1 – BRITT VAN DER LEEDEN
DEVELOPMENT AND CHARACTERIZATION OF A RECONSTRUCTED HUMAN SKIN BURN WOUND MODEL

Britt van der Leeden[1,2], H. Ibrahim Korkmaz[3,4,6,7], Sanne Roffel[10], Bouke K.H.L. Boekema[3,7], Chopie Hassan[5], Paul P.M. van Zuijlen[6,7], Hans W.M. Niessen[1,8,9], Paul A.J. Krijnen[1,9], Susan Gibbs[4,10]

[1]Department of Pathology, Amsterdam University Medical Centers (AUMC), Amsterdam; [2]Amsterdam Infection & Immunity, AUMC, Amsterdam; [3]Burn research lab, Alliance of Dutch Burn Care, Beverwijk; [4]Department of Molecular Cell Biology and Immunology, AUMC; [5]Pharming Technologies B.V., Leiden; [6]Alliance of Dutch Burn Care, Burn Center, Red Cross Hospital, Beverwijk; [7]Department of Plastic, Reconstructive and Hand Surgery, AUMC, Amsterdam; [8]Department of Cardiac Surgery, AUMC, Amsterdam; [9]Amsterdam Cardiovascular Sciences, AUMC, Amsterdam; [10]Department of Oral Cell Biology, Academic Centre for Dentistry, Amsterdam, The Netherlands.

Background Burn wound healing and deepening involve complex mechanisms that are not yet fully understood, necessitating human-based models for further research.
Objectives We aimed to develop an *in vitro* burn wound model, replicating partial-thickness and deeps burns in a three-dimensional (3D) reconstructed human skin (RhS) model to observe wound healing over time.
Methods Standard tissue engineered RhS consisting of human cell populated epidermal and dermal compartments, were used to mimic the human skin *in vitro*. Burn wounds were applied using a soldering iron at 70˚C, 110˚C or 140˚C for 30 seconds. RhS samples were analyzed on days 1, 3 and 7 post-burn using (immuno)histochemistry for wound depth (hematoxylin and eosin staining), activation (vimentin, fibroblast activating protein (FAP)), myofibroblasts (α-smooth muscle actin (α-SMA)) and cell proliferation (Ki67). Secretion of Neutrophil gelatinase-associated lipocalin (NGAL), matrix metalloprotease (MMP) 9, Serum Amyloid A (SAA), and Intercellular Adhesion Molecule 1 (ICAM-1) was measured using ELISA.
Results RhS with 70˚C burn injury showed no tissue damage, while 110˚C and 140˚C burns indicated re-epithelialization within one week. Vimentin staining showed a scarcely populated dermal wound edge, indicative for post-burn fibroblast migration. FAP stained in the lower dermal wound edge showing more papillary fibroblasts. One-week post-burn, fibroblast proliferation (Ki67) and myofibroblast (α-SMA) differentiation in the wound edge was observed. Significantly increased levels of secreted MMP-9, ICAM-1, and NGAL were found in burned RhS compared to control.
Conclusion We successfully generated an *in vitro* human burn wound model mimicking different burn depths with concurrent wound healing properties, that will serve as a basis to study burn wound deepening.

2 – JOLIENE WICHERS SCHREUR
DEVELOPMENT OF HUMAN SKIN EQUIVALENTS REPRESENTING CUTANEOUS T-CELL LYMPHOMA

Joliene H. Wichers Schreur[1], Marion H. Rietveld[1], Sanne de Haan[1], Koen D. Quint[1], Robert Rissmann[1-3], Maarten H. Vermeer[1], Abdoelwaheb El Ghalbzouri[1]

[1]Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; [2]Centre for Human Drug Research, Leiden, The Netherlands; [3]Leiden Academic Centre for Drug Research, Leiden, The Netherlands.

Background Cutaneous T-cell lymphomas (CTCL) are non-Hodgkin lymphomas from skin-homing CD4+ T-cells. The most common subtypes of CTCL are mycosis fungoides (MF) and Sézary syndrome (SS), representing around 60%-80% and less than 10% of all CTCL cases. In early-stage disease, lesional skin of CTCL often resemble chronic inflammatory dermatoses. Pathogenesis and pathophysiology of CTCL is not fully understood and a curative treatment option is not yet available. Human skin equivalents (HSEs) could help to better understand CTCL in order to improve disease stratification and to develop innovative targeted therapies.
Objective This study aims to develop HSEs that mimic key characteristics of CTCL by incorporating CTCL T-cell lines and cytokines, with a focus on investigating their effects on epidermal morphogenesis and T-cell behavior.
Methods We generated multiple types of HSEs using CTCL T-cell lines and relevant cytokines. Epidermal morphogenesis and T-cell dynamics were assessed in both epidermal and full-thickness models (FTM).
Results Morphological analysis showed the presence of a well-formed epidermis harboring all viable layers. In full-thickness model (FTM), T-cells formed clusters in the dermal matrix. T-cells were positive for CD4+, and exhibited both proliferation and caspase activity.
Conclusion FTMs displayed optimal epidermal morphology that closely mimics the characteristics of CTCL Further in-depth analysis is ongoing to validate the functional role of CTCL T-cell lines within these models.

3 – LUCA MEESTERS
IPSC-DERIVED KERATINOCYTE MODELS FOR IN VITRO ATOPIC DERMATITIS RESEARCH

Luca D. Meesters[1,2], Wietske Kieboom[2], Ivonne van Vlijmen-Willems[1], Diana Rodijk-Olthuis[1], Yavuz Kilic[2], Dulce Lima Cunha[2], Hanna Niehues[1], Ellen H. van den Bogaard[1] and Huiqing Zhou[2,3]

[1]Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; [2]Department of Molecular Developmental Biology, Faculty of Science, Radboud University, Nijmegen, The Netherlands; [3]Department of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands.

Background Induced pluripotent stem cells (iPSC) can be derived from patients or be genome-edited to introduce or correct disease-related genetic variants, and subsequently

be differentiated into any skin cell type. Yet, the potential of induced keratinocytes (iKC) derived from iPSC has not been explored to model AD, partially because iKC are still considered immature as compared to primary keratinocytes (pKC).
Objective To improve the culture and maturation of iKC and investigate their utility for epidermal differentiation studies and AD modeling.
Methods iPSC were differentiated using RA and BMP-4, stimulated at various passages with fetal bovine serum (FBS) and AD cytokine cocktail IL-4, IL-13 and IL-22. iKC were analyzed by morphology, gene and protein expression.
Results Single cell RNA sequencing of iKC revealed different cell populations in the iKC culture but indicated cell surface markers to enrich for keratinocyte-like cells. iKC appeared immature as compared to pKC (e.g., lower KRT14) but showed flattened morphology and increased IVL transcription upon FBS stimulation, which is typical for epidermal differentiation. Air exposure also induced 3D epidermal differentiation, including KRT10 expression. The AD cytokine cocktail reduced KRT1 and IVL expression in iKC mimicking epidermis defects in AD. Cell culture optimization by iKC passaging significantly enhanced KRT14 expression, reaching similar levels as pKC, while maintaining the cobblestone keratinocyte morphology.
Conclusion High passage iKC show promise for epidermal differentiation in 2D and 3D culture systems, and can be used to model inflammation-related epidermal differentiation defects. This improved cell source facilitates patient-derived skin tissue modeling in translational research.

4 – KIM SCHILDERS
GENERATION OF FULL SKIN CONSTRUCTS FROM HAIR FOLLICLE STEM CELLS

K.A.A. Schilders[1], S. Jekhmane[1,2], M. Vlig[1], A. Elgersma[1], L. Hazenkamp[3], C.G. Gho[3], M. Middelkoop[1,2,4], B.K.H.L. Boekema[1,2,4]
[1]Alliance of Dutch Burn Care, Burn Research Lab, Beverwijk, The Netherlands; [2]Department of Plastic, Reconstructive & Hand Surgery, Amsterdam University Medical Centre, Amsterdam, The Netherlands; [3]Hair Science Institute, Amsterdam, The Netherlands; [4]Amsterdam Movement Sciences, Amsterdam University Medical Centre, Amsterdam, The Netherlands.

Background Hair follicles (HF) are often lost in deep wounds and current treatments cannot restore them, impacting both skin function and patient well-being. HF contain epidermal and dermal stem cells involved in both hair regeneration and wound healing. Previous studies in animal models have shown that HF-derived stem cells can restore hair growth.
Objective We aim to develop full skin equivalents (FSEs) from HF-derived stem cells, capable of regenerating hair for human therapeutic applications.
Methods Dermal papilla (DPC), bulge stem (BSC), and dermal sheath cells (DSC) were isolated from human hair grafts and characterized using flow cytometry. DPC were cultured in a 3D environment to maintain their hair-inductive properties. BSC and DSC were seeded onto a collagen scaffold and cultured for three weeks to create full FSEs and analyzed by immunohistochemistry.
Results Flow cytometry confirmed that most DPC, BSC and DSC expressed CD71, indicating proliferation. Further analysis identified distinct subpopulations of these cells expressing markers such as CD90, CD29, CD73, CD49f, and CD200, suggesting multipotency. 3D cultures of DPC showed that cell passage is a critical factor in spheroid formation since cells above passage 5 resulted in smaller and less uniform spheroids. It was possible to generate FSEs from HF-derived cells but significant contraction was observed in contrast to skin derived FSEs.
Conclusion Reproducible protocols were developed for isolating and culturing HF-derived cells, which expressed multiple stem cell markers. These cells were used to create skin equivalents, now under evaluation for their regenerative potential in wound healing therapies.

5 – JONAS JÄGER
TOWARDS NEXT GENERATION RECONSTRUCTED HUMAN SKIN: MONOCYTE PERFUSION OF A VASCULARIZED DERMIS IN A MULTI-ORGAN-CHIP

Jonas Jäger[1,2], Phil Berger[3], Andrew I. Morrison[1,2], Hendrik Erfurth[3], Maria Thon[1,2], Eva-Maria Dehne[3], Susan Gibbs[1,2,4], Jasper J. Koning[1,2]
[1]Amsterdam UMC location Vrije Universiteit Amsterdam, Department of Molecular Cell Biology and Immunology, Amsterdam, The Netherlands; [2]Amsterdam institute for Infection and Immunity, Inflammatory diseases, Amsterdam, The Netherlands; [3]TissUse GmbH, Berlin, Germany; [4]Department of Oral Cell Biology, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit, Amsterdam, The Netherlands.

Background Skin vasculature plays an essential role in wound healing, drug delivery, toxicological and immunological studies. However, due to its complexity to generate and the necessity to combine it with perfusion, it is mostly disregarded in current *in vitro* skin models.
Objective To generate a healthy and diseased vascularized dermis in a multi-organ-chip (MOC) for the perfusion of monocytes.
Methods A 3D-printed, water dissolvable structure was incorporated inside a MOC to generate hollow channels in a collagen/fibrin fibroblast-populated hydrogel. The channels were seeded with dermal endothelial cells (ECs) to generate an endothelium which was perfused with monocytes for 24 hours. The vascularized dermis was characterized structurally by immunocytochemistry and functionally for barrier integrity and immune cell transmigration/differentiation.
Results A vascularized, perfusable dermis in a MOC platform was created. Angiogenic sprouting, angiogenesis-associated cytokine secretion and fibroblast morphology was influenced by the collagen/fibrinogen hydrogel composition, resembling characteristics of healthy or early granulation tissue.
EC vessels with dermal fibroblasts remained viable and metabolically active in the chip for up to 7 days. Perfusion of monocytes showed transmigration across the endothelium

into the hydrogel and differentiation into (predominantly M2) macrophages within 24 hours.
Conclusion As a first step towards immune-competent skin models, a method to construct a monocyte-perfused vascularized dermis in a MOC is presented. In the future, after addition of an epidermis, this can serve as the basis to build the next generation of vascularized reconstructed human skin and opens exciting new possibilities to study human skin in health and disease.

6 – FENNA DE BIE
FLOW CYTOMETRY OF SKIN BIOPSIES IN CTCL PATIENTS DURING MOGAMULIZUMAB TREATMENT

Fenna J. de Bie, Alita J. van der Sluijs-Gelling, Safa Najidh, Cornelis P. Tensen, Maarten H. Vermeer
Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands.

Background Cutaneous T-cell Lymphomas (CTCL) represent a group of mature T-cell-derived lymphomas. Mogamulizumab (Moga), a therapeutic monoclonal antibody against CCR4, is a novel treatment for CTCL patients with advanced disease. Detection and characterization of skin-resident tumor cells and tumor microenvironment and their correlation with circulating tumor cells during treatment of Moga has not yet been described.
Objective Our goal was to develop a method enabling detection and immunophenotypic characterization of leucocytes from skin biopsies and correlate findings with circulating tumor cells during Moga treatment.
Methods 29 skin biopsies and matched blood of 12 patients were assessed using flowcytometry. Skin biopsies were dissociated and the single cell suspensions were stained with 15 cell surface markers and a viability stain. At the same time, blood was drawn from patients and an overlapping 12 surface makers were assessed.
Results Skin biopsies before treatment showed tumor cells in 7/8 cases. Follow up biopsies showed tumor cells in 7 patients, while tumor cells had disappeared completely in 5 patients. The immunophenotype of tumor cells in skin with circulating tumor cells found that 80% of the samples had a consistent immunophenotype between blood and skin. Over time the phenotype of the tumor cells in skin did not change. Analysis of the tumor microenvironment is still ongoing.
Conclusion We can characterize, quantify, and monitor tumor cells and the tumor microenvironment in both skin and blood of CTCL patients. Under the pressure of Mogamulizumab therapy the phenotype of skin resident tumor cells in CTCL patients does not change.

7 – AHMED ELFIKY
IMPACT OF DUPILUMAB AND UPADACITINIB TREATMENT ON EPIGENETIC AND TRANSCRIPTOMIC ALTERATIONS IN SKIN-HOMING T CELLS OF ATOPIC DERMATITIS PATIENTS

Ahmed M.I. Elfiky[1,2,3], Hidde M. Smits[1], Marlot van der Wal[1], Coco Dekkers[2], Celeste M. Boesjes[2], Marlies de Graaf[2], Julia Drylewicz[1], Marjolein de Bruin-Weller[2#], Femke van Wijk[1#]
[1]Center for Translational Immunology, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands; [2]Department of Dermatology and Allergology, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands; [3]Regenerative Medicine Center Utrecht, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands. [#]Authors share joint senior authorship.

Background IL-4 receptor alpha blocker dupilumab, and Janus kinase (JAK) inhibitors like upadacitinib, have revolutionized the management of atopic dermatitis (AD). However, prolonged treatment is necessary to sustain disease remission. While both therapies are clinically effective, only dupilumab has demonstrated successful dose reduction, suggesting potential disease-modifying effects.
Objective Investigate the immune-modulating potential of prolonged dupilumab and upadacitinib treatment on the epigenetic and transcriptomic profiles of skin-homing T cells in AD.
Methods Using flow cytometry, CD4+CLA+ T cells were isolated from AD patients (n=12) at baseline and after 52 weeks of dupilumab (n=6) or upadacitinib (n=6) treatment. DNA methylome, RNA transcriptome, and cytokines expression analyses were conducted using the EPIC array, RNA sequencing and flow cytometry, respectively. Non-atopic healthy controls (HC) (n=6) were included.
Results Our analyses identified 303 significant differentially methylated regions (DMRs) between HC and AD patients, involving pathways like cytokine-cytokine receptor interactions, NF-kB, and T cell receptor signaling. Some of these DMRs were associated with corresponding changes in the transcriptome. Following treatment, dupilumab corrected 6 AD-related DMRs towards the HC profile. Conversely, upadacitinib modulated 40 AD-related DMRs, with the majority further aligning with the AD profile. Intriguingly, we identified 241 DMRs and 13 DMRs modulated in response to upadacitinib and dupilumab, respectively, independent of AD-related DMRs, suggesting a broader impact of upadacitinib on the epigenome.
Conclusion Our findings demonstrate distinct effects of dupilumab and upadacitinib treatment at the epigenetic level. The differences in the direction and extent of modification between treatments may have clinical implications upon therapy discontinuation.

8 – EMMA HOLTAPPELS
IDENTIFYING BIOLOGICAL PROCESSES INVOLVED IN CLINICAL RESPONSE TO TREATMENT IN THE AUTOIMMUNE DISEASE VITILIGO USING PROTEOMICS

Emma Holtappels[1], Wouter Ouwerkerk[1,2], Martin A. Schneider[3], Rasmus B. Kjellerup[3], Marcel W. Bekkenk[1,4], Albert Wolkerstorfer[1], Rosalie M. Luiten[1]
[1]Amsterdam University Medical Center, Department of Dermatology, Netherlands Institute for Pigment Disorders, University of Amsterdam, Amsterdam Institute for Infection

and Immunity, The Netherlands; [2]National Heart Centre Singapore, Hospital Drive, Singapore; [3]Novartis Institutes for BioMedical Research, Basel, Switzerland; [4]VU University Amsterdam, The Netherlands.

Background Vitiligo is an autoimmune disease characterized by depigmented lesions, caused by autoreactive CD8-T-cells inducing melanocyte apoptosis. Treating vitiligo remains a challenge, as the processes involved in repigmentation are still poorly understood.
Objective The aim of this study was to identify the biological processes involved in the response to vitiligo treatment, using large proteomic screening panels.
Methods This prospective exploratory study was done by analyzing blood plasma and blister fluid samples from a cohort of 30 vitiligo patients starting standard-of-care treatment. We performed a large proteomic screen (5080 proteins) using Somascan/Soma logics in blister fluid and blood plasma collected at baseline and after treatment. We performed over-representation analyses for the significant proteins.
Results 61 proteins were significantly differentially expressed at baseline in lesional vs non-lesional blister fluid, however, none were associated with repigmentation. Analyses of baseline and changes during therapy yielded 6 proteins associated with repigmentation. A higher expression of TIM-1, TFF3 and NLRP1 in blister fluid at baseline and a higher expression of KRT5 in plasma after treatment, are associated with more repigmentation. Pathways involved in the differences between lesional and non-lesional blister were associated with melanocytic-specific pathways, whereas the NLRP1-inflammasome was involved in repigmentation.
Conclusion Several proteins and biological processes were found to be associated with repigmentation, of which most were related to the NLRP1-inflammasome. Proteomic differences expressed at baseline between lesional and non-lesional skin were not associated with a repigmentation. This suggests that skin repigmentation in vitiligo involves other processes than directly reverting the lesional towards non-lesional skin.

9 – NICOLINE VAN BUCHEM
THE POTENTIAL ROLE OF TRAINED IMMUNITY IN THE PATHOGENESIS OF AUTOIMMUNE VITILIGO

N.F. van Buchem-Post[1], N.O.P. van Uden[1], W. Ouwerkerk[1], W.J. Bakker[1], R. Peters[1], A.Wolkerstorfer[1], M.G. Netea[2], M.W. Bekkenk[1], R.M. Luiten[1]
[1]Department of Dermatology, Amsterdam University Medical Center, Amsterdam, The Netherlands; [2]Department of Internal Medicine and Radboud Center for Infectious Diseases, Radboud University Medical Center, Nijmegen, The Netherlands.

Background Vitiligo is an autoimmunity against melanocytes, caused by an interaction between genetic susceptibility and environmental factors. Adaptive immune responses are found in vitiligo patients, as well as innate immune activation. Long-term increase in innate memory function, known as trained immunity, has been described in inflammatory diseases. Moreover, two monocyte or macrophage phenotypes have been characterized in trained immunity: the inflammatory MCI phenotype producing cytokines and the MC phenotype predominantly producing chemokines.
Objective Trained immunity might play a role as an enhancer and trigger in the pathogenesis of vitiligo, by reported increased IL-1b, IL-6 and IL-8 production in vitiligo, associated with the NLRP1 haplotype. We investigated the potential role of trained immunity in vitiligo.
Methods We analyzed the pro-inflammatory cytokine production by monocytes of 30 vitiligo patients, upon stimulation with LPS or Pam3Cys *in vitro*.
Results We found significantly lower IL-1b cytokine production by monocytes of vitiligo patients than healthy controls (n=30). This difference was found in patients independent of their NLRP1 haplotype. Stratification of healthy donors on NLRP1 haplotype did not show significant differences in cytokine production, which was confirmed in an independent cohort of 500 NLRP1 haplotyped healthy donors.
Conclusion Our data of decreased IL-1b in vitiligo thereby contradict published data. Further analysis of the MC and MCI macrophage signatures associated with trained immunity in scRNAseq datasets of vitiligo skin, also revealed lower cytokine expression, but increased chemokine expression. Together these findings point towards the presence of the MC phenotype of monocytes/macrophages that are associated with trained immunity.

