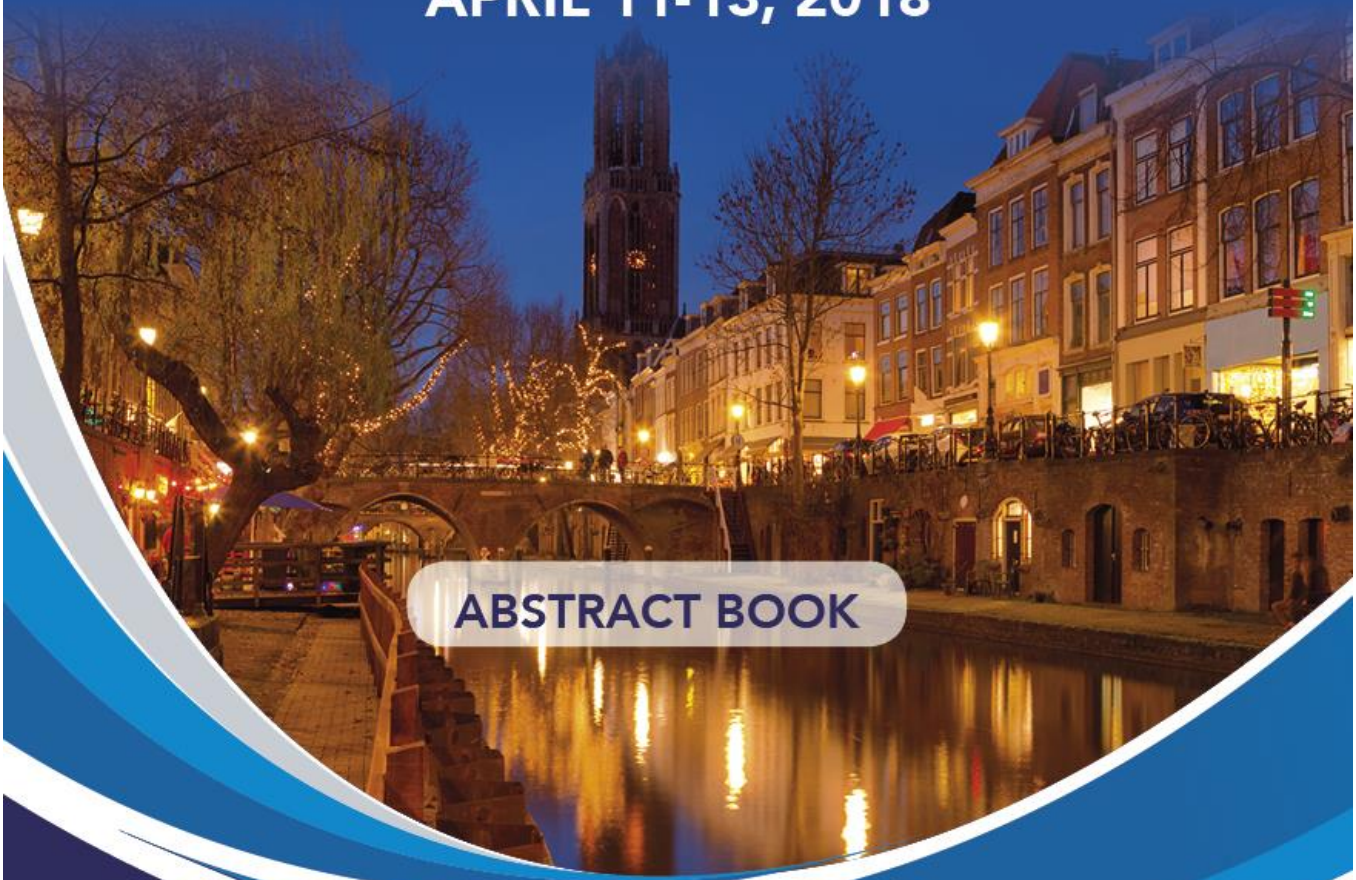
UTRECHT,
THE NETHERLANDS

10th GEORG RAJKA INTERNATIONAL SYMPOSIUM ON ATOPIC DERMATITIS

APRIL 11-13, 2018



ABSTRACT BOOK

ISAD

INTERNATIONAL SOCIETY OF ATOPIC DERMATITIS

Contents

Foreword by professor Carla Bruijnzeel-Koomen

Dear Colleagues and Friends,

We are proud to welcome you in the beautiful city of Utrecht.
It is a great honour for the eczema research community in the Netherlands to organize the 10th meeting of the International Society of Atopic Dermatitis.
The Board of the ISAD has chosen Utrecht as the location for the 10th ISAD congress since the department of Dermatology/Allergology in Utrecht has a longstanding focus on patient care and research in atopic dermatitis.
We hope you will enjoy the meeting in our charming University city with its characteristic houses and canals.
After decades of waiting for new drugs we recently entered an era with many promising new therapies, including biologics and small molecules. The introduction of these drugs will have an enormous impact on the quality of life of patients with moderate to severe atopic dermatitis. In addition, this will stimulate clinical and translational research in atopic dermatitis. There are still many 'research gaps'. Although we have made progress in the last decades we still do not completely understand the clinical phenotypes with their comorbidities, we lack objective disease parameters, and its genetics is still not understood. Furthermore, we need to study if the different clinical phenotypes are related to different therapeutic strategies and also to primary prevention strategies.
We are very grateful for the large number of outstanding abstracts that we received for the 10th ISAD meeting. Many important aspects of atopic dermatitis will be covered during the meeting. We are looking forward to discuss your data and strategies to fill in the remaining gaps of knowledge.

We hope you will enjoy and become inspired by the ISAD meeting in Utrecht.

On behalf of the Local Organizing Committee
Carla Bruijnzeel-Koomen, chair
Dirk Jan Hijnen, secretary
Bernd Arents, Marjolein de Bruin-Weller, Joost Schalkwijk, Marie-Louise Schuttelaar, Phyllis Spuls

Short history of ISAD

The International Society of Atopic Dermatitis (ISAD) developed out of the tradition of the international atopic dermatitis symposia created by the Hungarian dermatologist Georg Rajka in Oslo, starting back in 1979, when he as an enthusiast for Atopic Dermatitis, would for the first time personally select and invite colleagues to a conference on atopic dermatitis. The invitation always was “spiritual”, not financial in nature. He always also invited younger colleagues, who would have done good work in the past three years to present in a forum of experts in his chosen new homeland Norway. These meetings organized by George Rajka took place in Oslo (1979 and 1982), Loen (1985), Holmenkollen (1989) and Lillehammer (1992), and virtually all people travelling to Norway would take care of their own arrangements. It was in connection to one of those meetings, that the classic and famous “Hanifin and Rajka criteria” for diagnosis of atopic dermatitis were born.

With the retirement of George Rajka, the meeting started to travel around the world, and different organizers would add their specific touch to each meeting. We remember well the great meetings in Aarhus (1996) organized by Kristian Thestrup-Pedersen, in Davos (1999) organized by Johannes Ring, when the name “Georg Rajka Symposium” was added, in Portland (2001) organized by Jon Hanifin, in Rome (2003) organized by Alberto Giannetti, in Archachon (2005) organized by Alain Taieb, in Kyoto (2008) organized by Masahiro Takigawa, and in Munich (2010) organized again by Johannes Ring with the musical on King Ludwig II’s life, death and allergy.

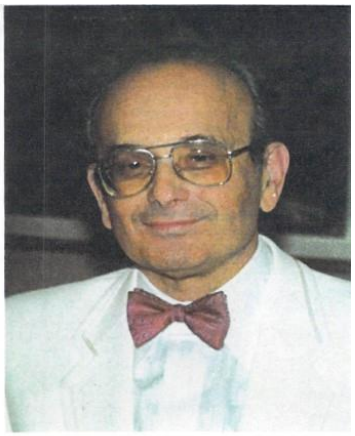
On the occasion of the 7th Georg Rajka International Symposium on Atopic Dermatitis in Moshi, Tanzania, in January 2012, organized by John Mazenga and Peter Schmid-Grendelmeier, a motion was made to found an International Society of Atopic Dermatitis which would organize future meetings, and also become active in various aspects of Atopic Dermatitis at a global level. This idea was brought forward and led finally to the founding of the International Society of Atopic Dermatitis in 2012. An alert bus driver can be thanked that the majority of attendants escaped an armed attack on the bus during the way back to the hotel.

The founding meeting of the ISAD took place on the 7th of June, 2012, during the EADV Spring Meeting in Verona in the Hotel Due Torri. In the early morning at 07:00 (!), Carlo Gelmetti (Milan), Amy Paller (Chicago), Johannes Ring (Munich), Zsuzsanna Szalai (Budapest), the late Kristian Thestrup-Pedersen (Aarhus) and Andreas Wollenberg (Munich) would meet in person for a working breakfast in close proximity to the famous St. Anastasia church in Verona. Peter Schmid-Grendelmeier (Zurich) was present by phone. A board and an executive committee were elected, and the basic rules for such a society would be discussed and agreed upon. The other founding members were unable to attend the meeting in person.

The ISAD meeting 2014 in Nottingham organized by Hywel Williams stood under the auspices of Robin Hood (with a short appearance of the Sheriff of Nottingham and the famous George Rajka song), and would emphasize evidence based medicine, structured reviews in AD and hands-on experience in Ye Olde Trip to Jerusalem, one of several pubs in England which claim to be the oldest.
The ISAD meeting 2016 in Sao Paulo organized by Roberto Takaoka had a focus on patient education and clinical care with demonstration of live patients.

In the year of 2018, atopic dermatitis is the target disease of many new drug developments, but the microbiome, biomarkers and genotype-phenotype correlations remain an important focus. We welcome all participants of the 2018 ISAD meeting in Utrecht, organized by Carla Bruijnzeel and Dirk Jan Hijnen, and hope that the spirit of the first meetings dedicated to disease and patients will remain active in the beginning era of biologics entering the field of Atopic Dermatitis.

Andreas Wollenberg and Johannes Ring



Georg Rajka

ISAD Society

Chair: Johannes Ring (Germany)

Carla Bruijnzeel-Koomen (The Netherlands)
Mette Deleuran (Denmark)
Carlo Gelmetti (Italy)
Norito Katoh (Japan)
Danielle Marcoux (Canada)
Amy Paller (USA)
Peter Schmid-Grendelmeier (Switzerland)
Eric Simpson (USA)
Zsuzsanna Szalai (Hungary)
Roberto Takaoka (Brazil)
Alain Taieb (France)
Gail Todd (South Africa)
Thomas Werfel (Germany)
Hywel Williams (UK)
Andreas Wollenberg (Germany)

Local organizing committee ISAD 2018:

Carla Bruijnzeel-Koomen, chair
DirkJan Hijnen, secretary
Bernd Arents
Marjolein de Bruin-Weller
Joost Schalkwijk
Marie-Louise Schuttelaar
Phyllis Spuls

Disclaimer

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Standard numbering of abstracts
The abstracts have been numbered following their order of presentation within each session.

Scientific program of the meeting

Wednesday April 11, 2018

11:30 AM – 1:00 PM Registration & Poster set up

1:00 – 1:30 PM Opening

Session 1 – 1:30-3:00 PM – Co-morbidities
Session chairs: Johannes Ring, Christian Vestergaard

1:30 – 2:00
Invited speaker: Jonathan Silverberg, USA

2:00 – 2:15
O01 HSV1- and influenza-specific T-cells are of a Th2/Tc2 type in patients with a history of eczema herpeticum, *L.M. Roesner, Germany*
2:15 – 2:30
O02 Atopic dermatitis and subsequent suicide: a matched case-control study, *A.M. Drucker, Canada*
2:30 – 2:45
O03 Eczema and mental health among pregnant women in the Japan environment and children's study (JECS), *K. Yamamoto-Hanada, Japan*
2:45 – 3:00
O04 Association with depression, anxiety and suicidal ideation in children and adults with atopic dermatitis: A systematic review and meta-analysis, *A. Halling-Overgaard, Denmark*

3:00 – 3:30 PM Break

Session 2 – 3:30-5:00 PM – Patients' perspectives/ Education/ eHealth
Session chairs: Roberto Takaoka, Sebastien Barbarot

3:30 – 4:00
Invited speaker: Matthew Ridd, United Kingdom

4:00 – 4:15
O05 Empowering physicians and educating patients in the 21st century: A novel, low-cost, multimodal intervention for atopic dermatitis care, *A. Han, USA*
4:15 – 4:30
O06 Improvement of atopic dermatitis, coping and quality of life in adult patients participating in a structured educational training, *A. Heratizadeh, Germany*
4:30 – 4:15
O07 Precision medicine in atopic dermatitis: generation of quantity-of-use estimates for topical therapies, *A. Kusari, USA*
4:45 – 5:00
O08 Development of at-home measurement device for skin barrier functions integrated with IOT technology for ad education, *H.J. Kim, South Korea*

Thursday April 12, 2018

Session 3a – 9:00-10:30 AM – Mechanisms of disease: genetics & -omics
Session chairs: Thomas Werfel, Kyu Han Kim

9:00 – 9:30
Invited speaker: John Common, Singapore

9:30 – 9:45
O09 The role of CXCR4-expressing skin-resident NKT cells in atopic dermatitis, *C.O. Park, South Korea*
9:45 – 10:00
O10 What is the evidence for interactions between filaggrin null mutations and environmental exposures in the aetiology of eczema? *H.C.J. Blakeway, United Kingdom*
10:00 – 10:15
O11 Role of brain-derived natriuretic peptide in atopic dermatitis, *M.S. Steinhoff, Qatar*
10:15 – 10:30
O12 Salivary chromogranin a levels correlate with disease severity but not reflect anxiety by questionnaire survey with adult atopic dermatitis patients, *S.K. Kaneko, Japan*

10:30 – 11:00 AM Break

Session 3b – 11:00 AM-12:30 PM – Mechanisms of disease: from phenotypes to endotypes
Session chairs: Emma Guttman, Norito Katoh

11:00 – 11:30
Invited speaker: Thomas Bieber, Germany

11:30 – 11:45
O13 Moving toward endotypes in atopic dermatitis: identification of patient clusters based on serum biomarker analysis, *J.L. Thijs, The Netherlands*
11:45 – 12:00
O14 Longitudinal latent class analysis identifies distinct subgroups of paediatric atopic eczema, *S.J. Brown, United Kingdom*
12:00 – 12:15
O15 Stratum corneum biomarkers of skin barrier and immune response in atopic dermatitis children with different skin types; an explorative study, *M.A. Middelkamp-Hup, The Netherlands*
12:15 – 12:30
O16 A model that integrates skin and blood atopic dermatitis biomarkers and clinical disease severity to advance personalized medicine, *A.B. Pavel, USA*

12:30 – 1:30 PM Lunch and poster viewing

Session 4a – 1:30-3:00 PM – New targets, systemic treatments and new treatments I
Session chairs: Andreas Wollenberg, Kenji Kabashima

1:30 – 2:00
Invited speaker: Lisa Beck, USA

2:00 – 2:15
O17 Comparison of the efficacy of dupilumab versus cyclosporine using EASI thresholds in adult patients with moderate to severe atopic dermatitis, *L.F.M. Ariëns, The Netherlands*

2:15 – 2:30
O18 From old king coal to novel treatments for atopic dermatitis: the aryl hydrocarbon receptor as a therapeutic target, *E.H. Van den Bogaard, The Netherlands*
2:30 – 2:45
O19 Effects of upadacitinib on atopic dermatitis signs, symptoms and patient-reported outcomes from a phase 2b randomized, placebo-controlled trial, *M.S. De Bruin-Weller, The Netherlands*
2:45 – 3:00
O20 MOR106, an anti-IL-17C MAb and a potential new approach for treatment of moderate to severe atopic dermatitis: Phase 1 study, *D. Thaci, Germany*

3:00 – 3:30 PM Break

Session 4b – 3:30-5:00 PM – New targets, systemic treatments and new treatments II
Session chairs: Andreas Wollenberg, Kenji Kabashima

3:30 – 3:45
O21 ZPL389, novel oral histamine H4 receptor antagonist for treatment of moderate-to-severe atopic dermatitis: results of a randomized, double-blind, placebo-controlled, proof-of-concept study, *T. Werfel, Germany*
3:45 – 4:00
O22 Novel AHR ligands for the treatment of atopic dermatitis, *G. Rikken, The Netherlands*
4:00 – 4:15
O23 Predictive factors for successful long-term control of “refractory” adult atopic dermatitis by biomarker-guided tight control strategy, *Y. Kataoka, Japan*
4:15 – 4:30
O24 Short-term VTP-38543 LXR agonist topical application improves epidermal barrier features in mild-to-moderate atopic dermatitis, *N.A. Guttman-Yassky, USA*

5:00 – 6:00 PM Poster viewing & drinks

6:00 – 7:00
Guest speaker - Stem cells and organoids in tomorrow’s clinical practice
H. Clevers, The Netherlands

Friday April 13, 2018

Session 5 – 9:00-10:30 AM – Outcome measures
Session chairs: Eric Simpson, Christian Apfelbacher

9:00 – 9:30
Invited speaker: Hywel Williams, United Kingdom

9:30 – 9:45
O25 EASI p-EASI: utilising a combination of serum biomarkers offers an objective measurement tool for disease severity in atopic dermatitis patients, *D.J. Hijnen, The Netherlands*
9:45 – 10:00
O26 Interpreting change in patient-oriented eczema measure scores: calculating the smallest detectable change and the minimally important change, *L.M. Howells, United Kingdom*
10:00 – 10:15
O27 What is long-term control of atopic eczema? International qualitative studies and results of the home V consensus meeting, *J.R. Chalmers, United Kingdom*
10:15 – 10:30
O28 Predicting short- and long-term outcomes of a systemic therapy for atopic dermatitis using machine learning methods, *G. Hurault, United Kingdom*

10:30 – 11:00 AM Break

Session 6 – 11:00 AM-12:30 PM – Gaps in evidence
Session chairs: Thomas Bieber, Hywel Williams

11:00 – 11:30
Invited speaker: Amy Paller, USA

11:30 – 11:45
O29 Early introduction of proactive therapy for infantile atopic dermatitis prevents onset of food allergy, *Y.O. Ohya, Japan*
11:45 – 12:00
O30 Treatment of atopic dermatitis (treat) registry taskforce: an international exercise to harmonise data collection for national atopic eczema registries, *L.A.A. Gerbens, The Netherlands*
12:00 – 12:15
O31 Evaluation of antimicrobial textiles for atopic dermatitis, *J. Srour, Germany*
12:15 – 12:30
O32 Salivary cortisol testing for Hypothalamic-Pituitary-Adrenal axis (HPA) suppression in children with atopic dermatitis treated with topical corticosteroids, *M. Kim, Australia*

12:30 PM Closing remarks and Farewell

Invited speakers presentations

Wednesday 11 April 2018

Session 1 – Co-morbidities
1:30 – 2:00 PM

Comorbidities of atopic dermatitis: association or systemic disease?
Jonathan Silverberg, USA

Atopic dermatitis (AD) is associated with a number of comorbid medical and mental health disorders. Some are direct or indirect symptoms of AD. While, others are standalone disorders associated with AD through shared risk factors and pathomechanisms. It can be challenging to decipher the clinical relevance of these comorbidities and their impact on therapeutic decision-making. In this talk, I will review the extra-cutaneous and systemic comorbid health conditions that occur in adults and children with atopic dermatitis, including atopic, neuropsychiatric, infectious and autoimmune comorbidities. I will elaborate on the epidemiology and associations for various comorbidities. In addition, I will touch upon some simple tools that can be used to screen for comorbidities in clinical practice. Finally, I will discuss the clinical relevance and therapeutic considerations for AD patients experiencing these comorbidities.

Session 2 – Patients' perspectives/ Education/ eHealth
3:30 – 4:00 PM

Atopic dermatitis – the patient perspective
Matthew Ridd, UK

From a medical viewpoint, atopic dermatitis/eczema is a fascinating condition and advances in our understanding of genetics and the skin-barrier hold promise for the possible prevention of the disease in the future. However, from the perspective of the patient or carer of a child with eczema, it's no fun at all. Many clinicians do not appreciate or acknowledge the psychological and social impact of living with the condition on the person affected and those living with them. This is compounded by uncertainty, and hence inconsistency of advice, about some of the core treatments used to manage the symptoms of eczema, and its relationship to food allergies. Patients/carer commonly turn to the internet for advice and support that they cannot find elsewhere, with the attendant risks of finding and following incorrect or downright dangerous information. What can general/family physicians, dermatology doctors/nurses and researchers do to help support patients and carers look after eczema in a safe and effective way?

Thursday 12 April 2018

Session 3a – Mechanisms of disease: genetics & -omics
9:00 – 9:30 AM

Metagenomics: new insights for atopic dermatitis
John Common, Singapore

Meta'omics is the study of the entire microbial community to give a detailed picture of a particular ecosystem. Each of the meta'omics technologies (such as, metagenomics, metatranscriptomics, metabolomics and metaproteomics) tells us something different about the microbial community and its activities, shifting our scientific questioning from "Who are you?" to "What do you do?". The skin is a challenging ecosystem to study meta'omics due to the low amount of biomass that can be recovered, which limits downstream techniques that are currently feasible on human volunteers. We have recently been using metagenomics to investigate microbial communities present on the skin of atopic dermatitis (AD) patients to understand shifts in community diversity and microbial functional characteristics. In our most recent study, we assessed temporal stability of the skin microbiome in AD patients and the impact of standard of care treatments. We observed that skin microbiome profiles of AD patients were mostly stable across visits when not in flare, however hierarchical clustering identified two distinct community types that varied in species and functional composition. To identify mechanistic biomarkers correlated with host properties, we found that community type B significantly correlated with higher

serum total IgE levels and objective SCORAD, but not increased transepidermal water loss or skin pH, and not linked to filaggrin mutations. This study suggests that skin metagenomics can distinguish specific subgroups of AD patients and therefore could aid in patient stratification and provide avenues to identify novel therapeutic targets or serve as biomarkers for predicting treatment efficacies. We envisage that additional integrative meta'omics analysis will help shed light on the contextual pathogenicity of microbes in AD.

Session 3b – Mechanisms of disease: from phenotypes to endotypes
11:00 – 11:30 AM

Mechanisms of disease: From phenotypes to endotypes
Thomas Bieber, Germany

Atopic eczema/dermatitis (AD) is a paradigmatic complex disease. Different ages of onset, natural histories with various trajectories and emergence of allergic asthma and/or allergic rhinitis (atopic march), various forms of severities, divergent therapeutic response to immunosuppressive drugs but also to new approaches such as biologics or small molecules are only some of the most important and striking aspects highlighting the phenotypic complexity of AD. This diversity is probably reflecting many underlying mechanisms such as the genetic and epigenetic background affecting the innate and adaptive immune mechanisms, neuro-immunological and environmental factors including the microbiomic signals. Currently, besides understanding the pathophysiology of AD, substantial progress in the discovery of biomarkers (BM) with a predictive/prognostic value for the management of this chronic disease is an unmet need. So far, mainly BM reflecting the severity of AD have been identified but their value as surrogate BM is questionable. Moreover, predictive BM for e.g. the therapeutic response or the selection of patients who will experience atopic and non-atopic comorbidities are still lacking. Thus, BM discovery and validation remains one of the key areas in translational medicine in AD. Only a detailed and extensive analysis of the clinical phenotype combined with a thorough exploration of the underlying mechanisms in the context of biobank projects including large cohorts of patients will pave the way for precision medicine in AD.

Session 4 – New targets, systemic treatments and new treatments
1:30 – 2:00 PM

The Gloves are Off – AD Therapeutics are Duking it Out
Lisa Beck, USA

Our understanding of AD pathogenesis remains incomplete, and consequently approved therapies are limited and inadequate. Since the Food and Drug Administration approved the topical calcineurin antagonists (protopic and elidel, in 2000 and 2001; respectively) and the corticosteroid, desonide (in 2006), no additional drugs had received approval. This changed in late 2016 and early 2017 when two new targeted treatments; a topical phosphodiesterase 4 inhibitor (crisaborole) and a biologic targeting IL-4R (dupilumab) were approved.
The success of these two anti-inflammatory therapies supports the inside-out hypothesis that posits that immune dysregulation is central feature of AD. In other words, a type 2 immune response, which is associated with activation of mast and innate lymphoid type 2 cells, leads to production of Th2-promoting cytokines including TSLP, IL-33, and IL-25 (IL-17c) that promote the development of Th2 cells. Th2 cytokines (IL-4, IL-5, and IL-13) upregulate IgE production, enhance the production and activation of eosinophils, activate sensory nerves - promoting itch and inhibit the expression of skin barrier proteins and lipids, antimicrobial peptides, and innate immune receptors. Additional therapies targeting components of the type 2 immune pathway include: anti-IL-13 strategies (lebrikizumab and tralokinumab), anti-OX40 (GBR830), anti-IL-33 (ANB020), anti-IL-31 (nemolizumab) and anti-IL17c [IL-25] (MOR106). The AD pipeline also includes therapies targeting Th22 (fezakinumab), Th17 (secukinimab) pathways as well as more global anti-inflammatory approaches as achieved with JAK (± Syk) inhibitors.
The so called "outside-in" hypothesis implicates defects in skin barrier (and epithelium in general) as the primary event. This hypothesis argues that reduction in epithelial proteins such as filaggrin or loricrin or tight junction proteins, dysregulation of serine proteases and/or protease inhibitors, or alterations in lipid composition and conformation, lead to microbial dysbiosis with Staphylococcus aureus colonization and collectively these changes promote a type 2 immune response. Several therapies have been developed with the rationale that they might normalize AD epithelial abnormalities and these include liver X receptors (LXR) ligands, aryl hydrocarbon receptor (AHR) ligands and histamine 4 receptor (H4R) antagonists.

We now know these two hypotheses are not mutually exclusive. For example, skin barrier defects enhance susceptibility to allergens, irritants and microbes, and promote cutaneous inflammation via epithelial expression of TSLP, IL-33, and IL-17c [IL-25]. Conversely, type 2 immunity induces upregulation of serine proteases and downregulation of epidermal differentiation genes like filaggrin, loricrin and involucrin, fatty acid elongases (ELOVL3 and ELOVL6) and TJ proteins, resulting in a compromised skin barrier. These new targeted therapies provide an unprecedented opportunity to investigate the relevance of inflammation vs epithelial abnormalities in AD clinical features (barrier dysfunction, S. aureus colonization and pruritus).

Friday 13 April 2018

Session 5 – Outcome measures
9:00 – 9:30 AM

Demystifying outcome measures
Hywel Williams, UK

"Outcome measures" have become a major industry in medicine with a profusion of scales clamouring for a foothold in the literature. Some of it is good, some of it is bad and a lot of it is confusing and technical. In this talk, I shall attempt to demystify outcome measures by giving an overview with special reference to outcomes in atopic eczema. I shall start with fundamental principles such as addressing the differences between domains and instruments and by tackling key questions such as what is an outcome – is it an end event, a transit event or an average event?, and who are they for – Trialists, funders, regulators, doctors, nurses or patients?. Are objective sign outcomes really that objective? Should there be a move to only use patient reported outcomes? I shall explore the differences between outcomes for intervention studies and those that might be used in routine care, and how outcomes can differ according to whether a study question relates to treatment, prognosis or prevention. I will then illustrate how core outcomes are an essential part of evidence-based dermatology by promoting fair comparisons of treatments, and I shall briefly update colleagues with the progress of the Harmonising Outcomes Measures for Eczema (HOME) initiative and what is happening elsewhere in dermatology with groups such as the Cochrane Skin Group Core Outcome Set Initiative (CSG-COUSIN). I will introduce the methods used to develop outcomes including classical test theory and item response theory, and hint at newer approaches such as those being developed by the Patient-Reported Outcomes Measurement Information System (PROMIS), along with the main international initiatives in the field of outcome measures. Finally, I will talk about the crucial aspect of clinical interpretability i.e. whether users or research are able to understand the results of outcome measures reported in studies, as well as the importance of balancing benefits and harms by means of tools such as decision aids. It is time for out-come measures to come out and be measured.
Key websites: HOME: http://www.homeforeczema.org/ and CSG-COUSIN: https://www.uniklinikum-dresden.de/de/das-klinikum/universitaetscentren/zegv/cousin

Session 6 – Gaps in evidence
11:00 – 11:30 AM

Mind the Gap: Prioritizing the Many Unmet Needs for Research in Atopic Dermatitis
Amy Paller, USA

Decision-making related to atopic dermatitis (AD) is ideally based on data derived from evidence-based research. However, many gaps remain in our understanding of atopic dermatitis and its optimal assessment and management. These gaps can be divided into several areas: i) understanding of AD mechanism, including the interplay between barrier, immune alterations, and the environment, including the microbiome, and the role of genetic differences; ii) definitions related to AD; iii) burden of AD, including its comorbidities and costs; iv) the natural course of the disease; v) the best measures of severity that take into account patient-reported outcomes, clinical observations, differences among various populations, and the development of new instrumentation towards noninvasive measurement; vi) the safety and efficacy of treatment options, including emerging therapies; vii) phenotyping and subphenotyping in an effort to be able to predict course, comorbidities, and treatment responses; and ix) how to best educate and engage patients and families in their management to improve adherence/ population health, including reaching the underserved. Prioritizing these gaps is a current goal of several organizations, and will help to focus research efforts.

Oral presentations

Wednesday April 11, 2018

Session 1 - Co-morbidities
1:30-3:00 PM

O01

HSV1- AND INFLUENZA-SPECIFIC T CELLS ARE OF A TH2/TC2 TYPE IN PATIENTS WITH A HISTORY OF ECZEMA HERPETICUM

L.M. Roesner[1], S. Traidl[1], P. Kienlin[1], G. Begemann[1], L. Jing[2], D.M. Koelle[3], T. Werfel[1]
[1]Division of Immunodermatology and Allergy Research, Hannover Medical School, HANNOVER, Germany
[2]University of Washington, Department of Medicine, SEATTLE, USA
[3]Departments of Medicine, Global Health, and Laboratory Medicine, University of Washington; Fred Hutchinson Cancer Res. Center; Benaroya Res. Inst, SEATTLE, USA

Background:
Around 3-8% of atopic dermatitis (AD) patients suffer from recurring severe forms of viral infections that affect larger areas of the skin, caused by molluscum contagiosum, papilloma virus, and most prominently, herpes simplex virus 1 (HSV1). The generalized cutaneous infection with HSV1, known as eczema herpeticum (EH), can lead to life threatening complications including herpes encephalitis. Adding to that, epidemiologic studies have shown that also the prevalence of respiratory tract infections, such as strep throat or influenza, is elevated in AD patients. So far, a reduced interferon(IFN)-γ response to viruses has been demonstrated in AD patients with a history of EH (AD/EH), but a precise profiling of virus-specific T cells has not been performed up to know.

Objective(s):
This study aimed to identify and characterize HSV1- and influenza-specific T cells in AD patients with and without a history of EH, compared to healthy controls.

Materials/methods:
Expression of polarization surface markers was assessed on HSV1- or influenza antigen-specific T helper ($CD4^+CD154^+$) and cytotoxic T cells ($CD8^+CD137^+$). In parallel, the secretion of IL-4 and IFN-γ was detected by ELISA in antigen- specific T cell lines. Finally, cytokine expression was assessed by intracellular staining in HSV-1 MHC class I tetramer-positive T cells.

Results:
Healthy individuals mounted a robust Th1/Tc1 response towards HSV1 and influenza antigens as expected. In AD patients, and even more pronounced in AD/EH, we were able to confirm a reduced IFN-γ secretion in our experimental approach. Interestingly, we further on detected specific type 2 immune responses in these patients consistently throughout our assays: HSV1-specific T cells were found to produce substantial amounts of IL-4 and to carry Th2 and Tc2 surface markers in higher frequencies compared to healthy controls. In contrast, influenza-specific T cells displayed the type 2 immune response mainly on T helper, not on cytotoxic T cells.

Conclusion:
We propose therefore that the combination of reduced T cell-derived IFN-γ and elevated IL-4 may negatively influence the resistance to viruses in AD and especially EH.

O02

ATOPIC DERMATITIS AND SUBSEQUENT SUICIDE: A MATCHED CASE-CONTROL STUDY

A.M. Drucker[1], D. Thiruchelvam[2], D.A. Redelmeier[3]
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[2]Institute for Clinical Evaluative Sciences, TORONTO, Canada
[3]Division of General Internal Medicine, University of Toronto, TORONTO, Canada

Background:
Atopic dermatitis can lead to decreased quality of life, anxiety and depression. Whether atopic dermatitis increases the risk of death from suicide is uncertain.

Objective(s):
To estimate the association of atopic dermatitis with a patient's subsequent risk of death from suicide.

Materials/methods:
We conducted a double matched case-control study among patients 15 to 55 years-old in Ontario, Canada's largest province. We identified consecutive cases of suicide deaths from Ontario coroners' reports between January 1, 1994 and December 31, 2014 (21 years) and matched individuals 1:2 with controls from the general population based on exact age, sex and socioeconomic status quintile. The primary predictor was a history of persistent atopic dermatitis defined by five or more physician visits for the diagnosis over the preceding five years. We estimated the association of atopic dermatitis with subsequent suicide using conditional logistic regression to calculate an odds ratio and 95% confidence interval.

Results:
We identified 18,441 cases of suicide over the twenty-year accrual period matched to 36,882 controls (matching rate = 100%). The median age of cases and controls was 39 years and 74% were male. A history of persistent atopic dermatitis occurred in 174 (0.94%) suicide cases and 280 (0.76%) controls. Persistent atopic dermatitis was associated with a 25% increased risk of suicide (odds ratio = 1.25, 95% confidence interval: 1.03 to 1.51, p=0.023). Secondary analyses using looser definitions of atopic dermatitis requiring one, two, three or four physician visits over 5 years yielded smaller associations with suicide. In analyses to assess the internal validity of our results, psychiatric diagnoses such as depression and anxiety were strongly associated with death from suicide whereas benign skin tumors were not.

Conclusion:
Adolescent and adult patients with persistent atopic dermatitis have an increased risk of death from suicide. Physicians may have opportunities to intervene for suicide prevention in this vulnerable patient population.

O03

ECZEMA AND MENTAL HEALTH AMONG PREGNANT WOMEN IN THE JAPAN ENVIRONMENT AND CHILDREN'S STUDY (JECS)

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Background:
The Japan Environment and Children's Study (JECS) is a nationwide, multicenter, prospective birth cohort study conducted by the Ministry of Environment of Japan. The association of mental health with allergy in pregnant women has not been well documented.

Objective(s):
We aimed to investigate the association of maternal mental health, including depression, anxiety, and quality of life, with eczema during pregnancy among JECS participants.

Materials/methods:
This is a cross-sectional study of a birth cohort. Participants in the JECS were recruited between January 2011 and March 2014.Lifetime prevalence of atopic dermatitis was assessed based on a self-reported doctor's diagnosis, obtained from the questionnaire during pregnancy. The Kessler's K-6 Non-Specific Psychological Distress Scale (K-6) was used to evaluate maternal anxiety and depression. Health-related quality of life (HRQOL) was measured using the Medical Outcomes Survey Short Form-8 questionnaire (SF-8). Logistic regression and linear regression were used to examine the associations of K-6 and SF-8 scores (MSC and PSC scores), respectively, with eczema, using the same potential confounders. We considered the following factors as possible confounders in the regression analyses: maternal age, place of residence, marital status, having another child, past history of abnormal pregnancy, current smoking status, employment status, and maternal education level.

Results:
K-6 scores ≥ 13 and ≥ 5 were seen in 3.5% and 31.9% of participants, respectively. The prevalence of eczema was 15.8%. Severe depression (K-6≥ 13) was statistically associated with eczema (aOR 1.22, 95% CI: 1.10–1.35). For PSC and MCS scores of the SF-8, eczema showed a significant negative association with PCS (regression coefficient of –0.587) and with MCS (regression coefficients of–0.375).

Conclusion:
Our study suggests that eczema in pregnant women is associated with depression and contribute to lower QoL. Our results highlight the importance of addressing eczema–mental health comorbidity. We should provide additional support to pregnant women with eczema, to help them maintain good mental health.

O04

ASSOCIATION WITH DEPRESSION, ANXIETY AND SUICIDAL IDEATION IN CHILDREN AND ADULTS WITH ATOPIC DERMATITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS
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Background:
Numerous studies have investigated the association between atopic dermatitis (AD) and psychiatric disease.

Objective(s):
In this systematic review and meta-analysis, we examined the association between AD in children and adults and, respectively, depression, anxiety, and suicidal behavior.

Materials/methods:
The medical databases, Pubmed, Embase and PsychInfo were searched and data extraction was performed independently by two authors.

Results:
A total of sixty studies were included in the qualitative analysis, and 24 of these were also included in a quantitative analysis. There was a significant association between adult AD and, respectively, depression (pooled odds ratio [OR] 2.19; 95% confidence interval [CI] 1.87-2.57) and anxiety (pooled OR 2.19; 95% CI 1.75-2.73). These data translate into clinically meaningful increased risk. While AD in children was associated with depression (pooled OR 1.27; 95% CI 1.12-1.45), no meta-analysis could be performed for anxiety. Finally, a positive association was found between AD in adults and adolescents and suicidal ideation (pooled OR 4.32; 95% CI 1.93-9.66).

Conclusion:
We conclude that associations between AD and depression, anxiety, and suicidal ideation, should be considered by doctors when treating AD patients, and that disease improvement reduce these risks.

