1 – EVA KORTE
THE PATIENT AND PARENT JOURNEY OF RECEIVING A DIAGNOSIS OF EPIDERMOLYSIS BULLOSA, AND BEYOND – A QUALITATIVE STUDY

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Background Epidermolysis bullosa (EB) encompasses a heterogeneous group of rare genetic skin fragility disorders resulting in chronic blistering and wounding. Although diagnostic advances have improved the speed and accuracy of EB diagnosis, little is known about the experiences and needs of individuals throughout their diagnostic journey.
Objective This qualitative study sought an in-depth understanding of the diagnostic journey in EB.
Methods Semi-structured video-call interviews conducted between January and March 2022 were thematically analysed using an inductive constructivist approach, ensuring the credibility of findings through member checking.
Results Twenty-six participants were interviewed, including parents of paediatric patients (n=18) and adult patients (n=8), covering all major EB types except Kindler EB. Three themes and eight subthemes revealed that individuals experience various needs diverse needs throughout their diagnostic and post-diagnostic journeys. In medically urgent EB cases, a rapid definite diagnosis was considered crucial. The process of EB diagnostics invoked a spectrum of emotional responses, ranging from clarity and confirmation to despair and uncertainty about the future. Participants expressed shortcomings in clinical practice, particularly the adverse effects of severity ratings in EB terminology on illness perception, healthcare-seeking behaviour, research participation, and engagement in peer support.
Conclusion Despite ongoing improvements in EB diagnostics, patients with EB and their families experience an urgent need for expedited diagnostics. They also need clear, realistic information about future expectations, proactive support and follow-up in specialized centres, and access to peer support. This study's findings provide insights for improving diagnostics and care for patients with EB and their families.

2 – CISSE VERMEER
ASO-MEDIATED EXON SKIPPING IN INTACT HUMAN SKIN POINTING TOWARDS A TREATMENT FOR RDEB

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Background Recessive dystrophic epidermolysis bullosa (RDEB) is a severe genetic skin condition, caused by a null variant COL7A1 (Type VII Collagen). No curative treatments are currently available for RDEB. Antisense oligonucleotides (ASOs) therapy has been shown to induce exon skipping of COL7A1 mRNA in human skin models. Bringing this therapy to the patient requires additional information with regards to safety of the antisense oligonucleotides.
Objective Our goal was to explore the distribution of ASOs designed to induce COL7A1 exon 105 skipping, and exon skipped mRNA in a 3D intact human skin model.
Methods ASO distribution and exon skipping was assessed using Basescope/miRNA-scope in-situ hybridization. Exon skipping was also assessed using quantitative PCR on healthy 3D intact skin models treated with ASOs designed to induce exon 105 skipping.
Results Exon skipping was observed in human skin donors using Basescope. after intradermal injection, ASOs were shown to migrate into the epidermis with nuclear localization in basal keratinocytes using miRNA-scope. Exon skipping was observed in cDNA from ASO-treated healthy skin using qPCR.
Conclusion Exon skipping therapy is a valid treatment strategy to treat pathogenic null variants of COL7A1. Intradermally injected ASOs reach the nuclei of COL7A1 expressing basal keratinocytes and induce exon skipping. Induction of exon skipping in intact human skin shows that exon skipping has potential as a systemic therapy for RDEB. Future steps include performing similar experiments on human skin xenografts generated from patient keratinocytes and fibroblasts containing a COL7A1 null variant in combination with assessment of type VII collagen restoration.

3 – JAIMY KLEIJNHOUT
MRNA-BASED CRISPR/CAS9 GENOME ENGINEERING IN EXPERIMENTAL DERMATOLOGY: A NOVEL CAS9 DELIVERY STRATEGY