10 – ALEX ROOKER
VITILIGO-ASSOCIATED BYSTANDER LYSIS IN BASAL CELL CARCINOMA

Alex Rooker, Nathalie O.P. van Uden, Rosalie M. Luiten, Walbert J. Bakker
Department of Dermatology and Netherlands Institute for Pigment Disorders, Amsterdam Infection & Immunity Institute, Amsterdam University Medical Centers, University of Amsterdam, Cancer Center Amsterdam, Amsterdam, The Netherlands.

Background Vitiligo is an autoimmune disorder characterized by T-cell mediated destruction of melanocytes, resulting in skin depigmentation. Lighter skin types are associated with a higher risk for skin cancer. However, in a previous meta-analysis the prevalence of non-melanoma skin cancer in vitiligo patients was decreased compared to healthy controls.
Objective The aim of this study is to investigate how vitiligo autoimmune reactions can combat basal cell carcinoma (BCC). As BCCs are populated with melanocytes, we hypothesize that vitiligo T-cells target melanocytes in BCCs and induce bystander lysis of adjacent BCC cells via T-cell-secreted IFNγ.
Methods HaCaT keratinocytes were exposed to IFNγ to assess their sensitivity. Next, HaCaT and MELakr melanoma cells were co-cultured with either melanoma-specific or control CD8+ T-cells, and cell viability was assessed. Additionally, HaCaT cells were preincubated with IFNγ and co-cultured with PBMCs to evaluate if IFNγ exposure increased their

susceptibility for killing.
Results HaCaT cells demonstrated sensitivity to IFNγ by increased levels of caspase-3 and CXCL9,10 and 11. Co-incubation with MELakr cells and CTLakr CD8+ T-cells resulted in increased levels of active caspase-3 in HaCat cells compared to co-incubation with control CD8+ T-cells. Furthermore, pre-incubation with IFNγ rendered HaCaT cells more susceptible to apoptosis when exposed to PBMCs.
Conclusion Our preliminary findings suggest that bystander keratinocytes can undergo apoptosis even when not directly targeted, potentially explaining the lower incidence of BCCs in vitiligo patients. Future studies will investigate if vitiligo induction in BCC mice models could inhibit or even stop BCC growth.

11 – ALESHA LOUIS
THE HUMAN SKIN MICROBIOME AND PHYSICAL BARRIER INTEGRITY IN AGING

Alesha Louis[1], Marion H. Rietveld[1], Bep Schonkeren-Ravensbergen[2], Catherine Mergen[3], Rym Halkoum[4], Gaëlle Gendronneau[4] and Abdoelwaheb El Ghalbzouri[1]
[1]Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; [2]Department of Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands; [3]Leiden Academic Centre for Drug Research/Drug Delivery Technology, Leiden University, Leiden, The Netherlands; [4]Chanel Parfums Beauté, Skin Biology Laboratory, Chanel Fragrance & Beauty, Paris, France.

Background Human dermis is separated into the papillary (Pfs) layer and the reticular (Rfs) layer. Human skin equivalents (HSEs) generated with Pfs or Rfs show that they have dissimilar effects on epidermal morphogenesis, and age-related modifications of the skin. Further, three microbial strains (*S. epidermidis*, *C. acnes*, *C. kroppenstedtii*) are found to be associated with skin aging. We question whether Pfs and Rfs have distinct roles in skin barrier organization and to what extent the aged skin microbiome interacts with the skin barrier.
Objective We aim to elucidate the role of Pfs and Rfs on the skin barrier structure and function and study the interaction between the skin microbiome and the lipidic barrier during aging
Methods We generated multiple types of HSEs using either Pfs or Rfs and inoculated them with a mixture of 3 major microbial strains. We studied both skin barrier organization and epidermal morphogenesis.
Results Pf-HSEs demonstrated an enhanced epidermal and dermal structure compared to Rf-HSEs, as is shown by a fully differentiated epidermal layer, upregulated expression of barrier-related markers and an uniform fibroblast orientation. Barrier organization is improved in Pf-HSEs. HSEs inoculated with the three bacterial strains showed improved epidermal morphology and distinct expression patterns of epidermal and barrier-related markers.
Conclusion Our study reveals distinct effects of Pfs and Rfs on barrier structure, and the potential influence of the skin microbiome herein, shedding light on lipidic barrier formation during skin aging. Further investigation is warranted to validate their role in the aging process of the skin.

12 – SARA MARCHISIO
EVALUATION OF CD39, CD73, AND CD38 AS POTENTIAL BIOMARKERS FOR MONITORING MOGAMULIZUMAB RESPONSE IN SÉZARY SYNDROME

S. Marchisio[1], Y. Yakymiv[1], L. Lin[1], E. Ortolan[1], G. Roccuzzo[2], F.J. de Bie[3], L. Marega[2], F.A. Scheeren[3], A. El Ghalbzouri[3], C.P. Tensen[3], M.H. Vermeer[3], P. Quaglino[2], A. Funaro[1]
[1]Laboratory of Immunogenetics, Department of Medical Sciences, University of Turin, Turin, Italy; [2]Dermatology Unit, Department of Medical Sciences, University of Turin, Turin, Italy; [3]Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands.

Background Recently, we demonstrated aberrant expression of CD39, CD73 and CD38 ectoenzymes levels on circulating and skin-homing CD4+ T-cells from patients with Sézary Syndrome (SS), an aggressive cutaneous T-cell lymphoma. The anti-CCR4 monoclonal antibody Mogamulizumab (Moga) increased progression-free survival in SS, though patients still ultimately progress.
Objective To explore novel biomarkers for monitoring SS, we monitored the expression of these ectoenzymes in circulating T-cells from 12 SS patients during Moga treatment.
Methods Patients were genotyped for the SNP rs10748643(A>G) in the ENTPD1/CD39 gene by Sanger sequencing and multiparametric flow cytometry was longitudinally performed on CD4+ and CD8+ T-cells before and during Moga treatment.
Results Before Moga, GG and AG patients showed significantly higher CD39+CD4+ T-cells levels compared to AA individuals. Notably, patients (11/12) who achieved a complete or partial response to Moga exhibited a marked reduction of CD39 expression (GG/AG patients) and/or CD73, along with a simultaneous increase in CD38 on residual CD4+ and CD8+ T cells. In contrast, the only non-responder (AA genotype) showed no variation in CD38 or CD39, but increased CD73 expression. Moreover, during treatment three responders experienced skin progression. Even without evidence of blood relapse, these patients were characterized by an opposite modulation of the ectoenzymes, with CD39 upregulation and CD38 downregulation on T-cells.
Conclusion The different modulation of these markers during Moga response and disease progression offers insights into the potential use of these ectoenzymes for monitoring patients' treatment response. A deeper characterization of the tumor and normal T-cell subsets expressing the ectoenzymes is ongoing.

13 – EDDY DE BOER
LONG-READ SEQUENCING CRACKS UNSOLVED CASES IN EPIDERMOLYSIS BULLOSA

Eddy N. de Boer[1], L.A. (Agnes) Grutters[1,2], Rosalie Baardman[2], Daniëlle Schoonhoven[1], Jeroen Bremer[2], Rindert R. Venema[2], Femke Boorsma[1], Jelkje de Boer-Bergsma[1], Gilles F.H. Diercks[2,3], Henny H. Lemmink[1], Sabrina Z. Commandeur-Jan[1], Lennart F. Johansson[1], Marieke C. Bolling[2], Cleo C. van Diemen[1] and Peter C. van den Akker[1,2]

Departments of [1]Genetics, [2]Dermatology, and [3]Pathology, University of Groningen, University Medical Center Groningen, UMCG Centers of Expertise for Blistering Diseases and Genodermatoses, Groningen, The Netherlands.

Background Standard genetic diagnostics of Epidermolysis Bullosa (EB) using short-read sequencing has a diagnostic yield of ~95% leaving 5% of EB patients in uncertainty about their genetic diagnosis.
Objective Here, we applied Oxford Nanopore Technologies (ONT) long-read sequencing (LRS) to diagnose unsolved cases.
Methods Nine patients were selected with either no causal variant identified or only one variant in a presumed recessive form of EB. Libraries were generated and 40 EB-related genes were sequenced.
Results In four patients, intermediate-sized (2.5-8 kb) multi-exon deletions were detected that were not found in public databases.
Two COL7A1 deletions were found in patients with dominant dystrophic EB (DDEB) in whom no previous variant was identified, which explained the phenotypes. In one family, co-segregation of the variant with the disease could be proven. The same ITGB4 deletion was identified in two patients. For one patient with junctional EB (JEB)-localized a heterozygous pathogenic frameshift variant had been identified previously, completing the genetic diagnosis, and explaining the phenotype. In the other patient no additional variant was found, leaving the EB simplex (EBS)-localized phenotype yet unexplained.
In a fifth patient with DDEB, we found a likely pathogenic intronic splice-variant in COL7A1 that had been missed in routine diagnostics. RT-PCR confirmed alternative splicing leading to the in-frame insertion of seven amino acids to the triple-helical region. The variant was found to co-segregate with the disease in the extended patients family.
Conclusion LRS yielded a genetic diagnosis for four out of nine patients, highlighting its added value to EB diagnostics.

14 – MERVE HATUN ERKAYMAN
IGA IS RELATED TO A MORE SEVERE MUCOUS MEMBRANE PEMPHIGOID

Merve H. Erkayman[1], Jeroen Bremer[1], Barbara Horvath[1], Gilles Diercks[2]

[1]Center for Blistering Diseases, Department of Dermatology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; [2]Departments of Medical Biology and Pathology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.

Background Mucous membrane pemphigoid (MMP) presents with predominant mucosal blisters, erosions, and subsequent scarring, which can lead to serious complications, such as blindness, strictures, and airway obstruction. Next to the clinical presentation, MMP is characterized by IgG and/or IgA autoantibodies mainly against BP180. Unfortunately, data on the clinical significance of IgA autoantibodies are scarce.
Objective To understand the impact of IgA autoantibodies on the clinical phenotype of MMP.
Methods In this retrospective study (2000-2024), we included 144 patients with predominant mucosal blistering disease showing linear IgG/IgA/C3c deposits in the basement membrane zone on direct immunofluorescence microscopy (DIF). Baseline DIF, serological tests, and clinical findings at presentation were retrospectively extracted from patient files.
Results Of 144 patients, 59,72% (n=86) had IgA deposition in DIF. The median age was 67,0 and 61,0 in the IgA-positive and IgA-negative groups, respectively. IgA-positive patients had 62,8% multisite disease and 37,2% ocular involvement, whereas IgA-negative patients had 45,8% multisite and 16,7% ocular disease. There was a trend towards an increased number of mucosal sites involved in the IgA-positive group (means: 2,05±1,03 and 1,73±1,05, respectively). Positive epidermal IgA autoantibodies (n=19) in salt-split-skin favored multisite (78,9% vs 51,6%), ocular (52,6% vs 24,2%), genital (47,4% vs 21,8%), and laryngeal disease (31,6% vs 12,1%), as well as an increased number of involved mucosal sites (means: 2,53 ±1,17 vs 1,80 ±,97).
Conclusion IgA appears to be associated with more severe (multisite) MMP. IgA-targeted therapies might become important in this subgroup of patients.

15 – MARIE-ELINE DEBEUF
EXPLORING THE THERAPEUTIC EFFECT OF ER:YAG LASER ON HAILEY-HAILEY DISEASE THROUGH TRANSCRIPTOMICS

Marie-Eline P.H. Debeuf[1,2], Michel van Geel[1,2,3], Michiel Adriaens[4], Janou Roubroeks[3], Antoni H. Gostynski[1,2], Peter M. Steijlen[1,2], Marieke C. Bolling[5], Jeroen Bremer[5], Valerie L.R.M. Verstraeten[1,2]

[1]Department of Dermatology, Centre of Expertise for Genodermatoses, Maastricht University Medical Centre+, Maastricht, The Netherlands; [2]GROW Research Institute for Oncology and Developmental Biology, Maastricht University, Maastricht, The Netherlands; [3]Department of Clinical Genetics, Maastricht University Medical Centre+, Maastricht, The Netherlands; [4]Department of Bioinformatics—BiGCaT, Maastricht University, Maastricht, The Netherlands; [5]University of Groningen, University Medical Center Groningen, UMCG Centre of Expertise for Genodermatoses and European Reference Network-Skin, Department of Dermatology, Groningen, The Netherlands.

Background Hailey-Hailey disease (HHD) is a rare autosomal dominant genodermatosis caused by defects in the Golgi-bound calcium pump hSPCA1. Although a variety of treatment options exist, long-term remission is rare. Our recent study showed long-term remission of HHD by one single Er:YAG laser with a median 38 months follow-up in 75 of 77 HHD

plaques. The pathophysiological mechanism underlying the therapeutic effect of Er:YAG laser in treating HHD, is unknown.
Objective To uncover the underlying mechanisms leading to the long-term remission of HHD by Er:YAG laser and to find potential new treatment targets in this therapy-resistant disease.
Methods Eight patients were included in this prospective study. In each patient, RNA sequencing was performed on skin samples obtained from a Hailey-Hailey plaque before and six weeks after Er:YAG laser. For control purposes, RNA sequencing was performed on skin samples from the clinically uninvolved skin in all patients. Differentially expressed genes were identified by DESeq2 analysis and enriched pathways by GO Enrichment Analysis.
Results DESeq2 analysis revealed 2168 significant dysregulated genes of which 1441 were upregulated and 727 downregulated when comparing treated to affected skin. Calcium-related pathways such as 'calcium ion transport' and 'calcium mediated signaling' were enriched, as were pathways associated with cell-cell adhesion. Other involved pathways are currently being evaluated.
Conclusion Both calcium signaling and cell-cell adhesion are known to be impaired in HHD. Current findings seem to imply a change in these pathways which may explain the long-term remission observed after Er:YAG laser.

16 – LISA VAN DER RIJST
IMPACT OF DUPILUMAB ON IMMUNE-RELATED PROTEINS IN SKIN TAPE STRIPS AND SERUM OF PEDIATRIC ATOPIC DERMATITIS PATIENTS

Lisa P. van der Rijst[1,2], Femke van Wijk[3], Edward F. Knol[3], Nicolaas P.A. Zuithoff[4], Constance F. den Hartog Jager[2], Marjolein S. de Bruin-Weller[2], Marlies de Graaf[1,2]
[1]Department of Dermatology and Allergology, University Medical Center Utrecht, Wilhelmina Children's Hospital, Department of Dermatology and Allergology, Utrecht University, The Netherlands; [2]Department of Dermatology and Allergology, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht, Utrecht University, The Netherlands; [3]Center for Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands; [4]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands.

Background The proteomic response to dupilumab in pediatric atopic dermatitis (AD) patients is not well characterized.
Objective To investigate immune-related proteins in the skin and serum of pediatric AD patients treated with dupilumab and assess their correlation with clinical severity.
Methods Twenty pediatric AD patients starting dupilumab treatment were included. Serum samples and tape strips from lesional and non-lesional skin were collected at baseline, 4 and 16 weeks of treatment. Fifteen pre-specified proteins were measured at each visit by Luminex multiplex immunoassay. Clinical effectiveness was assessed by Eczema Area and Severity Index (EASI) and Numeric Rating Scale (NRS) itch.
Results Along with clinical improvement, 16 weeks of dupilumab treatment resulted in a rapid and significant reduction of PARC and TARC levels in both tape strips and serum. Tape strips were superior in tracking proteomic changes in TH2-related chemokine CTACK, innate inflammatory markers (IL-8, IL-18) and tissue repair markers (OSF-2, MMP-1), while serum was superior in tracking changes in T-cell-derived cytokines (IL-4, IL-13). Moreover, inflammatory marker IL-1α significantly increased in lesional skin, while decreased in serum. In both skin and serum, PARC showed the strongest correlation with clinical severity (EASI and NRS itch).
Conclusion Skin tape strips and serum accurately captured changes in key AD-related proteins in pediatric patients treated with dupilumab, revealing distinct proteomic signatures. These findings underscore the complementary roles of skin tape strips and serum in profiling local and systemic proteins and highlight the value of minimally invasive tape strips for monitoring treatment response in pediatric AD.

17 – FLORENCE VROMAN
THE EFFECT OF DUPILUMAB ON THE MICROBIOME OF LESIONAL SKIN, FACIAL SKIN AND NOSE IN MODERATE TO SEVERE AD PATIENTS TREATED IN DAILY PRACTICE: DATA FROM THE BIODAY REGISTRY

Florence Vroman[1]; Celeste M. Boesjes[1]; Janetta Top[2]; Marco Viveen[2]; Daphne S. Bakker[1]; Bart P. Boogaard[2]; Malbert Rogers[2]; Lian F. van der Gang[1]; Marcel R. de Zoete[2]; Marlies de Graaf[1]; Rob J.L. Willems[2]; Marjolein S. de Bruin-Weller[1]
[1]National Expertise Center for Atopic Dermatitis, Department of Dermatology and Allergology, University Medical Center Utrecht, Utrecht, The Netherlands; [2]Department of Medical Microbiology, University Medical Center Utrecht, Utrecht, The Netherlands.

Background Atopic dermatitis (AD) is associated with an altered skin microbiome and both lesional and nasal *Staphylococcus aureus* (*S. aureus*) colonization. Dupilumab treatment reduces skin inflammation, but it is also associated with facial adverse events.
Objective The aim of this study was to evaluate the effect of dupilumab treatment on the (facial) skin and nasal microbiome of AD patients.
Methods Lesional, facial and nasal swabs were taken from AD patients at baseline (T0), after 4 (T4) and 28 (T28) weeks of dupilumab treatment. Relative abundance, microbial diversity and differential abundances were analysed using 16S rRNA gene sequencing. Data were compared with healthy controls (HCs). Whole genome sequencing was also performed.
Results In total, 31 AD patients and 30 matched HCs were included. In lesional skin, *S. aureus* was significantly more abundant at T0 compared to T4 and T28 with a Log Fold Change (LFC) of -5.14 and -5.54 to -9.18, respectively. Both the inverse Simpson and Shannon index revealed an increase in microbial diversity between T0 and T28 ($p<0.05$), where

the latter was comparable to HCs. Bray-Curtis dissimilarities showed a significant decrease in mean dissimilarity between HC and T0 versus T4/T28 samples. Similar changes, although mostly non-significant, were found in the facial microbiome of AD patients. No clear differences were observed in the nose.
Conclusion The lesional skin microbiome, and to a lesser extent the facial microbiome, of AD patients shifted towards healthy skin during 28-weeks of dupilumab treatment. No clear effect was found in the nasal microbiome.

18 – ARANKA GERRITSEN
RESTORING INTERLEUKIN-22 INDUCED SEVERE ATOPIC DERMATITIS HALLMARKS IN VITRO BY DUAL TARGETING OF EPIDERMAL DEFECTS AND INFLAMMATION

Aranka Gerritsen[1], Luca D. Meesters[1,2], Ellen H. van den Bogaard[1]
[1]Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; [2]Department of Molecular Developmental Biology, Faculty of Science, Radboud University, Nijmegen, The Netherlands.