Wednesday April 11, 2018

Session 2 - Patients' perspectives/ education/eHealth
3:30-5:00 PM

O05

EMPOWERING PHYSICIANS AND EDUCATING PATIENTS IN THE 21ST CENTURY: A NOVEL, LOW-COST, MULTIMODAL INTERVENTION FOR ATOPIC DERMATITIS CARE
A. Kusari, A. Han, L.F. Eichenfield
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Background:
Worldwide, atopic dermatitis is a prevalent disease whose prevalence appears to have increased substantially in

recent decades. It is associated with significant quality of life impairment and patients are susceptible to undertreatment and limited access to high-quality care. In the United States, 28 million people are currently estimated to have atopic dermatitis, but there are only 9,600 practicing dermatologists, and even fewer pediatric dermatologists, to meet this overwhelming need. Previous research has shown that most U.S. pediatricians have referred patients with even mild atopic dermatitis to specialists. We designed a unique, multimodal intervention for pediatric providers to facilitate the delivery of high-quality atopic dermatitis care.

Objective(s):
The intervention has three major objectives: (1) an educational session developed with active learning techniques and knowledge-based assessments for providers, (2) an electronic health record (EHR) “order set”, and (3) customized patient instructions/after visit summary templates designed with the principles of therapeutic patient education (TPE) in mind.

Materials/methods:
The educational session consists of a multiple-choice pre-test, a one hour PowerPoint-based oral presentation by an atopic dermatitis expert, a multiple-choice post-test, and a third multiple-choice exam three months following the oral presentation. The EHR “order set” includes a list of commonly-used topical and oral therapies appropriate for mild-to-moderate atopic dermatitis as well as built-in patient instructions for each therapy that are automatically customized to each patient. Customization occurs using the patient’s name, percent skin area involved, and an age-based estimate of the patient’s total body surface area. Because a major barrier to successful therapy in atopic dermatitis is nonadherance, we developed unique polynomial models that provide estimates of fingertip units (FTU) of topical medication that should be used per application, as well as estimates of how many grams of cream or ointment should be used per week. These estimates of FTU are automatically included in the patient instructions/after visit summary, along with other patient-specific instructions.

Results:
Proportion of atopic dermatitis-coded visits associated with prescription of appropriate therapy pre- and post-intervention are to be assessed, along with provider comfort with management and perceived work-burden.

Conclusion:
This project is currently ongoing; 20 physician providers have been recruited to participate and all educational materials and EHR tools have been developed.

O06

IMPROVEMENT OF ATOPIC DERMATITIS, COPING AND QUALITY OF LIFE IN ADULT PATIENTS PARTICIPATING IN A STRUCTURED EDUCATIONAL TRAINING

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Background:
The etiology of atopic dermatitis (AD) is multifactorial and complex. In adult AD patients subjective burden of the disease mainly results from its chronic course with persisting itch and sleeplessness. In fact, various medical and psychological needs of adult AD patients often cannot satisfactorily be addressed in routine outpatient practice.

Objective(s):
In a controlled, randomized multicenter study we aimed to evaluate effects of an outpatient, structured educational program on the disease activity and psychosocial factors in adult patients with AD.

Materials/methods:
The ARNE study group (“Arbeitsgemeinschaft Neurodermitisschulung für Erwachsene”) consisting of an interdisciplinary team of professionals who are well experienced in health care for AD patients, drafted a comprehensive 12-hours training for small groups of 5-8 AD patients. Adult patients with moderate to severe AD (SCORAD index ≥ 20) were randomly allocated either to the training or waiting control group. In the latter case, patients were educated after all study assessments had been completed. At baseline and after one year (1-year follow-up) study patients were examined for their disease signs and symptoms and filled in questionnaires. As

primary study endpoints a significantly higher decrease in 1) “catastrophizing cognitions” with respect to itching (JKF questionnaire), 2) “social anxiety” (MHF questionnaire), and a significantly higher improvement in 3) subjective burden by symptoms of the disease (SKINDEX questionnaire) and 4) disease severity (SCORAD index) in the training group compared to the waiting control group were defined. Primary data analysis was performed in an “intention to treat” population. Secondary endpoints focused on further variables for coping and quality of life.

Results:
A total of 315 AD patients were randomized for the study. At 1-year follow-up, patients of the training group (n=168) showed a significantly better improvement in coping behavior with respect to itching (*P*< .001), subjective burden by symptoms of the disease (*P*<.001) and the SCORAD index (*P*<.001) compared to the waiting control group (n=147). Moreover, significant improvement could also be observed for the majority of secondary endpoints.

Conclusion:
In this first randomized, controlled multicenter study on structured patient education in adults with AD we succeeded to demonstrate significant beneficial effects on psychological variables and the disease severity. These data indicate that educational programs conducted by an interdisciplinary team should be implemented in outpatient care for adult AD patients.

O07

PRECISION MEDICINE IN ATOPIC DERMATITIS: GENERATION OF QUANTITY-OF-USE ESTIMATES FOR TOPICAL THERAPIES

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Background:
Skin-directed management is the backbone of modern atopic dermatitis care. However, noncompliance is a particular challenge associated with topical therapies. Patients and families are likely to underutilize topical corticosteroids, which are a mainstay of atopic dermatitis care, due to fears about adverse effecs. To this end, Long *et al* promulgated the fingertip unit, defined as the quantity of cream or ointment that fits on the distal third of an adult index finger, when extruded from a tube with a 5 milimeter nozzle. One fingertip unit covers approximately 0.4% of an adult’s body surface area, and is equivalent to roughly 0.5 g of cream or ointment.

Objective(s):
Our objective was to apply these definitions and existing estimates of body surface area by age to generate new mathematical models to predict the ideal quantity of topical therapy to be used for patients at any given percent skin involvement.

Materials/methods:
Formulas for quantity of use per week, and time to tube completion (assuming a 30g tube) were also generated. We developed numerous least-squares polynomial regressions using published data, and used the *polyfit* function in MatLab to determine the closest fit. Because a different, often less-potent, topical therapy is used on the face and delicate areas, we generated separate models for quantities to be used on the face and body by age.

Results:
The quartic model, Q_F = -0.0000767986 A^4 + 0.00299617 A^3 - 0.0402166 A^2 + 0.283635 A + 1.01154, where Q_F is quantity in fingertip units needed to fully cover the face of a child of certain age A, was found to be the best model to predict facial quantity. The cubic model, Q_B = 0.00637765A^3 - 0.147516A^2 + 1.68967A + 5.18026, was found to be the best model for predicting full body quantity.

Conclusion:
For most patients under the age of 18, our models effectively estimate optimal quantity of use. Though it would be impractical for physicians to hand-calculate quantity of use in a clinic setting, these formulas can be incorporated into a suite of electronic health record tools and used to automatically generate customized instructions for patients of every age. As part of an integrated approach, generating precise quantities of use for each patient may help combat nonadherance to topical therapies in atopic dermatitis patients.

O08

DEVELOPMENT OF AT-HOME MEASUREMENT DEVICE FOR SKIN BARRIER FUNCTIONS INTEGRATED WITH IOT TECHNOLOGY FOR AD EDUCATION

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Background:
The most commonly adopted parameters for assessing the skin barrier functions are trans-epidermal water loss (TEWL) and stratum corneum hydration (SCH). Along with its advantage as a non-invasive method, the clinical importance of TEWL and hydration also have been supported by the series of studies reporting the higher correlation between skin barrier functions and severity of skin diseases. In addition to the potential application as a diagnostic tool, usage of TEWL as a prediction marker for atopic eczema has also been supported by the a few cohort studies. These results suggest that maintaining TEWL in a normal range may be interpreted as keeping the skin barrier in a normal condition, and therapeutic efficacy of skin disease treatment can be evaluated by measuring the TEWL. Recently, beneficial effects of regular measurement of body weight for weight management have been repeatedly reported.

Objective(s):
Our object of this study is that regular measurement of TEWL can be of help for improving the skin Barrier function, and of therapeutic benefit for skin diseases, such as Atopic Dermatitis.

Materials/methods:
We did the Clinical study of 25 AD patients to explore the therapeutic effectiveness of daily IoT base skin barrier function measurement for atopic dermatitis therapy (n=25, for 4wks, daily usage). We analyzed based on previous 4wks clinical data and did the Education for usage of device and Daily check. After one month usage, we did the analysis based on web based daily data and clinical data on re-visit.

Results:
This study demonstrates that this new device can easily measure the skin barrier function on a daily basis with the same performance as the existing equipment at low cost. This study is also the first to establish that daily measurements using an IoT-based skin barrier measurement device would prevent deterioration during atopic dermatitis treatment, reduce the use of steroids(39.8±38.1 mg, ->13.2±15.8mg, p<<0.001)and encourage number of additional application of moisturizer per day during 4wks(1.83±0.87times/day). .

Conclusion:
Before the lesion deteriorates, the device is used to recognize changes in the skin barrier function and immediately corrects with the moisturizer and nonsteroidal topical application. Through this study, we intend to open a new paradigm for the treatment of atopic dermatitis and to improve the efficiency of treatment by constructing predictive indices using artificial intelligence.

Thursday April 12, 2018

Session 3A - Mechanisms of disease; genetics & -omics
9:00-10:30 AM

O09

THE ROLE OF CXCR4-EXPRESSING SKIN-RESIDENT NKT CELLS IN ATOPIC DERMATITIS

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Background:
Adaptive allergic inflammation plays key roles in atopic dermatitis (AD). However, it is challenging for treating recalcitrant severe AD patients, which demand new immunological therapies such as targeting innate immunity to control these symptoms. NKT cells share cell-surface proteins with conventional T cells and NK cells that serve as unconventional T cells bridging between innate and adaptive immunity. NKT cells are known for a new player to develop AD, which are collaborated with several chemokines that increase in atopic dermatitis.

Objective(s):
We would like to explore the role of CXCR4+ NKT cells in atopic dermatititis.

Materials/methods:
We used normal human and AD skin/blood samples for proteomic and transcriptomic analyses. To further explore the role of CXCR4+ NKT cells, we developed an AD mouse model adoptively transfered with allergen-specific NKT cells.

Results:
We identified that CXCR4 and its cognate ligand, CXCL12 were significantly up-regulated in human AD skin by proteomic and transcriptomic analyses. We also found that CXCR4 and CXCL12 were consistently elevated in our AD mouse model. Adoptive transfer of allergen-specific NKT cells conferred antigen-specific cutaneous inflammation in our model. Interestingly, CXCR4 was uniquely expressed in skin NKT cells, rather than in liver, spleen, lymph nodes. CXCR4+ NKT cells were CD69+, indicating a type of resident memory T cells. By intravital imaging, we also found that CXCR4+ NKT preferentially traffic to CXCL12-rich area formed an enriched skin-resident NKT cluster.

Conclusion:
Our results indicate that CXCR4+ skin-resident NKT cells may play an essential role in the pathogenesis of atopic dermatitis, suggesting that inhibition of the CXCR4/CXCL12 might serve as a novel therapeutic strategy for atopic dermatitis.

O10

WHAT IS THE EVIDENCE FOR INTERACTIONS BETWEEN FILAGGRIN NULL MUTATIONS AND ENVIRONMENTAL EXPOSURES IN THE AETIOLOGY OF ECZEMA?

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Background:
Epidemiological studies alongside clinical observation indicate that gene-environment interactions are likely to play a role in the aetiology of eczema. Null mutations in the gene encoding filaggrin (*FLG*) represent the strongest genetic risk factor for atopic eczema identified to date. As filaggrin plays a key role in skin barrier function and *FLG* null mutations pre-dispose to atopic allergic disorders, this suggests that interactions between the environment and *FLG* genotype may contribute to atopic eczema pathogenesis.

Objective(s):
To systematically review the evidence for gene-environment interactions in the development of eczema, specifically focusing on those involving *FLG* null mutations.

Materials/methods:
A systematic search was undertaken from inception to February 2017 in EMBASE, MEDLINE and Web of Science to identify papers assessing the role of *FLG*-environment interactions in the aetiology of eczema. Search terms included all synonyms for eczema and filaggrin/*FLG*. All methodological approaches to genetic studies and studies of any classical epidemiological design were included. The review was prospectively registered and dual extraction of papers that met the inclusion criteria took place. Quality assessment was performed including assessment of study power using criteria modified from the Cochrane guidance for non-randomised studies and HuGENet for

genetic studies.

Results:
Of 1,571 papers identified, 12 fulfilled the inclusion criteria (nine cohort studies, one randomised-controlled trial, one family based study and one cross-sectional study). All 12 studies tested for interactions between *FLG* genotype and environment and calculated P values using regression models. Study populations ranged from N=336 to 6971. Six of the studies reported statistically significant (P≤0.05) *FLG*-environment interactions. These were early-life cat ownership tested in two separate cohorts (P<0.0001, P=0.003), older siblings (P<0.05), prolonged breastfeeding (P=0.02), water hardness (P<0.0001) and higher urine phthalate metabolite levels (P=0.026, P=0.049). Limitations of these studies included the low numbers of individuals who were exposed to both the environmental and genetic risk factors (N=4 to 94 per study) and the possibility of reverse causality.

Conclusion:
This systematic review highlighted limited evidence for *FLG*-environment interactions in the aetiology of eczema. Quality assessment indicated that many of the studies performed thus far have lacked large enough sample sizes to gain a full understanding of the nature of *FLG*-environment interactions and in relation to early onset eczema, they are liable to reverse causality. Further research is needed with larger sample sizes and clearly defined exposure assessment to determine whether important gene-environment interactions contribute to the aetiology of eczema.

O11

ROLE OF BRAIN-DERIVED NATRIURETIC PEPTIDE IN ATOPIC DERMATITIS

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Background:
IL-31 is a critical mediator in atopic dermatitis, a prevalent and debilitating chronic skin disorder. Brain-derived natriuretic peptide (BNP) has been described as a central itch mediator. The importance of BNP in peripheral (skin-derived) itch and its functional link to IL-31 within the neuro-immune axis of the skin is unknown.

Objective(s):
To investigate the function of BNP in the peripheral sensory system and skin in IL-31-induced itch and neuro-epidermal communication in atopic dermatitis.

Materials/methods:
We used Ca^{2+}-imaging, immunohistochemistry, quantitative real-time PCR, RNA-Seq, knockdown, cytokine/phosphor-kinase arrays, enzyme immune assay and pharmacological inhibition were subjected to examine the cellular basis of the IL-31-stimulated, BNP-related itch signaling in human DRG neurons (hDRG) and skin cells, transgenic atopic dermatitis-like mouse models, and human skin of atopic dermatitis and healthy subjects.

Results:
In hDRG, we confirmed expression and co-occurrence of OSMRβ and IL-31 receptor A in a small subset of neuronal population. Furthermore, IL-31 activated ~50% of endothelin-1-responsive neurons, and half of the latter also responded to histamine. In murine DRGs, IL-31 upregulated *Nppb* and induced soluble N-ethylmaleimide-sensitive factor attachment protein receptors-dependent BNP release. In the Grhl3PAR2$^{/+}$mice, house dust mite-induced severe atopic dermatitis-like dermatitis was associated with *Nppb* upregulation. Lesional IL-31-transgenic mice also exhibited increased *Nppb* transcripts in DRGs and skin; accordingly, skin BNP receptor was elevated. Moreover, expression of BNP and its receptor were increased in atopic dermatitis patient skin. In human skin cells, BNP stimulated a pro-inflammatory, itch-promoting phenotype.

Conclusion:
Our findings show that BNP is implicated in atopic dermatitis and that IL-31 regulates BNP in both DRGs and skin. IL-31 enhances BNP release and synthesis, and orchestrates cytokine and chemokine release from skin cells, thereby coordinating the signaling pathways involved in itch. Inhibiting peripheral BNP function may be a novel therapeutic strategy for atopic dermatitis and pruritic conditions.

O12

SALIVARY CHROMOGRANIN A LEVELS CORRELATE WITH DISEASE SEVERITY BUT NOT REFLECT ANXIETY BY QUESTIONNAIRE SURVEY WITH ADULT ATOPIC DERMATITIS PATIENTS

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Background:
Stress-induced scratching is an issue in patients with adult atopic dermatitis (AD). Although itching and stress are believed to be intimately related, no objective index is available; therefore, most evaluations are subjective.

Objective(s):
Using saliva, which is easily collected, we investigated the degree to which AD severity and patient stress levels are reflected in stress proteins in the saliva.

Materials/methods:
We evaluated the severity (SCORing Atopic Dermatitis [SCORAD] score), stress (State-Trait Anxiety Index [STAI] score), personality (Tokyo University Egogram [TEG] II score), and quality of life (Dermatology Life Quality Index [DLQI] score) of 51 patients with AD who were examined in the Department of Dermatology of Shimane University between April 2015 and May 2017. We collected saliva and measured salivary chromogranin A (CgA), amylase, and cortisol.

Results:
The amount of salivary CgA per protein in patients with AD was correlated with their SCORAD score. There was no correlation between cortisol or amylase levels and SCORAD score. SCORAD score was correlated with DLQI. CgA per protein was correlated with DLQI. The change in salivary CgA per protein in patients with AD was correlated with their changes in SCORAD score.

Conclusion:
The changes in salivary CgA level in patients with AD correlated with the changes in their condition. Our results suggested that patients with more severe AD may have high stress levels.

Thursday April 12, 2018

Session 3B - Mechanisms of disease; from phenotypes to endotypes
11:00 AM-12:30 PM

O13

MOVING TOWARD ENDOTYPES IN ATOPIC DERMATITIS: IDENTIFICATION OF PATIENT CLUSTERS BASED ON SERUM BIOMARKER ANALYSIS

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Background:
Atopic dermatitis (AD) is a complex, chronic, inflammatory skin disease with a diverse clinical presentation. It is however unclear whether this diversity exists at a biological level.

Objective(s):
To test the hypothesis that AD is heterogeneous at the biological level of individual inflammatory mediators.

Materials/methods:
Serum from 193 moderate to severe adult AD patients (geomean (95%CI) SASSAD of 22.3 (21.3, 23.3) and 39.1 (37.5, 40.9) respectively) and 30 non-AD healthy controls was analysed for 147 serum mediators, total IgE and 130 allergen specific IgEs. Population heterogeneity was assessed by principal component analysis (PCA) followed by unsupervised k-means cluster analysis of the principal components.

Results:
AD patients showed pronounced evidence of inflammation compared to healthy controls. PCA of AD serum data revealed the presence of four potential AD patient clusters. Fifty-seven principal components (PCs) described approximately 90% of the variance. Unsupervised k-means cluster analysis of the 57 largest PCs delivered 4 distinct clusters of AD patients. Cluster 1 had high SASSAD and BSA with the highest levels of PARC, TIMP-1 and sCD14. Cluster 2 had low SASSAD with the lowest levels of IFN-α, TIMP-1 and VEGF. Cluster 3 had high SASSAD with the lowest levels of IFN-β, IL-1 and epithelial cytokines. Cluster 4 had low SASSAD but highest levels of inflammatory markers: IL-1, IL-4, IL-13 and TSLP.

Conclusion:
AD is a heterogeneous disease both clinically and biologically. Four distinct AD patient clusters have been identified that could represent endotypes with unique biological mechanisms. Elucidation of these endotypes warrants further investigation and will require future intervention trials with specific agents such as biologics.

O14

LONGITUDINAL LATENT CLASS ANALYSIS IDENTIFIES DISTINCT SUBGROUPS OF PAEDIATRIC ATOPIC ECZEMA

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Background:
Atopic eczema is prevalent in childhood but displays a variable natural history; factors predicting prognosis and co-morbidity remain unclear. Longitudinal birth cohort studies provide an opportunity to define subgroups based on disease trajectories, which may represent different genetic and environmental pathomechanisms.

Objective(s):
To investigate the existence of distinct longitudinal phenotypes or subgroups of eczema in childhood using a mathematical modelling approach.

Materials/methods:
The presence or absence of eczema was recorded at regular intervals in two birth cohort studies: 9,894 children aged up to 16 years from the UK (ALSPAC cohort) and 3,652 children up to 11 years of age from the Netherlands (PIAMA cohort). Eczema was defined by parental report of a typical itchy and/or flexural rash. Longitudinal latent class analysis was used to investigate patterns of disease onset, persistence and resolution. We also investigated

associations with known eczema risk factors, including established genetic risk variants and selected atopic comorbidities.

Results:
Latent classes were identified, representing six subphenotypes of eczema, with remarkable consistency between the two cohorts. The most prevalent class of disease (13 and 15% in the UK and Dutch cohorts respectively) was early-onset-early-resolving eczema, which was associated with male gender (p=0.004 in the UK cohort). Two classes of persistent disease were identified (early-onset-persistent and early-onset-late-resolving, each representing 4-7% of the populations studied); these were most strongly associated with the eczema genetic risk score (odds ratio ~1.17 in UK and Dutch early-onset-persistent disease) as well as personal and parental history of atopic disease. A previously unrecognised class of mid-onset-resolving eczema was identified, comprising 7% of each cohort; these cases were not associated with *FLG* mutations, but strongly associated with asthma (OR 3.14, 95% CI 2.35-4.96) in the UK cohort. There was also a class of eczema (7% in the UK and 8% in the Netherlands) which showed onset later in childhood, at around 10 years of age, and tended to resolve towards the end of childhood. Finally, 58% of the UK cohort and 63% of the Dutch cohort were unaffected throughout childhood or had only very transient eczema.

Conclusion:
Distinct subgroups of paediatric eczema based on temporal trajectories of skin signs were identified and replicated in two independent population-based cohorts. The differing risk factor profiles and diverse prognoses indicate the importance of a stratified medicine approach for eczema.

O15

STRATUM CORNEUM BIOMARKERS OF SKIN BARRIER AND IMMUNE RESPONSE IN ATOPIC DERMATITIS CHILDREN WITH DIFFERENT SKIN TYPES; AN EXPLORATIVE STUDY.

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Background:
Atopic dermatitis (AD) affects children of all skin types. The wide variety of clinical symptoms and signs provide complexity in individualised approach in therapy and management. Biomarkers can aid in stratification, but the young age of children provides limitations in obtaining blood samples or skin biopsies, and detailed data of skin samples are lacking. A validated minimally invasive method to detect biomarkers would provide an important tool in dissection of childhood AD into disease endotypes.

Objective(s):
To explore the suitability of stratum corneum (SC) samples obtained by tape stripping in determining skin barrier and immune response biomarkers in AD children with different skin types.

Materials/methods:
SC samples were collected with adhesive tapes from lesional and visibly non-lesional forearm skin of 53 AD children and 50 healthy children. We analysed a panel of 28 immunomodulatory mediators analysed by multiplex technique, as well as natural moisturizing factors (NMF) levels and corneocyte morphology with atomic force microscopy (dermal texture index (DTI)) as markers for skin barrier.

Results:
Epidermal cytokines (IL 1β, and IL-18) and chemokines (CCL2, CCL22, CCL17) were significantly ($p<0.001$) higher in lesional AD skin as compared to non-lesional AD skin, while IL-1 α showed the opposite trend. The biomarkers IL8, CCL2, CCL17 showed the best correlation with AD severity (oSCORAD). Healthy skin showed highest NMF levels, with a gradual decrease in non-lesional and lesional AD skin. Children with skin type II also showed gradually decreasing NMF levels from healthy skin to non-lesional and lesional AD skin, but in skin type VI no differences in NMF levels were found between healthy skin, non-lesional and lesional AD skin. AD children with skin type VI showed higher NMF levels in both non-lesional and lesional AD skin compared to skin type II. DTI showed significant differences between lesional AD skin and both non-lesional AD skin and healthy skin.

Conclusion:
The minimally invasive method of collecting SC samples is suitable for determination of inflammatory and skin barrier biomarkers in AD children. This explorative study shows differences between AD children with skin type II and skin type VI in NMF levels, suggesting that some aspects of pathomechanisms may differ in AD children with light vs dark skin types.

O16

A MODEL THAT INTEGRATES SKIN AND BLOOD ATOPIC DERMATITIS BIOMARKERS AND CLINICAL DISEASE SEVERITY TO ADVANCE PERSONALIZED MEDICINE

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Background:
The evaluation of the atopic dermatitis/AD severity is limited to clinical scores, which have limitations, leading among other factors to high placebo responses in AD clinical trials. Several AD variants (i.e Asian vs. European American/EA) might have differences in cytokine polarity, and thus specific therapeutics may have varying efficacies in different AD phenotypes. While individual blood and tissue AD biomarkers have been studied, a biomarker study in both compartments across Asian and EA populations is lacking. Furthermore, since some of the best single correlations with severity/SCORAD are not only detected in lesional, but also non-lesional skin and blood, more complex biomarker models of AD are needed.

Objective(s):
To determine circulating and cutaneous AD biomarkers and integrate them with clinical severity, and determine differences between moderate-to-severe Asian and EA AD.

Materials/methods:
We analyzed skin and serum of moderate-to-severe Asian AD patients (n=27) and age/race-matched controls (n=15) using gene expression, and immunohistochemistry for skin analyses and MSD and Singulex serum immunoassays, comparing to EA AD patients (n=20) and controls (n=10).

Results:
Both EA and Asian AD showed significant elevations of Th2 markers in serum versus controls (IL-13, CCL13, CCL17, CCL26; $p<0.05$), highlighting the Th2 axis as the common denominator of AD across ethnicities, with even stronger induction of key Th2 markers (IL-13, CCL26) in Asians. While both EA and Asian AD showed significant IL-22 increases, IL-22 was significantly increased in Asians ($p<0.01$), concordant with Th17/Th22 up-regulations and more prominent epidermal hyperplasia in Asians. Serum and skin expressions of Th1-related markers (IFN-γ, CCL2; $p<0.05$) were significantly higher in EA vs. Asian AD.
In Asians, IFN-γ was negatively correlated with severity ($r=-0.44$, $p=0.09$). Conversely, most Th2 measures positively correlated with SCORAD, similar to EA AD ($p<0.05$). Non-lesional skin expressions of various Th2-attracting chemokines and Th22/IL-22 correlated with corresponding serum markers (CCL13, CCL26; $p<0.05$), while most lesional skin biomarkers were not correlated.

Conclusion:
Overall, Asian AD demonstrates a Th2/Th17/22 profile in both skin and serum, with lower Th1 compared with EA AD. Selective therapeutic approaches against the Th2, Th22, and Th17 cytokine axes, with associated biomarkers, are still needed in Asian AD to clarify the relative contribution of each axis to the Asian AD phenotype. These data highlight the systemic nature of AD regardless of ethnicity, and advocate for an integrated approach that includes clinical disease severity together with non-lesional, lesional and serum biomarkers to stratify patients in a personalized medicine approach.

Thursday April 12, 2018

Session 4A - New targets, systemic treatments and new treatments I
1:30-3:00 PM

O17

COMPARISON OF THE EFFICACY OF DUPILUMAB VERSUS CYCLOSPORINE USING EASI THRESHOLDS IN ADULT PATIENTS WITH MODERATE TO SEVERE ATOPIC DERMATITIS

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Background:
Dupilumab, a fully human anti-IL-4Rα mAb, inhibits signaling of both IL-4 and IL-13, which are key drivers of type 2/Th2-mediated inflammation. Dupilumab is approved in the EU, USA, Japan, and other countries for the treatment of adults with inadequately controlled moderate-to-severe atopic dermatitis (AD). Before dupilumab approval, cyclosporine was the only licensed oral immunosuppressive drug for AD treatment in many European countries. Most European guidelines advise limiting cyclosporine use to a maximum of 1 year. Although the efficacy of dupilumab and cyclosporine for AD has been studied separately, there is a lack of comparative evidence from head-to-head clinical trials.

Objective(s):
To assess the relative efficacy of dupilumab vs cyclosporine by estimating the proportion of responders using an improvement from baseline in the Eczema Area and Severity Index score of 50% (EASI-50) or 75% (EASI-75).

Materials/methods:
Patients treated with dupilumab 300mg every 2 weeks (q2w) in the Phase 3 CHRONOS (NCT02260986) trial and cyclosporine-treated patients from the UMC Utrecht Center, Netherlands were included. Patients achieving the EASI-50 or EASI-75 thresholds at weeks 12–16 and 24–30 were defined as responders. Regression models based on pooled patient-level data were used to estimate the proportion of EASI responders for each treatment in each population, adjusting for baseline characteristics.

Results:
156 patients were included in the analysis; 99 patients with complete data who were treated with 300mg dupilumab q2w (plus topical corticosteroids [TCS]) and 57 with cyclosporine (plus TCS). Among UMC patients, the estimated proportions of EASI-50 responders to dupilumab vs cyclosporine treatment were 93% vs 77% (P<0.02) for the first time-point (weeks 12–16) and 98% vs 67% (P<0.001) for the second time-point (weeks 24–30). For EASI-75, estimated responder proportions were 81% vs 56% (P<0.01) for the first time-point and 84% vs 47% (P<0.001) for the second time-point, respectively. Among CHRONOS trial patients, the estimated proportions of EASI-50 responders to dupilumab vs cyclosporine treatment were 92% vs 74% (P<0.02) for the first time-point and 95% vs 52% (P<0.001) for the second time-point; for EASI-75, responder proportions were 79% vs 53% (P<0.01) for the first time-point, and 79% vs 40% (P<0.001) for the second time-point, respectively.

Conclusion:
This analysis suggests a higher relative efficacy of dupilumab compared with cyclosporine in the treatment of patients with moderate-to-severe AD as captured by EASI. The relative efficacy for dupilumab vs cyclosporine showed a trend of improvement over time and for a higher efficacy threshold.

Key words:
dupilumab, EASI, cyclosporine

O18

FROM OLD KING COAL TO NOVEL TREATMENTS FOR ATOPIC DERMATITIS: THE ARYL HYDROCARBON RECEPTOR AS A THERAPEUTIC TARGET

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Background:
Despite the longstanding clinical use and efficacy of coal tar in dermatological practice, the molecular mechanism was unknown until the discovery that coal tar activates the aryl hydrocarbon receptor (AHR). The AHR is a ligand-activated transcription factor that we found to regulate keratinocyte differentiation and proliferation. In the past, the AHR was considered to mediate the metabolism of xenobiotics and was predominantly associated with toxicity. Nowadays, the AHR is considered a therapeutic target in many research fields, and clinical trials with AHR ligands for inflammatory diseases are ongoing.

Objective(s):
The identification of the AHR-dependent therapeutic effects of coal tar led us to fractionate coal tar in order to identify its active ingredients, to study the therapeutic activity of novel AHR ligands for atopic dermatitis (AD) and to investigate the downstream effects of AHR signaling in keratinocytes.

Materials/methods:
We fractionated coal tar (differential extraction, centrifugal partition chromatography and silica-based column chromatography) followed by gas chromatography-mass spectrometry. Therapeutic effects of coal tar fractions and AHR ligands were studied in keratinocyte monolayer cultures and in *in vitro* AD skin models. Genotoxicity was determined by the Ames test. We studied AHR-mediated signaling by genome-wide ChIP-sequencing and RNA-sequencing analysis of coal tar-treated keratinocytes.

Results:
The fractionation of coal tar resulted in 144 single fractions that were pooled to 11 fractions based on GC-MS data. Coal tar odor was restricted to the colorless fractions 1-5, while fractions 6-11 were fluorescent yellow to orange and having an unpleasant chemical odor. AHR activity and induction of epidermal differentiation was restricted to fractions 6-11, containing apolar compounds with a less favorable safety profile (potential mutagens). Three structurally different types of AHR ligands demonstrated no signs of cell toxicity or genotoxicity while therapeutic activities were similar to coal tar. Cluster and Gene Ontology analysis of the early and late responses of AHR signaling in keratinocytes after coal tar exposure (t=2 hours, t=24 hours) indicate that the AHR interacts with other transcription factors and signaling pathways to regulate the expression of genes involved in the cell cycle, keratinocyte differentiation and host defense responses.

Conclusion:
Our data indicate that components that cause the typical coal tar odor are dispensable for its therapeutic effect. However, they maybe indispensible for providing a counterbalance to other pharmacologically active and potentially toxic chemicals in coal tar. The herein identified novel non-mutagenic AHR ligands with similar therapeutic properties to coal tar may be key for developing new therapies for AD patients.

O19

EFFECTS OF UPADACITINIB ON ATOPIC DERMATITIS SIGNS, SYMPTOMS AND PATIENT-REPORTED OUTCOMES FROM A PHASE 2B RANDOMIZED, PLACEBO-CONTROLLED TRIAL

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Background:
Atopic dermatitis (AD) is a chronic, inflammatory, pruritic skin disease. Upadacitinib, an oral selective JAK-1 inhibitor, is being investigated for treatment of patients with AD and other inflammatory diseases.

Objective(s):
Evaluate the effects of upadacitinib treatment on AD signs, symptoms and patient-reported outcomes (PROs) during the study's first 16 weeks.

Materials/methods:
In the first 16-week, double-blind portion of this 88-week, dose-ranging trial, adults with moderate-to-severe AD (EASI ≥16, BSA ≥10%, IGA ≥3) not adequately controlled by topical treatment, or for whom topical treatments were not medically advisable, were randomized to once-daily upadacitinib monotherapy 7.5, 15, or 30 mg (N=42/42/42), or placebo (N=41). Tools measuring AD signs, symptoms and PROs included Eczema Area and Severity Index (EASI), Scoring Atopic Dermatitis (SCORAD), Patient Oriented Eczema Measure (POEM), and pruritus Numerical Rating Scale (NRS). For binary variables, pairwise comparison of each upadacitinib group and placebo was performed using the Cochran Mantel-Haenszel test adjusting for stratification factor (geographic region). For continuous variables, treatment groups were compared using analysis of covariance with treatment group and stratification factor (geographic region) as fixed effects, and the corresponding baseline value as covariates.

Results:
The study's primary endpoint, percent improvement in EASI, was met by the 7.5/15/30 mg upadacitinib groups (39.4%/61.7%/74.4%; p<0.05/<0.001/<0.001) vs placebo (23.0%). Mean percent improvement in SCORAD from baseline at week 16 (LOCF) was 32.5%/46.9%/60.4% upadacitinib groups (p<0.01/<0.001/<0.001; N=39/36/40) vs 12.4% placebo (N=33). SCORAD response at week 16 (NRI) for upadacitinib groups (N=42/42/42) vs placebo (N=41) was 28.6%/42.9%/61.9% vs 7.3% for SCORAD 50 (p<0.01/<0.001/<0.001), 4.8%/21.4%/40.5% vs 2.4% for SCORAD 75 (p>0.05/<0.01/<0.001), and 2.4%/9.5%/23.8% vs 0% for SCORAD 90 (p>0.05/<0.05/<0.001). Mean improvement [SE] from baseline to week 16 in POEM (LOCF), was 5.5 [1.43]/8.6 [1.41]/12.3 [1.40] (N=42/40/42) for upadacitinib groups (p<0.05/<0.001/<0.001) vs 1.6 [1.49] for placebo (N=37). For patients with baseline pruritus NRS of ≥4 (non-responder imputation), improvement in pruritus NRS ≥4 points from baseline to week 16, was observed in 24.3%/59.4%/52.8% on upadacitinib (p<0.05/<0.001/<0.001, N=37/32/36) vs 5.7% on placebo (N=35). The most common treatment-emergent adverse events (AEs), upadacitinib groups vs placebo, were upper respiratory tract infection (16.7%/11.9%/11.9% vs 10.0%) and AD exacerbation (16.7%/7.1%/11.9% vs 7.5%). 4.8%/2.4%/0% of upadacitinib patients (7.5/15/30 mg groups) had serious AEs vs 2.5% placebo.

Conclusion:
Upadacitinib 15 and 30 mg treatment for 16 weeks resulted in significant improvements in AD signs, symptoms and PROs. Upadacitinib treatment showed a positive benefit/risk profile that needs confirmation in larger trials.

O20

MOR106, AN ANTI-IL-17C MAB AND A POTENTIAL NEW APPROACH FOR TREATMENT OF MODERATE TO SEVERE ATOPIC DERMATITIS: PHASE 1 STUDY

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Background:
IL-17C induces expression of cytokines, pro-inflammatory mediators and antimicrobial peptides in epidermal keratinocytes. MOR106 is a fully human monoclonal antibody that binds with high affinity to human IL-17C, thereby neutralizing its biological activity. MOR106 was shown to be effective in animal models of atopic dermatitis and psoriasis and therefore could be a potential new treatment for these diseases.

Objective(s):
To evaluate safety, tolerability and PK of MOR106 and explore potential efficacy in Atopic Dermatitis (AD).

Materials/methods:
A randomized, double-blind, placebo-controlled, dose-escalation, phase I study evaluating single ascending doses (SAD) in healthy volunteers (HV), and multiple ascending doses (MAD) in patients with moderate-to-severe (AD).

In the SAD part of the study, 56 subjects received a single i.v. infusion of up to 20 mg/kg. In the MAD part, 25 AD patients received one i.v. infusion every week, for 4 weeks (4 administrations in total), with a 10 week follow up period. End points of both parts included safety and tolerability, and the pharmacokinetic profile and assessment of immunogenicity. Key exploratory endpoints in the MAD part for efficacy included percentage change in Eczema Area Severity Index (EASI) and Scoring Atopic Dermatitis (SCORAD) as well as the number of patients with a 50 % reduction in EASI (EASI-50) at week 4 compared to baseline.

Results:
MOR106 was well tolerated in healthy volunteers and AD patients with no serious or severe adverse events (AE) reported. All treatment-emergent AEs were transient.
A dose-proportional increase in drug exposure was observed, which was comparable between healthy volunteers and patients. Estimated half-life ranged between 13 and 17 days. A linear relationship between dose and MOR106 concentration in skin could be demonstrated in HV when measured 96 hours after administration.
The study was not statistically powered to show differences in efficacy between treatment groups; nevertheless, at the highest dose level (10 mg/kg) of MOR106, 83% of patients (5 out of 6) showed an improvement of at least 50% in signs and symptoms of atopic dermatitis as measured by the EASI score was recorded at week 4. The onset of activity, as measured by the percentage change in EASI score, was rapid, occurred within a few weeks, and was maintained for over 2 months after the last treatment. These results were corroborated by the SCORAD scores.