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Background In ten years after the introduction of the CRISPR/Cas9 system, various research fields have extensively used genome engineering to study cell biology and disease pathophysiology. While there is a growing interest in keratinocyte genome engineering, the number of studies using CRISPR/Cas9 within the field of experimental dermatology is limited. The generation of simple variants, e.g. a knockout, can be relatively easy through non-homologues end joining. Synthetic guide-RNAs and conventional Cas9 proteins are commercially available. Precision editing, via homology-directed repair is far less efficient and requires altered cutting

strategies with novel Cas9 proteins.
Objective To optimize the delivery of CRISPR/Cas9 machinery into N/TERT-2G immortalized keratinocytes and improve editing efficiencies by new optimized Cas9 proteins that are available in plasmid or mRNA form.
Methods N/TERT-2G immortalized keratinocytes were transfected with eGFP plasmids or mRNA using lipofectamine or electroporation to assess transfection and translation efficiency by fluorescence imaging.
Results The transfection efficiency of electroporated eGFP mRNA (~60%) outperforms electroporated plasmids (<5%), and lipofectamine transfected mRNA (~6%) and plasmids (<1%) in N/TERT-2G keratinocytes. mRNA transfection efficiency appeared to be dose-dependent.
Conclusion High efficiency genome engineering with the precision of a single nucleotide can expand our scientific toolbox in experimental dermatology. Here, we show that mRNA electroporation is a highly efficient transfection method in N/TERT-2G keratinocytes. This is the first step towards a transient precise editing strategy using optimized Cas9 proteins, and paves the way to improve existing disease models using a genetic component, recreate patient mutations and study genotype-phenotype correlations.

4 – JAAP VAN DER VELDEN
L12 LINKER DOMAIN SPECIFIC VARIANTS IN KRT10 CAUSE ATYPICAL EPIDERMOLYTIC ICHTHYOSIS

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Background Epidermolytic ichthyosis (EI) is a type of congenital ichthyosis, characterized by erythema and blistering at birth followed by hyperkeratosis. EI is caused by pathogenic variants in Keratin 1 (KRT1) or Keratin 10 (KRT10) and is primarily transmitted by autosomal dominant inheritance. The keratins form a network of intermediate filaments and are a structural component of the cytoskeleton, giving strength and resilience to the skin. Here, we present for the first time pathogenic variants in the L12 linker domain of KRT10 in three separate cases of EI.
Objective Identification of pathogenic variants for EI patients in KRT1 or KRT10 and establishing the pathogenicity of the found variations.
Methods We evaluated all patients and available family members clinically. Genetic analyses were performed using Sanger sequencing. Vectors containing wild-type or mutated forms of KRT10 were transfected into HaCaT cells and analyzed by high resolution confocal microscopy.
Results Genetic analysis of KRT10 identified three unique heterozygous variants in three affected patients with a mild EI phenotype. One variant occurred de novo while the other two where familial inherited. All identified missense variants are located in the L12 linker domain of KRT10. An in vitro study of aggregate formation of the missense variants in KRT10 only showed a very mild, not quantifiable aggregate formation in the KRT10 network, compared to the wild-type sequence.
Conclusion We identified, for the first time, three different pathogenic variants in the L12 linker domain of KRT10 in patients with an atypical, milder form of EI resembling peeling skin syndrome.

5 – DANIELA ANDREI
EPIDERMAL GROWTH FACTOR RECEPTOR INHIBITION LEADS TO CELLULAR PHENOTYPE CORRECTION OF DSP-MUTATED KERATINOCYTES

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Background Desmoplakin (DSP) is a desmosomal component expressed in skin and heart, essential for desmosome stability and intermediate filament connection. Pathogenic variants in the DSP gene encoding DSP, lead to heterogeneous skin, adnexa and heart related phenotypes, including skin fragility, woolly hair(WH), palmoplantar keratoderma(PPK) and arrhythmogenic/dilated cardiomyopathy(ACM/DCM). Epidermal growth factor receptor(EGFR) is a transmembrane protein expressed in the basal epidermal layer involved in proliferation and differentiation, processes that are disrupted in the development of PPK, and in the regulation of the desmosome.
Objective Considering the ambiguity of computer-based prediction analysis of DSP variants, our goal was to functionally analyse a DSP variant that was not previously described, NM_004415.4:c.3337C>T (NM_004415.4(NP_004406.2):p.(Arg1113*)). Additionally, our second aim was to investigate the effect of EGFR inhibition on patient cultured keratinocytes.
Methods RNA and protein analyses, in addition to immunofluorescence, electron microscopy, desmosomes morphometrics and keratinocytes dissociation assay.
Results We report a heterozygous DSP variant in a patient with PPK, WH and ACM. RNA and protein analysis revealed ~50% reduction of DSP. Patient's keratinocytes showed fragile cell-cell connections and perinuclear retracted intermediate

filaments. In skin of the patient, evident EGFR upregulation was observed. EGFR inhibition in patient's keratinocytes strongly increased DSP expression at the plasma membrane, improved intermediate filament connection with the membrane edges and reduced the cell-cell fragility. This cell phenotypic recovery was due to a translocation of DSP to the plasma membrane together with an increased number of desmosomes.
Conclusion These results indicate a therapeutic potential of EGFR inhibitors for disorders caused by DSP haploinsufficiency.