Background Atopic dermatitis (AD) is a chronic inflammatory skin disease that manifests in varying degrees of severity. Transcriptomic skin biomarkers for severe AD have been identified by the BIOMAP consortium, providing insights into potential underlying disease-associated mechanisms. This severity degree can be mimicked *in vitro* using organotypic epidermal models exposed to different AD-related cytokines.
Objective To compare the transcriptome of *in vitro* AD models with patient-derived transcriptomic signatures to identify pathophysiological mechanisms that can be targeted by therapeutics.
Methods The differential gene expression profiles of severe AD lesional skin were compared to that of interleukin (IL)-4, IL-13 and IL-22 stimulated human epidermal equivalents. These AD models were treated with known AD drugs tapinarof (AHR ligand) and/or tofacitinib (JAKi) and analyzed for morphology, gene/protein expression and epidermal barrier function.
Results The combination of IL-4, IL-13 and IL-22 induced differential gene expression that resembled severe AD lesional skin and most strongly impaired barrier function. Computational analyses identified novel 'bridge genes' (e.g. BIRC3, AKR1C3) involved in multiple severe disease-associated biological processes. In AD models, tapinarof reduced hyperproliferation and induced epidermal differentiation, while tofacitinib decreased inflammatory signaling. Combined treatment fully restored impaired barrier function and normalized the expression of severe AD transcriptomic markers, including bridge genes.
Conclusion We identified IL-22 and its intracellular signaling as a key driver of severe AD-related epidermal pathology in a Th2 cytokine milieu. The combined targeting of epidermal defects and inflammation by AHR activation and JAK/STAT inhibition could be an effective dual strategy in the treatment of severe AD.

19 – MARGOT STARRENBURG
IMPACT OF TRALOKINUMAB ON SKIN-HOMING T CELLS AND IL-4 AND IL-13 RECEPTOR DYNAMICS IN PATIENTS WITH ATOPIC DERMATITIS

Margot Starrenburg[1,2], Coco Dekkers[1,2], Maria van der Wal[2], Marloes Meermans[2], Daphne Bakker[1,2], Marjolein de Bruin-Weller[1], Femke van Wijk[2]
[1]National Expertise Center for Atopic Dermatitis, Department of Dermatology and Allergology, University Medical Center Utrecht, The Netherlands; [2]Center for Translational Immunology, University Medical Center Utrecht, The Netherlands.

Background Tralokinumab, an IL-13 targeting mAb, is an effective treatment for atopic dermatitis (AD).
Objective To study the effects of tralokinumab on IL-4 and IL-13 receptor expression and sensitivity and cytokine production in circulating lymphocytes and monocytes.
Methods 22 AD patients were included and sampled longitudinally for up to 28 (n=20) or 52 (n=10) weeks. PBMCs were characterized in flowcytometric assays.
Results Mean EASI and pruritus scores decreased significantly during treatment. We observed a significant decrease in IL-4, IL-13 and IL-17A in CLA+ CD4+ T-cells, and in the proportion of proliferating cells in both skin-homing (CLA+) and non-skin-homing (CLA-) T-cells, after 28 weeks of tralokinumab treatment. IL-22 expression was significantly higher in patients than in healthy control subjects (HCs) and showed a decreasing trend. Expression of IL-5, IFNγ, TNF-α in skin-homing T cells was similar in patients and HCs and did not change during tralokinumab treatment, as confirmed by stable (low) cytokine levels in the supernatants of PBMCs cultured for 72h with anti-CD3 stimulation. Monocyte and dendritic cell populations remained uninfluenced by tralokinumab treatment. While IL-4Rα and IL-13Rα expression on the cell surface of monocytes and T- and B-cells remained stable, the sensitivity to IL-4 or IL-13 stimulation measured by pSTAT6 activation decreased during treatment.
Conclusion We observed a reduction in Th2 cytokine production by CLA+ T-cells following tralokinumab treatment, without a concomitant increase in Th1, Th17 or Th22 inflammatory activity. There were no indications of upregulation of IL-4 or IL-13 receptor expression or enhanced receptor signaling during tralokinumab treatment.

20 – NIENKE VELDHUIS
LONG-TERM OPHTHALMOLOGICAL FOLLOW-UP OF ATOPIC DERMATITIS PATIENTS TREATED WITH DUPILUMAB

Nienke Veldhuis[1], Roselie Achten[1], Chantal van Luijk[2], Marlot van der Wal[3], Stans den Hartog-Jager[3], Marlies de Graaf[1], Joke de Boer[2], Femke van Wijk[3], Inge Haeck[1], Marjolein de Bruin-Weller[1]
[1]Department of Dermatology and Allergology, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht, Utrecht, The Netherlands; [2]Department of Ophthalmology, University Medical Center Utrecht, Utrecht, The Netherlands; [3]Center for Translational Immunology,

University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands.

Background Dupilumab-associated ocular surface disease (DAOSD) is a common side effect in dupilumab-treated atopic dermatitis (AD) patients. However, little is known about its long-term ocular safety.
Objective To investigate the effect of long-term dupilumab treatment on the frequency and severity of (DA)OSD and conjunctival goblet cells (GCs).
Methods This prospective study included moderate-to-severe dupilumab-treated AD patients between February 2020 and December 2021, with a single follow-up between December 2023 and August 2024 at the UMC Utrecht. Patients underwent ophthalmological and dermatological examinations at baseline (start of dupilumab), week 28, and last follow-up (≥2 years). Ocular surface disease (OSD) severity was assessed by the Utrecht Ophthalmic Inflammatory and Allergic disease (UTOPIA) score, with DAOSD defined as a ≥3-point increase from baseline. Conjunctival impression cytology was used to study the quantity and function of GCs.
Results OSD was present in 90.3% (28/31) patients at all time points. Median UTOPIA scores slightly decreased at week 28 and last follow-up compared to baseline. DAOSD was observed in 29.0% (9/31) patients during follow-up. At the last follow-up, 25.8% (8/31) patients were using anti-inflammatory ophthalmic treatment. Tear break-up time decreased over time, while tear production increased. GC numbers significantly decreased at last follow-up compared to baseline and week 28. Mucin 5AC (MUC5AC) production in Cytokeratin 19-CD45-MUC5AC+ cells remained stable between week 28 and last follow-up.
Conclusion (DA)OSD is common in AD patients undergoing long-term dupilumab treatment. Although MUC5AC production remained stable after week 28, the significant decrease in GC numbers suggests an overall reduction in MUC5AC.

21 – WOUTER OUWERKERK
CANCER-IMMUNOGRAM ANALYSES TO PREDICT THE HETEROGENEOUS CLINICAL RESPONSE TO IMMUNOTHERAPY IN METASTATIC MELANOMA PATIENTS

W. Ouwerkerk[1,2], A. Rooker[1], I. Bakker[1], S. Chielie[1], K.J. Willemsen[1], E.P.M. Tjin[3], J.A. van der Hage[4], M.W. Bekkenk[1,5], R.M. Luiten[1]
[1]Amsterdam University Medical Center, Department of Dermatology, Netherlands Institute for Pigment Disorders, University of Amsterdam, Amsterdam Institute for Infection and Immunity, The Netherlands; [2]National Heart Centre Singapore, Hospital Drive, Singapore; [3]Research Center Healthy and Sustainable Living, Research group Innovation in Healthcare Processes in Pharmacology, University of Applied Sciences Utrecht, Utrecht, The Netherlands; [4]Department of Surgery, Leiden University Medical Centre, Leiden, The Netherlands; [5]VU University Amsterdam, The Netherlands

Background Melanoma is an aggressive form of skin cancer that originates from melanocytes in which a multitude of processes are involved and with heterogeneous treatment responses.
Objective We developed a cancer-immunogram to predict the clinical and melanoma-specific immune response to MI immunotherapy in melanoma patients, using immunomonitoring data from a monobenzone and imiquimod (MI) therapy trial of patients with cutaneous melanoma metastases.
Methods The immunogram consisted of 9 different cancer immune-aspects (CIA), primarily based on the cancer immunity cycle, measured at baseline. We used logistic regression modelling to estimate the probability of response, defined by regression of tumor lesions, or melanoma-specific immune response, for each CIA.
Results The average response score of all CIA's resulted in mean scores 0.44 (±0.07) and 0.60 (±0.06) for non-responders and responders ($p<0.0001$), respectively. These scores had good discrimination capabilities with a sensitivity and specificity of 0.91 (95%CI 0.74-1.00) and 0.80 (95%CI 0.55-1.00), with an area under the ROC curve of 0.95. The AUROCs of the individual CIAs varied between 0.6 and 0.84 with a median AUROC of 0.72. Comparable Results were seen in the melanoma-specific immune response data.
Conclusion CIAs by themselves show limited ability to identify responding patients, where Tumor foreignness performed best. The combination of CIAs in an immunogram can fully harness the multifactorial nature of immune response to MI treatment against melanoma.

22 – MYRTHE MOERMANS
SURGICAL EXCISION VERSUS TOPICAL 5% 5-FLUOROURACIL AND PHOTODYNAMIC THERAPY IN TREATMENT OF BOWEN'S DISEASE: LONG-TERM RESULTS OF A MULTICENTER RANDOMIZED CONTROLLED TRIAL

Myrthe M.G. Moermans[1,2], Shima Ahmady[1,2], Patty J. Nelemans[3], Aimée H.M.M. Arits[4], Janneke P.H.M. Kessels[5], Han P.A. van Pelt[6], Nicole W.J. Kelleners-Smeets[1,2], Klara Mosterd[1,2]
[1]Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; [2]Grow Research Institute for Oncology and Reproduction, Maastricht University, Maastricht, The Netherlands; [3]Department of Epidemiology, Maastricht University, Maastricht, The Netherlands; [4]Department of Dermatology, Catharina Hospital, Eindhoven, The Netherlands; [5]Department of Dermatology, Zuyderland Medical Center, Heerlen, The Netherlands; [6]Department of Dermatology, VieCuri Medical Center, Venlo, The Netherlands.

Background Bowen's disease (BD) is an intra-epidermal neoplasm and usually treated by means of surgical excision (SE). Considering the superficial growth of BD, non-invasive treatments such as 5-Fluorouracil and methylaminolevulinate photodynamic therapy (MAL-PDT) are expected to be effective and safe. Randomized controlled trials (RCT) comparing the effectiveness of these treatments to SE are essential, but lacking and little is known about the long-term safety and efficacy.

Objective To evaluate the long-term probability of sustained clearance at least 3 years after treatment. As secondary outcome, we investigated the cumulative probability to develop cutaneous squamous cell carcinoma (cSCC) within the treatment area.
Methods In this multicenter, non-inferiority RCT, 250 patients with histologically confirmed BD were randomly assigned to SE, 5FU, or MAL-PDT in a 1:1:1 ratio between May 2019 and January 2021. All patients were invited for a long-term follow-up visit between February and September 2024. The follow-up period ranged from 3 to 4.5 years after finishing treatment. The treatment area was evaluated for recurrence and cSCC development by the investigator and supervising dermatologist, blinded to the assigned treatment.
Results In total 192 of the 250 randomized patients were seen for long-term follow-up. Results on recurrence and cSCC progression will be discussed during the NVED Annual Meeting 2025.
Conclusion This study shows which treatment for BD is most effective on the long-term. Based on these Results, recommendations can be made for optimizing treatment and follow-up.

23 – ELISE BELJAARDS
ASSOCIATION OF SKIN BARRIER FUNCTION, BACTERIAL COLONIZATION, AND INFLAMMATION WITH DISEASE ACTIVITY IN MYCOSIS FUNGOIDES AND SÉZARY SYNDROME

E.S.M. Beljaards[1,2], C. Mergen[1,2,3], S.S. Wind[1,2], R. Rijneveld[1], D. Balak[2], L. Bruijnincx[1], M. de Kam[1], K.D. Quint[2], J. Bosch[1,4], M.H. Vermeer[2], R. Rissmann[1,2,3] on behalf of the Next Generation ImmunoDermatology (NGID) Consortium
[1]Centre for Human Drug Research, Leiden, The Netherlands; [2]Department of Dermatology, Leiden University Medical Centre, Leiden, The Netherlands; [3]Leiden Academic Centre for Drug Research, Leiden, The Netherlands; [4]Department of Oncology, Leiden University Medical Centre, Leiden, The Netherlands.

Background The main subtypes of cutaneous T-cell lymphomas (CTCLs) are mycosis fungoides (MF) and Sézary syndrome (SS). Previous studies, often small-scale and limited to early-stage MF, reported impaired skin barrier function and increased bacterial colonization. To date, no comprehensive analyses have correlated trans-epidermal water loss (TEWL) with bacterial colonization and inflammation.
Objective To evaluate skin barrier function, bacterial colonization, and erythema (used as a proxy for inflammation) in patients with MF and SS.
Methods In this prospective, observational, cross-sectional study, TEWL was measured in lesional skin (LS) and non-lesional skin (NLS) using the GPSkin Barrier Pro-1. Swabs from nostrils, LS, and NLS were analyzed for bacterial colonization via culturing and sequencing. Erythema was assessed through multispectral imaging and clinical scores.
Results 16 MF-patch, 12 MF-plaque, 7 MF-tumor, 8 SS patients, and 10 healthy volunteers were included. TEWL was significantly higher in LS compared to NLS and healthy skin, and increased with disease stage (patch 17.2, plaque 34.4, tumor 47.2). Bacterial colonization was greater in LS, particularly in the tumor stage (*Staphylococcus aureus* frequency 43%). Subtyping of bacterial strains is ongoing and will be presented at the conference.
Conclusion Barrier dysfunction, increased bacterial colonization, and enhanced inflammation were observed in LS, worsening with disease progression. These findings align with previous studies suggesting that bacterial colonization is associated with CTCL progression and has a potential as therapeutic target. Further investigation, including ongoing bacterial sequencing, will further elucidate microbiome composition and its role in the pathogenesis of MF and SS.

24 – VEERLE MERKUS
TUMOR MICROENVIRONMENT OF METASTASIZED AND NON-METASTASIZED CUTANEOUS SQUAMOUS CELL CARCINOMA IN ORGAN TRANSPLANT PATIENTS

V.A. Merkus[1], E. de Jong[1], M.E. IJsselsteijn2, J.N. Bouwes Bavinck[1], N.F.C.C. de Miranda[2], C.P. Tensen[1], A. El Ghalbzouri[1], F.A. Scheeren[1], K. Schepers[1], M.H. Vermeer[1], K.D. Quint[1]
[1]Department of Dermatology, Leiden University Medical Centre, Leiden, The Netherlands; [2]Department of Pathology, Leiden University Medical Centre, Leiden, The Netherlands.

Background Solid organ transplant recipients (sOTRs) are at an increased risk of developing metastatic cutaneous squamous-cell carcinoma (cSCC). The tumor microenvironment (TME) plays a key role in cancer progression, but our understanding of its architecture and cellular composition during the metastatic process in cSCC is limited. Recent advances in single-cell technologies allow a detailed characterization of the TME.
Objective Compare the TME of cSCCs that metastasize (cSCC-M) and cSCCs that do not metastasize (cSCC-nonM) in sOTR patients by Imaging mass cytometry (IMC).
Methods We performed a comprehensive single-cell analysis using IMC on formalin fixed paraffin embedded (FFPE) biopsies from 5 sOTR patients with both cSCC-M (at least 1) and cSCC-nonM (at least 3).
Results We identified 25 cell clusters, including 18 immune cell clusters. Tumor cells were identified with D2-40, Ki-67 and Keratin. While no significant differences were observed in the immune cell counts between cSCC-M and cSCC-nonM, a higher frequency of CD4+ and CD8+ T cells expressing activation markers (Granzyme B, Ki-67, PD-1) was observed for cSCC-nonM. There were no notable differences in cell-cell interactions, spatial communities or distance to tumor cells between cell subsets in the two groups.
Conclusion The TME of metastasized and non-metastasized cSCCs in sOTRs appears comparable in regards to cell counts and interactions. However, the elevated frequency of CD4+ and CD8+ T cells expressing activation markers in SCC-nonM suggests a stronger immune response is present in SCC-nonM. Further studies should be aimed at understanding factors inducing immune activation in the TME in sOTR patients.

25 – INGER KREUGER
SPATIAL GENE EXPRESSION AND MICRO-ENVIRONMENTAL CHANGES DURING NEVUS TO MELANOMA TRANSITION

I.Z.M. Kreuger[1,2*], R.C. Slieker[2,3*], V.A. Merkus[1], S. de Haan[1], A.M.R. Schrader[4], T.J.B. van Groningen[1,2], R. van Doorn[1,2]
*[1]Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; [2]Leiden Center for Computational Oncology, Leiden University Medical Center, Leiden, The Netherlands; [3]Department of Cell & Chemical Biology, Leiden University Medical Center, Leiden, The Netherlands; [4]Department of Pathology, Leiden University Medical Center, Leiden, Netherlands. *These authors have contributed equally.*

Background Melanoma is an aggressive skin cancer, which can arise from benign nevi. Enhancing our understanding of melanoma development from nevi could improve early diagnosis and treatment. However, studies of early melanoma stages are limited, and the existing studies were mainly performed using bulk RNA sequencing, which reflects a mixture of cell types and more importantly lacks spatial context.
Objective Therefore, we have mapped the transition of nevi to melanoma using spatial transcriptomics.
Methods We analyzed nevus-associated melanoma FFPE samples from 18 patients using the 10X Genomics Visium Spatial Gene expression technology. Data analysis was conducted using Spaceranger, Semla and STdeconvolve. Additionally, validation immunostainings and cytometry by time of flight (CyTOF) experiments were performed.
Results We identified the main transcriptomic signatures in the skin, as well as nevus an melanoma signatures and their spatial location. Differential gene expression analysis identified potential biomarkers and key pathways in melanoma. Additionally, two melanoma signatures within the same patient with their own spatial location were detected. Micro-environmental analysis also showed changes in immune cells and keratinocytes near nevus and melanoma cells.
Conclusion Spatial analysis revealed gene expression alterations and micro-environmental changes during the transition of nevus to melanoma. This study advances our understanding of melanoma development, thereby providing a framework for the identification of novel biomarkers and treatment targets in melanoma.

26 – CATHERINE MERGEN
STRATUM CORNEUM CERAMIDE ALTERATIONS AND BARRIER DYSFUNCTION IN PSORIASIS NORMALIZE WITH GUSELKUMAB TREATMENT

Catherine Mergen[1], Jannik Rousel[1,2], Menthe E. Bergmans[2,3], Lisa J. Bruijnincx[2], Naomi B. Klarenbeek[2], Tessa Niemeyer-van der Kolk[2], Martijn B.A. van Doorn[2,4], Joke A. Bouwstra[1], Robert Rissmann[1,2,3], the Next-Generation ImmunoDermatology Consortium (NGID)
[1]Leiden Academic Centre for Drug Research, Leiden University, Leiden, The Netherlands; [2]Centre for Human Drug Research, Leiden, The Netherlands; [3]Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; [4]Department of Dermatology, Erasmus Medical Centre, Rotterdam, The Netherlands.

Background Psoriasis is a chronic, immune-mediated, inflammatory disease characterized by skin lesions with an impaired barrier. The skin barrier function is mainly provided by the lipid matrix surrounding the corneocytes in the stratum corneum, of which ceramides constitute important components. Changes in the ceramide composition have been associated with a reduced barrier function.
Objective In this study, we aimed to characterize the stratum corneum ceramide profile and barrier function in lesional and non-lesional psoriatic skin compared to controls, and during and after treatment with guselkumab.
Methods 26 patients with mild and moderate-to-severe psoriasis and 10 healthy volunteers participated in this study. Barrier function was measured by transepidermal water loss and ceramides were analyzed using liquid chromatography-mass spectrometry. Patients were randomized 3:1 to guselkumab or placebo and assessments were performed at baseline and after 4 and 16 weeks.
Results Lesional psoriasis was characterized by a reduced barrier function and alterations in the ceramide profile with significant changes in the ceramide subclass composition, degree of monounsaturation and chain length distribution. Both barrier dysfunction and ceramide alterations normalized to that of controls during treatment with guselkumab, but not placebo. Changes in the lesional ceramide profile during treatment correlated with barrier function and the target lesion severity. Non-lesional skin was similar to controls at baseline and did not change during treatment.
Conclusion Barrier dysfunction and ceramide abnormalities are observed in, and limited to, lesional psoriasis. Monitoring the ceramide profile might be exploited as an Objective biomarker for treatment responses.