Conclusion:
MOR106 was well tolerated, and the reported adverse events were not dose-limiting. The study supports IL-17C as a potential target in atopic dermatitis with encouraging signals of efficacy.

Thursday April 12, 2018

Session 4B - New targets, systemic treatments and new treatments II
3:30-5:00 PM

O21

ZPL389, NOVEL ORAL HISTAMINE H4 RECEPTOR ANTAGONIST FOR TREATMENT OF MODERATE-TO-SEVERE ATOPIC DERMATITIS:RESULTS OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PROOF-OF-CONCEPT STUDY

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Background:
Histamine 4 (H_4) receptors mediate pro-inflammatory functions, including histamine-induced inflammation. H_4 receptor antagonists are a potentially novel option for the treatment of inflammatory skin diseases including atopic dermatitis (AD).

Objective(s):
To investigate the efficacy and safety of ZPL-3893787, now ZPL389 (selective H_4 receptor antagonist) in moderate to severe AD.

Materials/methods:
The efficacy and safety of ZPL389 (30 mg) once daily oral therapy were evaluated in a randomized, double-blind, placebo-controlled, parallel-group study in which adult patients with moderate to severe AD were randomized (2:1), to ZPL389 (n=65) or placebo (n=33) for 8 weeks. In addition to emollient skin care, patients could have used the rescue medication mometasone furoate cream 0.1% during the 8-week treatment period. Eligible patients had Eczema Area and Severity Index (EASI) of ≥12 and ≤48, Investigator's Global Assessment (IGA) ≥3 (moderate), pruritus score of ≥5 (0-10 scale) and AD of ≥10% body surface area (BSA). Efficacy endpoints were measured by treatment group at each week. Significance was determined using one-sided p-values.

Results:
ZPL389 showed a 50% reduction in EASI score compared to 27% for placebo (placebo-adjusted reduction at Week 8 was 5.1; p=0.01). At week 8, 32.3% patients on ZPL389 vs 15.2% on placebo achieved EASI75 (p=0.088). Clear or almost-clear IGA scores were shown by 18.5% patients on ZPL389 vs 9.1% on placebo (p=0.033), respectively. There was a 41% reduction in SCORing Atopic Dermatitis (SCORAD) with ZPL389 vs 26% with placebo (placebo-adjusted reduction of 10.0; p=0.004). There was a 3-point reduction in NRS pruritus assessment (scale 1-10) with ZPL389, which was comparable to placebo. However, post hoc analysis with worst case imputation indicated a statistically significant 1.27-point higher reduction in pruritus assessment with ZPL389 than placebo (p=0.009). The SCORAD pruritus sub score showed a -3.57 point reduction in the score with ZPL389 compared to -2.71 with placebo. ZPL389 was well tolerated.

Conclusion:
This is the first report to demonstrate that ZPL389 improves skin lesions in patients with AD, confirming H_4 receptor antagonism as a novel therapeutic approach for the treatment of AD.

O22

NOVEL AHR LIGANDS FOR THE TREATMENT OF ATOPIC DERMATITIS

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Background:
The aryl hydrocarbon receptor (AHR) plays an important role in epidermal differentiation and mediates anti-inflammatory responses. Targeting the AHR, as seen in coal tar treatment, therefore alleviates the symptoms of chronic inflammatory skin diseases like atopic dermatitis (AD). AHR activity has been shown for quinoline-3-carboxamides (Q-3-C), and in experimental models for multiple sclerosis (MS) therapeutic effects of Q-3-C are completely AHR-mediated. Phase 2 and 3 trails with Q-3-C are ongoing in patients with MS and Huntington's disease.

Objective(s):
We studied novel Q-3-C metabolites for AHR activity in keratinocytes and potential therapeutic effects in AD.

Materials/methods:
Efficacy of six novel patented metabolites derivatives (IMA-06201, IMA-08401, IMA-06504, IMA-07101, IMA-05101 and IMA-01403) was evaluated in CYP1A1 reporter cells (AHR activity screening) followed by primary human keratinocyte monolayer cultures and 3D epidermal models for normal and AD skin. Epidermal morphology, keratinocyte differentiation and proliferation, inflammatory responses, CYP1A1 enzyme activity, cell toxicity and mutagenicity of the compounds were analysed.

Results:
IMA-08401 (prodrug to IMA-06201), IMA-06504 and IMA-07101 (prodrug to IMA-06504) were the most potent metabolites by 1) activating the AHR, 2) inducing epidermal differentiation, 3) reducing keratinocyte hyperproliferation, and 4) displaying anti-inflammatory effects in Th2 cytokine-stimulated primary human keratinocytes and 3D organotypic skin equivalents at a 1 nM concentration. IMA-06201 and IMA-05101 showed intermediate effects and IMA-01403 (inactive metabolite derivative) did not activate the AHR nor induced epidermal differentiation. The potency of the novel metabolites greatly exceeded the parent compound by a 10^3-10^4 fold. No cell toxicity or genotoxicity was observed for any of the metabolites. Furthermore, experimental in vivo studies showed no signs of toxicity up to 100 mg/kg after repeated oral dosing.

Conclusion:
Q-3-C metabolites are potent inducers of epidermal differentiation and downregulate Th2-mediated inflammatory processes similar to coal tar. The negligible in vitro toxicity, absence of mutagenicity, and in vivo tolerance of the metabolites, indicate a high potential for these compounds as novel candidate drugs for the treatment of AD.

O23

PREDICTIVE FACTORS FOR SUCCESSFUL LONG-TERM CONTROL OF 'REFRACTORY' ADULT ATOPIC DERMATITIS BY BIOMARKER-GUIDED TIGHT CONTROL STRATEGY

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Background:
Tight control, a treatment strategy that aims to achieve a predefined level of low disease activity or remission within a certain period, greatly improved treatment outcomes in rheumatoid arthritis patients. Considering atopic dermatitis as a similar chronic inflammatory disease, proactive therapy is a strategy for long-term control; however, remission level and time frames have not yet been defined. Since 2009 we have executed tight control strategy, which is initiated by a 2-week hospitalized remission induction with intensive topical corticosteroid [TCS] followed by serum biomarker “Thymus and Activation-Regulated Chemokine [TARC]”-guided weaning proactive treatment.

Objective(s):
To obtain predictive factors for subsequent successful long-term control by tight control strategy with “classic” medication, and to help identify patients who require new developing medication.

Materials/methods:
We performed a retrospective cohort study of 131 (M:F, 91:40) consenting patients with refractory moderate to severe adult atopic dermatitis (initial total Eczema Area and Severity Index [EASI], 2.1-72.0; median, 42.5; initial serum TARC, 381-81194; median, 4110 pg/ml). They were followed-up for more than 6 months with tight control strategy after intensive 2-week hospitalized topical treatment with an educational program in 2015. We compared backgrounds of patients in the favorable and unfavorable groups. Favorable was defined as Investigator’s Global Assessment [IGA] maintained at 0 or 1 with less than twice a week proactive TCS application 6 months after initial treatment. Predictive factors for future outcomes were retrospectively assessed by analyzing disease history and clinical and serum biomarker data in univariate and multivariate logistic regression models.

Results:
Six months later, 81 (61.8%) patients had favorable outcomes; 50 (38.2%) had unfavorable outcomes. Univariate analyses revealed that sex, presence of treatment-needed dermatitis in adolescence, refractory period duration, initial EASI total score, head EASI score, and severity of prurigo nodules were significantly different between groups. Multivariate analysis revealed that onset or relapse after adolescence (odds ratio [OR], 3.52; 95% confidence interval [CI], 1.14-10.88; P=.028), scarce prurigo nodules (OR, 3.38; 95% CI, 1.30-8.75; P=0.012), and shorter refractory duration (<5 years) (OR, 2.88: 95% CI, 1.24-6.70; P=0.014) were independent predictive factors for favorable outcomes. A 2-year observation revealed that 82% patients from the favorable group have been maintaining IGA 0 or 1 with less TCS dosage and showed significant decreases in serum total IgE levels (P<0.0001).

Conclusion:
Biomarker-guided tight control strategy by “classic” medication would achieve long-term control in half of the “refractory” atopic dermatitis patients. Patients who have negative predictive factors might require new medication.

O24

SHORT-TERM VTP-38543 LXR AGONIST TOPICAL APPLICATION IMPROVES EPIDERMAL BARRIER FEATURES IN MILD-TO-MODERATE ATOPIC DERMATITIS

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Background:
Atopic dermatitis/AD lacks safe and effective topical treatments. Liver X receptors/LXRs are involved in maintaining epidermal barrier and suppressing inflammatory responses in model systems. The LXR agonist VTP-38543 showed promising results in improving barrier function and inflammatory responses in mice.

Objective(s):
To assess clinical efficacy, cellular and molecular changes of the topical VTP-38543 in adults with mild-to-moderate AD.

Materials/methods:
104 mild-to-moderate AD patients were enrolled in a randomized, double-blind, vehicle-controlled comparison trial of VTP-38543 cream in three concentrations (0.05%, 0.15% and 1%), applied twice daily for 28d. Pre- and post-treatment skin biopsies were obtained from a subset of 33 patients. Changes in Scoring of Atopic Dermatitis (SCORAD), Eczema Area and Severity Index (EASI), and tissue biomarkers (by RT-PCR and immunohistochemistry) were evaluated.

Results:
In the biopsy cohort VTP-38543 0.05% significantly reduced baseline SCORAD and EASI at day 28 ($P \leq 0.05$ for both). VTP-38543 significantly increased mRNA expression of differentiation (FLG/LOR; $P=0.02$), and lipid (ABCG1, SREBP1c; $P<0.01$) measures, and dose-dependently reduced epidermal hyperplasia markers (thickness, K16 mRNA). VTP-38543 suppressed cellular infiltrates and downregulated mRNA expression of several Th17/Th22-related (PI3, S100A12) and Th2-related (IL-6) markers, in a dose-dependent but not significant fashion.

Conclusion:
Topical VTP-38543 application led to clinical AD alleviation, improvements in barrier differentiation and lipids, and a trend for dose-dependent cellular and molecular responses. Longer-term studies are needed to clarify whether a "barrier based" approach can induce meaningful suppression of immune abnormalities.

Friday April 13, 2018

Session 5 - Outcome measures
9:00-10:30 AM

O25

EASI P-EASI: UTILISING A COMBINATION OF SERUM BIOMARKERS OFFERS AN OBJECTIVE MEASUREMENT TOOL FOR DISEASE SEVERITY IN ATOPIC DERMATITIS PATIENTS

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Background:
Serum biomarkers offer an objective outcome measure for disease severity in atopic dermatitis (AD). Assessing disease severity with a single biomarker may not be sufficient in a complex and heterogeneous disease such as AD. We hypothesized that a combination of biomarkers is more suitable for assessing disease severity than a single biomarker.

Objective(s):
To combine multiple serum biomarkers as a surrogate measure for disease severity.

Materials/methods:
In a retrospective cohort of 193 AD patients, 147 serum biomarkers were measured to identify biomarkers that correlated with disease severity. Based on the findings in this retrospective cohort we selected ten biomarkers for validation in a prospective cohort of 65 AD patients. During a treatment period with topical steroids of two months, disease severity was assessed by the Eczema Area and Severity Index (EASI) and serum biomarkers were measured. Fourteen psoriasis vulgaris patients and 26 non-atopic subjects were included as controls.

Results:
In the retrospective cohort, IL-18, IL-22, IL-31, TARC, MDC, PARC, sIL-2R, sE-selectin, SDF-1α and I-309 showed correlation coefficients of >0.30 to disease severity. In the prospective cohort, all patients showed significantly decreasing EASI scores during treatment. Serum biomarkers IL-18, IL-22, I-309, MDC, PARC, sE-selectin, sIL-2R and TARC also significantly decreased upon treatment. Linear mixed model analyses in 55 randomly selected patients from the prospective cohort revealed an optimal combination of TARC, IL-22 and sIL-2R as a predictor of EASI scores. This model was validated in the ten remaining patients and showed a correct prediction of EASI scores in 90% of the cases (sensitivity: 100%, specificity: 88.9%). To test the robustness of our findings, the analysis was repeated five times. The predictive capacity of our model showed a sensitivity ranging from 83.3% to 100.0%, and a specificity ranging from 88.5% to 95.2%.

Conclusion:
Combining serum biomarkers TARC, IL-22 and sIL-2R as a signature offers an objective measurement tool for disease severity in AD patients.

O26

INTERPRETING CHANGE IN PATIENT-ORIENTED ECZEMA MEASURE SCORES: CALCULATING THE SMALLEST DETECTABLE CHANGE AND THE MINIMALLY IMPORTANT CHANGE

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Background:
The Patient Oriented Eczema Measure (POEM) is a 7-item questionnaire scored from 0-28 where either patients/parents document eczema symptoms experienced over the last week. Knowing how much POEM scores have changed over time is only helpful if we can interpret the *clinical significance* of the change. Interpretation can be aided by understanding what is an improvement beyond measurement error (smallest detectable change) and what improvement can be considered important to patients/parents/healthcare professionals (minimally important change).

Objective(s):
To calculate the smallest detectable change and the minimally important change on the POEM to aid interpretation of changes in POEM scores.

Materials/methods:
Firstly, we assessed the smallest detectable change and the minimally important change in a dataset of 300 UK children aged 1-14 with moderate to severe eczema. Minimally important change methods included both anchor-based (i.e. amount of change in the POEM that corresponds to a certain amount of change on a related, interpretable measure) and distribution-based approaches (i.e. amount of change in the POEM that corresponds with 0.5 or 0.2 baseline SD). Secondly, we combined data from five different UK trials including a total of 1372 children with eczema to compare the minimally important change (0.5 baseline SD) across age, sex, ethnicity and individual trials (eczema severity varied across trials).

Results:
The smallest detectable change was 2.12 points. The minimally important change estimates were 1.07 (0.2 baseline SD) and 2.68 (0.5 baseline SD) based on distribution-based methods, from 3.09 to 6.13 based on patient/parent-reported anchor-based methods, and from 3.23 to 5.38 based on investigator-reported anchor-based methods. The minimally important change was not differential by age (0-2 years = 3.25, 3-7 years = 3.40, 8-17 years = 3.44), sex (male = 3.43 female = 3.30), ethnicity (white = 3.45, non-white = 3.34) or trial (ranged from 2.68 to 2.95).

Conclusion:
A study including adults from the Netherlands with severe eczema estimated an MIC of 3.4 points. A study including UK children aged 1-5 estimated MIC results from 2.5 to 4.27. Considering our results alongside previous studies, we recommend the following thresholds are used to interpret changes in POEM scores: ≤ 2 points, unlikely to be a change beyond measurement error; 2.1 to 2.9 points, a small change detected that is likely to be beyond measurement error but may not be clinically important; 3 to 3.9 points, probably a clinically important change; ≥4 points, very likely to be a clinically important change.

O27

WHAT IS LONG-TERM CONTROL OF ATOPIC ECZEMA? INTERNATIONAL QUALITATIVE STUDIES AND RESULTS OF THE HOME V CONSENSUS MEETING

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Background:
The Harmonizing Outcome Measures for Eczema (HOME) initiative is a multi-disciplinary, evidence-based international group developing a core outcome set for atopic eczema trials. HOME has previously recommended four essential domains to be measured; signs, symptoms, quality of life and long-term control, with EASI and POEM as the instruments to measures signs and symptoms respectively.

Objective(s):
To define the domain of long-term control, and achieve consensus on what instrument(s) should be used to measure it.

Materials/methods:
Two qualitative studies were conducted by the long-term control working group: online focus groups involving patients/carers and an online qualitative survey of the HOME membership. These were analysed thematically and combined to provide evidence on what long-term control of atopic eczema means to patients/carers and clinicians. A face-to-face consensus meeting (HOME V) was held 12th–14th June 2017 in Nantes, France involving moderated

small interactive groups and whole group discussions with anonymous voting. The HOME roadmap and COSMIN/COMET guidelines on outcome measurement instrument selection were followed. Discussions and voting on the definition of long-term control and the face validity and feasibility of different ways of measuring long-term control were informed by these two international qualitative studies and other published evidence (systematic reviews and validation studies).

Results:
Focus groups involving 99 patients/carers were conducted in the UK, USA, the Netherlands, France, Sweden and Japan. The HOME survey included 62 responses, mainly clinicians, representing 16 countries. Patients/carers and clinicians considered long-term control to involve several related concepts: level of disease activity, impact on daily life, and treatment required (such as reducing treatment or using only maintenance treatment). Issues highlighted to consider when measuring long-term control included capturing patients/carers *and* clinicians perspective, burden of data collection, interpretability and including an objective assessment.
The consensus meeting in Nantes was attended by 81 participants from 13 countries. There was consensus (91% of participants voted in favour) that the long-term control domain consists of repeated measures of the agreed core domains (clinician-reported signs, patient-reported symptoms (including itch intensity) and quality of life) plus a patient global assessment. Pending further discussions, the existing recommended instruments for signs and symptoms (EASI and POEM) should be used.

Conclusion:
HOME recommends that long-term control of atopic eczema is captured in trials by repeated measures of the existing core domains plus a patient global assessment. Further work is required on timing of assessments and to determine the patient global assessment instrument.

O28

PREDICTING SHORT- AND LONG-TERM OUTCOMES OF A SYSTEMIC THERAPY FOR ATOPIC DERMATITIS USING MACHINE LEARNING METHODS

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Background:
Atopic dermatitis (AD) is one of the complex diseases that can largely benefit from systems medicine, as AD pathogenesis is governed by complex interactions between skin barrier, immune responses, and environmental stressors. Given a large variation in the disease severity and in responses to currently available treatment options from one individual to another, it is of high clinical relevance to design personalized treatment strategies for AD based on patient stratification, rather than the “one-fits-all” treatments. Better prognoses could help choose appropriate treatments for each patient effectively and seek alternatives when necessary.

Objective(s):
We aim to develop mathematical models that can predict the long-term and short-term outcomes of a systemic therapy.

Materials/methods:
We applied machine learning methods to the data from 43 adults AD patients who were treated with a systemic therapy (azathioprine or methotrexate). The data includes EASI assessed at weeks 0, 2, 4, 8, 12 and 24 of the therapy and concentrations of 26 serum biomarkers measured at week 0. A linear regression with Elastic Net regularisation identified a small number of biomarkers that could predict long-term outcomes of a systemic therapy, i.e. future EASI after 2, 4, 8, 12 and 24 weeks of systemic therapy. We also developed a linear mixed model that can predict the short-term outcomes of a systemic therapy, i.e. EASI at the next clinical visit from the present EASI measurement. The performance of both short-term and long-term models was evaluated by cross-validation.

Results:
We developed a mathematical model that predicts the long-term outcomes of a systemic therapy using concentrations of IL10, TNFa, IL7 and IL1b measured before the therapy starts. The model achieved 68% accuracy by cross-validation and allowed us to stratify patients as good or bad responders to the therapy. Moreover, we successfully predicted short-term evolution of AD severity assessed by EASI with 84% accuracy using a stochastic differential equation model. A parameter of this model represents a half-life, i.e. the duration of the treatment by

which the severity score becomes halved. The calculated EASI half-life could be used to compare the efficacy of different treatments. For example, the half-lives for the systemic therapy and a Dupilumab therapy were calculated to be 11 weeks and 4.5 weeks, respectively.

Conclusion:
Our results suggest that measurements of a few biomarkers could be used for short- and long-term prognosis of a systemic therapy, early identification of less-than-average responders, and patient stratification.

Friday April 13, 2018

Session 6 - Gaps in evidence
11:00 AM-12:30 PM

O29

EARLY INTRODUCTION OF PROACTIVE THERAPY FOR INFANTILE ATOPIC DERMATITIS PREVENTS ONSET OF FOOD ALLERGY

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Background:
Infantile atopic dermatitis has been found to be a strong risk factor for development of food allergy (FA) in children, however, it remains to be explored whether early proactive treatment with topical steroids for infantile atopic dermatitis could decrease the incidence of food allergy.

Objective(s):
The aim of this study was to investigate whether early introduction of proactive treatment for infantile atopic dermatitis could prevent the onset of FA.

Materials/methods:
Study design was a retrospective cohort study to analyze the data obtained from the electronic medical records of patients who visited the outpatient clinic in the National Center for Child Health and Development for the first time to receive eczema treatment in their infancy (age < 12 months) between April 2011 and December 2014. Regardless of the severity in their eczema, caregivers of all patients received education to treat their children's skin with proactive therapy resulting in sustained skin clearness thereafter.
They were divided into two groups of the early intervention group (EI) who started proactive therapy before 5 months of age, and the late intervention group (LI) who started it at 5 months of age or older. Primary outcome was the incidence of IgE mediated FA defined as those who experienced immediate allergic reaction to any food or avoided specific food due to high specific IgE level at 24 months of age

Results:
There were 77 patients in EI and 70 in LI. At the first visit, SCORAD (median: IQR) of EI was higher than that of LI (42.6: 24.0-61.0 vs 23.5: 11.9-40.0, p<0.01). The median age at first visit was 5 months of age in EI and 9 months of age in LI (p=0.66). At 24 months of age, incidence of FA in EI was lower than that of LI (24.7% vs 45.7%, p<0.01). Logistic regression analysis was carried out to examine the risk factors of food allergy at age 24 months by adjusting onset age of eczema(<=2 months, > 2 months) and SCORAD. Adjusted odds ratio (aOR) of LI was 4.1 (95% CI; 1.8 - 9.1, p= 0.001) and aOR of high SCORAD at the first visit was 1.3 (95%CI, 1.1 -1.5, p=0.003).

Conclusion:
Early introduction of proactive treatment for infantile atopic dermatitis could reduce the incidence of IgE mediated FA at 24 months of age.

O30

TREATMENT OF ATOPIC DERMATITIS (TREAT) REGISTRY TASKFORCE: AN INTERNATIONAL EXERCISE TO HARMONISE DATA COLLECTION FOR NATIONAL ATOPIC ECZEMA REGISTRIES

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Background:
The evidence-base on photo- and systemic therapies to guide clinical management for moderate-to-severe atopic eczema (AE) is small, despite its frequent and often off-label use. Patient registries could provide additional evidence on effectiveness, safety and cost-effectiveness. This would however require collection of uniform data (a core dataset), to allow direct comparisons across registries as well as to enable data sharing and pooling.

Objective(s):
The TREatment of ATopic eczema (TREAT) Registry Taskforce aims to seek consensus between key stakeholders internationally on a core dataset of domains, items and measurement tools ('what, how and when to measure') for AE registries with a research focus that collect data of children and adults on these therapies.

Materials/methods:
An eDelphi exercise was performed, followed by consensus meetings. Participants from six stakeholder groups were invited: doctors, nurses, non-clinical researchers, patients, industry and regulatory body representatives. The eDelphi comprised 3 sequential online rounds, requesting participants to rate the importance of each proposed domain. In addition, they could comment on the obvious list of domains (n=30) and they were able to add domains to round 2. A final consensus meeting was held to ratify the core dataset ('what to measure'). After the 'what to measure' core set was finalised, the 'how and when to measure' details were defined by three consensus meetings and a teleconference.

Results:
479 participants from 36 countries accessed the eDelphi platform, of whom 86%, 79% and 74% completed rounds 1, 2, and 3 respectively. At a consensus meeting attended by 42 participants, the final 'what to measure' core set was established containing 19 domains with 69 domain items (49 baseline and 20 follow up). In December 2017 the details of the 'how to measure' core set were finalised – taking into account feasibility, existing and validated tools (including the core outcome set defined by the HOME initiative) – as were the details on when those measurements should be collected ('when to measure').

Conclusion:
This international exercise to harmonise data collection for national AE registries has led to a standardised and uniform core dataset for those registries. When implemented, this will ultimately lead to a greater understanding of the effectiveness, safety and cost-effectiveness of photo- and systemic immunomodulatory therapies, to guide clinical decisions in the management of moderate-to-severe AE. Upcoming new systemic treatments have made this initiative even more urgent as comparative data of conventional and upcoming new treatments are lacking and necessary.

O31

EVALUATION OF ANTIMICROBIAL TEXTILES FOR ATOPIC DERMATITIS

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Background:
Functional textiles have been proposed as safe adjunct treatment for atopic dermatitis (AD). Some data has been published regarding their antimicrobial properties and their clinical efficacy.

Objective(s):
This study examined the physical and functional properties of 11 commercially available functional textiles, including their antimicrobial activity in vitro, as a function of multiple laundering cycles.

Materials/methods:
All materials were weighed and examined under scanning electron microscopy (SEM) before and after laundering for fiber morphology and silver coating. Bioburden of newly purchased textiles was assessed by measuring bacterial colony forming units (CFU). Deliverable antimicrobial efficacy was evaluated in vitro for each specimen, before and after 30, 70, 100, 150 and 200 laundering cycles.

Results:
Textile weight showed high variability. Damaged silver-coating of variable degree was observed under SEM in most materials after laundering. Products made of silk showed smoother and tighter fiber morphology compared to cotton. The bacterial load of unwashed material ranged from <1 CFU to 35 CFU per 50x50 mm specimen. Most silver-containing products lost their antimicrobial activity rapidly after laundering. Silk and cotton retrieved products had no deliverable antimicrobial effect even in their original state.

Conclusion:
Elastic, light weight textiles with smooth fibers are comfortable for daily use. Functional textiles rapidly losing their deliverable antimicrobial activity in vitro are not advisable for AD patients. Recommendations for functional textiles should be based on a combination of in vitro analysis of products in their original state and after laundering, together with real life data obtained from controlled clinical trials.

O32

SALIVARY CORTISOL TESTING FOR HYPOTHALAMIC-PITUITARY-ADRENAL AXIS (HPA) SUPPRESSION IN CHILDREN WITH ATOPIC DERMATITIS TREATED WITH TOPICAL CORTICOSTEROIDS

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Background:
Therapeutic monitoring of topical corticosteroids (TCS) use in atopic dermatitis (AD) is not well quantified in the literature, with limited safety data on high volume usage. Salivary cortisol correlates with circulating free cortisol and could be a potential non-invasive screening marker for detection of hypothalamic-pituitary-adrenal (HPA) axis suppression in TCS users.

Objective(s):
We performed a cross-sectional study measuring morning salivary cortisol level, assessing its feasibility as a novel, non-invasive screening test for HPA suppression in the pediatric AD.

Materials/methods:
Children aged between six months and 18 years with AD and healthy control subjects were included in the study. Patients on systemic corticosteroids were excluded. Saliva kits were provided to participants for sample collection within 30 minutes of awakening. Additional data were collected on patient demographics, AD severity measured by Eczema Area Severity Index (EASI), TCS use in the past week, wet dressing use, concurrent serum cortisol level where available, height, weight, and body surface area (BSA).

Results:
A total of 56 participants were included for analysis with 22 age matched controls and 34 cases with AD. A further 34 samples were collected but excluded from analysis due to incorrect specimen collection (n=20), incorrect collection time (n=6) and duplication of samples (n=8). The mean salivary cortisol level did not differ between “no TCS” and “low volume” users (<3 tubes-equivalent of 15g of 0.1% methylprednisolone per week). The mean salivary cortisol level for “high volume” users (≥3 tubes-equivalent of 15g of 0.1% methylprednisolone per week) was 3.9nmol/L and 7.4 nmol/L lower compared to the “no TCS” group (p=0.046), and the “low TCS” group (p=0.000). 3 AD cases had low morning serum cortisol (≤ 200nmol/L), all had low saliva cortisol (< 7 nmol/L). High saliva cortisol in this cohort had a negative predictive value of 88.6% (C.I. 76.9 – 94.8%) for high volume TCS use (AUC = 0.8, p = 0.001). Salivary cortisol concentration was inversely correlated with the total volume of TCS use, as well as TCS use adjusted for weight or BSA (Pearson’s coefficient= -0.405, -0.422, -0.427, respectively, p=0.002).

Conclusion:
Reported high volume use of TCS correlated with a decrease in morning salivary cortisol level. Saliva cortisol ≥ 7 nmol/L in this cohort ruled out high TCS use in 88.6%. Given the non-invasive, easy, and economical nature of saliva collection, this could be a potential future screening tool for HPA axis suppression in children using TCS considered to be at risk.

Posters

Co-morbidities

P001

CROSS-SECTIONAL STUDY OF PSYCHIATRIC COMORBITIDY IN PATIENT WITH ATOPIC DERMATITIS

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Background:
Recent data from Europe and the United States suggest that patients with atopic dermatitis (AD) might be at increased risk of depression.

Objective(s):
In this study, we investigated mental illnesses in patients with AD in Korea.

Materials/methods:
A cross-sectional study design was used analyzing data from the 2015 Korea National Health Insurance Research Database, a survey of 42,641 AD and of 139,486 non-AD included non-atopic eczema, urticaria and psoriasis. Multiple logistic regression analysis was performed and the prevalence of various mental illnesses was calculated for those with and without AD.

Results:
We found the prevalence of depression was not significantly different between AD and non-AD. From the severity of AD, severe AD showed a high odds ratio of depression (moderate odds, 1.75 vs. severe odds, 3.15, p-value <0.0001). Patients with AD have an increased prevalence of attention-deficit/hyperactivity disorder (ADHD) (odds,1.48; 95%CI, 1.27-1.72), autism spectrum disorder (ASD) (odds,1.54; 95%CI, 1.19-1.99), conduct disorder (odds,2.88; 95%CI, 1.52-5.45) significantly.

Conclusion:
In our results, ADHD, ASD and conduct disorder were increased in AD significantly compared to non-AD. We suggested that these mental illnesses could have more specific implications, such as genetic relation with AD. Patients with AD have not increased prevalence of depression compared to non-AD. However, severe AD have an increased the prevalence of depression significantly. Therefore, the severity of dermatitis is thought to contribute more to depression than the type of dermatitis.

Co-morbidities

P002

THE SEVERITY AND PROGNOSIS OF ACNE IN ATOPIC DERMATITIS PATIENTS: AN EXPERIENCE IN KOREAN TERTIARY CENTER

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Background:
Few study results have been reported about the severity and characteristics of acne vulgaris in patients with atopic dermatitis, so far.

Objective(s):
The aim of study was to estimate the severity and characteristics of acne vulgaris in the patients with atopic

dermatitis comparing to those without atopic dermatitis. We used the total counts of pills and the total grams of topical agents prescribed for the treatment of acne vulgaris.

Materials/methods:
A total of 141 patients with adult acne were selected who had visited Korea university Anam hospital dermatologic clinic from June 2015 to June 2016 . Among them, 16 patients had atopic dermatitis and 125 patients did not. We retrospectively reviewed the medical records of those patients and collected the pills and the topical agents prescribed for adult acne. The pills included doxycycline, minocycline, isotretinoin and the topical agents included 0.1% adapalene, fixed combination of 1 % clindamycin and 3% benzoyl peroxide, 1% clindamycin, fixed combination of 0.1% adapalene and 2.5% benzoyl peroxide.

Results:
Patients with atopic dermatitis were prescribed total 63.94 pills of antibiotics, 51.31 pills of isotretinoin and 47.81 gram of topical agents in average during a year. And patients without atopic dermatitis showed total 62.27 pills of antibiotics, 30.32 pills of isotretinoin and 43.64 gram of topical agents. There is no statistically significant result between two groups in the total antibiotics (*p=0.9552*), isotretinoin (*p=0.4814*) and the total gram of topical agents (*p=0.3165*).

Conclusion:
According to the above results, the severity and characteristics of acne vulgaris in patients with atopic dermatitis was not different from that in patients without atopic dermatitis. This study will be helpful for the future investigation to clarify the relationship between acne vulgaris and atopic dermatitis.

Co-morbidities

P003

ASSOCIATION BETWEEN OCULAR DISEASES AND ATOPIC DERMATITIS : A CROSS-SECTIONAL STUDY

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Background:
Atopic dermatitis (AD) is a chronic eczematous skin disorder. Several ocular diseases, including cataract, retinal detachment, blepharitis, glaucoma, keratoconjunctivitis, and keratoconus, have been reported to be associated with AD. However, the ocular disorders of AD patients are not of primary concern to most dermatologists and only a few studies using a large-sample, population-based study design have been reported so far.

Objective(s):
We investigated the association between cataract, glaucoma, and dry eye disease and AD in an adult population in the Republic of Korea.

Materials/methods:
A total of 14,900 adults who participated in the Korean National Health and Nutrition Examination Survey, a nationwide, population-based, cross-sectional survey, between 2010 and 2012 were included in the study. Multiple logistic regression analyses identified the possible association between cataract, glaucoma, and dry eye disease and AD relative to matched controls.

Results:
After adjusting for potential confounding variables, cataract and glaucoma were significantly associated with AD.

Conclusion:
Dermatologists should therefore be concerned with possible ocular disorders in patients with AD and should recommend regular ophthalmic screening for early detection.

Co-morbidities
P004

RELATIONSHIP BETWEEN THE CHARACTERISTICS OF CHRONIC PRURITUS AND PSYCHOLOGICAL STATUS

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Background:
Skin diseases could have a significant negative impact on patient's quality of life. Especially, chronic pruritus is a common problem with a deleterious effect on quality of life.

Objective(s):
We sought to evaluate the relationship between chronic pruritus and psychological status including insomnia and depression.

Materials/methods:
One hundred twenty two patients were intended to study using questionnaires, but 91 patients completed whole questionnaires and were analyzed. Demographic and clinical data were collected, including age, gender, underlying disease, smoking, and alcohol, onset of pruritus and skin diseases. Patient's skin disease were categorized into atopic dermatitis, chronic urticaria, other eczema, prurigo simplex, essential pruritus and others. The intensity of pruritus was assessed according to the 10-point Visual Analogue Scale (VAS) and the 4-Item Itch Questionnaire, insomnia symptoms according to Insomnia Severity Index (ISI), and depression symptoms with Beck's Depression Inventory (BDI).

Results:
The mean intensity of pruritus according to VAS(0-10points) was 6.0±2.5 points, and according to 4-Item Itch Questionnaire(0-19points) was 10.9±4.6 points. A significant correlation between pruritus and ISI was found (VAS: ρ=0.37, P=0.0003** , 4-Item Itch Questionnaire: ρ=0.46, P<0.0001**) as well as between pruritus and BDI (VAS: ρ=0.40, P<0.0001**, 4-Item Itch Questionnaire: ρ=0.43, P<0.0001**). Patients with symptoms suggesting sleep disturbance had more intense pruritus compared with the rest of patients (VAS:6.6±2.5 vs. 5.3±2.4 points, P=0.016*; 4-Item Itch Questionnaire: : 12.5±4.5 vs. 9.1±4.1 points, P=0.0003**) as well as with depression symptoms had more intense pruritus compared with the rest of patients (VAS:7.2±2.2 vs. 5.1±2.5 points, P=0.0001**; 4-Item Itch Questionnaire: : 13.5±4.3 vs. 8.8±3.8 points, P<0.0001**). There were no differences in degree of insomnia and depression symptoms among skin diseases.

Conclusion:
Itching intensity in patients with chronic pruritus plays an important role in determining patients' psychological well-being regardless of their skin diseases. 4-Item itch questionnaire is more correlated with insomnia and depression symptoms. Patients with chronic pruritus require an effective and long-term antipruritic therapy, which could improve their quality of life.

Co-morbidities
P005

CLINICAL CHARACTERISTICS AND GENETIC VARIATIONS OF ATOPIC DERMATITIS PATIENTS WITH AND WITHOUT ALLERGIC CONTACT DERMATITIS

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Background:
In patients with atopic dermatitis (AD), the risk of contact sensitization may be increased, as the disrupted barrier may increase the penetration of contact allergens. Therefore, it is necessary to screen for concurrent allergic contact dermatitis (ACD) in AD patients.

Objective(s):
To identify the clinical characteristics and genetic variations of patients with concurrent ACD and AD.

Materials/methods:
In total, 281 AD subjects who underwent patch testing were included. Subjects with any positive result were classified as “AD with ACD”, while the others as “AD only”. Their clinical characteristics and the prevalence of genetic variations (*FLG* 3321delA, *FLG* K4022X, *KLK7*, *SPINK5*, *DEFB1*, *KDR*, *IL5RA*, *IL9*, and *IL12RB1*) were compared.

Results:
Seventy-one subjects (25.3%) were found to be AD with ACD. Female, older age, older onset, self-reported personal or family history of ACD, and presence of prurigo nodularis were associated with concurrent ACD with AD. Patient age was useful for predicting concurrent ACD on the receiver operating characteristic curve. However, two groups showed no differences in the frequency of variations for the genes included in this study.

Conclusion:
No genetic difference was found between patients with AD only and AD with ACD in this study. Although the correlation was decreased after correcting for age and sex, a personal or family history of ACD, late onset age and prurigo nodularis can support to suspect concurrent ACD. Moreover, patch testing of AD patients over 20 years old in males and 14 in females may enable concurrent ACD diagnosed with high sensitivity and specificity.

Co-morbidities

P006

SERUM BIOMARKER PROFILES SUGGEST THAT ATOPIC DERMATITIS IS A SYSTEMIC DISEASE

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Background:
Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases and is associated with other atopic diseases such as asthma, allergic rhinitis and food allergy. Recent studies have also shown associations between AD and alopecia areata, neuropsychiatric and cardiovascular diseases (CVD).[1] This suggests that systemic inflammation in AD may contribute to the development of these comorbidities over time.

Objective(s):
The aim of the current study was to characterize systemic inflammation in AD patients compared to healthy controls by studying expression levels of inflammatory biomarkers in serum.