6 – MARCEL TEUNISSEN
IN-DEPTH PROTEOMIC ANALYSES OF INNATE LYMPHOID CELL SUBSETS FROM HEALTHY HUMAN SKIN REVEAL DISTINCTIVE PHENOTYPES AND FUNCTIONS

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Background Innate lymphoid cells (ILCs) play a crucial role in the skin-associated immune system, yet there is limited knowledge regarding their protein expression, proteomic diversity and function.
Objective As protein expression impacts cell function, we aimed to provide an in-depth proteomic analysis of cutaneous ILC2 and ILC3 subsets, representing the two major ILC populations in human skin.
Methods ILC2 and ILC3 subsets from healthy human skin were purified by fluorescence-activated cell sorting and state-of-the-art mass spectrometry-based proteomics was used for in-depth proteome analysis. The ILC2 and ILC3 counterparts in blood were isolated and analyzed in parallel.
Results We found over 6,600 proteins constitutively expressed by ILC2s and ILC3s from healthy human skin and blood. While the majority of proteins were expressed in both ILC subsets and in both skin and blood compartments, the skin ILC2s and ILC3s were more distinct than their counterparts in blood. Notably, only skin ILC3s expressed uniquely detected proteins. Our in-depth proteomic dataset enabled the characterization the cluster of differentiation marker profiles of the ILC subsets, examination of the distribution and abundance of proteins known to have immunological functions, and the identification of proteins (e.g. IL-14, IL-16, IL-36γ, and IL-37) that have not previously been implicated in ILC biology.
Conclusion Taken together, our analyses significantly enhance our knowledge on the protein expression profiles of ILC subsets. Moving forward, these proteomic datasets will serve as valuable resources for future investigations into ILC biology.

7 – ANNE-LISE STRANDMOE
ANALYSIS OF THE CIRCULATING IMMUNE PROFILE IN PEMPHIGUS VULGARIS REVEALS DISTINCT PATTERNS RELATED TO DISEASE STATE

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Background Fundamental research has led to life-saving treatments for multiple dermatological diseases such as pemphigus vulgaris (PV). Detailed research into the immune landscape is crucial for the development of targeted, personalized, and successful therapies. PV is a B-cell-driven autoimmune blistering disease characterized by loss of adhesion of the skin and/or mucosa due to autoantibodies against desmoglein 1 and/or 3. The exact mechanism resulting in disease onset and relapse after B-cell-depletion therapy with rituximab remains to be elucidated.
Objective We aim to establish immune signature profiles that can assist in disease monitoring of PV patients at active disease and remission after rituximab treatment.
Methods An established 40-marker spectral flow cytometry panel (OMIP-069) covering the major immune cell subsets was used to analyze PBMC samples from 29 PV patients and age/sex-matched healthy controls (HC). We examined rituximab-naïve (PVn) and rituximab non-naïve (PVnn) patients. Additionally, we profiled their serum for 46 cytokines/chemokines using a commercially available Luminex assay.
Results Data revealed a greater absolute count of classical monocytes in PV patients than in HCs. Various B-cell-subsets were significantly decreased in PVnn than in PVn patients. A significantly different pattern of inflammatory and immunoregulatory soluble analytes in PV patients compared to HCs.
Conclusion Our study reveals distinct immunological profiles in PVn and PVnn patients compared to HCs. These results underscore the utility of spectral flow cytometry and Luminex analyte analysis in characterizing the immunological landscape of PV as well as the influence exerted by prior rituximab treatment on the immune system of PV patients.