27 – LINDA GODDING
REAL-WORLD COST-PER-RESPONDER AMONG THE DIFFERENT CLASSES OF BIOLOGICS FOR PSORIASIS

L.T.H. Godding[1], M.M.B. Seyger[1], A. Duvetorp[2], P. Mateman[3], J. van Overhagen[3], E.M.G.J. de Jong[1], J.M.P.A. van den Reek[1], and the BioCAPTURE Network[5]
[1]Department of Dermatology, Radboud University Medical Centre, Nijmegen, The Netherlands; [2]Department of Dermatology and Venereology, Lund University, Skane University Hospital, Malmö, Sweden; [3]LEO Pharma BV, Amsterdam, The Netherlands; [4]https://biocapture.nl/deelnemende-centra/

Background Biologics have revolutionized psoriasis treatment, but pose a significant burden on the healthcare budget. Insights into real-world cost-per-responder (CPR) of biologics is scarce, due to a lack of studies incorporating real-world data.
Objective Evaluating the real-world CPR of adalimumab,

ustekinumab, IL17-, and IL23-inhibitors for the treatment of psoriasis.
Methods Data were retrieved from the prospective, multicentre, real-world BioCAPTURE registry. The one-year CPR were calculated for relative and absolute Psoriasis Area and Severity Index (PASI)-scores (PASI75/90/100 and PASI≤3/1), factoring in dose adjustments. For the primary analysis, Dutch list prices were used and approximate discounts for biologics with (upcoming) biosimilars. Sensitivity analyses were conducted with Swedish list prices, reflecting price transparency, and according to number of prior biologics.
Results Altogether, 987 patients with 1300 treatment episodes were included. Dose adjustments in the first year were common. In general, the cost-per-PASI≤1-responder was significantly lower than the cost-per-PASI100-responder. Among biologics without biosimilar availability, the lowest cost-per-PASI≤1-responder was seen for brodalumab, followed by risankizumab, and guselkumab. Assuming discounts of 80% on adalimumab's and ustekinumab's originator price, adalimumab showed the lowest CPR across all responder definitions. Same patterns were seen with Swedish list prices. Overall, the CPR was higher among patients with ≥2 prior biologics compared to 0-1 prior biologic. However, differences were smaller for newer biologics.
Conclusion This study highlights the significant difference between the real-world cost-per-PASI100-responder and cost-per-PASI≤1-responder, emphasizing the importance of incorporating different responder definitions into cost-effectiveness research. Additionally, price transparency is important, as price fluctuations have a major impact on CPR.

28 – MARJOLEIN HIEL
PHENOTYPE TRANSITION IN RELAPSED PEMPHIGUS PATIENTS AFTER RITUXIMAB THERAPY: A RETROSPECTIVE SINGLE-CENTER ANALYSIS

M.A.J. Hiel[1*], A. Strandmoe[1,2*], L.L. van Nijen-Vos[2], A.M. Nijenhuis[2], G.F.H. Diercks[2], H.J. Meijer[2], J. Bremer[2], J.M. Meijer[1], P. Heeringa[2], B. Horváth[1]
*[1]Department of Dermatology, Center of Expertise for Blistering Diseases, University Medical Center Groningen, The Netherlands; [2]Department of Medical Biology and Pathology, University Medical Center Groningen, The Netherlands. *These authors have contributed equally.*

Background Pemphigus is an autoimmune bullous disease (AIBD) and has two main subtypes: pemphigus vulgaris (PV) and pemphigus foliaceus (PF). Both are effectively treated with the CD20- targeting monoclonal antibody rituximab, a B cell-depleting therapy. However, 57% of rituximab-treated pemphigus patients experience relapse following remission, with a subset exhibiting a transition in clinical phenotype upon relapse.
Objective To determine the frequency of relapse and phenotype transition in rituximab-treated pemphigus patients, identify their predictive factors, and elucidate associated immunological trends.
Methods A national, single center, exploratory retrospective cohort study was performed, reviewing the medical records of patients with pemphigus who had received at least one treatment cycle of rituximab between December 2006 to December 2023.
Results A total of 103 patients were included, of which the majority was diagnosed with mcPV (49 %). A substantial number (54%) relapsed, with 29% experiencing phenotype transition. Among the patients exhibiting transition, only mucocutaneous PV (mcPV) patients were involved, with 75% transitioning to mucosal pemphigus (mPV) and 25% to PF. Elevated levels of CD19+ B cells at diagnosis were identified as a significant predictive factor for a reduced risk of relapse.
Conclusion Fifty-four percent of rituximab-treated pemphigus patients relapsed, with 29% experiencing phenotype transition. This transition occurred only in patients with mcPV, indicating that relapsed mcPV patients may transition to a milder subtype. In this cohort, phenotype transition could not be predicted immunologically; However, elevated levels of CD19+ B cells at diagnosis represents a significant predictive factor for a lower risk of relapse.

29 – JULIETTE SIMONS
EFFECTIVENESS OF CICLOSPORIN IN OMALIZUMAB-REFRACTORY CHRONIC URTICARIA PATIENTS

J.V.L. Simons, Menno R. te Riele, Reineke Soegiharto, André C. Knulst, Heike Röckmann
Urticaria Centre of Excellence and Reference (UCARE). Department of Dermatology/Allergology, University Medical Centre Utrecht, Utrecht University, Utrecht, The Netherlands.

Background Ciclosporin is a third-line treatment for chronic urticaria (CU) patients refractory to omalizumab. Ciclosporin effectiveness is mainly investigated in omalizumab naïve populations.
Objective To investigate the effectiveness of ciclosporin in omalizumab-refractory CU-patients after omalizumab treatment and to identify factors associated with ciclosporin response.
Methods All omalizumab-refractory CU-patients prescribed ciclosporin after omalizumab until May 2024 were retrospectively included. Ciclosporin effectiveness (based on UAS7 or physician estimation), treatment duration and reasons for discontinuation were assessed. Potential predictors of effectiveness were analyzed by multivariate Log regression.
Results 37 omalizumab-refractory CU-patients treated with ciclosporin were identified (81.1% female, median age 29 years, median UAS7 at start ciclosporin 25.8). Sixty percent (n=22) had a good or even complete response to ciclosporin with a median treatment duration of 10.3 months. At start of ciclosporin treatment, 28 patients (76%) had concurrent treatment with omalizumab. Time on subsequent combination treatment varied between 0.4-32.8 months. In 8 patients (8/22, 36%) good/complete response was probably due to combination treatment with omalizumab.
Median time on ciclosporin was 8.3 months, and 75%, 49% and 17% of patients were still on ciclosporin treatment after

6 months, 1 and 2 years respectively. Patients discontinued ciclosporin due to remission (n=14, 38%), ineffectiveness (n=9; 25%) or side effects (n=8; 22%) respectively.
Patients with symptoms of inducible urticaria (CIndU) were 87% less likely to respond to ciclosporin (OR 0.13, 95%CI 0.02-0.89).

Conclusion Ciclosporin is an effective third-line treatment in 60% of omalizumab-refractory CU-patients in daily practice, particularly in those without CIndU.

P1 – JULIETTE KERSTEN
MODIFIED RECOMMENDATIONS FOR THE RADIATION DOSE IN PATIENTS WITH CUTANEOUS T-CELL LYMPHOMA AND LOCALISED LESIONAL DISEASE: A RETROSPECTIVE ANALYSIS OF TREATMENT OUTCOMES

J.M. Kersten[1], R. Ottevanger[1], S.E. Rademakers[2], M.H. Vermeer[1], K.D. Quint[1], K.J. Neelis[2]
[1]Department of Dermatology, Leiden University Medical Centre, The Netherlands; [2]Department of Radiology, Leiden University Medical Centre, The Netherlands.

Background Primary cutaneous T-cell lymphomas (CTCLs) are rare non-Hodgkin lymphomas predominantly affecting the skin. Treatment strategies are often guided by disease stage and type, with low-dose radiotherapy (RT) being a common approach for localized lesions.
Objective This study aims to compare the efficacy of single-fraction low-dose RT (1x6 Gy) versus the standard two-fraction regimen (2x4 Gy) in patients with localized CTCLs.
Methods A cohort of 78 patients with confirmed diagnoses of classical mycosis fungoides (cMF), folliculotropic mycosis fungoides (FMF), or primary cutaneous anaplastic large cell lymphoma (C-ALCL) received low-dose RT between January 2017 and December 2022. Outcomes assessed included complete response (CR) rates, freedom from treatment failure (FFTF), and toxicity.
Results Among 312 treated lesions, 270 (87%) achieved CR, with no significant difference in response rates between the single (88%) and double (86%) fraction groups (p = .872). The median time to retreatment was similar for both regimens. Importantly, there were no treatment-related toxicities reported.
Conclusion Single-fraction low-dose RT (1x6 Gy) is non-inferior to the two-fraction regimen (2x4 Gy) in achieving CR for localized CTCLs, offering a more convenient and patient-friendly option without compromising efficacy or safety. These findings support the incorporation of 1x6 Gy into clinical guidelines for the palliative management of CTCL.

P2 – MALAK AL-GAWAHIRI
THE IMPORTANCE OF PSYCHOLOGICAL AND SOCIOECONOMIC RISK FACTORS FOR DEPRESSION AND ANXIETY AMONG DUTCH PATIENTS WITH MILD-TO-SEVERE PSORIASIS: A WEB-BASED SURVEY STUDY

M. Al-Gawahiri[1*], L.T.H. Godding[1*], E.M.G.J. de Jong[1], D.R. Limbeek[1], L.D. Breeman[2], J.M.P.A. van den Reek[1], M.M.B. Seyger[1]
*[1]Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; [2]Health, Medical, and Neuropsychology Unit, Leiden University, Leiden, The Netherlands. *These authors have contributed equally.*

Background Patients with psoriasis have an increased prevalence of depression and anxiety compared to the general population. In previous studies, sex, age and psoriasis severity were associated with depression and anxiety. However, other possible relevant factors, such as psoriasis in visible areas, stress, socioeconomic status and social support have hardly been studied.
Objective To determine the prevalence of depression and anxiety in patients with mild-to-severe psoriasis and to identify relevant associated factors.
Methods A web-based survey among Dutch psoriasis patients ≥16 years was conducted. The Patient Health Questionnaire (PHQ-9) and Generalized Anxiety Disorder scale (GAD-7) were used to assess depression and anxiety, respectively. Patient characteristics included were sex, age, psoriasis severity, psoriasis in visible areas, stress, income, education and social support (ENRICHD Social Support Instrument). Logistic regression analyses were conducted.
Results Of 267 patients, 48 patients (18.0%) screened positive for moderate-to-severe depression (PHQ-9≥10) and 31 patients (11.6%) for moderate-to-severe anxiety (GAD-7≥10), of which 25 patients (80.6%) also screened positive for depression. While stress and low income were associated with both depression and anxiety, low education level was solely associated with depression. Sensitivity analyses showed that low perceived social support was strongly associated with both psychiatric disorders.
Conclusion This study highlights that stress, low income, and low perceived social support showed a stronger association with depression and anxiety in patients with psoriasis than the commonly studied factors sex, age and psoriasis severity, emphasizing the need to include psychological and socioeconomic factors in future research.

P3 – DIGNA DE BRUIN
IMAGING AND IMMUNE-RESPONSE PROFILING AFTER UV-B PROVOCATION IN HEALTHY VOLUNTEERS FOR PROOF-OF-MECHANISM CLINICAL TRIALS

Digna T. de Bruin[1], Wenyan Miao[2], Jared Steranka[2], Jannik Rousel[1], Eric Jacobson[2], Matthijs Moerland[1], Tessa Niemeyer-van der Kolk[1], Robert Rissmann[1], Keith Wilcoxen[2]
[1]Centre for Human Drug Research, Leiden, The Netherlands. [2]ROME Therapeutics, Boston, MA, USA.

Background The ultraviolet-B (UV-B) model is a skin inflammation model that has been broadly used in inflammatory pain studies. Although there are some studies investigating the inflammatory response of the skin to UV-B, the in-depth characterization of the immune response in healthy volunteers is lacking.
Objective To characterize the dermal immune response of healthy volunteers following a UV-B skin challenge and to evaluate test-retest variability of the UV-B response for later integration into phase 1 proof-of-mechanism studies with novel immunomodulatory agents.
Methods In this clinical study, the skin on the upper back of 10 healthy participants was irradiated with two times the minimal erythema dose UV-B on two different study days, two weeks apart. The inflammatory response was evaluated using non-invasive imaging techniques to measure skin erythema and perfusion and skin biopsies were taken 3 hours, 6 hours, and 24 hours post-challenge in the first period and 24 hours

post-challenge in the second period. Biopsies were examined for interferon-stimulated genes (ISG) expression.
Results UV-B increased erythema which peaked 6 hours post-UV-B and remained elevated for 24 hours post-UV-B. UV-B increased perfusion from 3 hours post-UV-B and peaked at 24 hours post-UV-B. The level of induction was consistent between participants and between the two periods. RNA-sequencing data of the skin biopsies revealed ISG induction at 24 hours post-UV-B in both periods.
Conclusion This study demonstrated the feasibility of using UV-B provocation in healthy volunteers for proof-of-mechanism clinical studies with novel immunomodulatory agents.

P4 – ROSANNE OTTEVANGER
EXPLORING THE ASSOCIATION OF PRIMARY CUTANEOUS CD30+ LYMPHOPROLIFERATIVE DISORDERS AND INFLAMMATORY BOWEL DISEASE IN A DUTCH COHORT

R. Ottevanger[1], R. Willemze[1], P.M. Jansen[2], J.J. Goeman[3], R.C. Melchers[1], M.H. Vermeer[1] and K.D. Quint[1]
Departments of [1]Dermatology, [2]Pathology, and [3]Statistics, Leiden University Medical Center, The Netherlands.

Background This study explores the potential association between primary cutaneous CD30+ lymphoproliferative disorders (pcCD30+ LPDs) and inflammatory bowel disease (IBD). PcCD30+ LPDs encompass a spectrum ranging from cutaneous anaplastic large cell lymphoma (C-ALCL) to lymphomatoid papulosis (LyP), with intermediate cases in between. Previous reports have suggested a possible link between these disorders and IBD, as patients receiving treatments for IBD showed effects on their pcCD30+ LPDs.
Objective The aim of this study was to investigate the frequency of IBD in Dutch patients with pcCD30+ LPD.
Methods A cohort of 581 pcCD30+ LPD patients from the Dutch Cutaneous Lymphoma Registry (2000–2020) was analyzed. Patients were categorized into LyP, C-ALCL, and borderline cases. Histopathological and clinical data were collected, and histology reports suggesting IBD were screened. The incidence of IBD was calculated with a 95% confidence interval (CI).
Results Among the 581 patients, 3% (19 patients, 95% CI: 2–5%) had a diagnosis of IBD, which is higher than the reported prevalence in the general Dutch population (0.432–0.613%). This suggests a possible association between pcCD30+ LPD and IBD, warranting further investigation.
Conclusion The study indicates a potentially increased prevalence of IBD in patients with pcCD30+ LPD compared to the general population. Further research is needed to confirm and better understand this association, which could have important implications for diagnosis, screening, and treatment strategies for patients with both conditions.

P5 – LISA VAN DER RIJST
TREATMENT GOALS AND PREFERENCES OF PEDIATRIC ATOPIC DERMATITIS PATIENTS, YOUNG ADULTS, AND CAREGIVERS

Lisa P. van der Rijst[1,2], Marjolein S. de Bruin-Weller[2], Nicolaas P.A. Zuithoff[3], Saskia Spillekom-van Koulil[4], Marieke Seyger[5], Marlies de Graaf[1,2]
[1]Department of Dermatology and Allergology, University Medical Center Utrecht, Wilhelmina Children's Hospital, Department of Dermatology and Allergology, Utrecht, The Netherlands; [2]Department of Dermatology and Allergology, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht, Utrecht, The Netherlands; [3]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands; [4]Radboud Institute for Health Sciences, Department of Medical Psychology, Radboud University Medical Centre, Nijmegen, The Netherlands; [5]Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands.

Background Understanding the treatment goals and preferences of young AD patients and their caregivers is crucial for enhancing patient-centered care.
Objective This study aimed to identify treatment goals and preferences of young AD patients and their caregivers and explore heterogeneity among subgroups.
Methods A web-based survey was conducted among children (6-11 years), adolescents (12-17 years) and young adults (18-30 years) with AD and caregivers of AD patients. Survey questions included multiple-choice, 4-point Likert scale, and open-ended questions. Goals and preferences were stratified by age, gender, disease severity, current treatment, visible lesions, and atopic comorbidities.
Results A total of 286 respondents were included in the analyses. Prioritized treatment goals were 'no itch', 'preventing new lesions', and 'no lesions'. Prioritized treatment characteristics were 'high effectiveness' and 'long-term safety'. Young patients (6-30 years) considered convenience of treatment more important than caregivers, while caregivers considered short- and long-term safety more important than young patients. Pediatric patients (6-18 years) considered psychosocial goals more important than young adults. Goals and preferences also differed by gender, disease severity, current treatment, and atopic comorbidities.
Conclusion Young AD patients and caregivers strive to reduce itch and lesions with effective and safe treatment. Goals and preferences differ within individuals at different stages of life, highlighting the importance of addressing individual needs to improve patient-centered care.

P6 – LISA VAN DER RIJST
DUPILUMAB-ASSOCIATED OCULAR SURFACE DISEASE IN PEDIATRIC ATOPIC DERMATITIS PATIENTS: RESULTS FROM THE BIODAY REGISTRY

Lisa P. van der Rijst[1,2], Chantal M. van Luijk[3], Sara van der Kamp[2], Nicolaas P.A. Zuithoff[4], Joke H. de Boer[3], Marjolein S. de Bruin-Weller[2], Marlies de Graaf[1,2]

[1]Department of Dermatology and Allergology, University Medical Center Utrecht, Wilhelmina Children's Hospital, Department of Dermatology and Allergology, Utrecht University, The Netherlands; [2]Department of Dermatology and Allergology, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht, Utrecht University, The Netherlands; [3]Department of Ophthalmology, University Medical Center Utrecht, Utrecht University, The Netherlands; [4]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands.

Background Dupilumab-associated ocular surface disease (DAOSD) is a common side effect in pediatric atopic dermatitis (AD) patients treated with dupilumab. However, long-term real-world safety data are limited.
Objective To investigate the incidence of DAOSD in pediatric AD patients treated with dupilumab and identify associated risk factors.
Methods This prospective study included pediatric AD patients (aged 3-17 years) treated with dupilumab. Ocular symptoms were assessed every 4-12 weeks. DAOSD was considered mild if controlled with lubricating and/or antihistamine eye drops, and/or tacrolimus skin ointment on the external eyelids, and moderate-to-severe if ocular anti-inflammatory therapy was required. Ophthalmological examination was performed in moderate-to-severe DAOSD. Univariable and multivariable regression analyses were conducted to identify predictors for developing DAOSD.
Results Among 104 patients (11.7 ± 4.0 years) with a median follow-up of 70.5 weeks, 34.6% (36/104) developed DAOSD, with 69.4% (25/36) classified as mild and 30.6% (11/36) as moderate-to-severe. The development of DAOSD was not age-dependent. The most common symptoms were pruritus, redness, and tearing. Ophthalmological examination revealed tarsal conjunctivitis in all patients with moderate-to-severe DAOSD. Baseline serum IgE levels ≥3000 kU/L were independently associated with the development of DAOSD (OR 4.66; 95%CI 1.43-15.13, p=.011). DAOSD led to dupilumab discontinuation in 3.8% (4/104) of patients.
Conclusion This real-world study shows that 34.6% of dupilumab-treated pediatric AD patients develop DAOSD, with baseline serum IgE ≥3000 kU/L independently associated with the development of DAOSD. Awareness of ocular symptoms is crucial, particularly in younger patients, where reporting ocular symptoms can be challenging and may affect timely diagnosis.