Materials/methods:
In a population of 193 moderate to severe AD patients (median six area, six sign atopic dermatitis (SASSAD) score 31.0, IQR 23.0-37.5; median age 30.5 years IQR 21.0-42.0) and 30 healthy controls (mean age 39.1 years, IQR 34.3-44.6) we measured serum concentrations of 144 analytes via multiplex immunoassay, and serum total IgE, periostin, and DPP4, via ELISA-based assays. Hierarchical cluster analysis followed by principal component analysis (PCA) was performed to visualize the biomarker expression profiles from AD patients and healthy controls.

Results:
Hierarchical cluster analysis showed that AD patients can clearly be distinguished healthy controls based on their serum biomarker expression profile. In addition, when we applied PCA, the AD patients and healthy controls were separated into distinct groups based on combinations of the first three principal components. Serum levels of the biomarkers driving the principal components were significantly different between AD patients and controls.

Conclusion:
By using a purely data-driven analysis we have shown that biomarker expression profiles of AD patients are clearly different from healthy controls, confirming the presence of systemic inflammation in AD patients. This contributes to

the hypothesis that that AD is a systemic disorder, and that long term exposure of distant organs to systemic inflammation could have detrimental effects.

Co-morbidities

P007

ATOPIC DERMATITIS AND ALCOHOL USE: A META-ANALYSIS AND SYSTEMATIC REVIEW

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Background:
While several maternal exposures have been associated with an increased risk of atopic dermatitis (AD) in offspring, the effect of alcohol use during pregnancy on the risk of AD in offspring is unclear. Furthermore, it is unclear whether adults with AD have an increased alcohol use, though other poor health behaviors have been associated with AD including smoking and physical inactivity as well as psychiatric disease.

Objective(s):
In this systematic review and meta-analysis, the association between alcohol use and AD were investigated in two ways: 1) whether alcohol use (drinkers versus abstainers) during pregnancy is associated with AD in offspring, and 2) whether AD is associated with increased alcohol use.

Materials/methods:
The medical databases Pubmed, Embase and Web of Science were searched and data extraction was done by two independent reviewers.

Results:
Eighteen studies were included in the qualitative analysis (comparing alcohol drinkers to abstainers) and 12 studies were included in quantitative analysis. There was a positive association between alcohol use during pregnancy and development of AD in offspring (pooled odds ratio [OR] 1.16; 95% confidence interval [CI] 1.09-1.24). However, there was no consistent association between AD in adults and adolescents and alcohol use (pooled OR 1.06; 95% CI 0.92-1.23).

Conclusion:
There is a need for future well-designed prospective studies to firmly establish the association between alcohol use and AD.

Co-morbidities

P008

ASSOCIATION OF METABOLIC AND ATOPIC CO-MORBIDITIES WITH SEVERITY OF ATOPIC DERMATITIS IN A NATIONAL COHORT OF YOUNG ADULT MALES.

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Background:
There have been debates whether the risks of metabolic diseases were increased among adult AD patients. Recent studies have suggested this relationship to be non significant. It is also not widely known if the severity of AD might be related to the presence of these metabolic diseases. Such a relationship between could further lend support to the hypothesis that there might be a correlation between the two conditions. Similarly, the relationship of atopic conditions like allergic rhinitis and asthma with severity of AD has not been well described in adult AD populations although it has previously been reported in children with AD.

Objective(s):
We aimed to study the relationship between the severity of AD and metabolic conditions (obesity, hypertension, hyperlipidaemia, type II diabetes mellitus) and atopic conditions (allergic rhinitis, asthma and food allergies).

Materials/methods:
A retrospective national cohort study was done utilizing the military electronic medical records. It consisted of baseline medical screening information of young male adults conscripted in Singapore over a five-year period. All young male citizens are required to undergo compulsory military service in Singapore.

Results:
A total of 10,077 subjects of median age 20.0 years had AD giving a period prevalence of 9.76%. Up to 29.1% of them had moderate to severe AD. Those with hypertension, hyperlipidemia and type II diabetes mellitus were significantly more likely to have moderate or severe AD after adjusting for age, ethnicity, education level, year of screening and atopic diseases. (OR: 1.50, 95% CI: 1.19 - 1.88, p <0.001). Obesity was also noted to have a slightly higher risk of more severe AD. Those who have allergic rhinitis and/or asthma were also significantly more likely to have moderate or severe AD (OR 6.97 95% CI: 6.24- 7.77, p <0.001) in a similar logistic regression model.

Conclusion:
This study has demonstrated the significant relationship of metabolic and atopic diseases with the severity of adult AD. It adds to growing evidence that important co-morbidities such as metabolic and atopic diseases are closely related with AD and its severity. It also provides insight on the correlation of adult AD with cardiovascular risk factors and atopic diseases especially in an Asian population. With this understanding, further mitigating strategies might be required in the management of these co-morbidities, in order to reduce disease burden of adult AD.

Co-morbidities

P009

INTRALESIONAL IMMUNOTHERAPY OF MOLLUSCUM CONTAGIOSUM BY MEASLES, MUMPS, AND RUBELLA VACCINE IN CHILDREN WITH ATOPIC DERMATITIS: A PILOT STUDY

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Background:
Molluscum contagiosum (MC) is a viral infection of the skin and mucous membranes that often mainly affects in children. Generally, physical destruction by curettage is one of the most commonly used therapy of MC but the presence of concomitant atopic dermatitis (AD) is an important risk factor associated with relapse and treatment failure of MC. Recently, immunotherapy using *Measles, Mumps, and Rubella* (MMR) vaccine intralesional injection has been used for some viral diseases.

Objective(s):
The aim of this study was to evaluate the efficacy and safety of intralesional immunotherapy with MMR vaccine for MC in children with AD.

Materials/methods:
We enrolled 14 AD patients treated by MMR vaccine for MC in our dermatology clinic. Subjects had been treated with MMR vaccine being injected into the largest molluscum lesion at 2-week intervals until complete response was accomplished or for a maximum of 6 treatments, and were checked the efficacy and recurrence at 4 weeks and 12 weeks after final treatment, respectively.

Results:
Eleven of 14 patients (78.6%) experienced complete resolution of their treated MC, and the average number of treatments was 4. Three patients (21.4%) didn't show complete remission. Some patients felt mild discomfort at the time of injection, but no serious side effects were reported. No recurrences were noted.

Conclusion:
Our experience suggests that intralesional immunotherapy by MMR vaccine for MC is less painful and more comfortable option in contrast to curettage, therefore it could be a promising treatment modality, particularly in children with AD.

Co-morbidities
P010

ASSOCIATION BETWEEN ATOPIC DERMATITIS AND AUTOIMMUNE DISORDERS IN A HOSPITAL COHORT OF US ADULTS

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Background:
Atopic dermatitis (AD) is associated with systemic immune activation, altered microbiome of the skin and gastrointestinal tract, and possible autoimmune disease. Previous studies found associations between AD and autoimmune skin conditions, such as alopecia areata and vitiligo. However, few studies examined the association between AD and extra-cutaneous autoimmune disorders.

Objective(s):
We sought to whether AD is associated with autoimmune disorders in US adults.

Materials/methods:
Data from the 2002–2012 National Inpatient Sample were analyzed, including a representative 20% sample of all US hospitalizations (total n=72,108,077 adults).

Results:
In multivariable survey logistic regression models controlling for age, race/ethnicity, gender and insurance status, AD was associated with increased odds of higher odds of autoimmune disorders affecting the skin and mucosa (adjusted odds ratio [95% confidence interval] for alopecia areata: 18.98 [13.44-26.78]; Sjogren's syndrome: 1.72 [1.50-1.98]); chronic urticaria: 7.05 [6.32-7.87]; vitiligo: 6.36 [5.35-7.57]), hematologic (pernicious anemia: 1.64 [1.42-1.88]; immune thrombocytopenic purpura: 1.48 [1.28-1.71]), musculoskeletal (ankylosing spondylitis: 1.73 [1.40-2.14]; rheumatoid arthritis: 1.34 [1.28-1.40]; systemic lupus erythematosus: 1.71 [1.59-1.83]), gastrointestinal (eosinophilic esophagitis: 3.89 [2.27-6.64]; non-alcoholic steatohepatitis: 1.75 [1.63-1.87]; Crohn's disease: 1.41 [1.30-1.52]; ulcerative colitis: 1.55 [1.42-1.69]; celiac disease: 2.45 [2.13-2.82];), endocrine (Hashiomoto's disease: 1.28 [1.04-1.57];), renal (chronic glomerulonephritis: 1.22 [1.01-1.46]), and nervous (multiple sclerosis: 1.61 [1.49-1.74];) systems. AD was inversely associated with type 1 diabetes mellitus (0.83 [0.78-0.88]). Similar results were found in multivariable models that controlled for comorbid allergic disease. For many autoimmune disorders, higher prevalence was observed in patients who were female and non-white race/ethnicity.

Conclusion:
Adults with AD had significantly higher odds of cutaneous and extra-cutaneous autoimmune disorders. Further studies are needed to understand the mechanisms of autoimmune disorders in AD and to identify which AD patients are at risk for developing autoimmune disease.

Co-morbidities
P011

ALLERGIC CONTACT DERMATITIS TO PERSONAL CARE PRODUCTS AND MEDICAMENTS IN ADULT ATOPIC DERMATITIS PATIENTS

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Background:
Atopic dermatitis (AD) is associated with skin-barrier dysruption, cutaneous and systemic immune dysregulation, and frequent application of emollients and medicaments, all of which may predispose them toward developing allergic contact dermatitis.

Objective(s):
To determine the predictors of and relevant allergens in allergic contact dermatitis among patients with atopic dermatitis.

Materials/methods:
We performed a retrospective chart review of 395 adults (age ≥18 years), who were patch-tested at the Northwestern Medicine patch-testing clinic from 2014-2017. Patients were patch-tested with the North American Contact Dermatitis Group (NACDG) standard series and a supplemental allergen series. AD was diagnosed using the Hanifin and Rajka criteria.

Results:
Overall, 97 (24.6%) of the cohort were diagnosed with AD. Patients with AD compared to those without AD had similar proportions of any positive (+, ++ or +++: 72 [74.2%] vs. 197 [66.1%]; Chi-square, P=0.14), stronger (++, +++: 30 [30.9%] vs. 75 [25.2%]; P=0.27) and irritant (49 [50.5%] vs. 149 [50.0%]; P=0.93) patch test reactions. In particular, AD patients had significantly higher rates of positive patch test reactions to ingredients in their personal care products or medicaments, including lanolin (P=0.03), quaternium-15 (P=0.04), fragrance mix I (P=0.008), cinnamal (P=0.02), neomycin (P=0.02), bacitracin (P=0.04), chlorhexidine (P=0.04), and budesonide (P=0.01). Relevance was established in >90% of patients with positive reactions to one of these allergens. In particular, positive patch test reactions to lanolin, quaternium 15, fragrance mix I, cinnamal, budesonide and chlorhexidine were more common in females with AD (P<0.05), but not males. Similar rates of polysensitization (≥2 positive patch test reactions) were observed in AD vs. non-AD patients (P=0.33).

Conclusion:
Patients with AD did not have higher rates of positive patch test reactions overall. However, they had higher rates of positive patch test reactions to multiple ingredients in their personal care products and topical steroid and antibiotic medicaments.

Patients' perspectives/ education/eHealth

P015

A DECADE-LONG SURVEY OF ATOPIC DERMATITIS AMONG SCHOOL STUDENTS IN HOKKAIDO

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Background:
To date, several cohort surveys of infantile atopic dermatitis (AD) have been reported. However, there are few cohort surveys involving school students.

Objective(s):
The aim of this study was to investigate not only the prevalence rate of AD but also the prognosis of individuals with AD.

Materials/methods:
We examined school students (1st, 4th, 7th grade) every year. The total number of students examined from 2005 to 2015 was 4087. AD was diagnosed by experienced dermatologists based on the Japanese Dermatological Association criteria for the disease. We analyzed 162 students who were examined at least twice and diagnosed with AD at least once.

Results:
The total number of students with AD was 369 and the average prevalence rate of AD from 2006 to 2015 was 9.0% (1st, 9.6%; 4th, 9.9%; 7th, 7.6%). The number of students with AD at 1st grade was 72. Thirty-six (50%) students had persistent AD at 4th grade, while 36 (50%) demonstrated AD remission. However, 44 (55%) students had newly developed AD at 4th grade. The total number of 4th grade students with AD was 88. Thirty-five (40%) students had persistent AD at 7th grade, while 53 (60%) demonstrated AD remission. However, 37 (51%) students had newly developed AD at 7th grade. Sixty-seven students were examined for 6 years. Twenty-nine (66%) students with AD at 1st grade demonstrated AD remission until 7th grade, while 23 (61%) students with AD at 7th grade developed AD after 1st grade.

Conclusion:
We thought that infantile AD improves during school age and that most AD cases in students are persistent cases. However, in this study, about half of the children with AD at 7th grade had newly developed AD during school age. This observation suggests that it is necessary to decrease the prevalence of AD in school students by not only treating students with AD but also by preventing the occurrence of AD in them. The early skin care intervention for healthy students will be effective in preventing AD.

Patients' perspectives/ education/eHealth

P016

DEVELOPING A WRITTEN ACTION PLAN FOR CHILDREN WITH ECZEMA

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Background:
Eczema is common in children but adherence to treatments is poor. Written action plans (WAPs) have been shown to help in asthma but the potential value, format and content of an eczema WAP is unknown.

Objective(s):
To explore the potential role of an eczema WAP; and to design an eczema specific WAP.

Materials/methods:
Qualitative study with parents of children with eczema; primary and secondary care health professionals; and other stakeholders. Forty-one semi-structured one-to-one interviews and two focus groups were audio-recorded, transcribed and analysed thematically.

Results:
Reported challenges of managing eczema included: parental confusion about treatment application; lack of verbal and written advice from GPs; differing beliefs about the cause and management of eczema; re-prescribing of failed treatments; and parents feeling unsupported by their GP. An eczema WAP was viewed as an educational tool that could help address these problems. Participants expressed a preference for a WAP that gives clear, individualised guidance on treatment use, presented in a 'step up/down' approach. Participants also wanted more general information about eczema, its potential triggers and how to manage problem symptoms.

Conclusion:
An eczema WAP may help overcome some of the difficulties of managing eczema and support families and clinicians in the management of the condition. Further evaluation is needed to determine if the eczema WAP we have developed is both acceptable and improves the outcomes for affected children and their families.

Patients' perspectives/ education/eHealth

P017

ECZEMA CARE ONLINE - DEVELOPMENT AND TESTING OF ONLINE INTERVENTIONS TO SUPPORT SELF-CARE FOR PEOPLE WITH ECZEMA

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Background:
People with eczema often have difficulty using their prescribed treatments sufficiently to keep their eczema under control. There are many reasons why people face challenges managing their eczema, including time-consuming treatment applications, initial stinging when applied to inflamed skin, concerns about treatment safety, and receiving insufficient or conflicting advice about how and when to use treatments.
We will explore and seek to address barriers to effective treatment within a newly-funded programme of research, leading to the development and evaluation of digital interventions (websites/apps) that use behaviour change techniques to support eczema self-care.

Objective(s):
To improve the lives of people with eczema by developing and testing digital interventions that will support self-care and address common barriers to eczema self-care, including concerns around topical corticosteroid safety.

Materials/methods:
This work will take place over the next five years in an inter-linked research programme. Our five workstreams will: i) understand facilitators and barriers to effective self-care amongst people with eczema (children with eczema and their families, teenagers and young adults managing their own eczema); ii) review the evidence base regarding safety of topical corticosteroids and develop knowledge tools to support shared understanding between patients, parents/carers and clinicians; iii) develop two digital interventions to support eczema self-care: one for parents/carers of children with eczema and one for teenagers and young adults managing their own eczema; iv) determine the clinical and cost-effectiveness of digital self-care interventions compared to standard clinical care in a randomised controlled trial; and v) a process evaluation to explore how to integrate interventions into clinical practice and to facilitate their uptake should they prove clinically and cost-effective.

Results:
This programme of work will produce a clear summary of current best evidence on the safety of topical corticosteroids; develop knowledge tools to facilitate shared understanding between clinicians and patients; develop two new fully evaluated self-care support interventions for the groups described above; and develop plans for how to rapidly integrate these interventions into clinical practice (if effective).

Conclusion:
Improved self-care has the potential to benefit people with eczema through better use of treatments and improved quality of life. It also has potential benefits for the healthcare system through reducing primary care consultation rates for eczema, more appropriate prescribing, and reduced referrals to secondary care.

Patients' perspectives/ education/eHealth

P018

BURDEN OF DISEASE AND QUALITY OF LIFE OF ADULTS WITH SEVERE ATOPIC ECZEMA: AN ASSESSMENT IN NINE EU COUNTRIES

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Background:
Atopic eczema (AE) is one of the most common non-communicable inflammatory skin diseases that affects 1-3% of the adult population in the EU. Characteristic of AE is the chronic or relapsing nature, with itch as the predominant symptom. Signs and symptoms of AE can have a huge impact on physical wellbeing and quality of life, especially in patients with severe AE. This is the first study of this size in Europe that assesses the real world impact and the intensity of individual suffering in the daily living of eczema patients.

Objective(s):
To provide insight on the burden of disease and quality of life of adult patients with severe AE in a real world setting, as to create awareness and understanding for this severe disease within national and international healthcare professionals (dermatologists, allergists, primary-care-physicians, nurses, pharmacists), health journalists, patient organisations and EU policy makers including payers.

Materials/methods:
The questionnaire was devised partly using validated instruments (POEM, HADS, DLQI) to assess the economic burden, individual suffering, emotional impact and coping skills. Approval of Ethics Committees was given in each participating country before starting the survey.
The survey was carried out in nine European countries and is based on n=1.200 interviews in total (Germany/France/Italy/United Kingdom/Spain: 180 each; The Netherlands: 150; Czech Republic, Denmark, Sweden: 50 each) with an average interview time of 25 minutes.
For fieldwork a telephone approach (CATI) was chosen to ensure a national coverage with the greatest possible evaluation quality. Fieldwork started in October 2017 and will be completed by the end of February 2018.
A comparable methodology and identical questionnaire allows cross-country comparison. Recruitment was based on physician referral, in some countries also on additional sources like patients support groups. To ensure consistent quality, screening questions have been added before starting the interview.

Results:
Results will illustrate the current situation of severe AE patients with regard to individual suffering. A comparison between several EU countries will assess relevant differences. All results will be available in March and analysed before the time of the conference.

Conclusion:
Conclusions will focus on similarities and un-equalities to ensure in the future a smoother management and lower burden of disease and therefore better quality of life for adult patients with severe AE. The final goal of this study is to assist patients and their families to manage severe AE and help the lay-public, physicians and the healthcare community to better understand this disease.

Patients' perspectives/ education/eHealth

P019

INFLUENCE OF CLIMATIC AND WEATHER CONDITIONS ON THE PREVALENCE OF ATOPIC DERMATITIS

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Background:
Climate and weather may influence eczematous skin diseases such as atopic dermatitis (AD).

Objective(s):
We aim to investigate the relationships between the prevalence of AD and climatic and weather conditions, and compare its affected patterns with those of allergic contact dermatitis (ACD).

Materials/methods:
The monthly patient numbers of AD and ACD were extracted from the Healthcare Bigdata Hub of the Korean Health Insurance Review and Assessment (HIRA) service from 2012 to 2016. The climate or weather data of the 4 largest and distinct cities in Korea – Seoul (cold and dry), Incheon (cold and humid), Daegu (warm and dry), and Busan (warm and humid) - were obtained from Korea Meteorological Administration.

Results:
The prevalence of AD was higher but that of ACD was lower in cold cities than warm ones. The prevalence of both AD and ACD was higher in dry cities than humid ones. The prevalence of AD was differentially related to temperature depending on seasons and cities, while that of ACD was positively correlated with temperature. Both AD and ACD increased with large diurnal temperature change in cold and dry seasons. The low humidity was associated with increased prevalence of AD and ACD in dry cities.

Conclusion:
This study showed that climate and weather factors influence the prevalence of AD in a complex manner. Education and interventions considering specific climate and weather conditions may be more helpful for patients with AD.

Patients' perspectives/ education/eHealth

P020

PATIENT ENGAGEMENT IN PROFESSIONAL EDUCATION CURRICULUM DEVELOPMENT

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Background:
It is a commonly held belief (or principle) the end user of professional medical education is the learner, i.e. medical professional. However, the success of medical education is ultimately measured by the longitudinal improvement in the health outcomes of patients, who indirectly benefit from direct provider learning. Thus, in order to reach the penultimate outcome of improved patient health, the patients' voice and experiences need to be included in the development of medical education curricula accessed by their providers.

Objective(s):
To improve the quality of professional medical education and directly impact patient outcomes, the National Eczema Association (NEA) created a multidisciplinary, whole person curriculum regarding atopic dermatitis, titled the Coalition United for Better Eczema Care (CUBE-C). This educational platform, consisting of written text, PowerPoint slides, and lectures is aimed at optimizing patient outcomes and quality of life for patients with atopic dermatitis, while reminding providers that atopic dermatitis is a complex, multidisciplinary disease. The authors believe the engagement of patients in educational curricula creation will ultimately lead to improved patient health outcomes.

Materials/methods:
To discover real-world needs and barriers experienced by patients to better manage their disease, patients with atopic dermatitis were included in the development of the medical curriculum as part of the NEA Coalition United for Better Eczema Care (CUBE-C) initiative. Based on this engagement, the educational curricula included medical, psychosocial, and logistical needs of atopic dermatitis patients as identified jointly by participating patients and providers.

Results:
Initial feedback from CUBE-C faculty and patients were positive, resulting in a more comprehensive medical education curriculum informed by both patients and their providers. Incorporating patients into the curriculum development allowed the authors to gain insights into patient interests and needs. Patients reported interest in alternative management strategies, such as bleach baths, as well as using shared decision-making tools with their providers.

Conclusion:
Formal research is needed to comprehensively assess the quantitative impact of including patients in the medical curriculum development process. Early observation of patient inclusion in our curriculum development processes reinforced the importance of the patient perspective ("voice") to inform meaningful direction in medical education curriculum development. There must also be post-educational evaluation of participating learners to assess the health outcomes of patients impacted by the educational activity.

Patients' perspectives/ education/eHealth

P021

MULTI-STAKEHOLDER ENGAGEMENT IN THE TREATMENT OF ATOPIC DERMATITIS

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Background:
Atopic dermatitis (AD) is a complex, heterogeneous disease, ideally requiring multidisciplinary care. Thus, treatment strategies should differ amongst patients to optimize medical care and quality of life. There is emerging knowledge of the pathophysiology of AD, such that future state will allow targeted treatment, aimed at a patient's individual disease process. Most patients with atopic dermatitis receive their basic and advanced care from primary care providers due to the high prevalence of the disease and limited access to subspecialty experts. Patients who do obtain subspecialty care do so across a variety of specialties with varying knowledge in disease management. For most providers, regardless of discipline, optimal AD medical education is not readily available.

Objective(s):
To help close this gap in medical knowledge and patient care, professional medical education must be designed by and for stakeholders across various medical disciplines in order to achieve optimal learning.

Materials/methods:
The National Eczema Association convened medical experts from different subspecialties of medicine to organize and create a curriculum and educational platform for medical education regarding atopic dermatitis to be understandable and accessible across medical specialties to all providers who treat AD patients.

Results:
Through the AD medical education curriculum development initiative, the National Eczema Association convened patients, dermatologists, allergists, immunologists, pediatricians, primary care providers, nurse practitioners, and physician assistants, resulting in a collaboratively developed, comprehensive curriculum that includes perspectives and considerations of learners across multiple fields. By bringing together stakeholders from diverse disciplines and backgrounds into curriculum development, including patients, the understanding of the complexities in AD care emerged, which helped drive an improved curriculum model.

Conclusion:
The National Eczema Association will use resulting pre/post-assessment evaluations of the curriculum to gain insight which will assist in optimal medical education for providers treating AD patients, and also allowed continuous improvement of the curriculum developed to maximize utilization and retention.

Patients' perspectives/ education/eHealth

P022

ADHERENCE TO TOPICAL MEDICATIONS: PERSPECTIVES FROM PARENTS OF CHILDREN WITH ECZMEA

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Background:
Several studies have demonstrated poor adherence among children with atopic dermatitis (AD). For example, one study which used electronic monitoring to measure use of triamcinolone ointment 0.1% found that mean adherence from baseline to the end of the study (8 weeks) was just 32%.
Though adherence has been shown to be low among children with AD, the reasons for it are poorly understood. Few studies have examined parents' self-reported reasons for deviation from prescribed treatment instructions.

Objective(s):
To review and synthesize the existing literature related to adherence and AD;
To assess treatment adherence to topical therapy among parents of children with moderate to severe AD and drivers of topical treatment non-adherence among this group.

Materials/methods:
An online survey questionnaire was posted to members of Global Parents for Eczema Research and Eczema Parents Facebook groups. Both are international groups comprised of parents of children with eczema, the majority residing in the U.S., the UK, Canada and Australia.

Results:
Survey data collection will be complete in March 2018. We will highlight survey findings including reported adherence among parents of children with AD and drivers of non-adherence.

Conclusion:
Improvement in adherence to topical treatments among children with AD could yield large gains in quality of life improvements and reduce exposure to costlier systemic agents that have more concerning side effects. Given the large, documented gains in disease improvement, and even remission, achieved with interventions that address adherence among patients with other chronic diseases, strategies that address the underlying causes for poor adherence among parents of children with atopic dermatitis stand to provide a significant, untapped benefit.

Mechanisms of disease; genetics & -omics
P025

INCREASED EXPRESSION OF TRPV4 CHANNEL IN KERATINOCYTES UNDER TH2 INFLAMMATION
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Background:
Pruritus in the patients with atopic dermatitis is frequently affected by environmental temperature change. Transient receptor potential (TRP) channel which is a nonselective cation channel play a central role on sensory response to noxious physical and chemical stimuli. Populations of non-neuronal cells in the skin express many different types of TRP channels and TRP channels are involved in various key cutaneous functions including pruritus, differentiation, and inflammatory process.

Objective(s):
To evaluate the molecular expression of TRP channels in keratinocytes under Th2 inflammation.

Materials/methods:
Primary epidermal keratinocytes cell line was stimulated with IL-4, IL-13, IL-17A, and IFN-γ. Expression of TRPV1, TRPV3, TRPV4 and TRPA1 in keratinocytes was analyzed by quantitative real time PCR, and Western blot and flow cytometry. Itch related mediators (nerve growth factor, endothelin-1, thymic stromal lymphoprotein) were checked keratinocytes with IL-4 and TRPV4 agonist (4α-phorbol 12,13-didecanone).

Results:
RT-PCR and Western blotting analysis revealed elevated expression of TRPV3, TRPV4 and TRPA1 in keratinocyte stimulated with IL-4, IL-13, IL-17A. Especially, TRPV3 and TRPV4 expression were significantly increased under Th2 inflammation like IL-4 and IL-13. Flow cytometry analysis confirmed increased expression of TRPV3 and TRPV4 in keratinocytes stimulated with IL-4 and IL-13 at 24 hours. Nerve growth factor was significantly increased under IL-4 with TRPV4 agonist (4α-phorbol 12,13-didecanone).

Conclusion:
TRPV3 and TRPV4 channels are significantly expressed in keratinocytes under Th2 inflammation. Especially, TRPV4 (warm >28°C) may be more relevant TRP channels than TRPV1 (warm >43°C) on the mechanism of pruritus in atopic dermatitis.

Mechanisms of disease; genetics & -omics
P026

PHENOTYPIC PROFILE OF CLA+ NK CELLS IN ADULTS WITH ATOPIC DERMATITIS
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Background:
Atopic dermatitis (AD) is an inflammatory, chronic, and immune mediated skin disease characterized by intense pruritus and xerosis. Cellular elements of the innate immune response, such as natural killer (NK) cells, are capable to regulate immunological response through cytokine production; however, further studies regarding NK features and their role in AD are still lacking.

Objective(s):
To evaluate the phenotypic profile of peripheral blood NK cells through activation markers and skin homing molecules in adults with AD.

Materials/methods:
Ten healthy subjects (HC, n = 10) and 11 patients with AD (mild n = 5, and severe, n = 6, disease severity evaluated according to EASI), gender- and age-paired, were selected. To analyze the NK cells in the peripheral blood, venous blood was collected in EDTA-enriched tubes. Approximately 70mL of whole blood was stained with: anti-CD3, anti-CD19, anti-CD56, anti-CD16, anti-CLA (skin homing marker), anti-CD11b (NK cell functional maturation marker), anti-CD8 and anti-NKG2D (NK cell activation receptor marker), and further analyzed by flow cytometry.

Results:
Our results showed a significant increase of CLA frequency in individuals with severe AD both in $CD56^{bright}$ and $CD56^{dim}$ NK cell population. There was a significant decrease in CD8 and NKG2D frequency in the NK cell populations. The frequency of NKG2D receptor was also reduced in $CD56^{bright}$ NK cells in individuals with mild AD. We also observed a significant increase of CD11b frequency in NK cell populations of individuals with severe AD.

Conclusion:
Circulating CLA+ NK cells are elevated in severe AD, with high degree of functional maturity (CD11b), and reduced expression of activation receptors (CD8 and NKG2D), indicating that such NK cells showed phenotypical changes according to AD severity, and are chronically activated. Further studies are necessary to better elucidate the role of NK cells and innate immune response in AD pathogenesis.

Mechanisms of disease; genetics & -omics

P027

PROSPECTIVE BIRTH COHORT STUDY ON ENVIRONMENTAL FACTORS AND ATOPIC DERMATITIS DEVELOPMENT

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Background:
The influence of environmental factors on atopic dermatitis (AD) has been investigated in many cross-sectional studies. It remains however unclear whether certain environmental factors could influence AD development early in life.

Objective(s):
The aim of this prospective birth cohort study was to assess the relationship between a wide array of environmental factors and AD onset during infancy.

Materials/methods:
Caucasian infants were monitored over the first two years of life or up to AD onset for skin changes. Genetic predisposition was evaluated based on family history of atopy and filaggrin genotyping. Standardized questionnaires based on the recent literature were used to collect information on environmental factors.

Results:
Out of 149 included children, 36 developed AD, at an average age of 9.4 months. Infants with a family history of atopy developed AD 2.6 times as frequently (31%; 30 of 97) as infants without atopic predisposition (12%; 6 of 52). Filaggrin mutations (R501X, 2282del4, R2447X and S3247X) were however infrequent in our study population. We observed a reduced risk of AD in infants exposed to a moist housing environment or to tobacco smoke, and a tendency of higher household income to be associated with increased AD risk. No association was found between AD risk and parental level of education, number of siblings, prenatal exposure to alcohol or antibiotics, mode of delivery, duration of breastfeeding, urban living, presence of carpets in the house, fabric softener use or pet ownership.

Conclusion:
In our cohort, family history of atopy was a major risk factor regardless of the most common filaggrin mutations, which were infrequent in both AD and control infants. Postnatal exposure to tobacco smoke and a moist housing environment were associated with a reduced risk of AD.

Mechanisms of disease; genetics & -omics

P028

ASSOCIATIONS OF CLINICAL AND PARACLINICAL CHARACTERISTICS WITH SEVERITY OF ATOPIC DERMATITIS IN A HOSPITAL COHORT

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Background:
Atopic dermatitis (AD) is a complex disease with numerous underlying mechanisms of disease. Understanding the pathogenesis of AD is of great importance when developing preventive measures and selecting treatment targets.

Objective(s):
This study explores to what extent key clinical and para-clinical characteristics differ according to disease severity in a large hospital cohort of patients with AD.

Materials/methods:
Consecutive outpatients with AD referred to the Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark between January 2012 and December 2017, were separated into groups, based on disease severity (SCORAD); mild (<25), moderate (25-50) and severe (>50). Distribution of key clinical and para-clinical disease characteristics was compared between groups.

Results:
471 patients was scored using SCORAD and grouped by disease severity; 166 mild, 219 moderate and 86 severe. A significant difference between groups was observed for sex (36.7 vs. 48.4 vs. 54.7% males, p=0.012), serum total IgE (549 vs. 1201 vs. 1962 $*10^3$ IU/L, p<0.001), blood eosinophil count (0.31 vs. 0.42 vs. 0.60 * 10^9/L, p<0.001), *FLG*-mutation carrier status (16.7 vs. 15.5 vs. 30.2%, p=0.025), asthma (30.7 vs. 29.7 vs. 52.3%, p=0.002), extrinsic AD (43.0 vs. 62.7 vs. 75.8%, p<0.001), DLQI (6.8 vs. 9.4 vs. 13.2, p<0.001) and number of locations (in face, trunk, extremities) affected by eczema (6.5 vs. 9.0 vs. 10.8, p<0.001).

Conclusion:
Key clinical and para-clinical disease characteristics vary to a high degree according to the severity of AD measured by SCORAD. Patients with severe AD have a significantly higher frequency of atopic comorbidities, are more often *FLG*-carriers and have more impaired quality of life.

Mechanisms of disease; genetics & -omics

P029

TRANSCRIPTOME ANALYSIS OF HUMAN SKIN-RESIDENT MEMORY T CELLS IN ATOPIC DERMATITIS

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Background:
Memory T cells in human skin has been composed of two major subsets, called migratory memory T cells (T_{MM}) and skin-resident memory T cells (T_{RM}). The best characterized are T_{RM} cells that bear the CD69 and CD103 but lack of CCR7 and CD62L. However, the gene expression profile has not yet been determined in T_{RM} cells and T_{MM} cells using transcriptional analysis.

Objective(s):
Our aim was to characterize and identify a gene expression signature of human skin T_{MM} cells and T_{RM} cells in atopic dermatitis.

Materials/methods:
To distinguish between T_{MM} cells and T_{RM} cells, we attempted to generate human normal and AD skin using migration assay. Then, we respectively sorted T cells which migrated from the skin ($CD69^-$ T_{MM} cells) and remained on skin ($CD69^+$ T_{RM} cells). We further performed microarray analysis to evaluate and verify the cytokine signatures and various genes associated with tissue egress and residency.

Results:
We found that skin T_{RM} cells were transcriptionally distinct from T_{MM} cells using principal component analysis and correlation matrix analysis. AD $CD69^+$ T_{RM} cells also considerably showed significant level of genes related with tissue residency compared to T_{MM} cells. Gene set enrichment analysis further showed that skin T_{RM} cells were significantly enriched for various immune-related signature genes compared to T_{MM} cells from AD skin. Interestingly, AD T_{RM} produced multiple cytokines, such as IL-4, IL-17, IL-22, and IFN-γ.

Conclusion:
These results indicate that highly-multifunctional AD T_{RM} could be a main mechanism resistant to conventional treatments, suggesting a new therapeutic target for the treatment of AD.

Mechanisms of disease; genetics & -omics

P030

THE ROLE OF PATHOGENIC STAPHYLOCOCCUS AUREUS STRAINS AND THE SKIN COMMENSAL MICROBIOME ON IMMUNOLOGICAL RESPONSES IN ATOPIC DERMATITIS

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Background:
S. aureus (SA) is known to play an important role in atopic dermatitis (AD). Disease flares are associated with SA skin infection, and SA abundance correlates with flare and disease severity. Importantly, however, the extent to which SA is causative rather than a bystander of the inflammatory AD skin environment is not clear. If SA does have a causal role, the mechanisms through which it exerts its function on the skin immune system to drive inflammation are also not fully understood.

Objective(s):
This study aims to investigate the role of SA and commensal bacteria in AD pathogenesis through analysis of the skin metagenome and transcriptome.

Materials/methods:
Skin microbiome samples and underlying skin biopsies were obtained from lesional and non-lesional skin of adults with mild-severe AD (n=88), and healthy volunteers (n=117). The metagenome was sequenced to quantify microbial abundance by aligning metagenome reads to species-specific marker sequences. SA virulence factor gene abundances were measured by mapping metagenome reads to gene sequences.

Results:
There are clear differences in the microbiome between AD and healthy volunteers with increased SA and reduced commensals in AD. SA abundance correlates with AD severity. The data reveal a subset of AD patients whose microbiome is heavily dominated by SA. The SA virulence factor delta-toxin genes are present in a significantly higher proportion of AD samples compared to healthy volunteers.

Conclusion:
This work demonstrates that our methodology detects expected differences between AD patients and healthy controls. The subset of AD patients whose microbiome is heavily dominated by SA will be interrogated further to identify specific SA strains and virulence genes in AD. The AD host transcriptome profile associated with SA and commensal bacteria will be explored to reveal potential microbe-host interactions. These interactions may provide novel therapeutic targets for the disease. This work will be validated *in vitro* to test whether these relationships are causal and identify the mechanisms underlying host responses to SA in AD.

Mechanisms of disease; genetics & -omics

P031

FILAGGRIN-GENOTYPE AND ATOPIC DERMATITIS DO NOT AFFECT SEVERITY OF KERATOCONUS

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Background:
Filaggrin is a major structural protein in the skin barrier and the RX501 and/or 2282del4 null-mutations in the filaggrin-gene (*FLG*) increase the risk of atopic dermatitis (AD). Moreover, the inflammatory reaction in AD itself may downregulate the expression of filaggrin and thereby additionally impair the skin barrier function. Filaggrin is also present in the corneal epithelium and may play a significant role in the corneal epithelial barrier which shares structural similarities with the skin. Previous studies have hypothesized that *FLG* mutated (*FLG*mut) patients with concomitant AD may have a more severe keratoconus (KC).

Objective(s):
We investigated if *FLG* genotype in synergy with AD affects the risk and severity of KC in a Danish cohort.