8 – YIXIN LUO
ROLE OF HNRNPK DELETION IN INITIATING CUTANEOUS T-CELL LYMPHOMA PATHOGENESIS: AN INDUCIBLE KNOCKOUT MOUSE MODEL

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Background Recent genomic analysis has unveiled recurrent heterogeneous nuclear ribonucleoprotein K (HNRNPK) gene deletions in cutaneous T-cell lymphoma (CTCL). HNRNPK acts as a tumor suppressor by inhibiting the JAK-STAT pathway.
Objective This study investigates the pivotal role of Hnrnpk deletion in initiating CTCL pathogenesis using a transgenic mouse model.
Methods and **Results** Hnrnpk was knocked out in skin infiltrating CD4+ T cells in transgenic mice (topical oxazolone, OXA, followed by tamoxifen) which were then subjected to repeated applications of OXA (3-2/wk for 20 wks). After discontinuing OXA, autonomous inflammation persisted. Remarkably, Hnrnpk haploinsufficiency alone was sufficient to elicit these phenotypic changes. Comprehensive flow cytometry analyses of blood samples in the course of the experiment showed no evident effect but postmortem analyses of skin samples corroborated and characterized the persistent inflammation. Histological examinations revealed increased epidermal thickness and inflammatory cell infiltration, particularly CD3+ CD4+ T-cells, in Hnrnpk knockout mice exposed to long-term OXA treatment. Immunohistochemistry demonstrated heightened cell proliferation (Ki-67 expression) and augmented JAK/STAT signaling (p-Stat3) in these mice – all reminiscent of early CTCL.
Conclusion Our results underscore the significance of Hnrnpk deletion in CD4+ T-cells leading to autonomous skin inflammation, emulating early stages of CTCL, thereby confirming HNRNPK's tumor-suppressive role. This in vivo model gives experimental access to the intricate processes involving HNRNPK in T-cell modulation, affecting epidermal homeostasis, and in CTCL pathogenesis, opening new avenues for potential therapeutic interventions.

9 – WILLEM ZOUTMAN
AN IN-HOUSE DEVELOPED DIGITAL PCR-BASED METHOD FOR QUANTIFICATION OF DNA METHYLATION BIOMARKERS IS VALUABLE FOR DIAGNOSTIC CHALLENGING EARLY SÉZARY SYNDROME PATIENTS

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Background Sézary syndrome (SzS) is an aggressive type of cutaneous T-cell lymphoma. Diagnosing SzS can be challenging, especially in early stages of disease. Previously, we showed that promoter methylation of PROM1, G0S2, CMTM2, PAM, GNMT and NEXN is frequently observed in peripheral CD4+ T-cells from SzS patients, but is not found in healthy donors and benign erythrodermic inflammatory dermatoses (EID) patients.
Objective We investigated the diagnostic value of promoter methylation of these biomarkers in patients suspected for SzS but that did not fulfil diagnostic criteria (early SzS). Furthermore, we assessed the tumor-specificity of these biomarkers in SzS tumor cells.
Methods Promoter methylation was analyzed in blood samples from 13 early SzS, 13 EID patients and 10 healthy donors. Quantification was performed by using Methylation Sensitive Restriction Enzyme – digital PCR (MSRE-dPCR); This in-house developed method is free of bisulfite conversion. We assessed tumor-specificity in an independent cross-validation experiment using flowcytometric sorted tumor cells from confirmed SzS patients.
Results Diagnostic sensitivity of our biomarker panel was 94.4 % (specificity 100%). Tumor-specificity evaluation showed that at least 1 of the biomarkers is methylated in all sorted tumor cells and not in cells with a normal phenotype from the same patient.
Conclusion These data show that promoter methylation of PROM1, G0S2, CMTM2, PAM, GNMT and NEXN is highly specific for SzS cells and can be of value in diagnostic challenging early SzS patients. In addition, the dPCR-based quantification of tumor cells offers a method for monitoring tumor-load, disease progression and treatment efficacy.

10 – FENNA DE BIE
STANDARDIZATION OF MULTI CENTER FLOW CYTOMETRY FOR THE DETECTION OF CIRCULATING CUTANEOUS T-CELL LYMPHOMA CELLS

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Background Cutaneous T-cell Lymphomas (CTCL) represent a group of mature T-cell-derived lymphomas, often associated with a poor prognosis in advanced cases. Accurate detection of circulating neoplastic cells in CTCL relies on flow cytometric (FC) assessment, pivotal for diagnosis, hematologic staging, and monitoring immunophenotypic changes. Nevertheless, current FC procedures lack standardization, prompting a multicentric initiative to address this.