P7 – H. IBRAHIM KORKMAZ
THE POST-BURN IMMUNE RESPONSE IN BURN PATIENTS: A PIVOTAL ROLE FOR COMPLEMENT

H.I. Korkmaz[1,2,3,4,5,8], P.A.J. Krijnen[9,10], M. Vlig[7,8], G. van Mierlo[11], M.M. Stoop[5], A. Pijpe[1,2,5,8], E. de Jong[12], R.B. Pouw[4,11], H.W.M. Niessen[9,10,13], P.P.M. van Zuijlen[1,2,5,6,8,14]

[1]Department of Plastic, Reconstructive and Hand Surgery, [2]Amsterdam Movement Sciences (AMS) Institute, Amsterdam UMC, Location VUmc, Amsterdam, The Netherlands; [3]Department of Molecular Cell Biology and Immunology, [4]Amsterdam Infection and Immunity (AII) Institute, Amsterdam UMC, Location VUmc, Amsterdam, The Netherlands; [5]Burn Center and [6]Department of Plastic and Reconstructive Surgery, Red Cross Hospital, Beverwijk, The Netherlands; [7]Burn Research Lab, [8]Alliance of Dutch Burn Care, Beverwijk, The Netherlands; [9]Department of Pathology, [10]Amsterdam Cardiovascular Sciences, Amsterdam UMC, Location AMC, Amsterdam, The Netherlands; [11]Department of Research, Sanquin Blood Supply Foundation, and Landsteiner Laboratory, Amsterdam UMC, University of Amsterdam, The Netherlands; [12]Department of Intensive Care, Red Cross Hospital, Beverwijk, The Netherlands; [13]Department of Cardiac Surgery, Amsterdam University Medical Centers, Amsterdam, The Netherlands; [14]Paediatric Surgical Centre, Emma Children's Hospital, Amsterdam UMC, location AMC, Amsterdam, The Netherlands.

Background Burn injuries weaken the immune response, increasing infection risk. Dysregulation of the complement system, a key part of innate immunity, can cause excessive inflammation or immune dysfunction, further heightening infection risk, sepsis, and impairing wound healing.
Objective This study investigates burn wounds' impact on complement activation.
Methods In an observational study at Burn Center Beverwijk, Netherlands, adult burn patients (2016-2017) were grouped by burn size: <10% (n=7), 10-20% (n=6), and >20% (n=5) total body surface area (TBSA) burned. Weekly blood samples were collected for 30 days. C-reactive protein (CRP) and leukocyte levels were measured using turbidimetric and haematology analysers. Complement activation fragments (C3bc, C4bc) and C1-esterase inhibitor (C1inh) protein and activity levels were assessed using ELISA.
Results CRP levels peaked in all groups 2-6 days post-burn, with elevated leukocytes only in the <10% group, significantly higher than the 10-20% and >20% groups. By 9-14 days, CRP was higher in the >20% group compared to <10%, with slight leukocyte increases in all groups. By 21-30 days, CRP and leukocytes decreased but CRP remained above healthy levels. C3bc and C4bc increased significantly in the <10% group at 2-6 days. C3bc stayed elevated at 9-14 and 21-30 days. Endogenous C1inh protein was significantly increased after 9-14 up to 21-30 days. While the levels of functional C1inh were slightly, but significantly increased 9-14 days only. No correlation was found between burn size and C3bc, C4bc, or C1inh.
Conclusion In burn patients, there is a prolonged increase in complement activation, notwithstanding increased endogenous C1inh.

P8 – LEON MILTNER
MULTIMORBIDITY IN ADULTS WITH ATOPIC DERMATITIS IN A POPULATION-BASED COHORT

Leon A. Miltner[1], Laura Loman[1], Josué Almansa Ortiz[2], Junfen Zhang[1,3], Aline B. Sprikkelman[4,5], Marie-Louise A. Schuttelaar[1]
[1]Department of Dermatology, University Medical Center Groningen, Groningen, The Netherlands; [2]Department of Health Sciences, Community and Occupational Medicine, University Medical Center Groningen, Groningen, The Netherlands; [3]Dermatology Hospital, Southern Medical University, Guangzhou, China; [4]Department of Pediatric Pulmonology and Pediatric Allergy, University Medical Center Groningen, Groningen, The Netherlands; [5]Groningen Research Institute for Asthma and COPD (GRIAC), University Medical Center Groningen, Groningen, The Netherlands.

Background Atopic dermatitis (AD) is proposed as a systemic disease due to underlying systemic inflammation and various comorbidities.
Objective This study aimed to examine the associations between AD and multimorbidity (MM) in a cohort from the Northern Netherlands and to identify MM patterns in participants with AD.
Methods We assessed lifetime prevalence of 52 diseases, from 15 domains, combining data from questionnaires, medication records and clinical assessments within the Lifelines Cohort. Lifetime AD was self-reported, physician-diagnosed and severity evaluated using the POEM. MM was defined as lifetime presence of at least two diseases, excluding AD. A categorised morbidity score (cMS) indicated the number of diseases. We analysed associations of AD and AD severity with MM and cMS using binary and multinomial logistic regression, adjusting for age and sex. Patterns of MM based on disease domains were explored using Latent Class Analysis (LCA).
Results Among 37,193 participants, 8.7% had AD. The prevalence of MM was 64.9% in those with AD, increasing with severity (mild 62.4%; moderate-to-severe 68.4%) and 52.4% for those without. The risk for MM was 1.95-fold higher in participants with AD, particularly for moderate-to-severe cases (aOR 2.49 vs. mild AD aOR 1.73). The risk increased with additional morbidities, reaching 4.08-fold for ≥5 diseases. Results were additionally confirmed for non-atopic MM. LCA identified five distinct classes of multimorbid participants with AD.
Conclusion Participants with AD, especially moderate-to-severe cases, are at higher risk for both MM and non-atopic MM. Whether this is due to systemic inflammation in AD, needs further investigation.

P9 – LIANA BARENBRUG
INCORPORATING THE PATIENTS' VOICE IN HEALTHCARE PRACTICE AND INFORMATION PROVISION REGARDING FAMILY PLANNING AND PREGNANCY: A QUESTIONNAIRE STUDY AMONG DUTCH PATIENTS WITH PSORIASIS

L. Barenbrug[1], I. van Ee[2], R.G. van der Molen[3], E.G.M.J. de Jong[1], J.M.P.A van den Reek[1]
[1]Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; [2]Psoriasispatiënten Nederland, Nijkerk, The Netherlands; [3]Department of Laboratory Medicine, Laboratory of Medical Immunology, Radboud University Medical Center, Nijmegen The Netherlands.

Background Having a chronic disease and being treated with medication could raise concerns regarding family planning and pregnancy (FPP), for both female and male patients with psoriasis. Yet no guidelines are available that specify on when, how, and by whom information regarding FPP should be provided to patients.
Objective Gain insight in the perspectives of patients with psoriasis on healthcare and information provision regarding FPP in the Netherlands.
Methods We developed an online questionnaire in collaboration with the Dutch psoriasis patient association. Female and male patients with psoriasis ≥18 years in the Netherlands, independent of their treatment type, were eligible to participate in this study.
Results A total of 102 patients responded to the questionnaire (71 (70%) females, 31 (30%) males). Respondents preferred dermatologists or general practitioners as information provider, but also indicated that they would like to have a flyer/website they can access themselves. Topics of FPP information that patients would like to receive are fertility, heredity of psoriasis, use of psoriasis medication, and specifically for females the course of psoriasis during and after pregnancy and breastfeeding. Respondents desired FPP information at diagnosis and at the moment of medication changes. However, a considerable part (44%) of the respondents preferred to receive information only when they explicitly requested it.
Conclusion Dermatologists and general practitioners have a crucial role in providing FPP information. An information source aggregating all the relevant FPP information that guides physicians and is accessible for patients could be beneficial for improving healthcare for patients with psoriasis.

P10 – FLORENTINE DE BOER
EFFECT OF REPEATED LOW DOSE UVR EXPOSURE ON THE SKIN INFLAMMATION THRESHOLD, SKIN BIOMARKERS AND VITAMIN D IN HEALTHY ADULTS

F.L. de Boer[1], S. Kezic[1], G.E. van der Lelie[2], E. Motazedi[1], T. Rustemeyer[3], A. van Dijk[4], M. Almasian[5], I. Jakasa[6], H.F. van der Molen[1]
[1]Department of Public and Occupational Health, Amsterdam UMC location AMC, The Netherlands; [2]Vrije Universiteit van Amsterdam, The Netherlands; [3]Department of Dermatology and Allergology, Amsterdam UMC location AMC, The Netherlands; [4]RIVM; Rijksinstituut voor Volksgezondheid en Milieu, Bilthoven, The Netherlands; [5]Department of Bioengineering, Amsterdam UMC location AMC, The Netherlands; [6]Department of Food Technology, University Zagreb, Croatia.

Background Ultraviolet radiation (UVR) is the primary risk factor for skin cancer, but the skin adapts to counteract harmful effects of UVR through photoadaptation. Key factors in this process include melanin production, skin thickening and immune responses.
Objective We aim to investigate the effects of low-dose UVR on the skin's inflammation threshold assessed as minimal erythema dose (MED) across different skin phototypes (FP).
Methods Over nine-weeks, 31 subjects were exposed on the lower back to sub-erythemal UVR (0.8 standard erythema dose), three times per week. At three visits, we measured MED, epidermal and stratum corneum (SC) thickness, melanin index (MI), erythema index (EI), skin and systemic levels of immunological biomarkers and serum vitamin D.
Results We observed a 50% increase in MED, with a stronger effect in lighter phototypes. Increase in MED was paralleled with increase in EI. MI and SC thickness increased by 12% and 34%, respectively, with melanin playing a larger role in MED increase. Vitamin D levels rose by 21%, adjusting for seasonal decline. Immunological markers of Th1/Th2 response and vascular markers declined, indicating local immunosuppression, though no systemic effects were observed.
Conclusion These findings suggest that low-dose UVR promotes photoadaptation, but further research is required to evaluate the long-term risks and benefits of this exposure.

P11 – ANDREW MORRISON
LYMPHATIC ENDOTHELIAL CELLS ENHANCE THE PHYSIOLOGY OF A PERFUSED VASCULARISED LYMPH NODE-ON-CHIP FOR STUDYING SKIN-IMMUNE RESPONSES

Andrew I. Morrison[1,2*], Jonas Jäger[1,2*], Charlotte M. de Winde[1,2,3], Susan Gibbs[1,2,4], Jasper J. Koning[1,2], Reina E. Mebius[1,2]
*[1]Amsterdam UMC location Vrije Universiteit Amsterdam, Molecular Cell Biology & Immunology, Amsterdam, The Netherlands; [2]Amsterdam institute for Infection and Immunity, Amsterdam, The Netherlands; [3]Cancer Center Amsterdam, Amsterdam, The Netherlands; [4]Department Oral Cell Biology, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit, Amsterdam, The Netherlands. *These authors have contributed equally.*

Background Lymph nodes (LNs) play an integral part in systemic human immunology, aiding in tissue drainage of interstitial fluid and immune cell migration, particularly from skin via lymphatic endothelial cells (LECs) of the lymphatic vasculature. Representative LN models are needed to study immune responses *in vitro*, but recreating LN complexity with stromal and immune cells is challenging, especially for multiorgan-on-chip (MOC) systems.
Objective This study characterises the addition of LECs under a LN-on-chip model, lining a sacrificial structure in a TissUse HUMIMIC Chip2 to act as a lymphatic vessel.
Methods Human immune cells and LECs were isolated from LN biopsies. A LN hydrogel was cultured in the chip, with LECs seeded for vessel endothelialisation. After a 7-day flow culture, flow cytometry, 3D imaging, cytokine/chemokine analysis, and metabolic profiling were performed.
Results A stable culture maintained consistent immune cell populations, independent of LEC addition. LECs in the LN model displayed an enhanced lymphatic phenotype, upregulating markers such as ACKR4. LECs increased IL-7 and CCL21 levels in the vasculature, while homeostatic factors, like CXCL13, remained within the LN compartment. Immune cell clusters were observed in higher abundance near the LEC vessel, reflecting a more optimal immune cartography.
Conclusion This study demonstrates an enhanced physiological relevance of an immunocompetent LN-on-chip model containing LECs, characterised by the emergence of LN-specific factors essential for a migratory microenvironment. These findings support the suitability for MOC platforms, where a skin-draining LN model, in progress, can study immune cell trafficking and adaptive immune responses downstream from dermal pathology.

P12 – NOOR VAN HOUT
ENGINEERED LIVE BIOTHERAPEUTIC PRODUCTS AND THEIR EFFECTS ON UV LIGHT-IRRADIATED KERATINOCYTES

N.E van Hout[1], G. Nevot[2], P.A.M. Jansen[1], P.L.J.M. Zeeuwen[1], E.H. van den Bogaard[1]
[1]Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; [2]Department of Experimental and Health Sciences, Universitat Pompeu Fabra, Barcelona, Catalunya, Spain.

Background Current treatments for chronic skin conditions such as atopic dermatitis (AD) primarily focus on symptom control, often leading to side effects and economic burdens on healthcare systems. In the European project SKINDEV, we aim to harness the skin microbiome and engineer bacteria to create next-generation probiotics also known as engineered live biotherapeutic products (eLBPs). With synthetic biology, strains are created that can detect skin signals like immune responses and environmental factors, producing therapeutic treatments on demand.
Objective In this part of the project we aim to evaluate the potential of a skin-commensal eLBP that produces superoxide dismutase (SOD) to decrease UV light-induced oxidative stress.
Methods *In vitro* human epidermal equivalents (HEE) will be exposed to various doses of UV light to determine conditions that induce reactive oxygen species (ROS)-related gene expression. Following the selection of the optimal UV dosages, the eLBP will be cultured on top of the HEE. Supernatants will be collected to quantify H_2O_2 levels as an indicator of ROS production by keratinocytes. The production of SOD will be assessed using Western blot analysis of the total construct lysate. Additionally, SOD activity will be measured using specific activity assays on the same lysate samples.
Results Currently data are analyzed and will be presented in detail at the annual meeting of the NVED 2025.
Conclusion Will be discussed at the annual meeting of the NVED 2025.

P13 – LINDA GODDING
SEARCHING FOR RELEVANT BIOMARKERS IN DERMATOLOGICAL CARE: A SURVEY AMONG DUTCH PATIENTS AND DERMATOLOGICAL CARE PROVIDERS

L.T.H. Godding[1], M.M.B. Seyger[1], S. van Beugen[2], A.I.M. van Laarhoven[2], E. van der Pool[3], N. Olde[3], D. Trampe[3], H. Niehues[1], E.M.G.J. de Jong[1], J.M.P.A. van den Reek[1], on behalf of the Next Generation ImmunoDermatology project
[1]Department of Dermatology, Radboud University Medical Centre, Nijmegen, The Netherlands; [2]Institute Psychology, Health, Medical and Neuropsychology Unit, Leiden University, Leiden, The Netherlands; [3]Lectoraat Human Communication Development, HAN University of Applied Sciences, Nijmegen, The Netherlands.

Background The Next Generation ImmunoDermatology (NGID)-project, a unique Dutch nationwide flagship project, aims to enhance personalized care by identifying biomarkers for six skin diseases. Successful biomarker implementation requires insights into patients' and dermatological care providers' (DCPs) needs.
Objective Identifying biomarker needs and preferences of patients and DCPs regarding psoriasis, atopic dermatitis (AD), hidradenitis suppurativa, lupus erythematosus (LE), chronic urticaria (CU), and T-cell lymphoma (TCL).
Methods Questionnaires were developed for patients and DCPs separately. Demographics, biomarker needs, and uptake barriers and facilitators were assessed.
Results (preliminary September 2024) The preliminary sample consisted of 295 patients and 58 DCPs. Both patients and DCPs most frequently reported the need for a therapeutic response biomarker. For LE, CU, and TCL, a large proportion of both groups also expressed the need for a biomarker that predicts disease progression. Assuming a one-time biomarker collection, patients' willingness regarding biomarker uptake was generally high. Most important barriers were incomplete reimbursement or travel times >1 hour, although a substantial proportion of AD and CU patients also considered a biopsy a barrier. DCPs considered a well-validated biomarker and easy uptake in daily practice as main facilitators, while poor validation was the main barrier.
Conclusion Both patients and DCPs are in need for biomarkers that predict therapeutic response. However, findings also highlight differences in needs among patients with various skin diseases and differences in barriers and facilitators between patients and DCPs. Acknowledgement of these findings in early phases of biomarker research is essential and will facilitate implementation in daily practice.

P14 – JULIETTE SIMONS
DIAGNOSTIC MANAGEMENT AND MONITORING OF CHOLINERGIC URTICARIA PATIENTS IN DAILY PRACTICE

Juliette V.L. Simons, Hong Nho Le, Reineke Soegiharto, André C. Knulst, Heike Rockmann
Urticaria Centre of Excellence and Reference (UCARE). Department of Dermatology/Allergology, University Medical Centre Utrecht, Utrecht University, Utrecht, The Netherlands.

Background The pulse-controlled ergometry test (PCE test) and CholU Severity Index (CholUSI) are available instruments for diagnosis and severity assessment of cholinergic urticaria (CholU). However, both tools were only evaluated in a limited number of patients.
Objective To investigate the diagnostic value of the PCE test and the value of CholUSI for monitoring of CholU severity.
Methods Retrospective study including all patients with a clinical diagnosis of CholU, based on exercise induced wheals and pruritus by history and photo-documentation, between 2021 and 2024. We evaluated patient characteristics, CholU severity by UCT and CholUSI, diagnostic value of PCE-test (defined positive when wheals occurred).
Results Thirty-nine CholU patients (66.7% male, median age 25.0 years, median CholUSI 17.0; mean UCT 2.0) were included. Sixteen patients underwent a PCE test: wheals developed in 10 patients, indicating a PCE-test sensitivity of only 62.5% (95% CI 0.4-0.8). A positive PCE-test was associated with earlier sweating (5 vs. 20 minutes respectively, p=0.03) and higher disease severity by CholUSI (18.0 vs. 14.5, p<0.01). In 22 CholU patients treated with omalizumab median CholUSI decreased significantly from 17.0 (IQR 16.0-18.0), at baseline, to 4.0 (IQR 0.0-15.0) at end of treatment (p<0.01), and median UCT increased significantly from 2 (IQR 1-4) to 15.5 (IQR 7-16) (p<0.01) respectively. The correlation between CholUSI and UCT was strong and statistically significant (P=-0.821; p<0.01).
Conclusion The sensitivity of the PCE test was low and associated with early sweating and high disease severity. CholUSI might be a valuable tool for monitoring CholU.

P15 – SHIDI WU
TUMOR-STROMA INTERACTION FACILITATES CUTANEOUS T CELL LYMPHOMA CELL PROLIFERATION AND DYNAMIC PHENOTYPE CHANGE IN CANCER-ASSOCIATED FIBROBLASTS

Shidi Wu, Marion H. Rietveld, S. de Haan, C.P. Tensen, Maarten H. Vermeer, Abdoelwaheb El Ghalbzouri
Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands.

Background The tumor microenvironment (TME) is a complex ecosystem surrounding a tumor and supporting tumor progression in which cancer-associated fibroblasts (CAFs) are the major component. To date, the impact of the TME on mycosis fungoides (MF) progression remains underexplored, especially the contribution of CAFs on MF pathogenesis awaits further investigations.
Objective Explore the interaction between MF malignant T cells and CAFs.
Methods To examine the effect of CAFs on malignant T cell proliferation, conditioned media (CM) from CAFs was collected and used to culture two MF cell lines (Myla & HH) and their cell viability was examined via CCK8 assays. Then, 2D "Myla-CAFs" co-culture was carried out in transwell plates and the CAF morphology was observed via a microscope while the phenotypical changes of CAFs were examined via RT-PCR.

Results Compared to the control group, CAF-CM significantly induced Myla cell proliferation but not HH cells. 2D co-culture of CAFs with Myla cells switched the well-aligned, spindle-shaped morphology to a "stressed", more flattened and tangled appearance. RT-PCR Results showed a mild induction of myo-fibroblastic CAF panel genes (ACTA2, COL11A and POSTN) in CAFs co-cultured with Myla cells. Meanwhile, the expression of several cytokines and chemokines was drastically upregulated in Myla-co-cultured CAFs compared to control CAFs (CXCL1, CXCL2, CXCL5, CXCL6, IL1b, IL6, IL8 and CXCL12. N=6), indicating a dynamic inflammatory phenotype acquisition in CAFs enabled by Myla cells.
Conclusion Our findings suggest interaction between Myla cells and CAFs facilitates malignant T cell proliferation and yields an "inflammatory CAF-dominant" phenotype in CAFs.