Materials/methods:
One hundred and eight patients were recruited from the Department of Ophthalmology and the Department of Dermatology, Aarhus University Hospital, and distributed in four groups based on KC- and AD-status (KC+/AD+, KC+/AD-, KC-/AD+ and KC-/AD-). Patients with high-myopia comprised the reference group. All patients answered a six-question questionnaire or underwent clinical examination in order to diagnose AD. Bilateral corneal topography was performed using a Pentacam HR to assess KC status. We employed the topographical keratoconus classification (TKC) and K_{max} (steepness of the cornea-cone) for group comparison and analyzed *FLG*-genotype by DNA-sequencing.

Results:
Fifteen of the 108 patients (14%) in our cohort had *FLG*mut. There was no difference in the distribution of *FLG* genotypes in the four groups (*P=0.34*). Nine of 49 (18%) patients with AD and 6/59 (10%) without AD had *FLG*mut (P=0.22).
There was no difference in K_{max} between KC patients with and without AD (54.5 vs. 57.6; P=0.51). Median K_{max} in patients with *FLG*mut did not differ significantly from patients with *FLG* wildtype (66 vs. 59.9; P= 0.12).

Conclusion:
In our cohort, the frequency of *FLG* mutations was low and the genotype was equally distributed between patients with and without AD and KC. *FLG* mutated patients had a higher K_{max} compared to patients with *FLG* wildtype albeit the difference did not reach statistical significance.
The fact that filaggrin has a low expression in cornea compared to normal skin, may complicate the transference of the above hypothesis regarding KC severity. Also, the lower frequency of *FLG* mutations in our cohort impair the ability of this study to identify a potential aggravated condition in patients with both AD and *FLG* mutation.

Mechanisms of disease; genetics & -omics

P032

EVOLUTION OF SKIN MICROBIOTA OVER THE FIRST TWO YEARS OF LIFE AND ITS MODIFICATIONS PRECEDING ATOPIC DERMATITIS DEVELOPMENT

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Background:
In recent years, genomic sequencing surveys have looked at the skin microbiota in adults or older children, establishing baselines and providing invaluable insight into the complex interplay between the skin and its microbial ecosystem. However, few studies have investigated the evolution of skin microbiota in early life and alterations thereof which could increase the risk of atopic dermatitis (AD).

Objective(s):
We aimed to characterize the skin microbiota at birth, the impact of delivery mode and its evolution over the first two years of life, and to determine whether specific skin microbiota alterations can be observed before AD development.

Materials/methods:
We analyzed bacterial 16S rRNA gene sequences in axillary fossa swabs collected from 96 healthy Caucasian newborns at six different time points over a two-year period. We additionally used real-time PCR to quantify the level of colonization by five bacterial species with known or suspected association with AD.

Results:
Consistent with the ongoing structural and functional skin maturation in the first years of life, age was found to have a major impact on infant skin microbiota. Biodiversity increased from age one month onwards, and several bacterial families displayed distinctive patterns of evolution. The influence of delivery mode was mostly observed at age one day, but displayed a residual effect until age six months. In children developing AD, we uncovered several alterations in the skin microbiota at various time points before disease onset. Noteworthy, several taxa were more abundant in children who did not develop AD later on than in those who did, indicating a potentially protective role of certain resident bacteria against AD.

Conclusion:
Collectively, our findings provide novel insights into the evolution of skin microbiota in the first two years of life, and highlight the relationship between skin bacterial community and AD development in infancy. Early changes in skin colonization patterns might alter the maturation of both the skin and immune system, potentially with a long-term impact on cutaneous and general health.

Mechanisms of disease; genetics & -omics

P033

ROLE OF VDR GENE POLYMORPHISMS IN ATOPIC DERMATITIS SEVERITY IN CHILDREN

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Background:
Vitamin D is a pleiotropic hormone with multiple biological actions on the skin and immune system that exerts its functions by binding the vitamin D receptor (VDR). Clinical and epidemiological studies have suggested an association between vitamin D (VD) deficiency and the development and severity of atopic dermatitis (AD). A previous study in adults with AD showed a specific VDR haplotype to be more frequent in patients with severe AD, but no studies have been performed in children with AD.

Objective(s):
The objective of this study was to evaluate VD receptor polymorphisms FokI, ApaI and TaqI in AD patients, and assess the effect of these polymorphisms on disease severity and immune status at baseline and after VD supplementation.

Materials/methods:
Genomic DNA was obtained using BuccalAmp kit from 101 subjects and 99 healthy controls. We assessed the following single nucleotide polymorphisms (SNPs) of the vitamin D receptor (VDR): *Fok*I (rs2228570), *Taq*I (rs731236), and *Apa*I (rs7975232) in 101 AD patients and 93 healthy non-atopic controls.

Results:
For all polymorphisms, genotype frequencies were in line with Hardy-Weinberg equilibrium (HWE) in the AD patients (all p>0.05). In controls, *Fok*I and *Apa*I were in HWE (both p>0.05), but *Taq*I deviated from HWE (X2=4.7, p<0.03). Genotypic frequencies for *Fok*I, *Apa*I, and *Taq*I VDR SNPs were not significantly different between AD patients and healthy controls. Next, we compared allelic frequencies between AD and healthy control groups. No significant differences were found between AD and healthy control groups in all 6 alleles studies. We then evaluated if VDR SNPs were associated with AD severity, immunologic parameters and response to VD supplementation. The *Fok*I

TT-genotype was significantly associated with lower SCORAD (28±9 vs. 34±17, P=0.04), lower IgE concentration (160±271 vs. 541±1166, P=0.009), and lower eosinophils (270±193 vs. 594±818, P=0.003)

Conclusion:
The present study shows that *Fok*I TT-genotype is associated with a milder AD phenotype. Our data suggests that the VDR may influence AD severity by modulating response to VD.

Mechanisms of disease; from phenotypes to endotypes
P035

CHARACTERIZATION OF THE SKIN MYCOBIOME IN PATIENTS WITH ATOPIC DERMATITIS
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Background:
Most of the studies on skin mycobiome have been conducted based on traditional culture-dependent methods, which prone to vary with the isolation techniques and the culturing conditions.

Objective(s):
We aimed to sequence skin fungal community, so-called 'mycobiome' of patients with atopic dermatitis (AD) and compare to that of healthy controls. We also assessed *Malassezia* species in two groups to elucidate the role of *Malasseiza* in AD pathophysiology.

Materials/methods:
We enrolled 8 AD patients and 8 healthy controls. Skin swab samples from antecubital fossae of all subjects were obtained. The used phylogenic marker was internal transcribed spacer 2 regions of DNA.

Results:
Taxonomic identification at various levels, from phylum to species, with alpha diversity analysis revealed more diverse fungal genera in AD samples. *Malassezia* was the most dominant genus among 680 genera identified in both subject groups. Although interpersonal variation was observed, the diversity assessed by the Shannon diversity index indicated that AD samples had more diverse fungal communities than healthy controls at both genus and species level.

Conclusion:
Although this study was limited by its small number of cases and lack of precise clinical correlation, our data provide useful insights for further investigation.

Mechanisms of disease; from phenotypes to endotypes
P036

PROTEASE-ACTIVATED RECEPTOR-2 IN KERATINOCYTES CAN DRIVE ATOPIC DERMATITIS, ITCH AND NEUROEPIDERMAL COMMUNICATION
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Background:
Activation of protease-activated receptor-2 (PAR2) has been implicated in inflammation, pruritus, and skin barrier regulation, all characteristics of atopic dermatitis (AD), as well as Netherton syndrome which has similar characteristics. However, understanding the precise role of PAR2 on neuro-immune communication in AD has been hampered by the lack of appropriate animal models.

Objective(s):

Materials/methods:
We used a recently established mouse model with epidermal overexpression of Par2 (Par2OE) and littermate WT mice to study the impact of increased Par2 expression in epidermal cells on spontaneous and house dust mite (HDM)-induced skin inflammation, itch, and barrier dysfunction in AD, *in vivo* and *ex vivo*.

Results:
Par2OE newborns displayed no overt abnormalities, but spontaneously developed dry skin, severe pruritus, and eczema. Dermatological, neurophysiological, and immunological analyses revealed the hallmarks of AD-like skin disease. Skin barrier defects were observed before onset of skin lesions. Application of HDM onto Par2OE mice triggered pruritus and the skin phenotype. Par2OE mice displayed an increased density of nerve fibers, increased nerve growth factor and endothelin-1 expression levels, alloknesis, enhanced scratching (hyperknesis) and responses of DRG cells to non-histaminergic pruritogens.

Conclusion:
Par2 in keratinocytes, activated by exogenous and endogenous proteases, is sufficient to drive barrier dysfunction, inflammation, and pruritus and sensitize skin to the effects of HDM in a mouse model that mimics human AD. Par2 signaling in keratinocytes appears to be sufficient to drive several levels of neuro-epidermal communication, another feature of human AD.

Mechanisms of disease; from phenotypes to endotypes

P037

ALTERED ESPRESSION OF EPIDERMAL ENZYMES IN ATOPIC DERMATITIS SKIN IS AN UNDERLYING FACTOR IN STRATUM CORNEUM LIPID COMPOSITION

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Background:
The barrier dysfunction in atopic dermatitis (AD) skin correlates with stratum corneum (SC) lipid abnormalities including lipid/protein ratio, reduced ceramide (CER)chain length and free fatty acid (FFA) chain length. Furthermore the CER subclass levels play also an important role. However, the underlying causes in the biosynthesis of these lipids in the viable epidermis is largely unknown.

Objective(s):
We investigated whether the expression of CER and FFA biosynthesis enzymes are altered in AD skin compared with control skin and determined whether changes in enzyme expression can explain the changes in CER and FFA composition.

Materials/methods:
In 20 AD patients (variation in scorad between 0 and 43.5, 8 patients with filaggrin mutations, 12 without) and controls (no filaggrin mutations) the expression of enzymes involved in the biosynthesis of FFAs and CERs was analyzed on a protein level in relation to the SC lipid composition. In addition on gene level the same enzymes were examined in full thickness human skin equivalents generated with a cocktail of cytokines in the medium. The enzymes include stearoyl CoA desaturase (SCD), elongase 1 (ELOVL1) and ELOVL6 involved in FFA synthesis and β-glucocerebrosidase (GBA), acid-sphingomyelinase (aSmase), ceramide synthase 3 (CerS3) involved in CER synthesis.

Results:
The results reveal an altered expression of SCD and ELOVL1 in AD lesional skin, while the expression of enzymes in non-lesional skin is similar to control skin. This was accompanied by functional changes displayed by increased unsaturated FFAs (SCD) and reduced FFA C22-C28 (ELOVL1) in AD lesional skin. The CER composition in AD lesional skin shows corresponding changes such as increased CER AS and NS (aSmase) and decreased esterified ω-hydroxy CERs (CerS3). Changes in enzyme expression or lipid properties did not correlate to filaggrin expression.

To obtain more evidence about the effect of inflammation on the lipid analysis, mRNA levels in full thickness human skin we examined and we observed for almost all enzymes a reduction in mRNA level when human skin equivalents were generated with a cocktail of cytokines. This suggests that inflammation plays a role in the altered enzyme expression.

Conclusion:
This study shows that alterations in gene and protein expression of key enzymes involved in SC lipid synthesis contribute to changes in the lipid composition in AD skin. The results indicate that inflammation influences the expression of these enzymes.

Mechanisms of disease; from phenotypes to endotypes
P038

ORAL TOLERANCE MODULATES THE SKIN TRANSCRIPTOME IN MICE WITH ATOPIC DERMATITIS
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Background:
Defective gut immune reactions have been implicated in the development of atopic dermatitis (AD). The underlying immunologic interactions between the skin and intestine have been incompletely understood. Repeated epicutaneous exposure of murine skin to ovalbumin (OVA) induces AD-like lesions, and oral tolerance (OT) induction prior to epicutaneous sensitization protects mice from Th2 inflammation.

Objective(s):
To explore the effect of OT on AD-like skin responses, we compared the transcriptomic profiles of skin obtained from mice that were epicutaneously sensitized (EC), orally tolerated prior to epicutaneous sensitization (OT-EC), or neither (control).

Materials/methods:
To induce OT to OVA, mice were provided with drinking water containing 1% OVA for 5 days, while a control group were given standard drinking water. Two days after the oral treatment, epicutaneous sensitization was performed. The transcriptomic profiles of skin were obtained by high-throughput RNA sequencing from mice that were epicutaneously sensitized, orally tolerated prior to epicutaneous sensitization, or neither (control). Transcripts with fold change values ≥2 and $p \leq .05$ were included as differentially expressed genes. The mRNA expression of upregulated genes in OT-EC mice were observed in the skin specimens of patients with AD compared to healthy controls. Silencing of five upregulated genes were performed on HaCaT cells using siRNAs transfection.

Results:
Compared to the control group, OT-EC mice showed an upregulation of six genes. Five of those genes, which have human homologs and are known to regulate inflammation (*Scgb1a1,Tsc22d3*, and *Pon1*) or keratinocyte differentiation (*Btc* and *Per1*), were significantly downregulated in the skin specimens from patients with AD. The knockdown of *SCGB1A1* upregulated the expression of genes encoding Th2 inflammatory mediators (IL-13 and *CCL22*). Transfection with siRNA against *SCGB1A1* or *TSC22D3* decreased the expression of LOR, which encodes loricrin. This decrease in the expression of *LOR* corresponded with the decreased expression of *Lor, Lce1l* and *Lce1m* in EC relative to OT-EC.

Conclusion:
Our findings suggest that OT induction may protect skin against allergic inflammation by promoting the expression of genes that regulate Th2 inflammatory responses and skin barrier function.

Mechanisms of disease; from phenotypes to endotypes
P039

TSLP POLYMORPHISMS IN ATOPIC DERMATITIS AND ATOPIC MARCH IN KOREANS
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Background:
Atopic march (AM) is the progression from atopic dermatitis (AD) to allergic rhinitis and asthma. The development of AD is as high as 20% in children worldwide and continues to increase. AD seems to be caused by both genetic and environmental factors. Recently, polymorphisms of the thymic stromal lymphopoietin (*TSLP*) gene associated with allergic disorders were reported in ethnic groups from various countries.

Objective(s):
Identification of *TSLP* polymorphisms in Koreans with AD or AM.

Materials/methods:
Whole-exome sequencing (WES) was performed in 20 AD and 20 AM patients.

Results:
Nine single nucleotide polymorphisms (SNPs) of *TSLP* were detected (rs191607411, rs3806933, rs2289276, rs2289277, rs2289278, rs139817258, rs11466749, rs11466750, rs10073816). These SNPs have been correlated with susceptibility to allergic diseases in ethnic groups from China, Japan, Turkey, and Costa Rica in previous studies. Remarkably, one of 20 patients in the AD group lacked all SNPs, compared to six of 20 patients in the AM group. Odds ratios showed that Korean patients without the nine *TSLP* variants had an 8.14 times higher risk of moving from AD to AM. One (rs3806933, rs2289276 and rs2289277) of two haplotype blocks was validated in 60 AD and 59 AM patients using Sanger sequencing. rs3806933 and rs2289276 were in high linkage disequlibrium (*D'*=0.97).

Conclusion:
The increase of major allele frequency of respective nine *TSLP* variants may enhance the risk of AM. These data will contribute to improved genetic surveillance system in the early diagnosis technology of allergic disease.

Mechanisms of disease; from phenotypes to endotypes

P040

ASSOCIATION OF CDKAL1 POLYMORPHISMS WITH EARLY-ONSET ATOPIC DERMATITIS IN KOREANS

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Background:
Atopic dermatitis (AD) has increased in frequency to rates as high as 20% for children in developed countries. AD is one of the most common childhood diseases and has a complex etiology involving genetic and environmental factors. Thus, a broad understanding of genetic background is needed for early diagnosis of AD.

Objective(s):
Identification of candidate functional genetic variants associated with early-onset AD in Koreans.

Materials/methods:
Whole-exome sequencing (WES) was performed in three families. Sanger sequencing was used to validate detected variants in 112 AD patients and 61 controls.

Results:
Functional variants were filtered by WES, and then variants related to allergic immune diseases were selected through a literature search. Two candidate non-synonymous SNPs of *CDKAL1* (rs77152992) and *ERBB2* (rs1058808) were identified, c.1226C>T, p.Pro409Leu, and c.3463C>G, p. Pro1170Ala respectively. A case-control study was performed to determine whether rs77152992 and rs1058808 are candidate risk factors for early-onset AD. rs77152992 was significantly associated with early-onset AD (OR 0.42, 95% CI 0.21-0.83, *P* = 0.0133) in allele frequencies. The CC genotype of *CDKAL1* had significantly increased risk of AD (OR 2.16, 95% CI 1.0-4.6, *P* = 0.0475). rs1058808 had no correlation with AD. Total eosinophil count was significantly increased in AD patients with the CC genotype of *CDKAL1* (rs77152992).

Conclusion:
CDKAL1 (rs77152992) and *ERBB2* (rs1058808) were deemed functionally interesting based on WES. Our case-control study suggests that the CC genotype of rs77152992 may be associated with increased eosinophil counts. It may enhance the risk of early-onset AD.

Mechanisms of disease; from phenotypes to endotypes
P041

FILAGGRIN IMPACTS THE CUTANEOUS MICROBIOME

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Background:
Genetic deficiency or haploinsufficiency of the epidermal filaggrin (FLG) protein is associated with ichthyosis vulgaris (IV) and atopic dermatitis (AD). Epidermal barrier impairment as well as colonization with *Staphylococcus aureus* (*S. aureus*) are typical hallmarks for AD lesional skin and might therefore potentially be related to loss of FLG protein.

Objective(s):
The aim of our study was to investigate if the *FLG* genotype could either affect the skin barrier function and/or the composition of the cutaneous skin microbiome.

Materials/methods:
We established completely FLG-deficient human epidermal equivalents (HEEs) of primary adult keratinocytes from ichthyosis vulgaris patients carrying the homozygous mutation of *FLG.* Therein we compared the outside-in and inside-out epidermal barrier function of with control HEEs *in vitro. In vivo* non-lesional skin swabs of the lower leg of IV and AD patients carrying *FLG* mutations were taken to determine the bacterial composition of the skin depending of the FLG-genotype.

Results:
Different from earlier findings derived from *in vitro* knockdown studies, we found that FLG loss does not directly lead to alterations in the epidermal barrier function, nor does it drastically change epidermal morphology, differentiation or response to AD-typical T helper 2 cytokines. Microbiome analyses showed a lower abundance of Gram-positive anaerobe cocci (e.g. *Finegoldia magna*) on skin of *FLG*-deficient individuals. Furthermore, *F. magna* induced a stronger antimicrobial peptide response than *S. aureus*, whereas *S. aureus* caused a stronger pro-inflammatory cytokine response than *F. magna.*

Conclusion:
Our study provides novel findings towards the link between *FLG*-deficiency and AD. We contradict earlier findings that FLG loss directly impairs skin barrier function, and we reveal that a genetic variation shape the skin microbiome alterations, which in turn can contribute to an altered host-defense response. The latter generates new testable hypotheses regarding the disease mechanism of AD.

Mechanisms of disease; from phenotypes to endotypes
P042

STUDIES OF KERATINOCYTE-SPECIFIC REGULATORY INTERACTIONS BY 3D MAPPING WITH FOCUS ON ATOPIC DERMATITIS

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Background:
Atopic Dermatitis (AD) is a common complex disorder with high heritability in which genes together with environmental factors contribute to disease susceptibility. AD is a chronic inflammatory disease that often starts during childhood. It is characterized by pruritus, dryness, and inflammation of the skin. In developed countries, the prevalence is 20% in children and 3% in adults. Until today, more than 30 susceptibility loci have been identified, but those explain less than 20% of the estimated heritability. The main gene identified in AD is *FLG*, mutated in 20-30% of individuals with AD

Objective(s):
To understand the role of intergenic GWAS SNPs associated to AD in gene regulation and to identify active regulatory enhancer regions in human keratinocytes.

Materials/methods:
For identification of regulatory regions and their interactions in human primary keratinocytes we have used High throughput chromosome conformation and sequence capture (HiCap). Sets of capture probes were designed covering 21,000 promoters and 29 probes containing GWAS variants of AD. For validation, we are performing luciferase reporter assays.

Results:
HiCap was performed in two replicates. We detected >8,500 interactions, from which >5,000 were between probes and distal fragments and >3,300 between probes. The data analysis is ongoing for regions of interest. Ten hits potentially containing enhancer elements were chosen for further functional analysis (rs10995251, rs16999165, rs2164983, rs6661961, rs7130588, rs7927894, rs4085613, rs4780355, rs2201841 and rs17728338). We have performed RNAseq for correlation with targeted gene expression.

Conclusion:
Despite the advances in genomics and the availability and affordability of DNA sequencing only ~30% of mutations can be linked to disease. In the case of complex diseases many of the GWAS SNPs are in intergenic regions and it is challenging to link them to specific phenotypes. A big proportion of these SNPs are thought to be located in enhancer regions, distal from the genes that they regulate. Using our Hi-Cap AD targeted approach we are able to identify the genes that are affected and thus providing a better understanding of the disease mechanism.
Keywords: chromatin loops, complex disease genetics, gene regulation

Mechanisms of disease; from phenotypes to endotypes

P043

ATOPIC DERMATITIS SUBJECTS COLONIZED WITH STAPHYLOCOCCUS AUREUS HAVE A DISTINCT PHENOTYPE AND ENDOTYPE

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Background:
Atopic dermatitis (AD) patients are commonly colonized with *Staphylococcus aureus (*AD*S.aureus*+) but what differentiates this group from noncolonized AD subjects (AD*S.aureus*-) has not been well-studied.

Objective(s):
To evaluate whether these two groups have unique phenotypic or endotypic features we performed a multi-center, cross-sectional study enrolling AD*S.aureus*+ (N=51) and AD*S.aureus*- (N=45) subjects defined by the presence or absence of *S. aureus* by routine culture techniques and nonatopic, noncolonized controls NA*S.aureus*- (N=46).

Materials/methods:
Filaggrin (*FLG*) genotypes were determined and disease severity (EASI, RJL, IGA and NRS) was captured. Skin physiology was assessed (transepidermal water loss [TEWL], stratum corneum integrity, hydration and pH) and serum biomarkers measured.

Results:
We found that AD*S.aureus*+ had more severe disease based on all scoring systems except itch (NRS). They had higher levels of type 2 biomarkers (eosinophil count, tIgE, CCL17, and periostin). Additionally, AD*S.aureus*+ had significantly greater allergen sensitization (Phadiatop and tIgE), barrier dysfunction (TEWL and SC integrity) and serum LDH than both AD*S.aureus*- and NA*S.aureus*- groups. *FLG* mutations did not associate with *S.aureus*+ colonization.

Conclusion:
In conclusion, adult AD participants who are colonized on their skin with *S. aureus* have more severe disease, greater type 2 immune deviation, allergen sensitization, barrier disruption, and LDH elevation than noncolonized AD subjects.

Mechanisms of disease; from phenotypes to endotypes

P044

LOW VITAMIN D LEVELS ARE ASSOCIATED WITH IRRITABLE BOWEL SYNDROME (IBS) AND NUMMULAR ECZEMAS IN KOREAN ATOPIC DERMATITIS (AD) PATIENTS

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Background:
IBS is a group of symptoms such as diarrhea and constipation without any evidence of underlying damage. The causes of IBS are gut-brain axis problem, small intestinal bacterial overgrowth and food sensitivity. Vitamin D, a critical regulator of immunity, regulates the mucosal barrier and microbiome in the gut. Vitamin D deficiency could be associated with the prevalence of AD. AD is a common inflammatory skin disease; however the association with IBS and lower vitamin D levels in nummular type of AD remains unclear.

Objective(s):
We evaluated the presence of IBS and vitamin D levels in patients with AD to know the provoking factors in AD and to find some clinical subtypes among AD patients.

Materials/methods:
This study included 596 patients above adolescent AD. Serum vitamin D levels were measured, and we classified these AD cases into IBD positive or not, and clinically diagnosed these patients as typical or nummular (follicular) subtypes in these AD patients.

Results:
IBD(+) AD patients had lower vitamin D levels in serum than in IBD(-) cases. Nummular or follicular subtypes of AD also showed lower vitamin D levels than in typical AD. The vitamin D level was significantly lowered in nummular subtypes combined with IBD(+) AD patients (70 cases, 13.79 ng/ml) than in typical AD with IBD(-) AD patients (258 cases, 17.62ng/ml).

Conclusion:
Our results demonstrate that low vitamin D levels may link to IBD in AD patients and change the clinical manifestation of the AD patients. Further elucidation of the relationship vitamin D with IBD and nummular subtypes in AD patients may deepen into systemic view for the understanding of etiology of AD beyond skin barrier paradigm.

Mechanisms of disease; from phenotypes to endotypes

P045

IMMUNE RESPONSE PATTERNS IN CHRONIC INFLAMMATORY SKIN DISEASES - FUNDAMENTAL FOR TARGETED THERAPY

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Background:
The definition of Atopic eczema does not sharply distinguish from other forms of eczema such as nummular eczema, chronic contact dermatitis, or dyshidrotic eczema. More general, dermatology textbooks describe more than 100 different chronic inflammatory skin diseases (CISD`s) based on clinical phenotype and histological architecture.

Objective(s):
This historical description is complemented by increasing molecular knowledge about the interaction of epithelial and immune cells – and this knowledge is now being translated into specific therapeutics.

Materials/methods:
Here, we stimulated primary human skin equivalents with T cell supernatant of distinct T cell subsets and performed RNA sequencing. We compared the resulting transcriptome and histology with that of multiple CISD`s.

Results:
Combining the enormous advances made in lymphocyte immunology and molecular genetics with clinical and histological phenotyping revealed six predominant immune response patterns of the skin – the lichenoid pattern (IFN-g/TNF-a), the eczematous pattern (IL-4, IL-5, IL-13), the bullous pattern (IL-5, IL-13), the psoriatic pattern (IL-17´s, IL-22), the fibrogenic pattern (TGF-b), and the granulomatous pattern (IL-10).

Conclusion:
This classification allows to predict efficacy of novel and specific therapeutic agents of most CISD´s. With more and more specific therapeutic agents approved, classifying CISD`s also according to their immune response pattern will become indispensable.

Mechanisms of disease; from phenotypes to endotypes

P046

EXPRESSIONS OF CCL18 AND THE FCERI ARE UP-REGULATED BY TH2 CYTOKINES AND DIFFERENTIALLY REGULATED BY HISTAMINE IN HUMAN M2 MACROPHAGES

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Background:
Increased levels of CCL18 are found in the epidermis and dermis of atopic dermatitis skin lesions and lead to a pronounced migration of CCR8 expressing Th2 cells. The expression of the FceRI is up-regulated in atopic patients and supposed to play a role in the pathogenesis and effector phase of allergic diseases. The trimeric structure $\alpha\gamma_2$ of the FceRI consisting of an IgE binding α-chain and two y-chains is expressed on monocytes, macrophages, dendritic cells and eosinophils.

Objective(s):
The aim of this study was to investigate the role of histamine, in particular on CCL18 production and on FceRI expression, in human IL-4 or IL-13 activated M2a macrophages. To explore this issue also in pathophysiological conditions, we examined macrophages derived from patients with atopic dermatitis and healthy controls.

Materials/methods:
We differentiated human monocytes obtained from patients with atopic dermatitis or healthy controls in the presence of M-CSF to M2 macrophages and activated the cells with IL-4 or IL-13 to M2a macrophages. The M2- and M2a macrophages were stimulated with histamine and specific ligands targeting H1R, H2R and H4R. mRNA expression and protein production of CCL18 were analyzed by qPCR and ELISA respectively. The mRNA expression of the FceRI α and γ chain was quantified by qPCR.

Results:
We detected an up-regulation of CCL18 mRNA and protein expression and also of the FceRI α chain mRNA expression by IL-4 and IL-13 when compared to unstimulated macrophages. The CCL18 expression was

potentiated, whereas the FceRI α chain mRNA expression was reduced in response to histamine. Stimulating the histamine receptors on M2a macrophages with their specific ligands (agonists and antagonists), we observed that both effects were mainly attributed to the H2R. Interestingly, the IL-4- and H2R-mediated effects on CCL18- and on FceRI α chain expression were more pronounced in the AD group when compared to the healthy control group. The expression of the FceRI γ chain was not affected by IL4 or by histamine.

Conclusion:
Our data discover a novel function of the H2R, i.e. the up-regulation of the Th2 attracting chemokine CCL18 in human activated M2 macrophages. This provides additional evidence for a role of histamine to foster a Th2 dominated milieu. The down-regulation of the FceRI α chain expression via the H2R underlines the widely known immune modulatory role of the H2R. These ambivalent functions of the H2R may have an impact on the course of atopic dermatitis and for new therapeutic interventions.

Mechanisms of disease; from phenotypes to endotypes

P047

CELL TYPE- AND DISEASE-SPECIFIC SOCS3 EXPRESSION ABNORMALITIES IN KERATINOCYTES AND MACROPHAGES

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Background:
In chronic inflammatory skin diseases a de-regulated immune regulation occurs with a prolonged and increased expression of pro-inflammatory cytokines. Less is known about the impact of regulatory molecules in such diseases.

Objective(s):
It was the aim of this study to investigate the expression of Suppressor of Cytokine Signalling (SOCS)3 and its regulation in inflammatory skin diseases.

Materials/methods:
Skin biopsies from healthy donors and patients suffering from atopic dermatitis or psoriasis were analysed by immunohistological staining for the expression pattern of SOCS3. Moreover, keratinocytes and macrophages derived from patients and healthy controls were checked by qRT-PCR for their expression of SOCS3 mRNA under basal and under inflammatory conditions. A promoter reporter assay was performed to check for cell type specific differences in the regulation of SOCS3 expression. mRNA stability was measured after actinomycin D treatment. 5-aza-2´-deoxycytidine treatment was used to analyse the impact of DNA methylation. Finally, the DNA methylation pattern of different CpG sites in the SOCS3 gene and its promoter region was investigated by pyrosequencing.

Results:
We found a reduced expression profile of SOCS3 in the epidermis of lesional atopic dermatitis and psoriasis skin when compared to skin from healthy controls. Cell culture experiments confirmed these findings. A diminished SOCS3 expression was found in keratinocytes from atopic dermatitis patients when compared to cells from healthy donors. Interestingly, vice versa macrophages from patients suffering from psoriasis or atopic dermatitis showed increased SOCS3 mRNA expression levels. A promoter reporter assay revealed that in macrophages SOCS3 is mainly regulated on the level of transcription whereas in keratinocytes other mechanisms seemed to be involved. No differences were seen in SOCS3 mRNA stability between these both cell types. 5-aza-2´-deoxycytidine treatment significantly increased SOCS3 expression in keratinocytes and pyrosequencing revealed significant cell type and disease dependent differences in the DNA methylation of CpG site cg18181703.

Conclusion:
We concluded that SOCS3 expression is altered in a cell type-specific manner in atopic dermatitis and psoriasis patients which is due to epigenetic changes in the DNA methylation pattern. This may contribute to the dysregulated immune response seen in inflammatory skin diseases.

Mechanisms of disease; from phenotypes to endotypes
P048

QUANTIFICATION OF NATURAL MOISTURISING FACTORS AT THE SKIN SURFACE USING A PORTABLE INFRARED SPECTROMETER DEVICE: A PILOT, CALIBRATION MODEL

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Background:
Attenuated Total Reflectance (ATR) Fourier Transform Infrared Spectroscopy (FTIR) is a useful technique for the molecular analysis of surfaces, including the skin, with promising translational clinical potential. Skin surface levels of Natural Moisturising Factors (NMF) are a biomarker of filaggrin (FLG) status (both inherited and acquired) and skin dryness. FLG-related Atopic Dermatitis (AD) is associated with more severe/persistent disease

Objective(s):
To combine FTIR with chemometric analysis to generate a pilot calibration model for the *in vivo* quantification of NMF at the skin surface using a portable FTIR device

Materials/methods:
This study was performed in a climate-controlled, skin barrier suite located at the University of Sheffield, UK. Subjects with either healthy skin or AD were recruited from the local Sheffield community and informed consent was obtained prior to enrolment in the study. A diagnosis of AD was made using the UK working party criteria, and disease severity classified by the eczema area and severity index (EASI) score. Genotyping for the 5 most common European loss-of-function *FLG* mutations was performed from buccal swabs. FTIR spectra of 4cm^{-1} resolution were collected from the volar forearm and antecubital fossa in conjunction with tape strips for the quantification of NMF components by High Performance Liquid Chromatography and o-phthaldialdehyde derivatization. Transepidermal water loss (TEWL) and stratum corneum hydration (SCH) measurements were collected as an assessment of barrier function. Ethical permission for this study was granted by the NHS Trent research ethics committee

Results:
Partial least squares regression modelling of absorbance in the mid infrared spectral region (1710-1185cm^{-1}) with skin surface NMF components determined by HPLC generated a predictive r^2 value of 0.90. Modelling was superior on the antecubital fossa compared to the forearm presumably due to the increased FTIR signal obtained from this site. Predicted NMF values correlated with *FLG* status, TEWL and SCH

Conclusion:
FTIR combined with chemometric analysis is a suitable technique for the instantaneous *in vivo* quantification of NMF at the skin surface. The use of a portable FTIR device makes this methodology suitable for any clinical setting, with the potential to inform long-term treatment strategies in AD

Mechanisms of disease; from phenotypes to endotypes
P049

THE EXPRESSION OF AUTOPHAGY-REGULATING PROTEINS IN ATOPIC DERMATITIS

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Background:
Atopic dermatitis is a chronic inflammatory skin disease with a genetic predisposition involving an impaired skin barrier and T helper 2-type immune reaction. Autophagy is an intracellular degradation and recycling system that has been shown to be dysregulated in inflammatory and neoplastic disorders.

Objective(s):
This project aimed at investigating autophagy markers in atopic dermatitis in order to identify autophagic processes.

Materials/methods:
Skin tissues samples of six atopic dermatitis patients as well as normal skin were analyzed. Indirect

immunofluorescence staining technique with antibodies against tumor protein 73α (P73), autophagy-related protein (ATG) 5, ATG7, microtubule-associated proteins 1A/1B light chain 3B (LC3B), sequestosome-1 (p62) was applied followed by confocal laser microscopy and Imaris software analysis of images

Results:
The expression of autophagy markers ATG5, ATG7, P73, LC3B and sequestome-1 (P62) was significantly increased in atopic dermatitis compared with normal skin. There was a distinct expression pattern of these proteins with an expression of P73 in the stratum basal and lower levels of the stratum spinosum, while P62 was found in the upper stratum spinosum and granular layers in atopic dermatitis but not normal skin.

Conclusion:
These findings provide evidences that autophagy is enhanced in atopic dermatitis and thus might play a pathogenic role. The finding of autophagy markers in the lower layers of the epidermis are suggestive of a stimulation by proinflammatory cytokines in the dermis.

Mechanisms of disease; from phenotypes to endotypes

P050

IS THERE AN ASSOCIATION BETWEEN INDOOR ALLERGENS AND THE SEVERITY OF ATOPIC DERMATITIS?

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Background:
Atopic dermatitis (AD) is a prevalent inflammatory skin disease that affects 10-20% of children worldwide. Etiology and pathogenesis is complex and multifactorial, in which genetic and environmental factors combine. One of the few modifiable environmental factors that participate in AD is the presence of indoor allergens. However, the role of exposure to indoor allergens on AD severity is unclear and literature is scarce on the subject.

Objective(s):
To evaluate the association between indoor allergens and AD severity.

Materials/methods:
Children aged 0-17 years from Santiago, Chile who had active AD were recruited between september and December of 2017. SCORAD index was evaluated by a trained evaluator in all children. A qualitative survey about home environment was applied to the child's parents. A sample of home dust was collected from the child's bedroom floor and mattress using a standardized vacuum cleaner adapter (DUSTREAM®, Indoor Biotechnologies). Dust samples were analyzed using a multiplex assay for allergen detection (MARIA®, Indoor Biotechnologies) to quantify dust mite (Der p1, Der f1), cat pelt (Fel d1), dog pelt (Can f1), and alternaria alternata (Alt a1) allergens.

Results:
Twenty-five children were included in the study. Mean age was 3.9±3.8 and 52% were female. Twelve patients had mild AD (SCORAD 0-24.9), 11 moderate AD (25-49.9), and 2 had severe AD (50-103). All dust samples had cat and dog allergens, regardless of whether the home had pets. Forty percent of homes had dust mite allergens, and 0% had alternaria alternata. Homes that had dog or cat had significantly higher amounts of Can f1 and Fel d1, respectively ($p<0.001$). No association was found between the presence or amount of indoor allergens and AD severity determined by SCORAD. No association was found either between tobacco exposure, use of perfume, presence of visible dust or presence of carpets at home with AD severity.

Conclusion:
The presence of indoor allergens does not appear to directly influence disease severity in children with AD. The results of the present study show that children in Santiago, Chile, are permanently exposed to cat and dog allergens, regardless of pet ownership, although allergen loads are significantly higher with indoor pets. Dust mite allergens were less prevalent than expected, probably due to the relatively dry spring weather in Santiago. Further studies assessing indoor allergens and allergen sensitization in children with AD may be warranted to fully evaluate the role of indoor allergens on AD.

Mechanisms of disease; from phenotypes to endotypes
P051

CHILDHOOD NUMMULAR ATOPIC DERMATITIS: OVERLAP WITH CHILDHOOD PSORIASIS.
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Background:
Nummular atopic dermatitis consists of red oozing or scaly annular or nummular plaques, mainly over limb extensor surfaces. In children, it represents an atypical clinical form of atopic eczema. Nummular eczema can be difficult to distinguish from psoriasis and both conditions may overlap.

Objective(s):
We aimed to better define clinical features, frequency of overlapping presentations, evolution, and therapy of nummular atopic dermatitis.