Objective Our goal is to develop a standardized diagnostic tool enabling the detection of malignant skin-homing T-cells in participating reference laboratories throughout three continents.
Methods Fourteen participating laboratories processed peripheral blood samples from CTCL and healthy controls (HCs) over multiple sample-inclusion rounds using a newly developed 3-tube, 8-color FC panels and EuroFlow protocols for instrument setup and sample preparation. All data files underwent centralized analysis, evaluating the number of acquired events, scatter characteristics, and median fluorescence intensity (MedFI) values for individual markers through the calculation of performance scores.
Results The central data analysis revealed various technical challenges; targeted interventions were employed to address these technical hurdles and enhance data comparability. These interventions resulted in a notable improvement in the outcomes: reduced variability in MedFI values, scatter characteristics of leukocytes, and a more consistent number of acquired events. CTCL cells were accurately detected in all 90 CTCL patient samples.
Conclusion We conclude that the implementation of the novel FC panel leads to the accurate detection of circulating CTCL cells, and that EuroFlow-based workshops and interventions improved data reproducibility, demonstrating the feasibility of achieving robust inter-and intra-laboratory FC standardization across different sites and instruments.

11 – ALESHA LOUIS
DISSIMILAR EFFECT OF PAPILLARY AND RETICULAR FIBROBLASTS ON PIGMENTATION

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Background The dermis can be separated into the upper papillary fibroblast (Pfs) layer and the lower reticular fibroblast (Rfs) layer. Previous studies using human skin equivalents (HSEs) cultured with either Pfs or Rfs show that they have dissimilar effects on epidermal morphogenesis, barrier morphology and function, and invasive behavior of tumor cells. Also, HSEs cultured using Rfs show characteristics of skin aging, including a thinner epidermal layer and decreased barrier function. As skin aging involves the appearance of hyperpigmentary spots (solar lentigines) we question whether Rfs in HSEs have a dissimilar effect on pigmentation processes compared to Pfs in HSEs.
Objective We aim to elucidate the role of both Pfs and Rfs on pigmentation.
Methods We generated multiple types of HSEs using either Pfs or Rfs combined with a co-culture of keratinocytes and melanocytes, and studied both pigmentation processes and epidermal morphogenesis.
Results Culturing HSEs using Rfs led to increased macroscopic pigmentation as well as increased melanin content, increased number of melanocytes and increased expression of melanogenesis-related genes (DCT and MITF). Moreover, morphological differences were observed between Pfs or Rfs HSEs; PFs HSEs showing better epidermal structure.
Conclusion We found a dissimilar effect of Pfs and Rfs on pigmentation which provides new insights into the appearance of (hyper)pigmentary lesions upon skin aging.

12 – MARCEL VLIG
ANTIMICROBIAL ACTIVITY OF SUPPLEMENTED MEDICAL-GRADE HONEY AGAINST PSEUDOMONAS AERUGINOSA IN BURN WOUNDS

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Background Burns are often complicated by the presence of bacteria such as Pseudomonas aeruginosa in the wounds. Silver-based dressings are commonly used in the treatment of burns but can cause skin irritation and delay healing time. Medical-grade honey (MGH) provides an interesting alternative.
Objective This study investigated the antimicrobial effects and possible cytotoxicity of L-Mesitran Soft (MGH-gel) and its individual components, Medihoney (Manuka), Flammazine (silver sulphadiazine), and silver nitrate ($AgNO_3$) in an ex vivo human burn wound model.
Methods For bacterial survival, PAO1 was inoculated for 1 hour in wound models and treated for 24 hours with mentioned components, after which CFU were counted to assess bacterial survival. For wound healing, wound models were treated twice a week for 14 days, after which BRDU and H&E staining were performed to assess reepithelialisation and proliferation of keratinocytes.
Results L-Mesitran, Flammazine, and $AgNO_3$ reduced P. aeruginosa numbers below detection levels. L-Mesitran Soft exhibited a significantly stronger antimicrobial effect compared to Medihoney. The individual components of L-Mesitran contributed significantly to its antibacterial efficacy, thus suggesting synergistic activities. Moreover, L-Mesitran, Flammazine, and $AgNO_3$ slightly inhibited re-epithelialization while Medihoney treatment resulted in a complete lack of re-epithelialization and keratinocyte proliferation. Furthermore, six clinical cases of infected burn wounds illustrated the effectiveness of MGH therapy.
Conclusion Overall, L-Mesitran Soft had similar effects as silver-based products on bacterial load and epidermal regenera-

tion, but outperformed Medihoney. Therefore, supplemented MGH could be used as an effective alternative or complementary treatment for P. aeruginosa-infected burn wounds.