P16 – LIAN VAN DER GANG
EARLY EFFICACY OF DUPILUMAB IN ATOPIC DERMATITIS: PATIENT-REPORTED OUTCOMES VERSUS OBJECTIVE SLEEP AND SCRATCHING MEASURES

Lian F. van der Gang, Elise J. Leeman, Celeste M. Boesjes, Marlies de Graaf, Marjolein de Bruin-Weller
Department of Dermatology and Allergology, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht, Utrecht, The Netherlands.

Background Real-world data on early itch reduction and sleep improvement with dupilumab treatment for moderate-to-severe atopic dermatitis (AD) are limited and primarily rely on physician- or patient-reported outcomes (PROs) instead of Objective measures.
Objective To evaluate the early effect of dupilumab on nocturnal scratching and sleep using Objective measurements from actigraphy and photoplethysmography, alongside PROs.
Methods This single-center, prospective cohort study included adult patients with moderate-to-severe AD initiating dupilumab treatment at the labeled dose. Nocturnal scratching and sleep parameters were assessed nightly using wristbands that measured actigraphy, accelerometry (ACC), and photoplethysmography (PPG) for 7 days pre-treatment and 28 days post-treatment initiation. Daily Numeric Rating Scales (NRS) for itch and sleep disturbance were recorded as PROs. Generalized linear mixed models were used to assess changes in continuous outcomes over time, and random effect meta-analyses to evaluate correlations between Objective measures and PROs.
Results Twelve patients completed the study (median age 44 years, 25% male, mean baseline Eczema Area and Severity Index [EASI] score 18.1). Patient-reported NRS itch and sleep scores, along with physician-assessed EASI scores, significantly improved over 28 days, while actigraphy-measured nocturnal scratching events and ACC/PPG-measured sleep efficiency remained unchanged. Weak correlations were observed between total scratching time and patient-reported itch scores, with no significant association between patient-reported itch and sleep efficiency.
Conclusion Dupilumab significantly improved patient-reported itch and sleep quality within 28 days; however, **Objective** measures of nocturnal scratching and sleep did not show similar efficacy, potentially due to habitual nocturnal scratching.

P17 – LIAN VAN DER GANG
DAILY PRACTICE EXPERIENCE OF DUPILUMAB TREATMENT IN PATIENTS WITH PRURIGO NODULARIS: A 28-WEEK EVALUATION OF CLINICAL EFFECTIVENESS AND SAFETY FROM THE BIODAY REGISTRY

Lian F. van der Gang[1], Daphne S. Bakker[1], Florence Vroman[1], Keneshka Atash[1], Marijke Kamsteeg[2], Floor M. Garritsen[3], Francine C. van Erp[4], Simone A.E. Stadhouders-Keet[5], Wianda A. Christoffers[6], Femke van Wijk[7], Marlies de Graaf[1], Inge Haeck[1], Marie L.A. Schuttelaar[8], Marjolein de Bruin-Weller[1]
[1]Department of Dermatology and Allergology, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht, Utrecht, The Netherlands; [2]Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; [3]Department of Dermatology, HagaZiekenhuis, Den Haag, The Netherlands; [4]Department of Dermatology, TerGooi Medical Center, Hilversum, The Netherlands; [5]Department of Dermatology, Reinier de Graaf Gasthuis, Delft, The Netherlands; [6]Department of Dermatology, Reinier de Graaf Gasthuis, Delft, The Netherlands; [7]Center for Translational Immunology, University Medical Center Utrecht and Utrecht University, Utrecht, The Netherlands; [8]Department of Dermatology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.

Background Dupilumab is the first available targeted treatment for adults with moderate-to-severe prurigo nodularis (PN). While its safety and efficacy have been shown in phase III trials, real-world data is limited.
Objective To assess the 28-week real-world efficacy and safety of dupilumab in PN patients.
Methods Adult patients treated with dupilumab for PN from February 2023 to September 2024 were enrolled in the Dutch BioDay registry. Data were collected at baseline, 16 weeks, and 28 weeks. Efficacy was measured by clinical (Investigator Global Assessment for PN-Stage [IGA PN-S]) and patient-reported outcomes (weekly average itch Numeric Rating Scale [NRS]).
Results Forty-five patients with PN (mean age 60.2 years, 55.6% female, 62.2% with atopy) were included. Mean IGA PN-S decreased from 3.3 ± 0.7 (n=45) to 2.0 ± 1.0 (n=36) at 16 weeks, and 1.6 ± 1.0 (n=22) at 28 weeks. The proportion of patients achieving NRS ≤ 4 was 47% at 16 weeks and 59% at 28 weeks. Atopic PN patients had significantly lower IGA PN-S scores than non-atopic patients at weeks 16 and 28. Adverse events included ocular surface disease (n=7, 15.5%), arthralgia/myalgia (n=7, 15.5%), and headache (n=3, 6.7%). Three patients (6.7%) discontinued dupilumab treatment due to side effects (n=1), ineffectiveness (n=1), or patient preference (n=1).
Conclusion Real-world data from the BioDay registry confirms dupilumab's effectiveness in reducing skin lesions and itch in PN patients, consistent with clinical trial Results. Preliminary

Results suggest that atopic patients may respond better, and that safety aligns with the known dupilumab safety profile.

P18 – NIENKE VELDHUIS
OCULAR SURFACE DISEASE IN PEDIATRIC PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS

Nienke Veldhuis[1*] Lisa P. van der Rijst[1,2*], Sara van der Kamp[1]; Roselie E. Achten[1], Chantal M. van Luijk[3], Elsbeth S.M. Voskuil-Kerkhof[3], Inge M. Haeck[1], Marjolein S. de Bruin-Weller[1], Marlies de Graaf[1,2]

*[1]Department of Dermatology and Allergology, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht, Utrecht University, The Netherlands; [2]Department of Dermatology and Allergology, University Medical Center Utrecht, Wilhelmina Children's Hospital, Department of Dermatology and Allergology, Utrecht University, The Netherlands; [3]Department of Ophthalmology, University Medical Center Utrecht, Utrecht, The Netherlands. *These authors have contributed equally.*

Background Ocular surface disease (OSD) is a known comorbidity in patients with atopic dermatitis (AD), but its prevalence in pediatric patients with moderate-to-severe AD is currently unknown.
Objective To investigate the prevalence and severity of OSD in pediatric patients with moderate-to-severe AD.
Methods This prospective study included pediatric patients (aged <18 years) with moderate-to-severe AD eligible for systemic treatment between August 2019 and July 2024 at the Wilhelmina Children's Hospital and the University Medical Center Utrecht, the Netherlands. All patients were examined by an ophthalmologist and a dermatologist. The severity of OSD was assessed using the Utrecht Ophthalmic Inflammatory and Allergic disease (UTOPIA) score.
Results Fifty pediatric patients (median age 10.0 years [IQR 6.0-13.3]) were included. Self-reported allergic conjunctivitis was present in 70.0% (35/50) of patients, and 14.0% (7/50) of patients used concomitant ocular medication. Ocular symptoms were reported by 42.0% (21/50) of patients. OSD was observed in 74.0% (37/50) of patients, mostly (94.6%) classified as mild OSD (median UTOPIA score 2.0 [IQR 0.0-3.0]). In patients with OSD, 43.2% (16/37) of patients did not report any ocular symptoms. OSD development was significantly correlated with age (p<.001), EASI score (p=.015), pre-existing allergic conjunctivitis (p=.040), and total IgE levels (p=.019).
Conclusion OSD is prevalent and mostly mild in pediatric patients with moderate-to-severe AD, with its prevalence increasing with age. These findings highlight the potential underdiagnosis of OSD in pediatric moderate-to-severe AD patients, and may contribute to preventative strategies and earlier identification of ocular side effects in patients treated with biologics.

P19 – THIJS VAN DER MARK
DEVELOPMENT AND VALIDATION OF BLUNT TRAUMA IN A RECONSTRUCTED HUMAN SKIN MODEL

Thijs van der Mark[1], Paul A.J. Krijnen[2], Rico W. Balk[2,4,5], Ingeborg S.E. Waas[2], Maartje Goudswaard[1], Manon Ceelen[1], Udo J.L. Reijnders[1], Hans W.M. Niessen[2], H. Ibrahim Korkmaz[3,4,5,6]

[1]Department of Forensic Medicine and Medical Advisement, Public Health Service Amsterdam, The Netherlands; [2]Department of Pathology, Amsterdam Cardiovascular Sciences, Amsterdam UMC, Location AMC, Amsterdam, The Netherlands; [3]Department of Plastic, Reconstructive and Hand Surgery, Amsterdam Movement Sciences (AMS) Institute, Amsterdam UMC, Location VUmc, Amsterdam, The Netherlands; [4]Department of Molecular Cell Biology and Immunology, Amsterdam Infection and Immunity (AII) Institute, Amsterdam UMC, Location VUmc, Amsterdam, The Netherlands; [5]Alliance of Dutch Burn Care, Beverwijk, The Netherlands; [6]Burn Center and Department of Plastic, Reconstructive and Hand Surgery, Red Cross Hospital, Beverwijk, The Netherlands.

Background In the Netherlands, forensic medical injury reporting is deemed crucial and often lacking in criminal cases. Experts in justice have highlighted the need for more medical information in criminal cases. Injury dating Methods are limited, specifically for bruises. (Immuno)histological markers might be used in living individuals as is already done post mortem. Dating blunt injuries in living individuals using immunohistochemistry remains unexplored.
Objective An *in vitro* skin model of superficial blunt injuries could provide insights in novel injury dating markers for forensic applications; however, such a model has not yet been developed and validated. The aim of this study is to characterize and validate blunt trauma in a 3D reconstructed human skin (RhS) model.
Methods Human skin was mimicked *in vitro* using tissue engineered RhS model. In this model, human keratinocytes are cultured on fibroblast populated collagen-based hydrogels. Blunt trauma was induced by the impact of a dropped metal object (weight: 68.211g, diameter: 1cm) from a height of 5cm and 10cm onto the RhS. Morphological changes were assessed using histology.
Results After the application of blunt force, trauma was induced in the RhS. Basal keratinocyte nuclei deform from a cylindrical to a spherical shape upon trauma. Also, an disorganized keratinocyte structure is observed. The dermal layer of the RhS showed lacerations post trauma.
Conclusion This study successfully developed and validated an *in vitro* model for blunt trauma, providing a crucial tool for the identification of novel injury dating markers in forensic medical research.

P20 – REINEKE SOEGIHARTO
SIDE EFFECTS OF OMALIZUMAB IN PATIENTS WITH CHRONIC URTICARIA: A LONG-TERM MULTI-CENTRE REAL-WORLD STUDY

R. Soegiharto[1], E. van der Wind[1], M. Alizadeh Aghdam[1], J.A. Sørensen[2], E. van Lindonk[3], F. Bulut Demir[4], N. Mohammad Porras[5], Y. Matsuo[6], L. Kiefer[7,8], A.C. Knulst[1], M. Maurer[7,8†], C. Ritchie[9], M. Rudenko[10], E. Kocatürk[7,11], R.F.J. Criado[12], S. Gregoriou[13], T. Bobylev[14], A. Kleinheinz[14], S. Takahagi[6], M. Hide[6,15], A.M. Giménez-Arnau[5], A. Salman[4,16], R. Oztas Kara[17], B.S. Dikicier[17], M.B.A. van Doorn[3,18], S.F. Thomsen[2], J.M.P.A. van den Reek[19], H. Röckmann[1]

[1]Department of Dermatology/Allergology, University Medical Centre Utrecht, Utrecht University, Utrecht, The Netherlands; [2]Department of Dermato-Venereology and Wound Healing Centre, University of Copenhagen, Bispebjerg Hospital, Copenhagen, Denmark; [3]Department of Dermatology, Erasmus MC, Rotterdam, The Netherlands; [4]Department of Dermatology, Marmara University School of Medicine, İstanbul, Turkey; [5]Department of Dermatology, Hospital del Mar Research Institute, Universitat Pompeu Fabra de Barcelona, Barcelona, Spain; [6]Department of Dermatology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan; [7]Institute of Allergology, Charité, Freie Universität Berlin and Humboldt-Universität, Berlin, Germany; [8]Fraunhofer Institute for Translational Medicine and Pharmacology, Immunology and Allergology, Berlin, Germany; [9]Secciones Alergia Adultos y Pediátrica, Hospital Italiano de Buenos Aires, Ciudad Autónoma de Buenos Aires, Argentina; [10]London Allergy and Immunology Centre, London, United Kingdom; [11]Department of Dermatology, Bahcesehir University School of Medicine, Istanbul, Turkey; [12]Department of Dermatology, faculdade de medicina do ABC, Santo André, Brazil; [13]Department of Dermatology and Veneorology, National and Kapodistrian University of Athens, Athens, Greece; [14]Clinic for Dermatology, Elbe Klinikum Buxtehude, Buxtehude, Germany; [15]Department of Dermatology, Hiroshima City Hiroshima Citizens Hospital, Hiroshima, Japan; [16]Department of Dermatology, Acibadem Mehmet Ali Aydinlar University School of Medicine, Istanbul, Turkey; [17]Department of Dermatology, Sakarya University Faculty of Medicine, Sakarya, Turkey; [18]Centre for Human Drug Research, Leiden, The Netherlands; 19 Department of Dermatology, Radboud University Medical Centre, Nijmegen, The Netherlands.
†Author M. Maurer deceased

Background Omalizumab treatment in chronic urticaria (CU) is considered safe in RCTs and daily practice studies. Studies primarily investigating side effects (SEs) of omalizumab and associated factors are lacking.
Objective To investigate reported SEs in omalizumab treated CU patients in a large long-term daily practice cohort.
Methods A multi-national retrospective study was conducted at 14 UCAREs, including all CU patients ever treated with omalizumab until centre specific data lock. The prevalence of reported SEs was assessed.
Results 1,859 patients were included, of which 32.9% (n=612, range across centres 0%-75.5%) reported SEs during omalizumab treatment. Only 7.2% (n=44/612) discontinued treatment for this reason. Fatigue (15.8%, n=293), headache (11.6%, n=215) and flu-like symptoms (9.3%, n=172) were most commonly reported. No events suggestive for anaphylaxis and no new notably prevalent SEs were reported. Hair loss was reported by 2.9% (n=53) of patients, leading to omalizumab dosage decrease in 21.1% (n=8). Patients reporting SEs were more often female (78.3% versus 68.6%, p<.001), had worse disease control prior to omalizumab (UCT 4.0 versus 6.0, p<.001) and lower fast response rates (42.6% versus 59.5%, p<.001) compared to those without SEs.
Conclusion Omalizumab's safety and tolerability was confirmed, with no newly reported severe SEs and no suggestive anaphylaxis observed. Certain SEs of impact may lead to treatment adjustments and deserve more attention, e.g. hair loss. SEs were more often reported in difficult-to-treat CU patients, possibly related to a negative connotation with omalizumab. This potentially increased disease burden highlights the importance of achieving disease control in CU patients.

P21 – REINEKE SOEGIHARTO
EXPLORING THE DISEASE DURATION OF URTICARIA AND ASSOCIATED CLINICAL CHARACTERISTICS IN DUTCH PRIMARY CARE

R. Soegiharto[1], B. Hengevelt[1], N. Boekema-Bakker[2], I.A.M. Groenewegen[2], A.C. Knulst[1], J. van den Reek[3], H. Röckmann[1]
[1]Department of Dermatology/Allergology, University Medical Centre Utrecht, Utrecht University, Utrecht, The Netherlands; [2]Julius Center for Health Sciences and Primary Health Care, University Medical Centre Utrecht, Utrecht, The Netherlands; [3]Department of Dermatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.

Background While disease duration in urticaria is often expected to be short (acute), it is unclear which factors are associated with long disease duration (chronic). In The Netherlands, all urticaria patients are initially managed by general practitioners (GPs).
Objective To determine the rates of short- and long-duration urticaria in Dutch primary care and associated factors.
Methods All patients from the Julius General Practitioner Network database with at least one urticaria-related contact between 2010 and 2019 were included. Dates of urticaria-related contacts were used to estimate disease duration. Characteristics, comorbidities and comedication were used to analyse determinants of longer disease duration by multivariate logistic regression.
Results 18.087 urticaria patients were identified (mean age 30, 62.4% female); 69.6% (N=12.588) and 77.7% (N=14.059) had <1 and <6 weeks follow-up, respectively, suggesting acute urticaria. Twenty-two percent (N=4028) had a follow-up duration >6 weeks, suggesting chronic urticaria with median duration of 2 (IQR 0-5) years. Long duration (>6 weeks) was associated with female sex (OR 1.13, 95%CI 1.05-1.21), higher age (OR 1.01, 95%CI 1.0-1.01), and high BMI (OR 1.55, 95%CI 1.38-1.73), while

shorter duration was associated with fever (OR 0.61, 95%CI 0.37-1.00) and antibiotics prescription (OR 0.76, 95%CI 0.64-0.89) surrounding first urticaria contact.
Conclusion In primary care, the majority of urticaria patients had short disease duration, but a substantial part had longer duration with a median of 2 years. The identified determinants are potentially indicative of prolonged disease and may support expectation-management and guide clinicians in identifying patients who benefit from earlier treatment-strategy escalation.

P22 – NIKITA KOSTER
A PROSPECTIVE, MULTI-CENTER, OBSERVATIONAL BIOMARKER REAL-WORLD EVIDENCE STUDY FOR IN-DEPTH PROFILING OF PATIENTS WITH CHRONIC IMMUNE-MEDIATED INFLAMMATORY SKIN DISEASES IN DAILY PRACTICE

N.G. Koster[1,8,9], J. Simons[2], F. van den Berge[3], J.M.P.A. van den Reek[4], E.M.G.J. de Jong[4], S. van Beugen[5], A.I.M. van Laarhoven[5], I. Haeck[2], M. de Bruin-Weller[2], M.L. Schuttelaar[6], B. Horvath[6], A. Gostinsky[7], A. Knulst[2], D. Balak[8], M.H. Vermeer[8], L. Nguyen[8], L. Gerbens[10], P. Spuls[10], P. Middelkamp-Hup[10], V. Exadaktylos[9], T. Niemeyer-van der Kolk[9], H. van der Zee[3], J. Damman[3], DJ Hijnen[3], F. Wijk[11], M.M.B. Seyger[4], H. Röckmann[2], M.B.A. van Doorn[3], R. Rissmann[1,8,9]
[1]Research division BioTherapeutics, Leiden Academic Centre for Drug Research, Leiden University, The Netherlands; [2]University Medical Center Utrecht, Dermatology, Utrecht, The Netherlands; [3]Erasmus MC, Dermatology, Rotterdam, The Netherlands; [4]Radboud University Medical Centre, Dermatology, Nijmegen, The Netherlands; [5]Leiden University, Instituut Psychologie, sectie Gezondheids-, Medische en Neuropsychologie, Leiden, The Netherlands; [6]University Medical Center Groningen, Dermatology, Groningen, The Netherlands; [7]University Medical Center Maastricht+, Dermatology, Maastricht, The Netherlands; [8]Leiden University Medical Centre, Huidziekten, Leiden, The Netherlands; [9]Centre for Human Drug Research (CHDR), Leiden, The Netherlands; [10]Amsterdam University Medical Centre, Dermatology, Amsterdam, The Netherlands; [11]University Medical Center Utrecht, Center of Translational Immunology, Utrecht, The Netherlands.

Background The Next Generation ImmunoDermatology project aims to comprehensively profile six immune-mediated inflammatory diseases, including atopic dermatitis (AD), plaque psoriasis (PSO), hidradenitis suppurativa (HS), cutaneous T-cell lymphoma subtype mycosis fungoides (MF), chronic spontaneous urticaria (CSU), and cutaneous lupus erythematosus (CLE) in daily practice.
Objective The Objectives in this study include evaluating disease-related characteristics compared to healthy volunteers, and evaluation of biomarkers for disease stratification and (targeted) treatment response in patients in a real-world clinical setting. Additionally, changes in disease characteristics over time, differences and similarities in disease characteristics between diseases, and differences and similarities between responder and non-responder profiles will be evaluated.
Methods The study is a multicenter, healthy-subject controlled, parallel-cohort, open-label, observational, longitudinal basket study in real-world setting.
Patients with AD, HS, MF, CSU, CLE (N=120) and PSO (N=160) will be enrolled in groups of N≥40 patients per treatment, according to national guidelines. A cohort of healthy volunteers, closely matched to demographic patient characteristics, will serve as untreated control group. The following assessments will be performed: skin punch biopsies, tape stripping, swabs, imaging, patient-reported outcomes (PROMs), clinical parameters and blood-based biomarkers.
Results The Results of this study will provide data on changes in various biomarkers over time, including histology, gene expression levels, ceramide composition, skin microbiome, imaging biomarkers, PROMs, clinical parameters and blood-based biomarkers.
Conclusion The biomarkers identified in this study may contribute to better targeted treatment response in clinical practice and better understanding of disease pathology for patients with AD, PSO, HS, MF, CSU or CLE.