Materials/methods:
Retrospective observational study of patients under 20 with a diagnosis of nummular atopic dermatitis seen between January 2007 and April 2017 at two French university hospital outpatient clinics (Dijon and Lyon). A diagnosis of nummular atopic dermatitis was made on nummular dermatitis and criteria of atopic dermatitis from the American Academy of Dermatology consensus conference.

Results:
A total of 31 patients were included. Nine patients had signs consistent with or suggestive of psoriasis (29%). Skin biopsy in 3 of them showed spongiotic eczema. In this overlapping group, patients were mostly boys (77.8%); three had a family history of psoriasis, and 6 were resistant to topical corticosteroids. Four patients were treated with acitretin, considered effective in 2 cases.

Conclusion:
The overlapping condition between childhood nummular atopic dermatitis and psoriasis has been variously reported as “psema”, “psoriasis-dermatitis” or “eczemoriasis”. Various endophenotypes of atopic dermatitis have been described. For instance, Asian atopic dermatitis phenotype consists of a mixture of atopic dermatitis commonly observed in European patients, and psoriatic features. Acitretin efficacy suggests pathophysiological determinants common with psoriasis.

Mechanisms of disease; from phenotypes to endotypes
P052

USING NON-INVASIVE TAPE STRIPPING TO DIAGNOSE INFLAMMATORY SKIN PRESENTATIONS
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Background:
Eczematous skin morphologies are extremely common. Based solely on clinical presentation, diagnosis of the underlying pathology is often difficult and contact, irritant, atopic eczema, psoriasiform eczema, eczematised psoriasis are among the differential diagnoses. Uncertainties are common in cases where inflammation is minimal or in certain anatomic locations including scalp, auricular, palmoplantar or flexures. Establishing a clear diagnosis can be challenging even with histopathology as it is well described in the case of palmoplantar inflammation.

Objective(s):
To develop a simple, reliable diagnostic tool to distinguish the epidermal, molecular profile in inflammatory lesions.

Materials/methods:
Using non-invasive tape-stripping, protein was extracted, total protein content determined and epidermal mediators were measured with ELISA based approaches. Results were normalised to total protein content. We compared samples from healthy individuals (n= 20) and lesional as well as non-lesional skin from atopic dermatitis (n =32) or psoriasis (n=54).

Results:
From epidermal markers previously linked to atopic dermatitis, including thymic stromal lymphopoietin, CCL27 (CTACK), and CCL17 (TARC), only the latter showed diagnostic potential in our approach. When measurable, CCL17 was highly suggestive of atopic eczema inflammation (at a cut-point of 0.026 pg/µg, sensitivity was 74.07% and specificity was 71.88%). However, CCL17 was undetectable in a significant number of atopic eczema (25%) as well as psoriatic samples (57.4%). On the other hand we found that IL-36γ is a highly sensitive and selective biomarker upregulated in psoriatic epidermis and is superior to other proteins including IL-8, IL-18, HBD2 and CXCL1. IL-36γ proved to accurately differentiate psoriasis from AD in palmoplantar localisation and clinically challenging cases. Interestingly, we failed to find a significant difference in the expression of IL-1α, IL-1β, IL-18 or HBD2 between lesional psoriasis and eczema. Non-lesional skin failed to show diagnostically meaningful expression of inflammatory or antimicrobial markers.

Conclusion:
Our results demonstrate IL-36γ as a robust, and sensitive biomarker to discriminate psoriatic lesions, and that the detection of inflammatory and antimicrobial markers via non-invasive tape stripping shows diagnostic potential with regards to eczema. Further analysis and refinement of the methodology may allow the development of a reliable diagnostic tool for eczema subtypes.

Mechanisms of disease; from phenotypes to endotypes

P053

IS THERE A STAPHYLOCOCCUS AUREUS-DRIVEN ATOPIC DERMATITIS ENDOTYPE?

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Background:
Atopic dermatitis (AD) is an inflammatory skin disease with a heightened susceptibility to colonization by *Staphylococcus aureus*. This bacterium thrives during AD flares and is capable of inducing Th2 immune responses. Little information exists on the role of *Staphylococcus aureus* on the configuration of AD endotypes.

Objective(s):
The purpose of this work is to evaluate phenotypic and immune differences between children with AD with and without skin colonization by *Staphylococcus aureus.*

Materials/methods:
We performed a cross-sectional baseline analysis of 101 children with AD recruited for the VIDATOPIC trial who were stratified by skin *S. aureus* colonization assessed in lesional AD. SCORAD was assessed by trained evaluators in all subjects. Blood was collected from all patients to evaluate eosinophil counts and immune biomarkers. In moderate and severe AD patients, immunophenotypic studies were performed to evaluate T cell subsets, and T-cell cytokines were quantified by Luminex after culture with Staphylococcus aureus enterotoxin B (SEB).

Results:
At baseline 40% of study subjects had *S. aureus* colonization. Subjects colonized by *S. aureus* had significantly higher SCORAD than subjects that were *S. aureus* culture-negative (SCORAD 42.6 vs 25.8; P<0.001) with significantly larger extension of AD-affected skin (13.7% vs. 4.6%, P=0.005) and more pruritus (6.5±3.2 vs. 4.9±2.4, P=0.008). *S. aureus* culture-positive had higher blood eosinophil counts (820±1099 vs. 351±274, P=0.01), serum total IgE (927±1585 vs. 183±240 U/L, P=0.005), CCL22 (98±199 vs. 14±134 pg/ml, P=0.03), and CCL27 (65±115 vs. 21±74 pg/ml, P=0.03), but not CCL17 (194±58 vs. 179±64 pg/ml, P=0.24). Specific IgEs against Staphylococcal

enterotoxin A and B were significantly higher in subjects with skin *S. aureus* (both P=0.02). Percent of IL-17$^+$ CD4 T cells was higher in S. aureus colonized subjects (0.7±0.81% vs. 0.33±0.31%, P=0.041), but no differences were observed in circulating Tregs, Th1 or Th2 cells. No significant differences were observed between groups in T-cell production of IFN-y, IL-2, IL-4, IL-5, IL-9, IL-10, or IL-17 after stimulus with SEB.

Conclusion:
Skin colonization by Staphylococcus aureus in children with AD is associated to greater disease severity, higher levels of atopic biomarkers, and more circulating IL-17$^+$ T-cells. This skin commensal may drive disease pathogenesis in a subgroup of AD children constituting a specific AD endotype.

New targets, systemic treatments and new treatments
P055

USE OF ORAL IMMUNOSUPPRESSIVE DRUGS IN THE TREATMENT OF ATOPIC DERMATITIS IN THE NETHERLANDS

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Background:
Data on the percentage of patients with really difficult to treat atopic dermatitis (AD) are scarce. From socio-economic perspective it is important to have more insight in these numbers, as new very effective, but expensive, treatment options will be available in the near future. Estimating the number of AD patients using oral immunosuppressive drugs can give an impression of the percentage of difficult to treat patients in the total AD population.

Objective(s):
To give an overview of the use of oral immunosuppressive drugs in patients with AD in the Netherlands.

Materials/methods:
Prescription data of oral immunosuppressive drugs in the Netherlands were extracted from a pharmaceutical database containing data of 557 million prescriptions and 7.2 million patients. An algorithm, based on the WHO Anatomical Therapeutic Chemical (ATC) codes, was used to identify patients with AD. The prescription of oral immunosuppressive drugs between January 1st 2012 and January 1st 2017 was evaluated.

Results:
943 AD patients (1.4%) used cyclosporine A, methotrexate, azathioprine or mycophenolic acid. Methotrexate was most commonly used, followed by azathioprine and cyclosporine A. A switch in medication was rarely seen. In the evaluation period a decrease in the prescription of cyclosporine A was seen, together with an increase of the prescription of methotrexate. In 31% of the patients who stopped treatment, the discontinuation took place within the first months of treatment.

Conclusion:
Of the AD patients, 1.4% used oral immunosuppressive drugs. Methotrexate was the most commonly used systemic drug in the Netherlands for the treatment of AD.

New targets, systemic treatments and new treatments
P056

THE ECONOMIC IMPACT OF PATIENTS WITH MODERATE TO SEVERE ATOPIC DERMATITIS ELIGIBLE FOR SYSTEMIC TREATMENT

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Background:
The prevalence of atopic dermatitis (AD) has increased over the past decades. The disease burden in patients with AD and healthcare costs are often underestimated, partly due to the fact that the majority of AD has relatively mild disease. Given the increasing prevalence of AD, it is likely that healthcare costs have increased concomitantly. However, data about the economic impact of moderate to severe AD in daily practice in patients receiving adequate care and support are lacking. Given the introduction of new, costly, targeted therapies for AD, more information on the costs of AD in relation to disease severity is needed in patients eligible for systemic treatment.

Objective(s):
To investigate the economic impact of moderate to severe atopic dermatitis (AD) in daily practice, including direct and indirect costs in patients receiving adequate care and support.

Materials/methods:
A descriptive retrospective study was performed including patients with moderate to severe AD treated with oral immunosuppressive drugs. Burden of disease was determined at baseline by disease severity and quality of life according to validated questionnaires and measurements. Additional data including medication use and healthcare utilization were collected to calculate direct costs. Indirect costs including work productivity and days of work absenteeism were calculated using the work productivity and activity impairment (WPAI) questionnaire. All costs were calculated over the previous year according the Dutch guideline for economic evaluations in healthcare for patients with controlled and uncontrolled disease based on the investigator global assessment (IGA).

Results:
In total 99 patients with moderate to severe AD treated with oral immunosuppressive drugs were included for analysis including 51 patients with controlled AD (IGA 0-2) and 33 patients with uncontrolled AD (IGA 3-5). Mean total direct costs were €5009 per patient per year (PPY) for the total group and €4264 PPY for patients with controlled AD and €6754 PPY for patients with uncontrolled AD. Mean total indirect costs were €8834 PPY for the total group and €5329 PPY for patients with controlled AD compared to €13881 for patients with uncontrolled AD. Mean total costs including direct and indirect costs were €13846 PPY for the total group and €9593 for patients with controlled AD compared to €20635 for patients with uncontrolled AD.

Conclusion:
Patients with moderate to severe AD treated with oral immunosuppressive drugs generates considerable direct and indirect costs. Indirect costs generated by work productivity and activity impairment had the greatest impact on total costs, especially in patients with uncontrolled disease.

New targets, systemic treatments and new treatments

P057

THE BENEFICIAL EFFECT OF KOREAN RED GINSENG EXTRACT ON ATOPIC DERMATITIS PATIENTS: AN 8 WEEK OPEN, NON-COMPARATIVE CLINICAL STUDY

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Background:
Atopic dermatitis (AD) is a chronic or chronically relapsing, eczematous, severely pruritic inflammatory skin disorder. Korean red ginseng (KRG) has been shown previously to exhibit diverse biological effects including anti-inflammatory and antipruritic effects in a murine model.

Objective(s):
We aimed to investigate the beneficial effects of KRG on AD patients, to determine whether there was improvement in disease severity, skin barrier function, pruritus and sleep disturbance relief.

Materials/methods:
An open, noncomparative clinical study that utilized KRG tablets (500mg/tablet) was conducted. This study included 41 patients with mild to moderate AD diagnosed by the Korean atopic dermatitis guidelines. Three visits to the hospital at days 1, 28±7, and 56±7 for evaluation were made. The effects of KRG were assessed by measuring

Eczema Area and Severity Index (EASI) score, transepidermal water loss (TEWL), the visual analogue scale (VAS), total amount of topical agents used in recent 8 weeks and investigator global assessment (IGA).

Results:
Patients taking KRG tablets showed significant decreases in EASI score and TEWL, and the VAS of pruritus and sleep disturbance were significantly reduced. The amount of topical agents used was reduced but not by a statistically significant amount. IGA at the third visit showed improvement of AD compared to the second visit, but the difference was not statistically significant.

Conclusion:
KRG can be safely used as a health food to achieve clinical improvement of AD as well as improving overall quality of life, and has potential for further development.

New targets, systemic treatments and new treatments
P058

THE ROLE OF IFN-GAMMA-INDUCIBLE PROTEIN 10 (IP-10; CXCL10) IN HOUSE DUST MITE-INDUCED ATOPIC DERMATITIS-LIKE SKIN INFLAMMATION

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Background:
The chemokine interferon-γ inducible protein 10 kDa (CXCL10) play a key role in many inflammatory conditions, particularly those mediated by T cells. Therefore, the production of this chemokine in peripheral tissues could be instrumental in the pathophysiology of tissue-specific immunological diseases.

Objective(s):
We investigated whether CXCL10 was involved in house dust mite (HDM)-induced atopic dermatitis (AD)-like skin inflammation.

Materials/methods:
We assessed the role of CXCL10 in HDM-induced AD-like skin inflammation and their regulatory mechanism in epidermal keratinocytes, *Dermatophagoides farinae* extract (DFE)-induced murine AD model and human AD lesions.

Results:
In various types of keratinocytes and mouse model with AD-like lesion, DFE induced a significant increase of CXCL10. DFE also activated the expression of TLR1, TLR2, TLR3, and TLR6. Among them, knockdown of TLR3 inhibited DFE-induced upregulation of CXCL10. In addition, TLR3 agonists induced the expression of CXCL10. This finding suggests that CXCL10 production is mediated by TLR3 signalling. We also found evidence that immune master regulators, IRF3 and NFκB are directly involved in the production of CXCL10 in keratinocytes.

Conclusion:
This study provides understanding of CXCL 10 production and regulatory mechanism in keratinocytes and their role of HDM-induced AD-like skin inflammation.

New targets, systemic treatments and new treatments
P059

THE JANUS KINASE INHIBITOR AZD1480 SHOWS BROAD ANTI-PRURITIC EFFECTS ON ACTIVATED DORSAL ROOT GANGLIA AND ITCH BEHAVIOR IN MICE

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Background:
Janus Kinase (JAK) inhibitors like oclacitinib and tofacitinib are novel therapeutics for allergic inflammatory diseases, such as atopic dermatitis. We recently demonstrated these two JAK inhibitors can also inhibit the transient receptor potential cation channel subfamily V member 1 (TRPV1) or capsaicin receptor (Fukuyama et al., JACI, *140:306-309,* 2017). Interestingly, AZD1480 is a JAK inhibitor with similar inhibitory profile as oclacitinib; however, by molecular docking experiments it is predicted to lack significant binding activity to the capsaicin binding site of TRPV1.

Objective(s):
The objective of this study was to determine whether AZD1480 differs in its inhibitory profile *in vitro* on dorsal root ganglia and *in vivo* in itch experiments in mice compared to oclacitinib and tofacitinib.

Materials/methods:
In vitro, the dorsal root ganglia (DRG) of untreated female BALB/c mice were collected and enzymatically dissociated. Fura-2 ratiometric calcium imaging was used to evaluate response of DRG neurons to IL-31, histamine, chloroquine and capsaicin after being treated with different JAK-inhibitors. *In vivo* studies were performed with female BALB/c mice that were treated orally with AZD1480, 30 minutes prior to an intradermal injection of IL-31, histamine, and chloroquine. The mice's scratching behavior was recorded for 30 minutes after stimulus injection. In addition, wiping response to capsaicin was recorded.

Results:
Pre-treatment with AZD1480 resulted in significant reduction of the *in vitro* response of DRG neurons to IL-31, histamine, and chloroquine. Mice treated with AZD1480 also showed significant reduction in scratching behavior after stimulus with IL- 31, histamine, and chloroquine by 60.1%, 80.7%, and 83.0%, respectively. However, the capsaicin induced wiping behavior was only slightly reduced.

Conclusion:
Besides reducing pruritus induced by IL-31 as expected, AZD1480 lowered the reaction induced by histamine and chloroquine as we recently demonstrated for oclacitinib and tofacitinib. Histamine and chloroquine are pruritic mediators that are not controlled through the JAK-pathway. However, in contrast to oclacitinib and tofacitinib, slight inhibition of the capsaicin response was observed suggesting that JAK-inhibitors might work through more than one pathway involved in itch perception.

New targets, systemic treatments and new treatments

P060

CRISABOROLE OINTMENT IMPROVES GLOBAL ATOPIC DERMATITIS SEVERITY ACROSS PATIENTS WITH VARYING BASELINE CHARACTERISTICS: POOLED RESULTS FROM TWO PHASE 3 TRIALS

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Background:
Crisaborole ointment is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild to moderate atopic dermatitis (AD). Efficacy and safety of crisaborole for treatment of mild to moderate AD was evaluated in 2 Phase 3 studies (NCT02118766; NCT02118792).

Objective(s):
To evaluate efficacy and safety of crisaborole stratified by baseline characteristics from 2 Phase 3 studies.

Materials/methods:
Patients aged ≥2 years with mild to moderate AD were randomly assigned 2:1 to receive crisaborole:vehicle twice daily for 28 days. The primary endpoint was success in Investigator's Static Global Assessment (ISGA, 5-point scale graded from clear [0] to severe [4]), defined as achieving a score of clear (0) or almost clear (1), with a ≥2-grade improvement from baseline at day 29. Efficacy and safety were stratified by age group (2 to <7 years [n=506], 7 to

<12 years [n=436], 12 to <18 years [n=371], ≥18 years [n=209]), sex, use of prior AD treatment, disease severity (mild or moderate), and percentage affected body surface area (%BSA; 5% to <16% [mild], ≥16% [moderate to severe]).

Results:
1016 patients received crisaborole and 506 received vehicle. Per age group, the proportion of crisaborole-treated patients who achieved success in ISGA vs vehicle-treated patients was 30.5% vs 21.8% (2 to <7 years; *P*=0.0644), 36.6% vs 22.9% (7 to <12 years; *P*=0.0037), 30.3% vs 19.4% (12 to <18 years; *P*=0.0257), and 29.7% vs 24.7% (≥18 years; *P*=0.4622). Treatment success was achieved in 33.8% vs 24.6% (*P*=0.0150) in male patients and 30.8% vs 19.8% (*P*=0.0009) in female patients. Among those who underwent prior AD treatment, 28.0% vs 15.9% (*P*=0.0009) achieved treatment success. Among those who did not undergo prior treatment, 35.0% vs 26.8% (*P*=0.0173) achieved treatment success. Treatment success was achieved in 24.9% vs 21.2% (*P*=0.3470) in those with mild disease and 36.7% vs 22.3% (*P*<0.0001) in those with moderate disease. Clear or almost clear status at day 29 occurred in 71.4% vs 56.7% (*P*=0.0024) with mild disease and 36.7% vs 22.3% (p<0.0001) with moderate disease. Among those with mild disease per %BSA, 32.2% vs 24.4% (*P*=0.0153) achieved treatment success. In those with moderate to severe disease per %BSA, treatment success was achieved in 32.0% vs 17.9% (*P*=0.0004). The rate of application site pain, the most common treatment-related adverse event, ranged from 2.3% to 7.0% in crisaborole-treated patients across subgroups.

Conclusion:
Pooled analysis from 2 large Phase 3 trials showed that crisaborole ointment improved global disease severity across multiple baseline characteristic subgroups.

New targets, systemic treatments and new treatments

P061

PSORIASIN EXPRESSION CAN BE INDCUED BY SILVER NANOPARTICLES THROUGH THE EGR-1-MAPK PATHWAYS

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Background:
The innate defense of the skin against microbial threats is influenced by antimicrobial proteins (AMP). Silver nanoparticles (Ag-NPs) can prevent bacterial infection and improve cutaneous wound healing owing to their antimicrobial activity. However, the mechanism of Ag-NPs' antimicrobial activity is poorly understood.

Objective(s):
The aim of this work was to determine the mechanistic relationship between Ag-NP treatment and expression of psoriasin.

Materials/methods:
Human neonatal epidermal keratinocytes (HEKns) were used. Psoriasin mRNA expression was measured by RT-PCR and real-time PCR. Western blotting was performed to verify early growth response-1 (Egr-1) and psoriasin expression, as well as mitogen-activated protein kinase (MAPK) phosphorylation. Psoriasin promoter activity by Egr-1 was detected by a luciferase assay.

Results:
Treatment of HEKn cells with Ag-NPs induced psoriasin mRNA and protein expression. Upregulation of psoriasin promoter activity was also observed in the luciferase assay. Ag-NPs increased Egr-1 expression, promoter activity, and its nuclear translocation in HEKn cells. Psoriasin luciferase activity was increased in Egr-1 pcDNA 3.1-transfected HEKn cells. Ag-NPs activated MAPK pathways including the extracellular signal-regulated kinase (ERK), p38, and c-Jun-N-terminal kinase (JNK) pathways. The upregulation of Egr-1 expression by Ag-NP stimulation was inhibited by ERK and p38 inhibitors, but not by a JNK inhibitor. Psoriasin expression was reduced in Egr-1 siRNA-transfected HEKn cells.

Conclusion:
Ag-NP treatment induces upregulation of psoriasin expression through Egr-1 expression. We suggest that the ERK and p38 pathways are involved in Egr-1-dependent psoriasin expression.

New targets, systemic treatments and new treatments
P062

PREDICTORS OF TREATMENT SUCCESS IN CHILDREN WITH DIFFICULT TO TREAT ATOPIC DERMATITIS USING A PERSONALIZED INTEGRATIVE MULTIDISCIPLINARY TREATMENT PROGRAM (PIM)

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Background:
A personalized integrative multidisciplinary 6 week treatment program (PIM) was developed for children with difficult to treat AD who are unresponsive to treatment according to current guidelines.

Objective(s):
The aim of the present study was to identify child and parent clinical and psychosocial characteristics that predict long-term treatment success after PIM.

Materials/methods:
Treatment was considered successful when there was a 75% reduction on the Self-Administered Eczema Area and Severity Index and/or little impact of AD on the Children's Dermatology Life Quality Index, six months after PIM.

Results:
The majority (77%) of children demonstrated long-term treatment success with PIM. Predictors of long-term treatment success included maternal disease acceptance OR (95%CI) 1.84 (1.15 – 2.94). A group (23%) of children, mostly girls OR (95%CI) 0.10 (0.02 – 0.54) with multiple somatic complaints OR (95%CI) 0.88(0.80 – 0.97), from families where the mother has anxiety for the use of topical corticosteroids OR (95%CI) 0.62(0.40 – 0.94), is less likely to obtain long-term treatment success.

Conclusion:
The majority (77%) of children with difficult to treat AD, seemingly unresponsive to conventional treatment according to current guidelines, are able to improve with PIM. Identifying children based on psychosocial and family but not clinical variables, predicted long-term treatment success after participating in PIM. Attention should be paid to a small group of children, mostly girls with multiple somatic complaints, from families where the mother has anxiety for the use of topical corticosteroids and difficulties with disease acceptance.

New targets, systemic treatments and new treatments
P063

EFFICACY, SAFETY AND PHARMACOLOGY OF ORAL ASN002, A NOVEL JAK/SYK INHIBITOR, IN MODERATE-TO-SEVERE ATOPIC DERMATITIS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Background:
Dysregulation of Th2 and Th22 cytokine pathways are implicated in the pathogenesis of atopic dermatitis (AD). ASN002 is a novel oral inhibitor of JAK and SYK signaling (including Tyk2), that diminishes production of Th2 and Th22 cytokines. Syk also regulates keratinocyte differentiation.

Objective(s):
Efficacy, Safety, Pharmacokinetic and pharmacodynamic measurements of ASN002 were evaluated in moderate-to-severe AD patients in a Phase 1b randomized, double-blind, placebo-controlled study (NCT03139981).

Materials/methods:
Patients were randomized 1:3 placebo or ASN002 at 20, 40 or 80 mg once daily for 4weeks (n=36). Inclusion criteria were Eczema Area and Severity Index (EASI) ≥16, body surface area (BSA) involvement ≥10% and an Investigator's Global Assessment (IGA) of ≥3 at baseline visit. No concomitant administration of topical corticosteroids or other immunosuppressants was permitted during or prior to study.

Results:
ASN002 was very well tolerated at all dose levels. The most common adverse events were transient, mild headache and nausea, mostly restricted to Day 1 of dosing. Subjects in the ASN002 treatment arms showed rapid onset and dose-related declines after 4 weeks in EASI50 of 29%, 100% and 88% and EASI75 of 0%, 63% and 50% for the 20, 40 and 80 mg cohorts respectively. Baseline EASI scores were 29.0, 21.3 and 29.0, respectively. The average decreases in EASI and in Itch Numeric Rating Scale (NRS) at week 4 for the 20, 40 and 80 mg cohorts were 21%, 79% and 70% and 15%, 47% and 71% respectively. In the 80 mg cohort, reduction in itch was seen as early as Day 2, (~45%) and improvements were also observed in the 40 and 80 mg cohorts in IGA assessments (up to 38% reaching 0-1). These clinical improvements were also associated with reversal of cutaneous biomarkers (cellular infiltrates, immune and hyperplasia markers) particularly in the mid and high dose.

Conclusion:
This is the first clinical report on safety, efficacy and effect on the pathologic lesional skin phenotype with oral JAK/SYK inhibitor ASN002 in moderate-to-severe AD. ASN002 was very well tolerated and demonstrated early improvements in pruritus and robust activity in EASI after 4 weeks with associated reversal of cutaneous biomarkers of inflammation.

New targets, systemic treatments and new treatments

P064

THE TRIPLE ACTION OF LEFLUNOMIDE: A NOVEL THERAPEUTIC MECHANISM OF ACTION IN THE TREATMENT OF INFLAMMATORY SKIN DISEASES.

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Background:
Leflunomide, a FDA approved drug for the treatment of rheumatoid arthritis (RA), shows therapeutic efficacy in case reports of atopic dermatitis (AD) and psoriasis patients and has recently been described to activate the aryl hydrocarbon receptor (AHR). Targeting the AHR, as seen in coal tar treatment, alleviates the symptoms of chronic inflammatory skin diseases like AD. The active metabolite of leflunomide, teriflunomide, is known to inhibit the synthesis of pyrimidine, leading to a reduction of lymphocytes in RA patients which explains it therapeutic effects.

Objective(s):
We studied the leflunomide-induced AHR activation in keratinocytes and evaluated its therapeutic effects for the treatment of AD.

Materials/methods:
AHR-activating properties of leflunomide were evaluated in CYP1A1 reporter cells (AHR activity screening) followed

by primary human keratinocyte monolayer cultures and 3D epidermal models for normal and AD skin. Epidermal morphology, keratinocyte differentiation and proliferation, inflammatory responses, CYP1A1 enzyme activity and cell toxicity were analysed.

Results:
At a concentration of 10 µM, leflunomide activated the AHR in keratinocyte and induced epidermal differentiation. Furthermore, leflunomide counteracted the Th2 cytokine-mediated effects in a 3D AD skin model and strongly downregulated keratinocyte proliferation. Cell toxicity (LDH release) was only observed at a concentration of 100 µM and higher. Surprisingly, CYP1A1 enzyme activity was not induced by leflunomide in keratinocytes despite the 50 fold induction of *CYP1A1* mRNA.

Conclusion:
The excellent skin permeation of leflunomide and the reported metabolism to its active metabolite in skin, suggests that leflunomide could be a successful topical drug for inflammatory diseases. Indeed, the efficacy of topical leflunomide was similar to systemic treatment in experimentally-induced arthritis models while adverse events were reduced. Therefore, we propose that leflunomide may be a good candidate drug for topical treatment of AD due to its triple action by 1) reducing lymphocyte and keratinocyte proliferation, 2) interference with the IL-4 mediated JAK/STAT pathway and 3) AHR-mediated epidermal differentiation leading to increased expression of important barrier proteins like filaggrin.

New targets, systemic treatments and new treatments

P065

ANALYSIS OF LONG-TERM CONSISTENCY OF CLINICAL RESPONSE WITH DUPILUMAB PLUS CONCOMITANT TOPICAL CORTICOSTEROIDS

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Background:
Dupilumab, a fully human anti-interleukin-4 receptor α monoclonal antibody, is approved in the USA, EU, and other countries for the treatment of adults with inadequately controlled moderate-to-severe atopic dermatitis (AD). Commonly, AD signs and symptoms have a chronic relapsing course, which limits the utility of single-time point analyses.

Objective(s):
We report consistency of response over time using repeated measures from a 52-week phase 3 trial of dupilumab with concomitant topical corticosteroids (TCS) in AD patients (LIBERTY AD CHRONOS: NCT02260986).

Materials/methods:
This double-blinded, placebo (PBO)-controlled trial enrolled adults with moderate-to-severe AD inadequately controlled with topical medication. Patients were randomized to subcutaneous dupilumab 300mg every 2 weeks (q2w) or PBO qw, and applied medium-potency TCS daily on active lesions. Clinical and patient-reported outcomes were recorded between week 16 and 52 every 4 weeks (10 time points); endpoints included proportion of patients with ≥50% and ≥75% improvement from baseline in Eczema Area and Severity Index, and ≥3-point improvement in peak pruritus Numerical Rating Scale (NRS). We defined consistent response as achieving the response threshold most of the time (i.e., at ≥6 out of the 10 time points). Safety was also assessed.

Results:
106 patients received dupilumab 300mg q2w+TCS; 315 patients received PBO+TCS. For EASI-50, consistent response was reported in 33.3% for patients receiving PBO+TCS vs 78.3% for patients receiving DUP+TCS (P<0.001). For EASI-75, consistent response was reported in 22.9% of patients receiving PBO+TCS vs 67.9% of patients receiving dupilumab+TCS (P<0.001). For ≥3-point improvement in peak pruritus NRS, consistent response

was reported in 17.1% of patients receiving PBO+TCS vs 65.1% of patients receiving dupilumab+TCS (*P*<0.001). When examining EASI and NRS as continuous assessment the sustained nature of the treatment response was also demonstrated by a LS-mean % change (SE) in EASI of -60.9 (4.29) and -84.9 (6.73) (*P*<0.0001), and a LS-mean % change (SE) in NRS of -31.7 (3.95) and -57.0 (6.17) (*P*<0.0001) for PBO and dupilumab arms from baseline to week 52. Overall, treatment-emergent adverse event (TEAE) rates were similar in all treatment groups. Commonly-occurring TEAEs attributable to dupilumab were injection-site reactions and conjunctivitis.

Conclusion:
These repeat-measure responder analyses provide an assessment of patient-level response consistency over 52 weeks, supplementing the continuous endpoint analyses. Compared to PBO+TCS, dupilumab+TCS results in higher rates of responders, and the response is also more consistent and better sustained over time.

New targets, systemic treatments and new treatments
P066

THE REGULATION OF HISTAMINE H4 RECEPTOR (H4R) DURING TH2 DIFFERENTIATION AND ITS ROLE IN TH2-MEDIATED IMMUNE RESPONSES

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Background:
Atopic dermatitis (AD) is mainly a T_H2-driven, chronic inflammatory skin disease, which is characterized by pruritus and skin lesions. One of the major mediators of pruritus in AD is the pleiotropic mediator histamine. There are four different G-protein coupled receptors (H_1R-H_4R) for histamine. Specifically the H_4R has been found to be upregulated in keratinocytes, antigen presenting cells, eosinophils as well as in *in vitro* differentiated T_H2 cells in presence of IL-4. Moreover, the use of specific H_4R antagonists led to amelioration of the skin lesions and to reduction of pruritus in both mouse models and clinical studies.

Objective(s):
In this study we aim to elucidate the role of H_4R in T_H2-driven immune responses as well as to identify the major factors which regulate the expression of the H_4R on T_H2 cells.

Materials/methods:
$CD4^+$ naïve T cells were enriched from total PBMCs and differentiated *in vitro* into T_H2 cells in presence of H_4R specific agonist for 14 days. Subsequently, the mRNA expression of the cytokines IL-5 and IL-13 was analyzed by qPCR.The expression of H_4R was analyzed at mRNA level as well as at protein level with a specific anti-H_4R antibody by flow cytometry i) in freshly isolated $CD4^+$ T cells, ii) at different time points (day 1, 4, 7 and 11) on T_H2 differentiated cells which were cultured with different doses of IL-4.

Results:
Preliminary results showed that the presence of H_4R specific agonist during the *in vitro* differentiation of T_H2 cells resulted in increased mRNA levels of the cytokines IL-5 and IL-13 compared to the control, where no H_4R agonist was added. Additionally, dose titration of IL-4 and time kinetics revealed that H_4R mRNA is upregulated progressively during the differentiation of T_H2 cells. Cell surface H_4R expression in response to IL-4 on $CD4^+$ T cells and T_H2 cells deriving from AD patients or healthy individuals is currently under investigation.

Conclusion:
Our data provide further evidence that H_4R is functionally upregulated on T_H2 cells. Thus, H_4R could be a new therapeutic target for diseases with T_H2 predominance, such as AD.

New targets, systemic treatments and new treatments
P067

TRADIPITANT IMPROVES WORST ITCH AND DISEASE SEVERITY IN PATIENTS WITH ATOPIC DERMATITIS

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Background:
Earlier work has suggested that tradipitant, a neurokinin-1 receptor antagonist, may improve the symptom of pruritus in patients with atopic dermatitis (AD) and that this effect is exposure dependent. We are now reporting the results of a 168 patient Phase II study examining the efficacy and safety of tradipitant in patients with AD.

Objective(s):
To examine the efficacy and safety of tradipitant in treating patients with AD.

Materials/methods:
Tradipitant Study VP-VLY-686-2102 was a randomized, double-blind, placebo-controlled, multicenter study that randomized 168 subjects with chronic pruritus associated with AD that was refractory to prior treatment with antihistamine or corticosteroid medication. Inclusion criteria included baseline pruritus score on a Visual Analog Scale (VAS) of ≥ 70 and a baseline disease severity that ranged from mild to severe while excluding very severe patients with a SCORAD > 80. Subjects received 85 mg of tradipitant or placebo orally twice a day and were assessed for pruritus symptoms, disease severity, and quality of life measures over 8 weeks. Itch was assessed by the Average Itch and Worst Itch VAS scales. Disease severity was assessed by the EASI and SCORAD scales. Global impressions of change were measured by the Clinician Global Impression of Change (CGI-C) scale, and Patient Global Impression of Change (PGI-C) scales for both itch and disease. Quality of life measures were assessed by the Patient Benefit Index (PBI) and SKINDEX scales.

Results:
Subjects receiving tradipitant improved on the Worst Itch VAS scale compared to placebo (-44.2 vs -30.6, p=0.019), the total SCORAD index (-21.3 vs -13.6, p=0.008), objective SCORAD (-13.3 vs -7.2, p=0.005), CGI-C (2.6 vs 3.3, p=0.007), PGI-C itch (2.6 vs 3.2, p=0.025), PGI-C AD (2.7 vs 3.5, p=0.007) and PBI (1.7 vs 1.2, p=0.038)/ Improvements favoring tradipitant were also observed for Average Itch VAS, subjective SCORAD, and SKINDEX 16, although the differences did not reach significance for these measures. No common AEs were identified in the treatment group as defined by >5% incidence and having a higher frequency than placebo.

Conclusion:
Tradipitant demonstrated a clinically meaningful and statistically significant improvement in measures of itch, disease severity, and quality of life in patients with AD refractory to treatment with antihistamines and corticosteroids. Tradipitant was safe and well tolerated.

New targets, systemic treatments and new treatments

P068

DIFFERENTIAL EFFECT SIZE OF TRADIPITANT IN ATOPIC DERMATITIS ACCORDING TO BASELINE IGE LEVELS

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Background:
Tradipitant, a neurokinin-1 receptor antagonist, improved itch and disease severity in VP-VLY-686-2102, a phase II study, which examined the efficacy and safety of tradipitant in patients with atopic dermatitis (AD). We present the results of an analysis aimed to examine the interaction between baseline IgE levels and treatment response with tradipitant.

Objective(s):
The objective of this analysis was to examine the effect of IgE levels at baseline on treatment response in the VP-VLY-686-2102 study.

Materials/methods:
Tradipitant study VP-VLY-686-2102 was a randomized, double-blind, placebo-controlled, multi-center study that randomized 168 subjects with AD that was refractory to prior treatment with antihistamine or corticosteroid medication. Inclusion criteria included baseline pruritus score on a Visual Analog Scale (VAS) of ≥70 and a baseline disease severity that ranged from mild to severe while excluding very severe patients with a baseline SCORAD > 80. Subjects received 85 mg of tradipitant or placebo orally twice a day and were assessed for pruritus symptoms, disease severity, and quality of life measures over 8 weeks. IgE subgroups were classified as either “low” or “high” based on a cutoff baseline value ≥100 kU/L. Treatment effect size was calculated within each subgroup for the parameters collected. Analysis was conducted based on MMRM.

Results:
Tradipitant demonstrated significant treatment effect size in measures of itch and disease severity in the overall population and the high IgE subgroup population. While tradipitant performed similarly in both IgE subgroups, placebo treated patients performed significantly worse in the high IgE subgroup as compared to the low IgE subgroup. Tradipitant's treatment effect size in measures of itch and disease severity was particularly significant and meaningful in patients in the high IgE subgroup.

Conclusion:
Baseline IgE level in patients with atopic dermatitis may serve as a useful tool in enriching for treatment response of tradipitant in further studies and in clinical practice.

New targets, systemic treatments and new treatments

P069

TRADIPITANT DEMONSTRATES IMPROVEMENTS IN THE PATIENT BENEFIT INDEX IN ATOPIC DERMATITIS

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Background:
Tradipitant, a neurokinin-1 receptor antagonist, improved itch and disease severity in patients with chronic pruritus associated with atopic dermatitis (AD) in study VP-VLY-686-2102. Substance P and the neurokinin-1 receptor have been implicated in itch related to AD. VP-VLY-686-2102 was a randomized, double-blind, placebo-controlled, multi-center study that randomized 168 patients with AD that was refractory to prior treatment with antihistamine or corticosteroid medication. Inclusion criteria included baseline pruritus score on a Visual Analog Scale (VAS) of ≥70 and a baseline disease severity that ranged from mild to severe while excluding very severe patients with a baseline SCORAD > 80. This study examined the efficacy and safety of tradipitant in patients with AD.