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

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Background Burn wound healing is a complex process that is mostly studied in animals models. To investigate human burn wound healing and to study interactions with the immune system or the drug effects, there is need for human based models.
Objective Our aim was to develop a standardized and scalable in vitro burn wound model, with different burn depths in a three-dimensional (3D) reconstructed human skin (RhS) model and investigate wound healing over time.
Methods Tissue engineered RhS models, in which human keratinocytes are cultured on fibroblast populated fibrinogen-collagen hydrogels, were used to mimic the human skin in vitro. Burn wounds were applied with an soldering iron for 30 seconds at 50˚C, 70˚C, 90˚C, 110˚C and 140˚C. At day 1, 3 and 7 RhS tissue samples were collected and assessed for viability (LDH), and (immuno)histological changes (hematoxylin and eosin (H&E), vimentin, fibroblast activating protein (FAP) and Ki67).
Results An in vitro human skin model with burn wounds was successfully constructed and was monitored over one week. Superficial, partial-thickness and deep-partial thickness wounds were produced in 30 seconds in RhS and confirmed by H&E and LDH staining. A post-burn migrating front of the epidermis is seen, which indicates re-epithelialization. This coincided with activation and proliferation of dermal fibroblasts (based on FAP and Ki67) in the wound edges, indicating wound healing.
Conclusion Our study shows the development of a standardized and scalable in vitro human burn wound model with different burn depths that successfully shows re-epithelialization and wound healing properties over time.

14 – ANDREW MORRISON
GENERATION OF AN ORGANOTYPIC 3D HUMAN LYMPH NODE MODEL TO STUDY SKIN IMMUNE RESPONSES

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Background Lymph nodes are secondary lymphoid organs that are fundamental in orchestrating adaptive immune responses. Their highly specialized architecture is regulated by non-hematopoietic Fibroblast Reticular Cells (FRCs), which support immune cell function, e.g. facilitating arrival of Dendritic Cells (DCs) after exposure-induced migration from skin. The study of skin-related human adaptive immune responses arising from inflammatory stimuli requires competent in vitro models recapitulating the physiological microenvironment.
Objective To create an organotypic 3D human lymph node model using FRCs as foundation that can be implemented into microfluidic devices for organ-on-chip, specifically a skin-draining lymph node.
Methods Primary human FRCs were isolated from lymph node biopsies and co-cultured with either DCs or immune cell suspensions in a 3D hydrogel. At the end of the culture period, cell profiles were characterized through flow cytometry and cytokine/chemokine analysis, as well as histology and 3D imaging.
Results The presence of FRCs in the hydrogel improved the viability of immune cell subsets. In the FRC-DC models, FRCs influenced DC differentiation under inflammatory stimuli to a lymph node resident-like DC phenotype. In the FRC-immune cell model, B cells benefited from the addition of FRCs due to stromal-secreted CXCL12, CXCL13 and BAFF.
Conclusion These models highlight the importance of FRCs in regulating immune cell behaviour in 3D, proving useful for further in-depth studies of stroma-immune cell interactions emerging from allergens and inflammatory stimuli. Such 3D platforms present a beneficial opportunity for skin-draining lymph node on chip, which can be applied in future toxicological risk assessments or tumour-metastasis studies.