P23 – RINDERT VENEMA
ISOLATION AND GENERATION OF A MONOCLONAL HUMAN ANTI-DESMOGLEIN 3 ANTIBODY

R.R. Venema[1], K. Mennega[2], A.M. Nijenhuis[1], B. Horváth[1], P.C. van den Akker[1], J. Bremer[1]
[1]University of Groningen, University Medical Center Groningen, Department of Dermatology, Center of Expertise for Blistering Diseases, Groningen, The Netherlands. [2]University Medical Center Groningen, Department of Pathology & Medical Biology, Groningen, The Netherlands.

Background Previously, we investigated antisense oligonucleotide (ASO)-mediated exon skipping as potential RNA-therapy approach for the severe genetic blistering disease Recessive Dystrophic Epidermolysis (RDEB), however optimization of delivery is essential for ASO-mediated exon skipping to be a viable approach for systemic treatment of RDEB. Therefore, we are currently developing a systemic targeted delivery platform for the skin inspired by the autoimmune disease Pemphigus Vulgaris (PV). PV patients present with autoantibodies directed against desmosomal proteins found in skin and mucosa, both of pathogenic origin and non-pathogenic origin. Non-pathogenic variants could potentially serve as an excellent systemic delivery platform for the skin.
Objective Isolate and sequence the B-cell receptor of multiple selected anti-DSG3 clones, (2) incorporate this sequence in cloning and expression plasmids, (3) recombinantly express the monoclonal, human anti-desmoglein 3 IgG (hu-a-dsg3) in HEK cells, and (4) fully characterize the hu-a-dsg3 by extensive *in vitro* diagnostic assays.
Methods To Isolate the anti-DSG3 B cells, we labeled recombinant DSG3 with two different fluorochromes and tested these protein conjugates in a 2G4 anti-DSG3 B cell hybridoma line and PR3 B cell hybridoma control line by

fluorescence-activated cell-sorting (FACS). Next, when optimized, we will test this dual labelling in the PBMC fraction of a healthy control and single cell sort double-positive cells.
Results/Conclusion In preliminary experiments, we observed excellent separation of positive and negative cell populations with AF647 labeled DSG3 by FACS, however AF488 labeled DSG3 needs further optimization. At the NVED we will present the data gathered in the coming months.

P24 – MARGOT STARRENBURG
DUPILUMAB TREATMENT DECREASES MBC2S, CORRELATING WITH REDUCED IGE LEVELS IN PEDIATRIC ATOPIC DERMATITIS

Margot E. Starrenburg[1,2], Manal Bel Imam[2], Juan F. Lopez[2], Laura Buergi[2], N. Tan Nguyen[1], Anouk E. M. Nouwen[1], Nicolette J. T. Arends[3], Peter J. Caspers[1], Mübeccel Akdis[2], Suzanne G.M.A. Pasmans[1], Willem van de Veen[2]
[1]Center of Pediatric Dermatology-department of Dermatology, Erasmus University Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands; [2]Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland; [3]Center of Pediatric Allergology-department of Pediatrics, Erasmus University Medical Center, Rotterdam, The Netherlands.

Background A preference for type 2 immunity plays a central role in the pathogenesis of atopic dermatitis (AD). Dupilumab, an mAb targeting the IL-4 receptor α (IL-4Rα) subunit, inhibits IL-4 and IL-13 signaling. These cytokines contribute significantly to IgE class switch recombination in B cells, critical in atopic diseases. Recent studies indicate IgG+CD23hiIL-4Rα+ type 2 memory B cells (MBC2s) as IgE-producing B-cell precursors, linked to total IgE serum levels in atopic patients. Total IgE serum levels decreased during dupilumab treatment in previous studies.
Objective We sought to assess the effects of dupilumab treatment in comparison with alternative therapies on the frequency of MBC2s and the correlation to total IgE levels in pediatric patients with AD.
Methods Pediatric patients with AD, participating in an ongoing clinical trial, underwent randomization into 3 treatment groups: dupilumab (n = 12), cyclosporine (n = 12), and topical treatment (n = 12). Plasma samples and PBMCs were collected at baseline (T0) and at 6 months after starting therapy (T6). Flow cytometry was used for PBMC phenotyping, and ELISA to assess total IgE levels in plasma.
Results Our findings revealed a significant reduction in MBC2 frequency and total IgE levels among patients treated with dupilumab. Also, a significant correlation was observed between MBC2s and total IgE levels.
Conclusion Systemic blocking of the IL-4Rα subunit leads to a decrease in circulating MBC2 cells and total IgE levels in pediatric patients with AD. Our findings unveiled a novel mechanism through which dupilumab exerts its influence on the atopic signature.

P25 – MARJOLEIN BRANDS
THE VALIDITY AND RELIABILITY OF PATIENT-PROVIDED PHOTOGRAPHS FOR THE DIAGNOSIS AND SEVERITY OF HAND ECZEMA – PRELIMINARY RESULTS

Marjolein J. Brands[1], Manon M. Sloot[1], Ute Bültmann[2], Klaziena Politiek[3], Elke Weisshaar[4], Laura Loman[1#], Marie L. A. Schuttelaar[1#]
[1]Department of Dermatology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; [2]Department of Health Sciences, Community and Occupational Medicine, University of Groningen, University Medical Center Groningen, The Netherlands; [3]Medical Center Leeuwarden, Department of Dermatology, Leeuwarden, the Netherlands; [4]Unit for Occupational Dermatology, Department of Dermatology, Ruprecht-Karls University Heidelberg, Heidelberg, Germany. #Authors share joint senior authorship.

Background Hand eczema (HE) is a common disease, with a clinical diagnosis. However, data on remote assessment of HE is limited.
Objective To assess the criterion validity and inter- and intra-rater reliability of patient-provided photographs to diagnose HE and assess its severity.
Methods Patients with and without HE were eligible. Presence and severity of HE (HECSI/photographic guide) were assessed by one of the two experienced raters at the outpatient clinic. Patients took four photographs of their hands, following instructions. All photographs were assessed twice by four experienced raters. Criterion validity was based on the photographic assessment of the identical rater who conducted the clinical assessment. Inter- and intra-rater reliability were based on the photographic assessment of all raters combined.
Results In total, 75 patients were included. The sensitivity, specificity, positive and negative predictive value for diagnosing HE based on photographs were 85.7%, 84.2%, 94.1% and 66.7%, with kappa values of 0.32 and 0.69 for the inter- and intra-rater reliability. For the severity, ICC values of ≥0.92 (HECSI), and kappa values of 0.74, 0.48-0.75 and 0.75 (photographic guide) were found for the criterion validity, inter- and intra-rater reliability.
Conclusion Remote assessment showed a sensitivity, specificity, and positive predictive value >84% for diagnosing HE, with a negative predictive value of 66.7%, and fair inter- and substantial intra-rater reliability. Severity assessment showed excellent (HECSI) and substantial, fair-substantial and substantial (photographic guide) criterion validity, inter- and intra-rater reliability. These Results indicate a potential role for remote assessment of HE in clinical and research settings.

P26 – ROLAND VALENTIN BUMBUC
THE ACUTE PHASE RESPONSE TO BURN INJURY: AN IN-SILICO MODELING APPROACH

R.V. Bumbuc[1,2,5], V.M. Sheraton[5], P.P.G. Mulder[1,4], B.K.H.L. Boekema[1,4], A. Hoekstra[5], P.P.M. van Zuijlen[1,3,4,6], H.I. Korkmaz[1,2,3,4]
[1]Department of Plastic, Reconstructive and Hand Surgery, Amsterdam Movement Sciences (AMS) Institute, Amsterdam University Medical Center (UMC), Location VUmc, Amsterdam,

The Netherlands; [2]Department of Molecular Cell Biology and Immunology, Amsterdam Infection and Immunity (AII) Institute, Amsterdam University Medical Center (UMC), Location VUmc, Amsterdam, The Netherlands; [3]Burn Center and Department of Plastic and Reconstructive Surgery, Red Cross Hospital, Beverwijk, The Netherlands; [4]Burn Research Lab, Alliance of Dutch Burn Care, Beverwijk, The Netherlands; [5]Computational Science Lab, Informatics Institute, University of Amsterdam, UvA - LAB42, Amsterdam, The Netherlands; [6]Amsterdam UMC location University of Amsterdam, Pediatric Surgical Centre, Emma Children's Hospital, Amsterdam, The Netherlands.

Background Burn injuries trigger complex events, including acute inflammation, which play a crucial role in tissue repair and regeneration. Activation of the complement system following burn injury is essential to the inflammatory response, influencing various immune pathways during healing.
Objective To develop and validate a computational model that simulates the acute inflammatory phase during the first 18 days post-burn injury, using animal data.
Methods Our Agent-Based Cellular Potts model incorporates different cell types as individual agents, along with cytokines and growth factors that interact within a defined tissue environment in a two-dimensional wound simulation. The model considers both systemic factors, such as cytokine and chemokine concentrations and immune cell recruitment, and local factors, including Damage-Associated Molecular Patterns (DAMPs) that signal tissue damage. We integrated experimental data from animal burn models, obtained through meta-analyses, to validate the interactions of key players in the acute inflammation cascade. The goal was to create a representation of complement activation, inflammatory events, and their associated consequences over time.
Results Our simulations demonstrated how various factors, such as burn injury severity, prolonged inflammation, and fluctuations in complement factor concentrations, influence the dynamics of the acute inflammatory phase. Additionally, we examined the interactions between complement activation and other signaling pathways involved in burn wound healing, including the effects of IL-6, IL-8, IL-1β, TNF-α, and TGF-β1 concentrations, alongside increasing CRP levels (in both blood and wound) and complement activation.
Conclusion This computational model offers insights into the spatio-temporal dynamics of key drivers of acute inflammation following burn injuries.

P27 – TRISTAN BRUIJN
A SYSTEMATIC REVIEW OF CHANGES IN MELANOCYTIC NAEVI DURING IMMUNE CHECKPOINT INHIBITION AND TARGETED THERAPY

Tristan V.M. Bruijn[1,2], S.T. Dinh[1], Yannick S. Elshot[1,2], S. van der Mierden[3], H.P. Soyer[4], C.M. Olsen[4,5], B. Betz-Stablein[4], M.W. Bekkenk[2], T. Rustemeyer[2], Elsemieke I. Plasmeijer[1,6]
[1]Department of Dermatology, The Netherlands Cancer Institute – Antoni van Leeuwenhoek, Amsterdam, The Netherlands; [2]Department of Dermatology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands; [3]Scientific Information Service – NKI Library, The Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, The Netherlands; [4]Frazer Institute, The University of Queensland, Dermatology Research Centre, Brisbane, Queensland, Australia; [5]Department of Population Health, QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia; [6]Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands.

Background Immune checkpoint inhibitors (ICIs) and targeted therapies (TTs) are effective in treating metastatic cancers, but they regularly cause cutaneous adverse events (cAEs) due to autoimmune or autoinflammatory reactions. These reactions can alter the clinical and dermatoscopic features of melanocytic nevi, and new benign or malignant melanocytic lesions may develop during treatment.
Objective This systematic review aimed to evaluate the literature on morphological changes in melanocytic nevi associated with ICIs and TTs to guide clinical practice.
Methods A search (PROSPERO: CRD42023416858) of the Ovid (Medline), Embase, and Scopus databases (up to December 1, 2023) was conducted to identify peer-reviewed studies reporting changes in nevi or new melanocytic eruptions following ICI and TT treatment in cancer patients. Studies focused on pigmentation disorders or other oncological conditions were excluded. Outcomes assessed included clinical and histopathological changes and the development of secondary primary melanomas.
Results A total of 104 studies were identified, including 57 case reports, 6 case series, 12 (non-) randomized controlled trials, and 29 observational studies (13 prospective, 16 retrospective). Among 967 patients from 24 countries, affected nevi or new melanocytic lesions developed in 22% of ICI and 78% of TT cases. Commonly reported changes included increased clinical atypia, growth, hyperpigmentation, and involution, with or without a halo phenomena. There were 49 cases of eruptive nevi and 132 newly diagnosed melanomas.
Conclusion Melanocytic nevi should be examined by a dermatologist before ICI or TT treatment to determine the baseline clinical and dermatoscopic morphology, as secondary primary melanoma may occur.

P28 – BIRTE HELL
IN VITRO SKIN MODELS FOR SENSITIZATION IN FOOD ALLERGY

Birte Hell[1], Silvia Letasiova[2], Jan Markus[2], Edward F. Knol[1], Kitty C. Verhoeckx[1]
[1]University Medical Center Utrecht, Department of Dermatology and Allergology, Utrecht, The Netherlands; [2]MatTek In Vitro Life Science Laboratory s.r.o., Bratislava, Slovakia.

Background Food allergies (FA) impact 1-4% of Western Europeans and can lead to fatal anaphylaxis. The skin is, together with the lungs and GI tract, one of the possible

sensitization routes. Currently, only *in vivo* models are used to study FA mechanisms in the skin, but human *in vitro* 3D skin models could potentially serve as a model for skin sensitization to food allergens. For example, the impact of the epidermal barrier function on allergen uptake and allergic inflammation can be studied.
Objective To develop an assay based on *in vitro* 3D skin models to investigate sensitizing capacity of different food components.
Methods Reconstructed epidermal models (EpiDerm™) were exposed to different concentrations of purified allergens or non-allergenic controls in presence or absence of LPS for 24 to 48 hours, single or repeated dosing. Tissues and supernatants were collected for further analysis.
Results No significant differences between allergens and non-allergens were found for epithelial barrier integrity or viability but dose-dependent trends were observed for peanut allergen Ara h 1 in independent experiments. Presence of LPS during apical exposure had no significant effects.
Conclusion Purified food allergens alone or in presence of LPS had no significant effects on viability or barrier function in healthy epidermal models. Next, gene expression and cytokine release will be analyzed to identify possible differences between allergens and non-allergens in order to evaluate the assay as a tool to study food sensitizing capacity.

P29 – EMILY KALLEN
ALMOND ALLERGY IN ADULTS: LOW DISCRIMINATIVE ABILITY FOR BOTH ALMOND SIGE AND SPT

E.J.J. Kallen[1], P.M.J Welsing[1], Pedro Botelho Alves[2], J.E. Kuiken[1], A.C. Knulst[1,3], R. van Ree[4#], T.M. Le[1,3#]
[1]Department of Dermatology/Allergology, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands; [2]Department of Allergy and Clinical Immunology, Coimbra University Hospital, Coimbra, Portugal; [3]Departments of Experimental Immunology and of Otorhinolaryngology, Amsterdam University Medical Centers, location AMC, Amsterdam, The Netherlands; [4]Centre of Translational Immunology, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands. #Authors share joint senior authorship.

Background No studies have investigated the clinical characteristics and diagnostics of almond allergy in a well-defined adult population.
Objective This study aims to 1) describe the clinical characteristics of adults with suspected almond allergy, 2) describe the clinical characteristics of the subgroup of patients who underwent an open food challenge (OFC) for almond and 3) evaluate the diagnostic value of almond-specific IgE (sIgE) and SPT for the presence of almond allergy.
Methods Adult patients who reported symptoms to almond within two hours after ingestion (n=221) and who underwent an OFC with raw almond (n=90) were included. The diagnostic value of almond-sIgE, SPT, and their combination was assessed using receiver operating characteristics (ROC) analysis.
Results Of the 221 patients reporting symptoms to almond, 29.1% reported severe symptoms. Of the 90 OFCs, 33.3% were positive, of which 36.7% had severe symptoms. All patients with a positive OFC reported subjective symptoms and 56.7% also reported Objective symptoms. Although not statistically significant, there were more tolerant (37.5%) than allergic (26.1%) patients sensitized to almond sIgE. ROC-analysis showed low area under the curves (AUCs) in predicting almond allergy for almond sIgE (0.54; 95% CI=0.38 – 0.71), SPT to almond extract (0.64; 95% CI=0.49– 0.80), and their combination (0.68; 95% CI=0.53 - 0.83).
Conclusion Almond allergy is severe in one third of the patients. Both almond-sIgE and SPT have a low diagnostic value for predicting almond allergy. Therefore, there is a high need for better diagnostic tools such as improved extracts and almond components-based tests.

P30 – FAUVE VAN VEEN
EXPLORING EXPERIENCES AND CONSIDERATIONS IN REPRODUCTIVE DECISION-MAKING FOR PATIENTS WITH GENODERMATOSES: A QUALITATIVE INTERVIEW STUDY

Fauve C.A.P. van Veen[1,2], Otte Borghouts[1,2], Peter M. Steijlen[1,2], Liesbeth van Osch[2], Sonja de Munnik[3], Malou Heijligers[2,3#], Antoni H. Gostyński[1,2#]
[1]Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; [2]GROW school for Oncology and Reproduction, Maastricht University, Maastricht, The Netherlands; [3]Department of Clinical Genetics, Maastricht University Medical Center+, Maastricht, The Netherlands. #Authors share joint senior authorship.

Background Genodermatoses are a heterogeneous group of inherited skin disorders that impact patients' quality of life. This, in turn, may influence the reproductive decision-making process for patients considering parenthood, given the risk of transmitting a genodermatosis. However, little is known about this decision-making process and perspectives.
Objective This qualitative study sought an in-depth understanding of the reproductive decision-making for patients affected by genodermatoses.
Methods Between January and September 2024, semi-structured interviews were conducted, recorded, transcribed, and analyzed using an inductive and reflexive thematic content approach. Eligible participants were purposively sampled from Dutch medical expertise centers and patient associations to ensure diverse representation and broad recruitment.
Results Twenty-eight participants were interviewed, covering several genodermatoses (n=11; epidermal differentiation disorders and Hailey-Hailey), (n=6; epidermolysis bullosa), (n=4; types of ectodermal dysplasia), and (n=7; basal-cell-nevus syndrome, FAMMM syndrome). Three key themes and thirteen subthemes emerged, indicating that most participants prefer to avoid transmitting their condition, and therefore consider reproductive options like pre-implantation genetic testing. This decision process was influenced by negative personal experiences with a genodermatosis,

resulting in fear and uncertainty about severe manifestations in offspring. Furthermore, participants wanted to prevent having to serve as a caregiver instead of a parent. Most participants were unaware of all the available reproductive options, and those who had received reproductive counseling, perceived it as positive. However, routine reproductive counseling was mostly lacking or inadequate, giving much room for improvement.
Conclusion This study offers insights into reproductive decision-making for patients affected by genodermatoses, underscoring the importance of reproductive counseling.

P31 – JAIMY KLIJNHOUT
STAPHYLOCOCCUS AUREUS STRAIN-SPECIFIC HOST DEFENSE RESPONSES IN KERATINOCYTES

Jaimy A. Klijnhout[1], Zoltán Radai[2], Patrick L.J.M. Zeeuwen[1], Bernhard Homey[2], Ellen H. van den Bogaard[1], Jos P.H. Smits[1,2]
[1]Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; [2]Department of Dermatology, University Hospital Düsseldorf, Medical Faculty, Heinrich Heine University, Düsseldorf, Germany.