Objective(s):
To study the effects of the novel neurokinin-1 antagonist, tradipitant, on the quality of life of AD patients utilizing the skin disease validated Patient Benefit Index (PBI) scale.

Materials/methods:
168 patients received 85 mg of tradipitant or placebo orally BID and were assessed for pruritus symptoms, disease severity, and quality of life measures over 8 weeks. The PBI is a self-reported questionnaire that has two components. In the PBI scale, patients rate the relative importance of treatment outcome at baseline from 0 to 4 and they then rate the treatment benefit in a 5-point scale that ranges from 0 to 4. Statistical analysis was performed using MMRM.

Results:
In an analysis assessing the PBI score at 8 weeks post-baseline, tradipitant-treated patients showed significant improvement compared to placebo-treated patients (tradipitant=1.72, placebo=1.24, p=0.0377). At baseline, AD patients rated the "free of itching" item as the most important PBI item to improve (tradipitant=3.8; placebo=3.7). Analysis at 8 weeks post-baseline showed that patients on tradipitant significantly improved in the "free of itching" item (tradipitant=2.37, placebo=1.49, p=0.0016).

Conclusion:
In an 8 week randomized, double-blind, placebo-controlled, multi-center study of tradipitant in patients with AD, tradipitant-treated patients demonstrated a significant improvement in the overall Patient Benefit Index, a scale that assesses quality of life in patients with skin diseases. The significant effect of improvement in quality of life measures by tradipitant in this study is consistent with its previously demonstrated antipruritic and disease modifying effects.

New targets, systemic treatments and new treatments

P070

PROTEASE-ACTIVATED RECEPTOR 2 ACTIVATION IS ASSOCIATED TO CLAUDIN-1 DOWN-REGULATION AND TIGHT JUNCTION IMPAIRMENT

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Background:
Protease-Activated Receptors (PAR1-4) are transmembrane G-protein-coupled receptors that can be activated by proteases-mediated cleavage of the N-terminal domain. In the skin, activation of PAR2 has been associated to inflammation, altered epidermal barrier function (e.g. increased proteolysis of filaggrin) and pruritus. PAR2 can be activated by endogenous serine proteases and by environmental proteases (e.g. bacteria products, dust mites, allergens). Increased proteases activity has been shown in atopic skin. In several epithelial (e.g. intestine, lung, kidney) and in endothelial cells, it has been shown that PAR2 activation induced impairment of Tight Junction (TJ) function. However, this has not yet been fully investigated in primary human keratinocytes (PHK). Several PAR2 downstream signaling pathways (e.g. NFkB, MAPK, ERK, IP_3/PKC, β-arrestin/actin) might be involved in epithelial TJ regulation. We have recently showed PAR2 activation reduced TJ integrity in PHK.

Objective(s):
Goal of this study was to validate and expand on our preliminarey study to investigate the effect of PAR2 activation on TJ function and composition in PHK. Additionally, we started to investigate PAR2 downstream signaling pathway(s) potentially involved in epidermal TJ regulation.

Materials/methods:
PHK were differentiated in high-Ca^{+2} media in the presence of the selective PAR2 agonist SLIGKV-NH_2 or reverse peptide as control (100 µM). TJ integrity was assessed by trans-epithelial electrical resistance (TEER) and permeability to Na-Fluorescein. Expression of epidermal barrier components was evaluated at the RNA (qPCR) and protein (e.g. immunostaining) level. PD98059 (MEK inhibitor) and SB203580 (MAPK inhibitor) were used to investigate selected PAR2 pathways.

Results:
Treatment with SLIGKV-NH_2 significantly reduced TEER at 96hr and 120hr ($p<0.01$ and $p<0.001$; n=9) and increased permeability to Na-Fluorescein at 96, 120 and 144hr time points as it compared to control ($p<0.01$; n=8-9). Importantly, PAR2 activation reduced and disrupted claudin-1, ZO-1 and occludin membrane staining pattern. This was associated with reduced expression of claudin, occludin and ZO-1 at the RNA level (qPCR, $p<0.05$; n=7; 72hours). Treatment with PD98059 or SB203580 was not able to rescue the SLIGKV-NH_2 induced TEER reduction; although both the inhibitors reduced baseline TEER as it compared to control samples.

Conclusion:
Our studies revealed that PAR2 might contribute to epidermal barrier impairment of atopic skin, by compromising both TJ function and composition. Further studies are needed to uncover the mechanism(s) involved in PAR2 mediated TJ. All together a strategy to selectively block PAR2 downstream signaling could result in much needed therapeutic interventions for AD by targeting both barrier and inflammation/itch.

New targets, systemic treatments and new treatments

P071

VALIDATION OF THE PRURITUS AND SYMPTOMS ASSESSMENT FOR ATOPIC DERMATITIS IN ADULTS WITH MODERATE TO SEVERE ATOPIC DERMATITIS

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Background:
The Pruritus and Symptoms Assessment for Atopic Dermatitis (PSAAD) symptom diary is an 11-question, symptom-based patient-reported outcomes (PROs) instrument that assesses the daily symptom experience of adults and adolescents with moderate to severe atopic dermatitis (AD). Concepts measured include severity of itch, dryness,

pain, flaking, cracking, bumps, redness, discoloration, bleeding, fluid (exudate), and swelling. It was developed in accordance with Food and Drug Administration (FDA) PRO guidance.

Objective(s):
To assess the reliability, validity, and responsiveness of PSAAD scores and define clinically meaningful changes/differences using data from a Phase 2 study of the oral Janus kinase 1 inhibitor PF-04965842 (NCT02780167) in adult patients with moderate to severe AD.

Materials/methods:
Several psychometric analyses were done to further validate the PSAAD in a clinical trial setting, including evaluation of the following: test-retest reliability, internal consistency reliability, known-group validity, convergent validity (Pearson correlations with scores from other PRO measures), clinically important difference (CID), and clinically important responder (CIR).

Results:
Test-retest reliability and internal consistency were acceptable (intraclass correlation coefficient = 0.81, Cronbach's alpha >0.9, respectively). Convergent validity was confirmed by significant correlations (all $P \leq 0.01$) between PSAAD overall score and other PROs, including pruritus numerical rating scale (r=0.82), Patient Global Assessment (r=0.70), Patient Global Impression of Severity (r=0.91), Patient Global Impression of Change (r=0.68), Patient Oriented Eczema Measure (r=0.82), and SCORing Atopic Dermatitis (r=0.60). Differences in the PSAAD overall scores between groups with Dermatology Life Quality Index (DLQI) scores of 0 or 1 (representing no effect at all on patient's life) and DLQI scores of 2 or more (representing small to extremely large effect on patient's life) were statistically significant ($P \leq 0.0001$) and supported the known-groups validity of the PSAAD, with greater symptom severity (assessed by the PSAAD) associated with greater deficits in quality of life (assessed by the DLQI). The CID and CIR were estimated to be 0.63 and 1.0 points, respectively.

Conclusion:
Evidence supports the reliability, validity, responsiveness, and definitions of clinically meaningful changes/differences for PSAAD scores to assess symptoms among adult patients with moderate to severe AD in accordance with FDA PRO guidance.

New targets, systemic treatments and new treatments

P072

RESULTS FROM A PHASE 2A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, EXPLORATORY, MULTICENTER STUDY OF GBR 830 IN ADULTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS

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Background:
GBR 830 is an investigational, first-in-class, humanized, monoclonal IgG1 antibody specific for inhibiting OX40, a costimulatory receptor on activated T cells. By blocking the binding of OX40 to its ligand OX40L, GBR 830 reduces longevity and efficacy of effector and memory T cells. This mechanism gives GBR 830 the potential to treat T cell-mediated autoimmune diseases, including atopic dermatitis (AD).

Objective(s):
To investigate the effects of GBR 830 on AD biomarkers and generate the first clinical evidence of its biological activity.

Materials/methods:
In this study (NCT02683928), adults with BSA ≥10%, EASI ≥12, SCORAD ≥20, IGA ≥3, and history of inadequate response to topical treatments were randomized 3:1 to GBR 830 (10 mg/kg IV, at baseline and Day 29) or placebo. Forty subjects had evaluable skin biopsies at baseline, 39 at Day 29 (GBR 830=28; placebo=11), and 29 at Day 71 (GBR 830=22; placebo=7). Primary endpoints were treatment-emergent adverse events (TEAEs) and change from baseline in gene expression signatures of key Th2, Th22, Th17, and Th1 immune pathway biomarkers from skin biopsies. Secondary endpoints included EASI 50 and EASI 75 response (≥50% or ≥75% score reduction from baseline, respectively) and IGA response (score of 0 [clear] or 1 [almost clear]).

Results:
Demographics and baseline disease characteristics were generally similar between treatment groups. Approximately one-half of subjects in both groups completed the study. 63% (39/62) of AD subjects had ≥1 TEAE; headache was the most common TEAE (GBR 830=13%; placebo=25%). A greater proportion of subjects achieved an EASI response with GBR 830 vs placebo: EASI 50 (Day 29: 43.6% vs 20.0%; Day 71: 76.9% vs 37.5% [p=0.04]); EASI 75 (Day 29: 12.8% vs 6.7%; Day 71: 42.3% vs 25.0%). The proportion of subjects with IGA response was also greater with GBR 830 vs placebo (Day 29: 5.1% vs 0%; Day 71: 23.1% vs 12.5%). A decline in epidermal hyperplasia measures and mRNA expression of key Th2, Th22, and Th1 skin biomarkers was observed in the GBR 830 group throughout the study period. A positive association was seen between improvements in clinical assessments and changes in tissue AD biomarkers.

Conclusion:
GBR 830 was generally well tolerated in adults with moderate-to-severe AD. Clinically meaningful and sustained improvement of AD symptoms were found following GBR 830 treatment through Day 71, with consistency between molecular and clinical responses.

Keywords:
atopic dermatitis, OX40, monoclonal antibody

New targets, systemic treatments and new treatments

P073

METHOTREXATE AND AZATHIOPRINE IN SEVERE ATOPIC DERMATITIS; A RANDOMISED CONTROLLED TRIAL AND OPEN LABEL EXTENSION STUDY

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Background:
In many patients with moderate-to-severe atopic dermatitis (AD) systemic treatment is needed to achieve adequate disease control. However, systemic treatments in adult patients with AD have rarely been compared for effectiveness and safety.

Objective(s):
To investigate long-term effectiveness, safety and drug survival of (off-label) methotrexate and azathioprine in adult patients with severe AD.

Materials/methods:
Patients with severe AD were randomly assigned in a 1:1 ratio to receive either methotrexate or azathioprine. After 12 weeks of treatment patients could continue in an open label extension study to be evaluated 3 monthly for 5 years. Treatments were continued, stopped, or switched, reflecting normal clinical practice.
Primary effectiveness outcomes were mean absolute and relative reduction in SCORing Atopic Dermatitis (SCORAD) index and Investigator Global Assessment (IGA) after 12 weeks (intention-to-treat analyses) and 2 (intention-to-treat and per-protocol analyses) and 5 years (intention-to-treat and descriptive analyses) compared to baseline. For safety, type, frequency, severity and relatedness to treatment of adverse events were investigated. Drug survival was analysed by Kaplan-Meier curves.

Results:
Of the 45 patients screened, 42 were included at baseline. Thirty-five patients participated in the open label extension study, of which 27 completed the total of 5 years. Twelve weeks after baseline, the methotrexate group (n=20) showed a mean relative reduction in SCORAD of 42% (P<0.01) compared with 39% (P<0.01) in the azathioprine group (n=22) (P 0.52). Two years after baseline, the methotrexate group (n=17) showed a mean relative reduction in SCORAD of 63% (P<0.01) compared with 53% (P<0.01) in the azathioprine group (n=18) (P 0.33). Five year after baseline the relative reduction in SCORAD was similar in methotrexate (n=14) and azathioprine group (n=11): 53% and 54% by descriptive analyses.

Thirteen serious adverse events (SAEs) occurred in 5 years. Nine SAEs were most likely not related to study medication and 4 possibly related (bladder carcinoma, hospitalizations due to exacerbation AD, hospitalization due to pneumonia). Drug survival was longer for methotrexate, but survival on the allocated drug in both groups was low after 5 years.

Conclusion:
Based on this relatively small study, methotrexate and azathioprine seem to be effective and safe as treatments in patients with severe AD after 5 years. Few patients in both groups survive on their originally allocated drug although some discontinued due to controlled AD.
The presentation is a summary of 3 abstracts, with 3 first authors.
*Mandy Elvira Schram, MD, PhD > first Author 12-24 weeks data
*Evelien Roekevisch, MD > first author 2 years data
*Louise Anna Andrea Gerbens, MD >first author 5 years data

New targets, systemic treatments and new treatments

P074

A PROTOCOL FOR A TRIAL ASSESSING THE EFFICACY OF ANTENATAL MATERNAL SUPPLEMENTATION WITH PREBIOTICS ON ATOPIC DERMATITIS PREVALENCE IN CHILDREN

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Background:
Atopic diseases are increasing worldwide; affecting 30-40% of the population and Atopic Dermatitis (AD) is the earliest and the most common manifestation of these diseases (prevalence 20%). Recent research has indicated atopic diseases are associated with a disrupted gut microbial 'balance' raising the possibility that very early interventions which restore an optimal pattern of microflora could improve host's health.. So far, most human intervention studies have mainly focused on improving *postnatal* infant colonization.

Objective(s):
Our study will test the hypothesis that a maternal *antenatal* prebiotics (GOS/inulin) supplementation is superior to placebo for AD prevention in high-risk children (PREGRALL study NCT03183440).

Materials/methods:
The PREGRALL study is a parallel - multicenter double-blind randomized controlled trial funded by the French Ministry of Health (PHRC-I 2015). PREGRALL will recruit 374 pregnant women, at risk of having an allergic infant, from 4 centres. Participants will be randomised to receive prebiotic supplementation or placebo, from 20 weeks of pregnancy to delivery. Primary outcome is AD prevalence at one year (*UK working group* criteria). Secondary outcomes are AD severity, quality of life, prebiotic tolerance, PREGRALL will allow to lead a translational study based on human biological samples collected from 100 infant-mother dyads involved in the trial. Three sample types will be collected from dyads (50 per intervention group): maternal blood (baseline: 20 weeks gestation, 32 weeks gestation, delivery and 2-month visit); infant blood (cord blood at birth, blood at 1 year old); maternal stools (baseline, 32 weeks gestation, delivery and 2-month visit); infant stools (newborn at day 1-5, 2 months and 1 year); breastmilk manually expressed at day 1 (colostrum), day 3 after the flow of milk and 1-month postpartum.

Results:
We hypothesize that the intervention will (i) reduce AD prevalence in high-risk children. (ii) favourably influence maternal gut colonization and increase SCFA metabolites ; (iii) have immunomodulatory effects associated with markers of immune homeostasis (at birth and in the postnatal period) in mothers and offspring .The 100 mother-baby dyads will be used for an ancillary study to analyze the mechanistic effects of prebiotics on immune system, gut microbiota and milk composition and function.

Conclusion:
To our knowledge PREGRALL will be the first clinical trial assessing the effects of prebiotics exclusively in pregnancy for AD prevention. It will contribute to our understanding of mechanisms involved in allergy prevention and may help to define new strategies involving prebiotic use during the antenatal period for reducing the incidence of AD in high-risk families.

Outcome measures
P077

EFFICACY AND UTILITY OF WET WRAP DRESSING FOR PATIENTS WITH PEDIATRIC ATOPIC DERMATITIS
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Background:
Management of atopic dermatitis (AD) is based on the regular use of emollients, together with topical steroids or calcineurin inhibitors for acute flares. However, oral medications have some limitations for long-term use and use by young children. Wet wrap dressing (WWD) is an interesting alternative for short-term control in patients with severe or refractory flares that avoids the use of systemic treatments.

Objective(s):
This study was done to compare the efficacy of wet wrap dressing group with topical steroid agents with control and estimate the utility of WWD in pediatric atopic dermatitis.

Materials/methods:
Total 40 cases with moderate to severe atopic dermatitis (mean eczema area and severity index, EASI≥7) and less than 13 years old were included in this study. Twenty cases were treated with WWD under two layers of cotton bandages or garments (Tubifast^{TM}) and the rest were applied with topical steroid agents without cotton bandages. The improvement of severity was evaluated by EASI and transepidermal water loss (TEWL). We compared two groups at 1 week treatment using analysis of covariance (ANCOVA) and t-test. Furthermore, we surveyed the questionnaire about the utility and adverse effect of WWD to evaluate the subjective outcomes of WWD.

Results:
After 1 week of WWD treatment, the statistically significant reductions in mean EASI (-6.138, 95% CI -7.328 to -4.947, p=0.013), and TEWL (-26.714, 95% CI -31.162 to -22.266, p=0.002) were observed compared to EASI (-4.048, 95% CI -5.205 to -2.892) and TEWL (-15.359, 95% CI -19.807 to -10.911) of control group. Patient self-assessment and visual analogue scale (VAS) were improved in both group, but there was no statistically significance between both groups in the VAS. Utility of WWD through the questionnaire was satisfactory.

Conclusion:
This study is meaningful in that it estimates both subjective and objective efficacy about WWD. In view of these findings, WWD has superior therapeutic effects than conventional steroid application in the treatment of atopic dermatitis of children with good compliance of patients and parent-caregivers.

Outcome measures
P078

EFFECT OF EVENING PRIMROSE OIL ON KOREAN PATIENTS WITH MILD ATOPIC DERMATITIS
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Background:
Atopic dermatitis (AD) is related to a deficiency of delta-6-desaturase, an enzyme responsible for converting linoleic acid to gamma-linolenic acid (GLA). Evening primrose oil (EPO) as a source of GLA has been of interest in the management of AD.

Objective(s):
The aim of this randomized, double blinded, placebo-controlled clinical study is to evaluate the efficacy and safety of EPO in Korean patients with AD.

Materials/methods:
50 AD patients were enrolled for the study and randomly divided into two groups. The first group received an oval unmarked capsule containing 450 mg of EPO (40 mg of GLA) per capsule, while placebo capsules identical in appearance and containing 450 mg of soybean oil were given to the other group. Treatment continued for a period of four months. The Eczema Area Severity Index (EASI) scores, transepidermal water loss (TEWL), and skin hydration were evaluated in all the AD patients at the baseline, and in months 1, 2, 3, and 4 of the study.

Results:
At the end of month 4, the patients of the EPO group showed a significant improvement in the EASI score (p = 0.040), whereas the patients of the placebo group did not. There was a significant difference in the EASI score between the EPO and placebo groups (p = 0.001). Although not statistically significant, the TEWL and skin hydration also improved in the EPO patients group.

Conclusion:
We suggest that EPO is a safe and effective medicine for Korean patients with mild AD.

Outcome measures

P079

CONSTRUCT VALIDITY OF SELF-REPORTED GLOBAL ATOPIC DERMATITIS SEVERITY IN A POPULATION-BASED COHORT OF ADULTS

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Background:
Atopic dermatitis (AD) is chronic inflammatory skin disease associated with skin signs, profound symptom burden and impact on quality of life, all of which factor into disease severity. Self-reported global AD severity may be a valid assessment of disease severity for epidemiological research.

Objective(s):
We sought to validate self-reported global AD severity in a representative cohort of US adults with AD.

Materials/methods:
A cross-sectional, population-based study of 8,217 adults was performed using a structured questionnaire. A diagnosis of AD was determined using modified UK Diagnostic Criteria for AD (N=602). AD severity was assessed using self-reported global AD severity, PO-SCORAD, PO-SCORAD itch, PO-SCORAD sleep, POEM, DLQI, HADS and SF-12. Correlations between these measures were analyzed using Spearman's correlation coefficient (rho). Agreement between self-reported global AD severity and PO-SCORAD, POEM and DLQI was further explored (kappa coefficient, κ).

Results:
Self-reported global AD severity showed moderate, statistically significant (P<0.0001) correlation with PO-SCORAD (rho=0.54), DLQI (rho=0.55), POEM (rho=0.49), PO-SCORAD itch (rho=0.43), HADS (rho=0.36), SF-12 mental health (rho=-0.35) (P<0.0001 for all). Similar results were observed in stratified analyses by age, sex, race/ethnicity and level of education. Fair to moderate agreement between self-reported AD severity and PO-SCORAD (k=0.40), POEM (k=0.40) and DLQI (k=0.45) was observed; as well as fair agreement with PO-SCORAD itch (k=0.29). We also observed a stepwise increase in PO-SCORAD, PO-SCORAD itch, PO-SCORAD sleep, POEM, DLQI, HADS, and a stepwise decrease in SF-12 mental and physical health with increasing self-reported global AD severity (Kruskal Wallis test, P<0.01).

Conclusion:
Based on these results, self-reported AD severity demonstrates construct validity for assessing AD severity in adults when performing epidemiological studies.

Outcome measures

P080

ERYTHEMA, PAPULATION, EXCORIATION AND LICHENIFICATION SEVERITY CORING BY DEEP NEURAL NETWORK

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Background:
The Eczema Area and Severity Index (EASI) score is one of the important scoring tool for evaluating eczema severity and treatment outcome, which requires validation and training of evaluators. It is still challenging to score the severity of eczema objectively and reproducibly with EASI score. Automated standardization of erythema, papulation, excoriation and lichenification severity using images has not been investigated yet.

Objective(s):
Our aim was to determine whether the deep convolutional neural networks (CNNs) could assess erythema, papulation, excoriation and lichenification severity at the level of competence comparable to dermatologists' scoring.

Materials/methods:
We made a standard dataset of 6,540 clinical images showing eczema. These images were scored 0 to 3 for each sign by three dermatologists. We trained four CNNs (ResNet V1, ResNet V2, GoogLnet and VGG-Net) with the image dataset, and then examined which CNN was most suitable for erythema, papulation, excoriation and lichenification scoring.

Results:
ResNet V1 and VGG-net showed the highest accuracy in scoring erythema, and lichenification, respectively. ResNet V2 showed the highest accuracy in scoring papulation and excoriation. Compared to dermatologists' scoring, the accuracy rates of CNNs for erythema, papulation, excoriation and lichenification were 98.93%, 96.00%, 97.00% and 89.00%, respectively.

Conclusion:
These results suggest some CNNs have a performance capacity for erythema, papulation, excoriation and lichenification scoring at the level of competence comparable to dermatologists. It is expected that CNNs can assess EASI score if CNNs can classify area score in the further study.

Outcome measures

P081

DOES EARLY EFFECTIVE TOPICAL TREATMENT OF ATOPIC DERMATITIS IN TODDLERS WITH EITHER CORTICOSTEROIDS OR TACROLIMUS AFFECT EARLY SENSITIZATION?

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Background:
The aim was to study if effective treatment of atopic dermatitis (AD) in early childhood prevents the development of respiratory symptoms including asthma and allergic rhinitis. This is an interim analysis when half of the children have been to the 1 year control to see if there are differences in the corticosteroid vs tacrolimus treated groups.

Objective(s):
This study is a part of an ongoing three-year randomized open-label comparative follow-up study of tacrolimus ointment (0.03%, if needed 0.1%) vs. corticosteroid (hydrocortisone, if needed hydrocortisone 17-butyrate) treatment in infants.

Materials/methods:
Children aged from 1 to 3.9 years who have been sent to Skin and Allergy Hospital in Helsinki due to moderate to severe AD according to Rajka & Langeland Eczema Severity Score (40) were enrolled in the study. Atopic eczema was diagnosed by a dermatologist. Patients with continuous need for inhaled corticosteroids were excluded from the

study. In total 152 patients were enrolled. This is a one-year follow-up analysis of 75 patients, who have reached the 12 months' control. The primary aim was to evaluate if there are statistically significant differences between the tacrolimus and corticosteroid therapy groups. EASI, IGA, TEWL, area of eczema, serum total IgE level and blood eosinophil count were used as efficacy measures.

Results:
Baseline characteristics were similar in both treatment groups. EASI, area of eczema, IGA and TEWLs improved in both therapy groups during the 12 months follow-up period with active treatment and no statistically significant differences were seen between the treatment groups. However, those patients with elevated serum total IgE, elevated eosinophil counts, positive prick tests or signs of sensitization to aeroallergens or food allergens at baseline had statistically significantly lower TEWL on eczema site on 12 months' control and smaller affected area of eczema in tacrolimus therapy group than in corticosteroid group.

Conclusion:
It is estimated that one third to half of patients with AD will develop asthma and especially children with multiple sensitizations and familial history of asthma are shown to be at greater risk. These results of our study point out that especially these high-risk patients could benefit from early effective tacrolimus treatment.

Outcome measures

P082

COMPARISON OF PATIENT (POEM), OBSERVER (EASI, SASSAD, TIS) AND CORNEOMETRY MEASURES OF EMOLLIENT EFFECTIVENESS IN CHILDREN WITH ECZEMA

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Background:
Eczema affects ~20% of children but multiple different outcome measures have hampered research into the effectiveness of different treatments.

Objective(s):
To compare the change in scores and correlations within and between five measures of eczema severity: Patient Orientated Eczema Measure (POEM), Eczema Area Severity Index (EASI), Six Area Six Sign Atopic Dermatitis (SASSAD), Three Item Severity (TIS), and skin hydration (corneometry).

Materials/methods:
Data from a feasibility trial that randomised young children with eczema to one of four emollients were used. Participants were followed for three months (84 days). Descriptive statistics (by emollient over time) and Spearman's correlation coefficients comparing scores at each time-point and absolute change (between adjacent time-points) for each outcome measure were calculated.

Results:
197 children, mean age (SD) of 21.7 (12.8) months, were randomised. POEM and TIS appeared to capture a range of eczema severity at baseline but only POEM had close approximation to normal distribution. Mean POEM, EASI, SASSAD and TIS scores improved month-by-month, with POEM showing the greatest sensitivity (effect size 0.42). Correlations within POEM, EASI, SASSAD and TIS were moderate-to-good, decreasing over time. Correlations between measures were strongest for EASI, SASSAD and TIS. By contrast, corneometry scores were more variable, correlated less well over time, and were poorly correlated with the other measures.

Conclusion:
Except for corneometry, all measures appear to change in relation to emollient use over time and correlate well with themselves. POEM demonstrated the greatest range of scores at baseline and change in eczema severity over the first 28 days.

Outcome measures

P083

MEMORY BUTTONS AND A SUPPORTIVE MOBILE APPLICATION INDUCED OBJECTIVE AND SUBJECTIVE EFFECTS IN PATIENTS WITH ATOPIC DERMATITIS

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Background:
Atopic dermatitis (AD) is a chronic skin condition where poor adherence is a major problem, affecting negatively the treatment outcome. Motivational interventions, such as digital tools (i.e. Internet-of-Things (IoT) and applications), in health behavior may result in better treatment outcomes through increased adherence.

Objective(s):
To determine whether the combination of a memory-button recording medication use and supportive mobile application (app) affect quality of life as well as subjective and objective severity measures in AD patients over one month following the patient's normal routine treatment schedules.

Materials/methods:
This was a non-interventional feasibility study, investigating a memory bluetooth connected button and supportive app (KlikKit™, Copenhagen, Denmark) in patients with AD (Inclusion criteria: >18 years of age, diagnosed with AD, daily use of a topical treatment, read Danish, and own an iPhone/Android phone). 118 subjects were voluntarily recruited online via facebook advertising (Studies&Me™, Copenhagen, Denmark). 96 patients did show up for the first consultation, of these 6 were excluded (did not bring their treatment to the consultation or had the wrong diagnosis). The patient should attend two consultations with a preferred 28 +/- 3 days interval in Denmark (Aarhus and Copenhagen). Patients were randomized in 3 groups: 1) control group who followed routine treatment schedules 2) received 1-3 memory buttons to click every time they used their topical products/emollients as part of their treatment plan, or 3) received the memory-buttons and supportive app to click every time they used their topical products and with possibility to overall monitor treatment progression as part of their treatment plan. SCORAD, EASI, POEM and DLQI were obtained at each consultation for all groups.

Results:
Digital recruitment for the study was highly effective and fast (total of 53 days). The study population comprised of a total of 83 out of 90 subjects who fulfilled two consultations. EASI and SCORAD scores were lower in all groups after 2nd consultation ($p<0.03$), however in group 3 ($p<0.0003$). Further, subjects in group 3 had a statistically significant decrease in their POEM score ($p=0.024$) compared to patients in group 1 and 2. No difference in DLQI was observed.

Conclusion:
Memory buttons and supportive app significantly improved objective and subjective clinical outcomes. These results are indicative of this digital solution may be capable of improving adherence in patients suffering from AD. Future studies will need to validate these findings.

Outcome measures

P084

UNDERSTANDING THE BARRIERS AND FACILITATORS TO EFFECTIVE PATIENT INVOLVEMENT IN CORE OUTCOME SET DEVELOPMENT CONSENSUS MEETINGS; EXPERIENCES OF HOME

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Background:
Harmonizing Outcome Measures for Eczema (HOME) is a global initiative developing a core outcome set for atopic eczema trials. Core outcome sets include outcomes of importance to both patients and clinicians, and to achieve this, patients have been key stakeholders in HOME since its inception. The term “patients” within HOME refers to adults with atopic eczema, parents of children with atopic eczema and leaders of atopic eczema support groups.

Objective(s):
The aim of this qualitative study was to understand how patients perceived their involvement in the HOME V consensus meeting to guide improvements at future consensus meetings.

Materials/methods:
Patients who attended the HOME V meeting in Nantes, France (June 2017) were invited to participate in semi-structured interviews via telephone with a researcher who was not directly involved with the planning or delivery of the meeting. Interviews were recorded, transcribed and thematically analysed. A subsequent ideas generation workshop involving patients and researchers from two core outcome set groups was held.

Results:
Eleven HOME V patient participants were interviewed. Several initiatives already implemented were helpful for facilitating active patient involvement in HOME consensus meetings. The inclusion of a patients-only pre-meeting was welcomed and helped patients get to know each other. During the main meeting, the smaller breakout groups provided a good opportunity to express opinions. There was a sense of community amongst the patients who had been involved in several HOME meetings, and patients felt their viewpoint was valued by the wider group. The opportunity to share experiences and network was appreciated.
A number of areas for improvement were identified. Patients wanted more information regarding what to expect at the meeting, and whether their own viewpoint was sufficient or expected to represent patients more widely. At times the “experts” took over and the patient voice was felt to be less important. Technical language and methods were used at times without explanation. The consensus meetings are fast-paced and time to discuss and reflect during the meeting was lacking. More attention should be paid to accommodating the health needs of patients at meetings. The workshop conducted subsequent to the interviews generated ways to address these weaknesses, and will be published in a guide to patient involvement for others planning consensus meetings.

Conclusion:
Although there was a largely positive response from patients when asked about their involvement in HOME meetings, these findings will be used to make improvements in key areas at future meetings.

Outcome measures

P085

THE IMPORTANCE OF PATIENT-REPORTED PAIN INTERFERENCE IN ATOPIC DERMATITIS

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Background:
Patient-Reported Outcomes Measurement Information System (PROMIS®), developed by NIH, is a biopsychosocial health outcomes tool encompassing multiple domains in physical, mental, and social health and is used to track specific health domains across all diseases.

Objective(s):
This study evaluated the clinical relevance of three PROMIS® domains (Pain Interference, Mood/Depression, and Anxiety) in atopic dermatitis (AD).

Materials/methods:
A PROMIS® health assessment, using computer adaptive tests for three domains, was administered on iPads during routine care in three Dermatology clinics at University of Rochester. Domain scores range from 0-100 where a score of 50 is the “average health of the general population.” Minimally important differences have been recognized as ≥5points off the average or in a score change (1,2). Domain scores >55 were considered “notable”. All statistical analyses (two-tailed ANOVA and Fisher Exact tests) were performed at significance level of 0.05 using JMP Pro12.

Results:
Of the 4,523 office visits that captured PROMIS® data, 101 (2.2%) were for AD. Mean Mood and Anxiety scores, but not Pain Interference, were significantly higher for AD patients than all other dermatology patients (49.9±10.4 vs. 47.6±9.8, p=0.030; 52.1±9.8 vs. 49.8±10.4, p=0.017; 50.5±10.5 vs. 50.2±10.2, p=0.748). The percentage of AD patients with “notable” scores was 36% in Anxiety, 33% in Mood, and 34% in Pain Interference. Systematic chart reviews of age and gender-matched patients with “notable” and “not notable” domain scores (n=20 in both groups) revealed significant associations with Pain Interference. “Notable” Pain Interference scores associated with severe disease (p=0.020), higher percentage body surface area (BSA) of disease (p=0.002), uncontrolled disease (p=0.004), and/or unsuccessful treatment (p=0.001). Chi-square tests revealed one-way trends of “notable” Anxiety with uncontrolled disease and higher BSA and “notable” Mood scores with severe disease (p=0.050).

Conclusion:
PROMIS® Pain Interference reflects the impact of AD and treatment on patients’ physical health. The association of Anxiety and Mood scores in AD requires further exploration. Assessing the effectiveness of therapeutic interventions in AD patients would be improved with PROMIS utilization.
1. Jensen RE *et al*. (2017) United States Population-Based Estimates of Patient-Reported Outcomes Measurement Information System Symptom and Functional Status Reference Values for Individuals With Cancer.Journal of Clinical Oncology. 35(17):1913-20. PMC5466008.
2. www.healthmeasures.net

Outcome measures

P086

NAIL DYSTROPHY IN PATIENTS WITH ATOPIC DERMATITIS AND ITS ASSOCIATION WITH DISEASE SEVERITY

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Background:
Nail dystrophy arises from various inflammatory dermatologic diseases. However, there have been few reports on the prevalence of nail abnormality in atopic dermatitis (AD) or on the relationship of this condition with the severity of the disease.

Objective(s):
This study was intended to determine the prevalence and types of nail abnormalities associated with AD and to evaluate the relation between nail abnormalities and the severity of AD.

Materials/methods:
AD patients aged 2 to 19 who visited the outpatient clinic were thoroughly examined for nail abnormalities. Demographic information was collected and eczema area and severity index (EASI) score for severity of AD were checked.

Results:
A total of 235 AD patients (children and adolescents) were investigated. There were 24 (10.2%) patients with nail abnormalities: transverse groove (Beau’s line) (25%), nail pitting (16.7%), koilonychia (16.7%), trachyonychia (12.5%), leukonychia (12.5%), brachyonychia (8.3%), melanonychia (8.3%), onychomadesis (8.3%), onychoschizia (8.3%), and onycholysis (8.3%). There was no statistically significant difference in the total EASI score associated with development of nail abnormalities (p = 0.236). However, when the EASI score was confined to the lower extremities, it showed a relation to the prevalence of toe nail dystrophy (odds ratio: 1.115; 95% confidence interval: 1.01–1.32; p = 0.03).

Conclusion:
Nail abnormalities in AD are thought to be caused mainly by pathologic change in the nail matrix region, and the EASI score confined to lower limbs, might be used as a predictor of toe nail changes in patients with AD.

Outcome measures
P087

WHAT IS THE QUALITY OF QUALITY-OF-LIFE MEASUREMENT INSTRUMENTS FOR CAREGIVERS OF CHILDREN WITH ECZEMA? SYSTEMATIC REVIEW

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Background:
Eczema often has detrimental impacts on affected children and their family and caregivers. It is therefore of interest to assess the impact on quality of life (QoL) of caregivers of children with eczema in clinical trials. There is uncertainty regarding the quality of existing measurement instruments.

Objective(s):
The objective of this systematic review was to investigate the quality of existing instruments developed to measure the QoL of caregivers of children with eczema to inform recommendations for their use in clinical trials.

Materials/methods:
We systematically searched the literature for studies on measurement instruments developed and/or validated for the measurement of QoL in caregivers of children/adolescents with eczema. For the included studies, we assessed their methodological quality using the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) checklist as well as the adequacy of investigated measurement properties. Findings from both assessments were summarized in a best-evidence synthesis for each measurement property.

Results:
Sixteen studies were included reporting on 20 instruments used to measure QoL in caregivers of children with eczema: the Parents' Index of Quality of Life in Atopic Dermatitis (PIQOL-AD) in seven languages, the Dermatitis Family Impact (DFI) in six languages, the Childhood Atopic Dermatitis Impact Scale (CADIS) in four languages, the Family Dermatology Life Quality Index (FDLQI) in Ukrainian, the Quality of Life in Primary Caregivers of Children with Atopic Dermatitis (QPCAD) in Japanese and a German questionnaire by Rueden at al. 1999. Overall, we found substantial validation gaps. For instance, no study investigated measurement error. Currently, no instrument can be recommended for measuring QoL in caregivers of children with eczema because none fulfilled all required adequacy criteria. With adequate internal consistency and reliability, the US version of the CADIS has the potential to be recommended pending future validation studies.

Conclusion:
Currently, no instrument used to measure QoL in caregivers of children with eczema can be highly recommended. Further studies filling validation gaps are warranted.

Outcome measures
P088

CLINICAL FEATURES OF ATOPIC DERMATITIS IN ADULTS ARE DIFFERENT ACCORDING TO AGE OF ONSET

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Background:
Few studies in atopic dermatitis (AD) in adult patients have evaluated differences according to onset age about epidemiological associations and clinical features.

Objective(s):
The objective of the study is to compare the clinical features of AD in adult patients according to age of onset.

Materials/methods:
This study recruited subjects with AD visiting the dermatology outpatient department of Kangnam Sacred Heart Hospital and comprised clinical evaluation by a dermatologist and a survey of demographics and onset of AD-associated signs and symptoms. They are also tested total IgE and multiple allergen simultaneous test (MAST).