Background Atopic dermatitis (AD) is strongly associated with overabundant *Staphylococcus aureus* (*S. aureus*) colonization. Interpatient variability in *S. aureus* strains found on lesional skin of AD patients may contribute to disease pathophysiology and severity. The genetic composition and therefore the transcriptome of *S. aureus* differs among bacterial strains. Previous data has shown that clinically isolated *S. aureus* induce strain-specific host-defense responses in keratinocytes.
Objective We aim to identify *S. aureus* specific genes or gene clusters that induce transcriptional responses upon co-culture with keratinocytes to elucidate *S. aureus* host-microbe interactions that relate to AD pathophysiology.
Methods Monolayer and human epidermal equivalent cultures of primary keratinocytes or N/TERT-2G immortalized keratinocytes were co-cultured with AD clinical isolates (N=10) and commercially available *S. aureus* ATCC strains (N=2). Host defense gene expression (RNAseq, qPCR) was correlated to whole genome sequencing data of *S. aureus* strains.
Results Five *S. aureus* clinical isolate strains induced a strong host defense response (IL6, IL8, CCL20, DEFB4A, S100A7, LCE3A), four clinical isolate strains and ATCC29213 induced a moderate response, and one clinical isolate strain and ATCC6538 induced a mild response in human epidermal equivalents after 24h co-culture. These strains expressed a subset of bacterial genes, including Glu-specific serine endopeptidase (SspA), which positively correlated to keratinocyte host defense induction.
Conclusion The genetic heterogeneity between *S. aureus* strains should be considered in AD disease pathophysiology. Specific bacterial genes may drive keratinocyte defense mechanisms. Next steps are aimed to validate bacterial whole genome sequencing data at gene and protein expression level.

P32 – FAUVE VAN DEN BERGE
SKINERGY CINDU: AN EXPLORATORY MULTI-CENTRE, TWO-PART STUDY TO DEEP-PHENOTYPE CHRONIC INDUCIBLE URTICARIA AND EXPLORE BIOMARKERS FOR OMALIZUMAB RESPONSE USING A MULTIMODAL PROFILING APPROACH

I. Abdisalaam[1,2,3], F.R. van den Berge[4], J.V.L. Simons[5], N.G. Koster[1,2], J.T. Niemeyer-van der Kolk[1], E.S. Klaassen[2], M.F.J.M. Vissers[2], R. Rissmann[1,2], H. Rockmann-Helmbach[5], M.B.A. van Doorn[1,4]
[1]Centre for Human Drug Research, Leiden The Netherlands; [2]Leiden Academic Centre for Drug Research, Leiden University, Leiden The Netherlands; [3]Leiden University Medical Center, Leiden The Netherlands; [4]Erasmus Medical Center, Rotterdam The Netherlands; 5University Medical Center Utrecht, Utrecht, The Netherlands.

Background Chronic inducible urticaria (CIndU) is a heterogenous group of urticarias induced by specific triggers (e.g. friction, cold or pressure), whereas in chronic spontaneous urticaria (CSU) no trigger is apparent. Symptomatic dermographism (SD) and cold urticaria (ColdU) are the most frequent CIndU subtypes, but their pathogenesis is largely unknown. This is a pilot study for the Next Generation Immuno-Dermatology consortium SKINERGY trials.
Objective The aim of this clinical study is to facilitate an in-depth characterization (deep-phenotyping) of SD and ColdU. Biomarkers for (new) disease characteristics and diagnosis using a multimodal approach will be explored. Additionally, disease characteristics and biomarkers in response to treatment with omalizumab will be evaluated between subtypes and within patients over time.
Methods This multi-centre, two-part, observational study compares SD and ColdU patients with CSU patients and matched healthy volunteers. Each group includes up to 10 individuals. In part A, the biology of SD and ColdU will be investigated. In part B, the response of biomarkers to real-world treatment with omalizumab will be monitored. To this end, invasive (skin biopsies and blood sampling) and non-invasive (questionnaires, imaging, tape stripping, skin and faecal microbiome) assessments will be performed.
Conclusion Identifying specific characteristics of CIndU subtypes SD and ColdU and a deeper understanding of the mechanisms involved in the pathophysiology of CIndU may potentially lead to better stratification between and possibly within CIndU subtypes. Additionally, biomarkers for the prediction and monitoring of treatment response to omalizumab may facilitate personalized treatment of CIndU patients in the future.

P33 – MENGYAO ZHOU
POLARIZATION SECOND HARMONIC GENERATION IMAGING OF COLLAGEN FIBER ORGANIZATION IN HUMAN HEALTHY AND SCARRED SKIN

Mengyao Zhou[1], Madalena P. Gomes[2,4,5,6], H. Ibrahim Korkmaz[2,3,4,6,7,8], Bouke K.H.L. Boekema[2,4,6], Marie L. Groot[1]
[1]Faculty of Science, Department of Physics, Laserlab, Vrije

Universiteit Amsterdam, Amsterdam, The Netherlands; [2]Department of Plastic, Reconstructive and Hand Surgery, Amsterdam UMC location VUmc, Amsterdam, The Netherlands; [3]Alliance of Dutch Burn Care, Red Cross Hospital, Beverwijk, The Netherlands; [4]Alliance of Dutch Burn Care, Burn Research Lab, Beverwijk, The Netherlands; [5]Department of Pathology, Amsterdam UMC location AMC, The Netherlands; [6]Amsterdam Movement Sciences Research Institute, Vrije Universiteit Amsterdam, The Netherlands; [7]Department of Molecular Cell Biology and Immunology, Amsterdam University Medical Center (UMC), Location VUmc, Amsterdam, The Netherlands; [8]Amsterdam Infection and Immunity (AII) Institute, Amsterdam University Medical Center (UMC), Location VUmc, Amsterdam, The Netherlands.

Background Collagen I and III proportions play an important role in tissue remodelling and wound healing. The Col I/III ratio regulates fibrillogenesis and determines the final fibril diameter and bundle structure, which affect skin mechanics. Abnormal collagen fiber organization can impair skin function and visual outcomes. Traditional Methods for detecting collagen isoforms, like immunohistochemistry (IHC), are invasive and labor-intensive. A label-free, highly specific method to assess collagen fiber composition and organization can provide valuable insights into understanding extra cellular matrix changes.
Objective To analyze how alterations in collagen composition affect fiber organization and substructural features by using polarization second harmonic generation (PSHG) microscope. An automated pixel-based method was developed to quantify collagen fibers in healthy and scarred skin
Methods Collagen gels with Col I/III ratios 1:0, 9:1, 4:1, 7:3 and 3:2 were created. Images were captured at different polarization angles by PSHG microscope to analyze second-order susceptibility ratios (χ_{15}/χ_{31} and χ_{33}/χ_{31}) and the alpha-helix pitch angle. Collagen structures were examined in healthy (n=5) and scarred skin (n=7), including hypertrophic (n=2), normotrophic (n=2), and burn scar (n=1) with PSHG microscope and IHC staining.
Results Increased Col III content correlated with decreased PSHG intensity and higher anisotropy. Healthy skin exhibited 24% higher standard deviation in fiber orientation than scarred skin as visualized by PSHG. The ratio of Col I/III was 2.2 in healthy skin and 1.6 in scar tissue as determined by IHC.
Conclusion PSHG microscope offers a rapid, label-free, quantitative approach for collagen structure analysis of intact skin.

P34 – NIKKI HENCKENS
PATIENTS' AND CLINICIANS' PERSPECTIVES ON TELEMEDICINE TO MONITOR PATIENTS ON SYSTEMIC TREATMENT FOR PSORIASIS OR ATOPIC DERMATITIS - A MIXED METHODS STUDY

N.F.T. Henckens[1], M.E. Pawlak[1], S.A.C. Wanten[1], Y.C. Weng[2], I. van Ee[3], B.W.M Arents[4], L. Witkamp[5], M.S. de Bruin-Weller[6], E.M. Baerveldt[7], M.M.B. Seyger[1], E.M.G.J. de Jong[1], J.M.P.A van den Reek[1], W.A. van Enst[2]

[1]Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; [2]Dutch Society for Dermatology and Venereology, Utrecht, The Netherlands; [3]Dutch National Psoriasis Patient Association, Nijkerk, The Netherlands; [4]Dutch Association for People with Atopic Dermatitis, Nijkerk, The Netherlands; [5]Ksyos Health Management Research, Amstelveen, The Netherlands; [6]Department of Dermatology and Allergology, University Medical Center Utrecht, Utrecht, The Netherlands; [7]IJsselland Medical Centre, Capelle a/d IJssel, The Netherlands.

Background Psoriasis and atopic dermatitis (AD) often require lifelong treatment and consequently frequent hospital visits. In stable disease, telemedicine may partly replace face-to-face consultations. However, perspectives of dermatological care providers (DCPs) and patients regarding telemedicine are underexplored.
Objective To assess perspectives of patients and DCPs regarding telemedicine for patients with psoriasis or AD on systemic treatment, focusing on current experiences and future preferences.
Methods A cross-sectional mixed-Methods study was conducted by surveys and semi-structured interviews with patients and DPCs. Telemedicine was defined as consultations by phone, video, online health platforms, email or applications. Interviews were conducted using a grounded theory approach and analyzed through inductive thematic analysis.
Results Surveys were completed by 162 patients and 152 DCPs; interviews were conducted with 12 patients and 5 DCPs. The majority of both groups expressed a positive outlook on telemedicine, provided the disease was stable. Patients valued telemedicine for practical benefits (e.g., time and cost savings). Patients preferred an established treatment relationship before replacing face-to-face consultations. DPCs highlighted the need for enhanced ICT support, user-friendly systems, and appropriate reimbursement. The majority of patients and DCPs (50.8% and 72.4%, respectively) preferred implementation of telemedicine, with 59.2% of DCPs believing ≥50% of their consultations could be conducted through telemedicine. Telephonic appointments were the preferred type in both groups.
Conclusion This study demonstrates the positive outlook on future telemedicine implementation among patients and DCPs for stable patients with psoriasis or AD using systemic treatment, but also emphasizes perspectives that should be addressed to ensure its success.

P35 – MARIE CHEVALIER
TUMOUR MICRO-ENVIRONMENT IN CHLORMETHINE RESPONDERS AND NON-RESPONDERS IN AN EARLY-STAGE MYCOSIS FUNGOIDES COHORT, USING IMAGING MASS CYTOMETRY

M.S.N. Chevalier[1,2], S.S. Wind[1,2,3],M.E. IJsselsteijn[2], V.A. Merkus[1], R. Rijneveld[3], K.D. Quint[1], A.M.R. Schrader[2], R. Rissmann[1,3], M.H. Vermeer[1]

[1]Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; [2]Department of Pathology, Leiden

University Medical Center, Leiden, The Netherlands; [3]Centre for Human Drug Research, Leiden, The Netherlands.

Background Mycosis fungoides (MF) is the most prevalent subtype of cutaneous T-cell lymphoma (CTCL). Treatment with topical chlormethine (Ledaga®) poses a significant clinical challenge due to unpredictable treatment responses and limited understanding of possible changes within the tumour-microenvironment (TME) contributing to therapeutical success.
Objective Firstly, the aim is to establish whether chlormethine therapy in early-stage MF is associated with a shift from a Th1/Th2 TME equilibrium towards a Th1-dominant inflammatory TME. Secondly, the Objective is to identify differences in TME patterns between responders and non-responders in early-stage MF baseline samples, in order to detect novel biomarkers that could help future selection of potential chlormethine responders.
Methods Formalin fixed paraffin embedded (FFPE) skin biopsy samples (n=54) were processed using the Hyperion (imaging mass cytometry): responders (n=8) and non-responders (n=8), application site reactions (n=5) and healthy volunteers (n=4). The IMC panel developed by Veerle Merkus, which has been presented at the NVED last year, was applied to our samples. Data from 102 regions of interest (ROIs) were extracted for computational analysis.
Results Preliminary Results show a drop in abundance across all cells in the responder group compared to non-responders. Moreover, most application site reactions are from responders (n=4). Further analyses are underway to perform more stringent cell clustering, assess cell abundance and explore the interactions between tumour cells and surrounding immune cells.
Conclusion The TME of responders appears to be more sensitive to chlormethine treatment, considering the differences in cell abundancy and side effects between responders and non-responders. Further analyses are ongoing.

P36 – MARJOLEIN HIEL
NAVIGATING THE CHALLENGES IN CLINICAL TRIALS FOR BULLOUS PEMPHIGOID AND PEMPHIGUS: LEARNINGS FROM THE CLINICAL TRIAL GRAVEYARD AND AN INTERNATIONAL EXPERT SURVEY

Eva W.H. Korte[1*], Marjolein A.J. Hiel[1*], Maria C. Bolling[1], Patrick Dunn[2], Dédée F. Murrell[3], Victoria P. Werth[4,5], Marc Yale[2], Phyllis I. Spuls[6,7], Joost M. Meijer[1#], Barbara Horváth[1#]
*[1]Department of Dermatology, UMCG Center of Expertise for Blistering Diseases, European Reference Network for Rare Skin Diseases (ERN SKIN), University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; [2]International Pemphigus & Pemphigoid Foundation, Roseville, California, USA; [3]Department of Dermatology, St George Hospital, University of New South Wales, Sydney, Australia; [4]Division of Dermatology, Corporal Micheal J. Crescenz Veterans Affairs Medical Center, Philadelphia, Pennsylvania, USA; [5]Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; [6]Department of Dermatology, Amsterdam UMC, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; [7]Amsterdam Public Health, Infection and Immunity, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; *These authors have contributed equally. #Authors share joint senior authorship.*

Background Autoimmune bullous diseases (AIBD) like bullous pemphigoid (BP) and pemphigus still lack effective approved drugs despite decades of clinical trials.
Objective To analyze failed BP and pemphigus trials and explore challenges in trial setup and conduct as perceived by AIBD experts.
Methods A mixed-Methods study was performed; a scoping review of failed trials from trial registries and an expert survey gathering insights on perceived challenges and potential solutions.
Results Thirty-two failed trials were identified (10 BP, 22 pemphigus). BP trials mainly failed due to unmet primary efficacy endpoints (67%), while pemphigus trials mostly struggled with recruitment (35%). Among 56 surveyed experts, challenges were perceived in trial setup (BP:85%, pemphigus:86%) and conduct (BP:88%, pemphigus:81%), predominantly related to patient recruitment (BP:85%, pemphigus:83%) and protocol development, such as the selection of endpoints (BP:77%, pemphigus:84%). Identified challenges further included overly strict and complex endpoints, patient fragility, corticosteroid therapy, and lack of funding.
Conclusion Critical analysis of failed AIBD trials underscores the importance of international stakeholder collaboration to redefine endpoints and adopting innovative patient-centric trial designs to prevent future trial failures and accelerating the clinical translation of critically needed drugs for AIBD patients.

P37 – ZIXIAN LIANG
DIAGNOSTIC VALUE OF COMPLEMENT FIXATION TEST IN ROUTINE DIAGNOSTICS OF PEMPHIGOID DISEASES: ONE YEAR OF PROSPECTIVE ANALYSIS

Z. Liang, S.M. van der Molen, J. Bremer, J.M. Meijer, G.F.H. Diercks
University of Groningen, University Medical Center Groningen, Department of Dermatology, Center of Expertise for Blistering Diseases, Groningen, The Netherlands.

Background activation of the complement system contributes to blistering in pemphigoid diseases. Routine diagnostics only detect C3c deposition during direct immunofluorescence (DIF). The additional diagnostic value of autoantibody-induced complement activation in serum is unclear.
Objective To evaluate the additional diagnostic value of the Complement Fixation Test (CFT) in pemphigoid diseases.
Methods Prospective analysis of serum samples from patients with suspected pemphigoid at UMCG for routine diagnostics (January-December 2023). Indirect immunofluorescence on Salt-Split human Skin sections (IIF SSS) and Complement Fixation Test (CFT) were performed in all samples. For CFT,

patient serum was incubated on salt-split skin sections to allow autoantibodies to bind the basement membrane zone (BMZ). Fresh complement was added, followed by a fluorescent anti-C3 antibody to detect C3 deposition at the BMZ.
Results During a 12-month prospective analysis, a total of 806 serum samples were included in this study from 446 female patients (55.3%) and 360 male patients (44.7%), with an average age of 67.3 years. The positive rate for IIF SSS IgG was 20.6% (166/806), while the overall positive rate for CFT was 9.1% (73/806), with 0.9% (7/806) being +/- positive, 1.7% (14/806) being + positive, 2.5% (20/806) being 2+ positive, and 4.1% (33/806) being 3+ positive. Three patients were identified with confirmed diagnoses of pemphigoid with negative IIF SSS and positive CFT Results.
Conclusion CFT can be used as a diagnostic method for pemphigoid diagnosis, but does not add significant value to routine IIF SSS diagnostics. The clinical importance of complement binding is further investigated.

P38 – CISSE VERMEER
SAFETY OF ANTISENSE OLIGONUCLEOTIDE THERAPY: A SYSTEMATIC REVIEW AND META-ANALYSIS ON ADVERSE EVENTS IN CLINICAL STUDIES

F.C. Vermeer[1], E. Birnie[1], R.R. Venema[2], M.C. Bolling[2], N.V.A.M. Knoers[1], J. Bremer[2], P.C. van den Akker[1,2]
[1]University of Groningen, University Medical Center Groningen, Department of Genetics, Groningen, The Netherlands; [2]University of Groningen, University Medical Center Groningen, Department of Dermatology, Groningen, The Netherlands.

Background Antisense oligonucleotide (ASO) therapies are a promising approach for treating genetic skin diseases such as epidermolysis bullosa by targeting specific RNA molecules. ASOs can modulate gene expression, splicing, or restore gene function. However, their safety profile in skin remains unclear, as data on ASO-based dermatological clinical studies are limited. The small, heterogeneous patient cohorts further complicate risk assessment, highlighting the need for a unified risk profile to ensure safe clinical implementation.
Objective This study aims to understand the risks of adverse events (AEs) associated with ASO therapies through meta-analysis and provide insights to improve future clinical study design for ASO-based N of 1 skin treatments.
Methods Meta-analysis was performed on 105 studies, including 48 placebo-controlled trials. Using MedDRA medical dictionary, AEs were categorized into 378 categories which could be used to assess prevalence and risk difference.
Results Comparative analysis found a significant increase in thrombocytopenic events in patients treated with 2'-MOE-PS ASOs (10%, 95CI: 5/15%) but not 2'-OMe-PS ASOs (-6%, 95 CI: -11/-2%). Analysis of prevalence shows that injection site reactions are significantly higher in subcutaneous (64%, 95 CI: 48/77%) versus intravenous (13%, 95 CI: 8/19%) administration.
Conclusion Meta analysis can explain differences in adverse event prevalence or risk difference between studies. For example, due to chemistry or administration. Our study also emphasizes the need for improved AE reporting and tailored safety monitoring in skin-specific ASO trials. Insight into prevalence and risk difference provides us with safety information for events that are relevant to EB patients in ASO trials.

P39 – FIEKE ROSENBERG
A GENOME-WIDE ASSOCIATION STUDY OF CONTACT ALLERGY TO P-PHENYLENEDIAMINE

Fieke M. Rosenberg[1], Ilja Nolte[2], Peter J. van der Most[2], Harold Snieder[2], Marie L.A. Schuttelaar[1]
[1]Department of Dermatology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; [2]Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.

Background There is variability in interindividual susceptibility to develop allergic contact dermatitis under uniform conditions, which may be driven by genetic factors. p-Phenylenediamine (PPD), a potent sensitizer and component in oxidative permanent hair dyes and temporary black henna tattoos, has been the focus of several candidate gene studies on contact allergy. However, the genetics of contact allergy remain unclear.
Objective To identify and characterize genetic loci associated with contact allergy to PPD by performing a genome-wide association study (GWAS).
Methods This GWAS employed a case-control design. Cases were patients with a positive patch test reaction to PPD, prospectively recruited from the Dermatology outpatient clinic at the University Medical Center Groningen (Netherlands) between 2006 and 2022. Controls were selected based on questionnaire-derived data from Lifelines, a population-based cohort and biobank in the Netherlands. Controls were participants without a history of eczema, contact allergy, hand eczema, skin reactions to hair dye, had never applied/had a skin reaction to black henna tattoos, and had no positive patch test for hair dye or black henna tattoo substances. GWAS analyses are being performed, both unmatched and age- and sex-matched (1:5 cases to controls).
Results A total of 176 cases (81% female, 19% male; mean age 43.3 years) and 7,554 controls (79% female, 21% male; mean age 45.4 years) were selected. Among the PPD cases, 42.6% had a positive patch test reaction (+), 27.8% a strong positive reaction (++) and 29.6% an extreme positive reaction (+++). GWAS analysis is currently ongoing.
Conclusion No Conclusions yet.