Results:
A total of 280 adult AD patients were enrolled. Among 280 adult AD patients, 232 patients (82.86%) showed early-onset (before 18yr-old) and 48 patients (17.14%) had late-onset (above 18yr-old) of AD. Between two groups, there were significantly different in initial involvement area (p=0.017) and treatment history (p=0.010). Interestingly, patients with BMI≥25 showed significantly higher EASI score than patients with BMI<25 in early-onset adult AD (p=0.048). On the other hand, there were not significantly different in sex, family history, body mass index (BMI), Eczema Area and Severity Index (EASI) and total immunoglobulin E (IgE).

Conclusion:
Significant differences of clinical characteristics exist between early-onset and late-onset AD subgroups in adult patients with AD. Our results suggest that the heterogeneity of AD in adult exist.

Outcome measures

P089

INVERSE ASSOCIATION BETWEEN TRANSEPIDERMAL WATER LOSS AND GESTIONAL AGE IN PRETERM INFANTS

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Background:
Skin barrier development begins *in utero* during the first trimester, with the stratum corneum developing around gestational week 34. In very preterm infants the skin barrier is immature and the postpartum maturation of the skin is delayed several weeks.

Objective(s):
To determine the transepidermal water loss (TEWL) at birth in preterm infants born at different gestational ages.

Materials/methods:
A birth cohort of 39 premature infants (gestational age 28-37 weeks, postnatal age 1-31 days) was established at the neonatal ward at Rigshospitalet, University of Copenhagen, Denmark. TEWL was measured noninvasively on the volar side of the forearm with a closed chamber system from AquaFlux. A mean of three measurements was calculated.

Results:
TEWL decreased significantly with 2.64 g/m^2/h (95% confidence interval 2.08-3.20 g/m^2/h) per increasing week of gestation adjusted for postnatal age (p>0.0001). TEWL decreased nearly 50% from infants born at 28 weeks of gestation (mean TEWL 31.72 g/m^2/h, n=4) to infants born at 35 weeks (mean TEWL 16.64 g/m^2/h, n=10).

Conclusion:
Our results show an inverse association between TEWL and gestational age, indicating that the skin barrier in very preterm infants is more permeable than the skin barrier in late preterm infants.

Outcome measures

P090

THE USEFULNESS OF SCCA2 AND PERIOSTIN AS CLINICAL BIOMARKERS FOR SEVERE ADULT ATOPIC DERMATITIS

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Background:
Thymus and activation-regulated chemokine (TARC/CCL17) is a member of the T-helper 2 chemokine family. Since 2009 we have executed tight control which initiates 2-week hospitalized remission induction with intensive topical corticosteroid (TCS) followed by serum biomarker-TARC-guided weaning proactive treatment. Then, we found that 40% patients have difficulty in maintaining long-term control only by proactive treatment despite normal serum TARC level at discharge. The problem is to detect them earlier and to prescribe further treatment. Periostin, an extracellular matrix protein induced by T helper 2 cytokines which act in chronic inflammation. Serum levels of squamous cell carcinoma antigen (SCCA) 1 and 2 induced by type 2 cytokines are increased in patients with atopic dermatitis. These seem to predict the prognosis in addition to TARC.

Objective(s):
To investigate correlation among serum periostin, SCCA2, clinical signs and other biomarkers in severe atopic dermatitis. To obtain a predictive biomarker of subsequent successful long-term control by tight control strategy with “classic” medication in addition to TARC.

Materials/methods:
We performed retrospective cohort study of 131 informed consented patients with moderate to severe adult atopic dermatitis who have been followed up for more than 6 months along our tight control strategy after initial 2-week hospitalized intensive topical treatment with educational program in 2015. We compared the backgrounds of favorable and unfavorable group and we also compared serum biomarker levels before and after treatment between two groups.

Results:
At the time of 6 months later 81(61.8%) patients were in favorable, 50(38.2%) patients were unfavorable outcome. Serum periostin levels were 35 ~ 1138ng/ml (M:143) before hospitalization, and 21 ~ 211ng/ml(M:55) at discharge. Serum SCCA2 were 0.3 ~ 261.5ng/ml (M:9.2) before hospitalization, and 0 ~ 3.7ng/ml (M:0.4) at discharge. They significantly decreased after 2-week treatment. Initial SCCA2 and initial periostin showed correlations with initial total EASI score(r=0.333,P<0.01,r=0.335,P<0.01), initial serum TARC(r=0.589,P<0.01,r=0.516,P<0.01). However, distribution of those two biomarkers were not significantly difference between favorable and unfavorable groups. A part of the unfavorable group showed SCCA2 over 1.4ng/ml with TARC less than 600ng/ml.

Conclusion:
Both periostin and SCCA2 levels rise in severe adult atopic dermatitis, and decrease after intensive topical treatment. These don’t seem to play an significant role to predict the prognosis. But, SCCA2 can be a predictive biomarker for some patients.

Outcome measures

P091

WORK LIMITATIONS AND HEALTH ECONOMIC IMPACT OF ATOPIC ECZEMA: RESULTS OF THE GERMAN REGISTRY TREATGERMANY

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Background:
Clinical registries may provide high quality evidence on the use and effectiveness of therapeutic interventions under real-life conditions. They are an indispensable prerequisite of evidence-based health care and translation of research evidence into clinical practice.

Objective(s):
Initiated in 2011 and relaunched in 2016, the German Atopic Dermatitis (AD) Registry TREATgermany is the first registry of patients with moderate to severe AD worldwide. Adults with moderate-to-severe AD (current/prior systemic anti-inflammatory treatment and/or objective SCORAD≥20) are prospectively followed over the course of at least 24 months. Herein, we present findings on the association of DLQI and WLQ of patients enrolled in the registry from June 2016 until December 2017 to analyze the health economic impact of AD.

Materials/methods:
Employed treatment modalities and a broad set of physician and patient reported outcome measures are documented using validated measurement instruments to assess clinical disease severity (EASI, objective SCORAD), quality of life (DLQI), symptoms (POEM), global disease severity, as well as patient satisfaction and work limitations including presentism (WLQ).

Results:
Overall, 243 individuals (mean age 42.8±14.6 years, 60.9% men) were enrolled at 19 recruitment centers. 68.7% of them were currently employed (73.0% of males, 63.4% of females, mean age 41.9±12.1 years). Employed persons had DLQI and WLQ scores of 10.6±6.9 points and 17.7±18.1%, respectively. Mean presentism, i.e. productivity loss while on the job, was substantial accounting for 9.2%. With coefficients of 0.388 and 0.326 WLQ and presentism scores significantly correlate with DLQI ($p<0.000$).
Bootstrapped regression models (corrected $R^2=0.15$) showed that the limitations in coping with work requirements increase by 1.7% as DLQI increases by one point. If the subscales of WLQ are considered, it becomes apparent that lower quality of life due to AD is most strongly associated with limitations in the area of physical and performance requirements in general. Presentism decreases by 0.5% as DLQI increases by one point.

Conclusion:
Moderate-to-severe AD has substantial adverse economic impact with mean productivity loss of patients of almost 10%. Future analyses from TREATgermany will address the impact of innovative treatment modalities on quality of life and work productivity of patients with moderate-to-severe AD.

Outcome measures

P092

BASELINE CHARACTERISTICS AND QUALITY OF LIFE OF PATIENTS WITH ATOPIC DERMATITIS OBSERVED IN THE GERMAN AD REGISTRY TREATGERMANY

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Background:
For analysis and descriptive reporting, clinical registries document and manage longitudinal patient data regarding utilization and effectiveness of treatments as well as aspects of patient and quality management under real-life conditions.

Objective(s):
From June 2016 until December 2017, 243 patients were included in the registry in 19 recruitment centers. The presentation will report baseline characteristics of AD and aspects of quality of life.

Materials/methods:
The German Atopic Dermatitis (AD) Registry *TREATgermany* is a prospective multicentered registry. It emerged from TREATeczema and is part of the European registry family TREAT.
Adults with moderate-to-severe atopic dermatitis (current/previous anti-inflammatory systemic treatment and/or objective SCORAD≥20) are prospectively followed over at least 24 months. Objective clinical severity (EASI, objective SCORAD), disease symptoms (POEM), severity of pruritus and sleeping problems (VAS), flares, quality of life (DLQI) as well as patient and physician treatment satisfaction are assessed by validated measurement instruments, and treatments are documented.

Results:
The total of 243 enrolled patients (mean age of 42.8±14.6 years, 38.6% females) had mean objective SCORAD of 39.1 ± 14.4 and mean EASI of 13.3± 10.9. Of these patients 54.8% reported an early disease onset, 22.4% had developed AD in adulthood. Severity of pruritus, pain and sleeping problems were assessed as 5.2±2.6, 3.1±2.6 and 3.9±3.3 of 10 points, respectively. Patients reported mean DLQI and POEM scores of 10.7±7.1 and 15.3±7.3, respectively. With 2.93±0.99 and 2.80±1.10 of 5 possible points IGA and PGA differed significantly (p=0.05) at baseline. Oral glucocorticosteroids (60.5%) was the most frequently applied medication followed by cyclosporine (42.0%). Patients were fairly satisfied with medical supply (7.1±2.6, scale 0-10) and treatment (6.4±2.8, scale 0-10), however AD was poorly controlled (<4 of 12 weeks) in 52.1% of the patients and only in 4.6% completely controlled (>10 of 12 weeks).

Conclusion:
This baseline analysis of the first 243 patients from TREATgermany provides valuable information about the usual treatment of adults with moderate-to-severe AD in Germany. It shows high burden of disease, effectiveness and utility of the current treatment as well as the need for additional effective and safe treatment alternatives for long term control.

Outcome measures

P093

IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES ARE OBSERVED IN ADULT ATOPIC DERMATITIS PATIENTS INITIATING SYSTEMIC MEDICATIONS

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Background:
Patient-Reported Outcomes Measurement Information System (PROMIS®) is a biopsychosocial tool used to track multiple domains in physical, mental, and social health across diseases.

Objective(s):
To determine whether initiation of systemic treatments for adults with atopic dermatitis (AD) correlated with an improvement in any of the PROMIS® domains (pain interference, depression, anxiety, and physical function).

Materials/methods:
PROMIS® assessments were administered by iPad during routine outpatient clinics at University of Rochester between April 2016 to January 2018. Domain scores range from 0-100, where a score of 50 is the "average health of the general population." Selected patients included: patients with AD who initiated a systemic medication (e.g. dupilumab, cyclosporine, methotrexate, and/or mycophenolate mofetil) for treatment of their disease and had PROMIS® domain data for a baseline visit (i.e., pre-treatment) and a follow-up (F/U) visit. Minimally clinically important improvements in PROMIS® domains (i.e. ≥ 5 points lower in pain interference, depression, and anxiety and ≥ 5 points higher in physical function) were evaluated using one-tailed paired t test.

Results:
We report preliminary data from N=14 subjects who were primarily Caucasian (11/14; 78.6%) females (8/14; 57.1%) with a mean age of 41 years (age range = 19-75 years). All patients completed at least one PROMIS® domain at both baseline and F/U visits. Pain interference decreased by a clinically important amount, 7.0 ± 11 points from baseline to F/U visit (53.9 to 46.9, p=0.029). Depression decreased by 3.8 ± 8.4 points (51.6 to 47.8, p=0.050) and physical function increased by 3.9 ± 6.4 points (49.2 to 53.3, p=0.030). The anxiety domain did not significantly change with treatment 53.6 to 51.2 p=0.100), although scores did improve. Of the 3 patients who started treatment with severe pain interference scores (greater than 55), 2 (66%) were no longer in the severe range at F/U.

Conclusion:
Pain interference, physical function and depression all improved – reflecting important changes with initiation of systemic treatment in our small AD cohort. PROMIS® anxiety measures improved, but did not reach statistical significance. These patient-reported outcomes may aid in monitoring AD patients' response to systemic treatments.

Gaps in evidence

P095

ATOPIC DERMATITIS IN INDIA

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Background:
Coloured skin shows different features of atopic dermatitis varying from hypopigmentation to hyperpigmentation . Term "Atopy" (strange) was coined by Coca & Cooke in 1923.Dark skin often shows features different from white skin which are often confused with vitiligo and leprosy.

Objective(s):
To establish the frequency of minor criteria of AD in a patient diagnosed on the basis of major criteria.
To establish a set of minor diagnostic criteria for AD in the Indian context

Materials/methods:
Ethical committee approval taken
Informed consent taken from the parent/guardian
Study of children less than 12 years of age, was conducted over a period of one year
The children were diagnosed on the basis of major criteria
All clinically diagnosed cases of atopic dermatitis (3/4 major criteria) were taken in to study.
The prevalence & significance of all minor criteria were analysed statistically

Results:
Most common features were xerosis,facial pallor,pityriasis alba,palmar hyperlinearity and itching when sweating found in more than 50% of patients.

catarct conjuctivitis were found in less than 5% of cases.
Atopic dermatitis is increasing in India, onset in the 1st year of life is 60%, progressed to 85% in 5 years.As of today there is no single clinical / biochemical feature diagnostic of AD.This is a preliminary attempt to evolve such criteria in order to aid practising dermatologist in a busy clinic.Hence, we arbitrarily chose the cut off point of 50% prevalence for each of the minor criteriaHowever. we found that only 5 of the minor criteria were found to have >50% prevalence.

Conclusion:
we propose a set of 5 minor criteria which have a higher relevance in the Indian context for busy dermatologist.

Gaps in evidence

P096

EMOLLIENT BATH ADDITIVES FOR THE TREATMENT OF CHILDHOOD ECZEMA (BATHE): MULTI-CENTRE PRAGMATIC RANDOMISED CONTROLLED TRIAL OF CLINICAL AND COST-EFFECTIVENESS

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Background:
There have been no adequately powered trials exploring the effectiveness of emollient bath additives in childhood eczema.

Objective(s):
The BATHE trial aimed to determine the clinical and cost-effectiveness of including emollient bath additives in the management of childhood eczema.

Materials/methods:
Participants were recruited from 96 general practices in England and Wales. Children were eligible if aged over 12 months and less than 12 years, fulfilling UK Diagnostic Criteria for Atopic Dermatitis. Children with inactive or very mild eczema (Nottingham Eczema Severity Scale 5 or less) were excluded, as were children who bathed less than once a week, or whose carers were not willing to accept randomisation. 483 were randomised and one withdrew, leaving 482 children in the trial, mean age 5 years.
The intervention group were prescribed emollient bath additives and were asked to use them regularly for 12 months. The control group were asked to use no bath additives for 12 months. Both groups continued with standard eczema management and received standardised advice on how to wash.

Results:
The primary outcome measure was eczema control assessed by Patient Oriented Eczema Measure (POEM, range 0-28) weekly for 16 weeks. Secondary outcomes included eczema severity over 1 year (4-weekly POEM); number of consultations for eczema exacerbations; Dermatitis Family Impact questionnaire; generic QoL (Child Health Utility-9D); and resource utilisation.
At least one post-baseline POEM was completed by 96.5% (465/482) of participants. Mean baseline POEM was 9.5 (s.d. 5.7) in the bath additives group and 10.1 (s.d. 5.8) in the no bath additives group. Mean POEM over the 16-week period was 7.5 (s.d. 6.0) in the bath additives group and 8.4 (6.0) in the no bath additives group. There was no statistically significant difference in weekly POEM scores between groups over 16 weeks. After controlling for baseline severity and confounders (ethnicity, topical corticosteroid use, soap substitute use) and allowing for clustering within centres and responses within participants over time, POEM scores in the no bath additives group were 0.41 points higher than in the bath additives group (95% CI -0.27 to 1.10), below the published minimal clinically important difference of 3 points. There was no difference between groups in secondary outcomes, economic outcomes or adverse effects.

Conclusion:
We found no evidence of clinical benefit from including emollient bath additives in the management of childhood eczema. Further research is needed into optimal regimens for leave-on emollient and soap substitutes for children with eczema.

Gaps in evidence
P097

THE SAFETY OF TOPICAL CORTICOSTEROIDS IN ATOPIC ECZEMA: AN OVERVIEW OF SYSTEMATIC REVIEWS

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Background:
Atopic eczema can significantly affect the quality of life of both children and adults. Topical corticosteroids were introduced in the 1950s, but incorrect use led to widespread concerns about their safety, especially when used in the longer-term. These concerns still persist amongst both patients and healthcare professionals, and can be a barrier to the use of these effective treatments.

Objective(s):
This overview aims to assess the safety of topical corticosteroids for the treatment of atopic eczema using data from published systematic reviews.

Materials/methods:
Included studies: systematic reviews of randomised controlled trials or observational studies (with a reproducible search strategy and searched at least one database); included participants of any age and gender with atopic eczema; and included a comparison of topical corticosteroids against a different strategy of using topical corticosteroids, another topical treatment, vehicle or no treatment. Outcomes include: total number of adverse events per group; non-immediate local adverse events (e.g. skin thinning); immediate local adverse events (e.g. stinging); systemic adverse events (e.g. impact on growth and development); and rebound symptoms/steroid withdrawal.
Comprehensive searches were conducted on the 24th October 2017 in five databases from inception: PubMed, MEDLINE, Embase, Cochrane Database of Systematic Reviews and Epistemonikos.

Results:
After de-duplication, 542 records were identified and screened; 113 records were eligible for full text screening and 36 systematic reviews met the inclusion criteria. The 36 systematic reviews covered a wide range of topics regarding the safety of topical corticosteroids in atopic eczema. The most commonly covered comparison was the safety of topical corticosteroids against topical calcineurin inhibitors. The next stage will be to extract safety data from each systematic review, and assess the quality of each review using the ROBIS tool. The full results will be available by March 2018.

Conclusion:
This overview of systematic reviews will provide an improved evidence base for clinicians and patients when making treatment decisions. Results will be used to develop a shared understanding tool for talking about topical corticosteroid safety in clinical practice. This work is being undertaken as part of a National Institute for Health Research-funded programme grant (RP-PG-0216-20007; Eczema Care Online (ECO)). The aims of ECO are to identify barriers and facilitators to the use of treatments for atopic eczema, and then to develop and test digital interventions (websites / apps) to support atopic eczema self-care. The results of this review will provide an evidence base which will form part of the digital interventions.

Gaps in evidence
P098

DIFFERENT POTENCIES OF TOPICAL STEROIDS FOR CHILDREN WITH ECZEMA: PROTOCOL FOR AN OBSERVATIONAL COHORT STUDY WITH EMBEDDED RANDOMIZED CONTROLLED TRIAL

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Background:
Topical corticosteroids (CS) of different potencies are the main treatment to control atopic dermatitis (AD). The Dutch GP-guideline concerning atopic dermatitis advocates a stepwise approach, in which treatment steps are tailored to the severity of the disease. The Dutch GP-guideline recommends to use a potency as low as possible which will be effective to treat the AD. When treatment is insufficient, a higher potency can be used. Whether the stepwise approach advocated in guidelines, or an initial start with a potent topical CS is more efficient is still unclear.

Objective(s):
We aim to determine whether a potent topical CS is more effective than a topical CS with low potency in the initial treatment of children with a moderate flare-up of AD in primary care in the short- and long-term control of the disease.

Materials/methods:
The Rotterdam Eczema study is an observational cohort study with an embedded pragmatic randomized controlled, open-label trial. Patients with the diagnosis AD, aged between 12 weeks and 18 years, who visited the GP for AD or received repeated prescriptions for AD in the previous 12 months are eligible for the cohort. The follow-up of the cohort will be 12 months. Patients will be enrolled in the trial if they have a flare-up of AD during follow up in the cohort. Eligible patients will be randomized in two groups, the intervention group or the GP-guideline care group. The intervention group will start with a potent CS once daily (i.e. fluticasone propionate cream 0.05% and ointment 0.005%). Patients in the GP-guideline care group will start with a low potency CS (i.e. hydrocortisone acetate 1%). The primary outcome will be the difference in the average subjective disease severity over 24 weeks follow-up in the trial, measured with the Patient Oriented Eczema Measure (POEM). The Eczema Area and Severity Index (EASI) will be measured as secondary outcome. Other secondary outcomes concerning the trial part of the study include QoL, compliance, local, and systemic side-effects, time to recovery, frequency of flare-ups, medication use and healthcare use.

Results:
Not applicable.

Conclusion:
This study will test the hypothesis that immediate treatment with a potent CS during a flare-up may lead to faster and better results as compared to starting with a CS with low potency, with eventually less overall use of CS. Besides improvements in disease-control and patients' satisfaction, this may also lead to less medical consultations and prescriptions, and may therefore be more cost-effective.

Gaps in evidence

P099

BEST EMOLLIENTS FOR ECZEMA (BEE) TRIAL PROTOCOL: A STUDY COMPARING THE CLINICAL EFFECTIVENESS AND ACCEPTABILITY OF FOUR TYPES OF EMOLLIENTS

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Background:
Emollients are used universally as part of atopic eczema (atopic dermatitis) treatment, yet there is a lack of good quality, head-to-head trials comparing their clinical effectiveness and acceptability. Consequently, clinicians take a "trial and error" approach to finding which emollient, out of the many different products available, suits the patient and their family.

Objective(s):
To compare the clinical effectiveness and acceptability of four different types of emollient (lotion, cream, gel and ointment) for the treatment of children with eczema.

Materials/methods:
BEE is a pragmatic, parallel, individually randomised, multi-centre, superiority trial with nested qualitative study. Children 6 months to 12 years with eczema (POEM>2) will be recruited via their General Practice (GP) in England. Participants must be willing to be randomised to and use their allocated emollient type as sole leave on treatment for 16 weeks; and not have any known sensitivity to the study emollients. Study emollients are all paraffin-based and do not contain antimicrobials or urea: lotions (glycerol-containing only); creams (no humectant or lanolin); gels (no povidine); and ointments (no additives). All other treatment for eczema will be as per usual care. Participants will be followed-up for 52 weeks. Data will be collected via online or paper questionnaires and GP electronic medical record review. Recruitment began in January 2018, with follow-up due to be complete by August 2020. In the nested qualitative study, semi-structured interviews will be conducted with ~20 participants in first four weeks of taking part and ~40 participants after 16 weeks. Interviews will explore acceptability and experiences of use for the assigned emollient, prior experiences and beliefs about emollient use, and elicit barriers and facilitators to use.

Results:
The primary outcome is the carer-reported POEM score, measured weekly for 16 weeks. 520 (130 per group) children will be recruited to detect a difference of 3.0 in POEM scores between any two groups with 90% power, assuming POEM SD 5.5 and 20% loss to follow-up. Secondary outcomes include: eczema signs (EASI, by masked assessor at baseline and 16 weeks), use of study emollient/other eczema treatments, satisfaction with emollient and adverse effects. Qualitative study: thematic analysis of interview data to evaluate acceptability of study emollients.

Conclusion:
The findings will provide important, much-needed information on the relative clinical effectiveness and acceptability of four types of emollients, that will directly inform prescribing of emollients for children with eczema.

Gaps in evidence

P100

TRIAL OF ECZEMA ALLERGY SCREENING TESTS (TEST) STUDY PROTOCOL: FEASIBILITY RCT WITH ECONOMIC SCOPING AND NESTED QUALITATIVE STUDY

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Background:
Because of the known association between food allergy and atopic eczema/dermatitis in children, parents often ask their doctor for allergy tests. Parental belief that food allergy is the cause of their child's eczema can be a barrier to use of effective treatments, lead to potentially harmful dietary restrictions, and result in frustration for parents and professionals. Some guidelines (e.g. NICE) suggest that food allergy testing may have a role in eczema management. However, the role of routine food allergy testing in childhood eczema is unclear, and there is little evidence available to inform such decisions.

Objective(s):
To determine the feasibility of conducting a definitive trial comparing food allergy testing and dietary advice plus usual eczema care versus usual eczema care alone.

Materials/methods:
80 children with mild-severe eczema (>3 months, <5 years) without diagnosed food allergy will be recruited from 12 GP surgeries and randomised in a 1:1 ratio to usual care or food allergy testing. The latter will comprise a structured allergy history, skin prick test (SPT) to six common food allergens (cow's milk, peanut, hen's egg, codfish, wheat & cashew), dietary advice, and oral food challenge if necessary. A standard protocol will be developed and used to determine what action is required based on the allergy test results. Participants will be followed-up for six months. In-depth qualitative interviews (n=~35) will be conducted with GPs and parents, sampled purposively by demographic/clinical characteristics and trial arm, including parents who decline trial participation. Interview data will be analysed thematically.

Results:
Key outcomes will include: recruitment and retention rates; number of negative, equivocal or positive allergy tests; adherence to dietary advice; data completeness for putative definitive trial outcomes (eczema severity, quality of life). Data on costs and outcomes will inform the feasibility of an associated cost-effectiveness study. In-depth interviews with GPs and parents and questionnaires will elicit parents' and GP's perceptions, beliefs and behaviour regarding diet, food allergies and allergy tests, and evaluate acceptability of trial procedures.

Conclusion:
At the end of this project, we will have established the feasibility and likely design of a robust full-scale RCT exploring the role of food allergy testing in the management of childhood eczema. We will also have better insight into what parents and GPs think and understand about food allergies and tests in children with eczema.

Gaps in evidence

P101

TEMPORAL VARIATION OF STAPHYLOCOCCUS AUREUS COLONIZATION AND CC-TYPES IN ATOPIC DERMATITIS - A FOLLOW UP STUDY

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Background:
A strong link between disease severity and *S. aureus* colonization of the skin has been reported in patients with atopic dermatitis (AD). In the present study temporal variations in *S. aureus* colonization and *S. aureus* CC-type is examined in AD patients, and linked to disease severity, skin barrier properties and filaggrin (*FLG)* gene mutation.

Objective(s):
Investigate temporal variations of *S. aureus* clonal type in AD patients, and relate this to disease severity, skin barrier properties and filaggrin gene mutations

Materials/methods:
A follow-up study of a cohort of 101 adult AD patients enrolled in a previous study, recruited from an outpatient clinic, and followed up after 1.5-4 years. Bacterial swabs were taken from lesional skin, non-lesional skin and nose. Swabs positive for *S. aureus* were characterized by *spa* and the respective clonal complex (CC) type assigned. Patients were characterized with respect to disease severity (SCORAD), skin barrier assessment (TEWL, pH) and *FLG* gene mutations.

Results:
A total of 63 patients participated in the follow-up study. Thirty-four patients (54.0%) were colonized in one or more sites at follow-up. Twenty-seven patients (42.9%) were colonized at both visits, 27 were colonized only at one visit and 9 patients (14.3%) were not colonized at either visit. Patients carrying a *FLG* gene mutation were more frequently colonized with *S. aureus* (p=0.05). Temporal variation in *S. aureus* CC-type of patients colonized at both visits showed that 14 carried identical CC-type at baseline and follow-up, whereas 11 had a different CC-type. Mean SCORAD was 47.4 in patients who changed CC-type compared to 30.3 in patients who did not (p=0.03). Patients who changed CC-type had an increase in SCORAD of 10.7 from baseline visit (36.7) to follow-up visit (47.4)

compared to patients who carried the same CC-type who had a reduction in SCORAD of 4.4 from 34.7 at baseline to 30.3 at follow-up.

Conclusion:
Data supports previous findings that *S. aureus* colonization is associated with *FLG* mutations, and indicates that change in CC-type is linked to flares of the disease.

Gaps in evidence

P102

INTERVENTIONS TO REDUCE STAPHYLOCOCCUS AUREUS IN THE MANAGEMENT OF ATOPIC ECZEMA: A COCHRANE SYSTEMATIC REVIEW

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Background:
Staphylococcus aureus can cause secondary infection in atopic eczema, and may promote inflammation in eczema that does not look infected. It is unclear whether antimicrobial treatments help eczema or promote bacterial resistance. We undertook an update of a Cochrane review first published in 2008.

Objective(s):
To assess the effects of interventions to reduce *S. aureus* for treating infected or uninfected atopic eczema.

Materials/methods:
We updated our searches of the following databases to April 2017: Cochrane Skin Group Specialised Register, CENTRAL, MEDLINE, Embase and LILACS. We searched trials registers, conference proceedings, and checked reference lists of trials and reviews. Randomised controlled trials of people with atopic eczema treated with a product intended to reduce *S. aureus* on the skin were eligible. Two people independently performed the study selection, data abstraction and assessed risk of bias.

Results:
We included 39 studies (18 new) with 1740 participants, covering nine treatment categories: oral antibiotic; topical antiseptic/antibiotic; topical steroid plus antiseptic/antibiotic; topical steroid plus antibiotic and antifungal; antibacterial soap; antibacterial bath additive (e.g. bleach baths); antibacterial bath additive plus antibiotic; textiles (e.g. silver-impregnated clothing); protease inhibitor. Quality of reporting was generally poor. High risk of bias for blinding, incomplete outcome data and selective reporting occurred in 25% of studies.
We pooled results for one comparison: topical steroid plus antibiotic compared with topical steroid alone (10 studies). The three studies (one in clinically infected eczema, two unspecified) that reported global degree of improvement in signs and symptoms showed a very small improvement in the steroid/antibiotic group compared with steroid alone (risk ratio [RR] for a good or excellent outcome 1.10, 95% confidence interval [CI] 1.00 to 1.21). No studies reported quality of life. Rates of adverse events requiring treatment withdrawal were low, resulting in considerable uncertainty (RR 0.49, 95% CI 0.09 to 2.78, three studies). There was a significant reduction in minor adverse events in the steroid/antibiotic group compared with steroid alone (RR 0.34, 95% CI 0.15 to 0.77) which was very different in the two studies reporting this outcome. No studies reported antibiotic resistance.
The one high-quality study comparing both oral and topical antibiotics versus placebo in children with clinically infected eczema showed no clinically useful benefit.

Conclusion:
We did not find any good evidence to support the use of interventions to reduce *S. aureus* for infected or uninfected eczema. High-quality trials including evaluation of quality of life and antibiotic resistance are required.

Gaps in evidence
P103

PROGNOSIS OF PRESCHOOL ECZEMA AND FACTORS OF IMPORTANCE FOR REMISSION
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Background:
Information on important factors for eczema remission is scarce.

Objective(s):
We aimed to explore the course of preschool eczema from birth to age 16 years, to identify factors related to the remission of preschool eczema, and to explore whether or not prognostic models could be useful to predict the remission of preschool eczema.

Materials/methods:
This study among 889 children with preschool eczema (eczema at 1, 2, and/or 4 years) was performed in a population-based cohort from birth until age 16 years. Information on background factors and eczema was obtained from regular questionnaires. Information on IgE sensitization at age 4 years and filaggrin mutations (R501X, R2447X, 2282del4) were available for a subset of children (n=671 and n=764, respectively).

Results:
Half of the children (51%) were in complete remission by school age (i.e. no eczema at age 8, 12, or 16 years), and by age 16 years 82% were in remission. In multivariate prognostic models, persistent preschool eczema (eczema at 1, 2, and 4 years) (odds ratio 0.27 [95% confidence interval 0.18-0.41]), preschool eczema with sleep disturbance due to itch (0.59 [0.43-0.81]), parental allergy (0.73 [0.55-0.96]), parental smoking at child's birth (0.70 [0.50-0.99]) and filaggrin mutation (0.47 [0.26-0.85]) were inversely associated with complete remission by school age. Male sex (1.37 [1.03-1.82]) and exclusive breastfeeding ≥ 4 months (1.44 [1.01-2.05]) were positively associated with complete remission by school age. The prognostic models developed had correct classification rates of 63-65%.

Conclusion:
Half of the children with preschool eczema were in complete remission by school age. The most important prognostic factors were persistent preschool eczema and preschool eczema with sleep disturbance due to itch. Both these factors were inversely associated with complete remission by school age. The prognostic models created could only predict 63% of cases with complete remission of PSE by school age, indicating that additional factors contribute to the prognosis. Therefore, future studies should focus on identifying such factors.

Gaps in evidence
P104

THE PREVALENCE OF ATOPIC ECZEMA ACROSS THE LIFESPAN: A UK POPULATION-BASED COHORT STUDY
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Background:
Atopic eczema (also known as atopic dermatitis or eczema) has been widely studied in childhood, but little is known about adult disease. Although traditionally characterized as a skin condition that remits in most children by

adolescence, increasing genetic and epidemiologic evidence suggest it may be better characterized as an episodic systemic inflammatory disorder that also occurs in adulthood.

Objective(s):
To estimate the age-specific prevalence of active atopic eczema and examine how it varies by demographic factors.

Materials/methods:
Longitudinal cohort study using data from The Health Information Network (THIN), a primary care electronic medical record database that is representative of the general population in the United Kingdom. The main outcome measure was active atopic eczema prevalence by age. All individuals who met a previously validated definition of atopic eczema (at least one of five diagnosis codes and at least two treatment codes) and had acceptable records in THIN between 1994 and 2013 were identified. For the primary analysis, an individual was considered to have active disease if he/she had at least one eczema-associated code (either a diagnosis or treatment code) in any given year based on chronologic age.

Results:
There were 848,435 individuals (9.86%) who ever received a code for atopic eczema. The prevalence of active eczema by age followed a u-shaped curve: it was highest in childhood (7% at ages 0-17), declined to 3% in adulthood (ages 18-74), and increased in older age (8% ages 75+). Overall, eczema was more common among females and those of higher social class, but the relative prevalence differed by age: active disease was more common among males than females over age 75, and more common among those of lower social class in mid-adulthood. The distribution among those who live rural and urban areas was similar at all ages.

Conclusion:
The prevalence of active physician-diagnosed eczema is highest during infancy and older age. Additional research is needed to characterize the natural history of the disease over the life course and understand disease etiology in older individuals.

Gaps in evidence

P105

ASSESMENT OF STRATUM CORNEUM THICKNESS AFTER TAPE STRIPPING BY CONFOCAL LASER SCANNING MICROSCOPY

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Background:
Tape stripping poses a minimal-invasive alternative to skin biopsies for assessment of cutaneous biomarkers in inflammatory skin diseases. It is generally assumed that stratum corneum is removed after 30-40 consecutive tape strips, however literature on this aspect is scarce.

Objective(s):
This explorative study aimed to determine the advancement into stratum corneum after 5, 15 and 35 consecutive tape strips in skin from healthy volunteers and patients with atopic dermatitis.

Materials/methods:
The study included 10 healthy volunteers and 4 patients with atopic dermatitis. D-squame tape strips were used, and 5, 15 and 35 consecutive tape strips were taken from the middle volar forearm (non-lesional skin). Each tape was pressed against the skin for 10 seconds using standardized pressure with D-squame pressurizer. Confocal laser scanning microscopy (CLSM) was performed at each location to assess the remaining thickness of epidermis. Transepidermal water loss (TEWL) was measured before and after 35 tape strips. The total amount of protein removed was assessed by scanning each tape with Squame Scan.

Results:
Visually evaluated by CLSM, stratum corneum was completely removed after 35 tape strips in all participants. A significant decrease in epidermal thickness and a significant increase in TEWL was found after 35 tape strips ($p=0.001$ and $p=0.002$). For normal skin the average decrease in epidermal thickness was 6.4 µm after 5 tape strips,

14.2 µm after 15 tape strips and 18.6 µm after 35 tape strips. The corresponding values for AD-skin were 5.6 µm, 11.2 µm and 16.6 µm. The total amount of protein removed after 35 tapes was 288 µg/cm^2 for healthy volunteers and 487.9 µg/cm^2 for patients with atopic dermatitis. There was no marked correlation between decrease in epidermal thickness and amount of protein removed.

Conclusion:
Stratum corneum was completely removed after 35 tape strips in all participants. The epidermal thickness was significantly decreased and TEWL was significantly increased after 35 tape strips. These results contribute with important information on the tape stripping method relevant for skin barrier research.

Gaps in evidence

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IS DRY SKIN IN INFANTS 3 MONTHS OF AGE ASSOCIATED WITH AN INCREASED TRANSEPIDERMAL WATER LOSS?

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Background:
Dry skin is often a forerunner for atopic dermatitis (AD), which is associated with impaired skin barrier, which in turn may be measured objectively by increased transepidermal water loss (TEWL). High TEWL levels are reported to precede and possibly predict the development of AD, but it is not known if TEWL is increased with clinical signs of dry skin in infants.

Objective(s):
To assess if dry skin is associated with increased TEWL in infants, 3 months old, in a general population. If TEWL is increased, early clinical detection of dry skin could be an easy way of selecting children for primary prevention with emollients and/or bath-oil.

Materials/methods:
The Preventing Atopic Dermatitis and Allergies in children (PreventADALL) study enrolled 2697 women (2701 pregnancies), with their last baby enrolled April 11th 2017, and 2397 newborn children were randomized to one of the following four groups in a 2 by 2 factorial design: 1. Observation only, 2. Early allergenic food introduction, 3. Skin barrier therapy or 4. Early allergenic food introduction and skin barrier therapy. In the present study we included the 1143/1239 infants in groups 1 and 2 that attended the 3-month follow-up when the skin was examined for dryness, AD and other exanthemas. TEWL was measured using an open chamber system with recording of humidity and temperature.

Results:
The included infants (46.6% girls), mean (CI) age 93.3 days (92.8, 93.8) measured a mean length of 61.9 cm (61.8, 62.0) and a mean weight of 6.3 kg (6.2, 6.3). TEWL measurements were completed in 1075 (94%) infants, out of whom 135 infants had signs of AD (12.6%), 504 (46.8%) had dry skin without signs of AD, and 436 (40.6%) infants had neither AD nor dry skin on skin examination. The mean TEWL (measured in g/m2/h) in children with signs of AD was 12.3 (10.9, 13.8), in children with dry skin 7.6 (7.1, 8.0) and in those with neither 6.7 (6.3, 7.0) ($p < 0.0001$, between all three groups).

Conclusion:
Three months old infants with dry skin had increased TEWL, significantly higher than infants without dry skin, but significantly lower than infants with signs of AD as found in a general population. This finding may help selecting infants, which may benefit the most from primary prevention of AD by emollients and/or bath-oil.