15 – ELISABETTA MICHIELON
AN IMMUNE COMPETENT HUMAN MELANOMA-IN-SKIN MODEL AS IN VITRO TOOL FOR TESTING CELL-BASED THERAPIES

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Background Despite recent extraordinary clinical success in treating melanoma with immune checkpoint blockade, a majority of patients do not respond or develop adaptive resistance resulting in poor prognosis. Therefore, a clear need exists for additional therapy options. The ability of Vγ9Vδ2-T-cells to recognize and kill transformed cells independently of HLA-matching makes them a promising candidate for immunotherapy. In vitro melanoma reconstructed human skin (Mel-RhS) models have been developed to mimic features of melanoma progression and thus have an attractive potential to test melanoma-targeted therapies in preclinical studies.
Objective Investigate the capacity of Vγ9Vδ2-T-cells to target tumors in Mel-RhS.
Methods A375 melanoma cells and keratinocytes were co-seeded onto fibroblast-populated dermal equivalents. Expanded peripheral blood-derived Vγ9Vδ2-T-cells were injected into Mel-RhS or healthy controls (RhS), assessed for activation markers by flow cytometry, and their tissue localization was assessed by immunohistochemistry.
Results Vγ9Vδ2-T-cells were viable up to three days in RhS and Mel-RhS and some were found to migrate through the dermal layer into the (sub-)epidermal tumor fields. Close contact with the tumor cells was evidenced by cross-dressing of the T cells with the Melanoma-associated Chondroitin Sulfate Proteoglycan (MCSP) antigen. MCSP+ Vγ9Vδ2-T-cells isolated from the Mel-RhS expressed higher levels of the activation marker 4-1BB. Moreover, CXCL10 secretion, involved in T-cell recruitment into the tumor, was also upregulated in supernatants from Vγ9Vδ2-T-cell-containing Mel-RhS.
Conclusion Vγ9Vδ2-T-cells injected into Mel-RhS could demonstrably migrate to the tumor and engage melanoma cells, leading to their selective activation. The novel Mel-RhS thus presents a promising tool to test T-cell-based therapies.

16 – JASPER KONING
ENDOTHELIALIZATION OF MULTI-ORGAN-ON-CHIPS WITH BLOOD AND LYMPHATIC ENDOTHELIAL CELLS FOR THE GENERATION OF IMMUNOCOMPETENT SKIN MODELS

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Background Until now, 3D human skin models fail to include both blood (BEC) and lymphatic endothelial cells (LEC) despite their essential role for homeostasis and immune responses, limiting their relevance for disease modeling and safety testing. Therefore, establishment of vascularized Organ-on-Chip microfluidic bioreactors with BECs and LECs are a pre-requisite to further improve human skin models to study human diseases.
Objective Set up a robust and reproducible method for the vascularization of organ-on-chip microfluidics with human BECs or LECs which allows long term culturing under physiologic flow conditions for future immunocompetent multi-Organ-on-Chip models.
Methods Human skin endothelial cells were separated into BECs and LECs, expanded, used to vascularize multi-Organ-on-Chips and cultured for up to 14 days under dynamic flow conditions mimicking blood and lymph flow pressures. Morphology, mRNA expression and biomarkers profiles in culture supernatants was investigated upon homeostatic and inflammatory conditions.
Results The new method results in large numbers of pure BECs and LECs. Upon vascularization and prolonged culture periods in Organ-on-Chips, cells retained their endothelial specific phenotype. Biomarker expression of BECs and LECs was different and the cells respond to inflammatory conditions by upregulating various biomarkers. mRNA levels of endothelial junction markers did not substantially change, while the LEC specific markers were reduced in LECs upon inflammatory conditions.
Conclusion The presented method can be used to further enhance organ-on-chip models through the incorporation of functional BECs and LECs resulting in relevant healthy and diseased tissue models to investigate human disease and safety testing.

17 – OLIVIA STEIJLEN
BEYOND ROUTINELY SCORED HISTOPATHOLOGY VARIABLES IN CUTANEOUS SQUAMOUS CELL CARCINOMA: A NESTED CASE-CONTROL STUDY

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Background In daily practice tumor characteristics like diameter, perineural invasion, tissue involvement, and differentiation are used to stage cutaneous squamous cell carcinoma (cSCC) for metastatic risk. Identifying high risk cSCC remains suboptimal and additional histopathological variables have been suggested to refine staging systems. However, evidence for more refined variables is predominantly based on small datasets or single-center investigations, underscoring the need for a more comprehensive exploration.
Objective To evaluate the association between refined his-

topathological variables and the risk of metastasis in cSCC and its value relative to routinely available variables.
Methods We conducted a nested case-control study involving cSCC patients, utilizing data from the Netherlands Cancer Registry and the National Pathology Registry. The primary cSCC of metastatic cases was selected and matched to non-metastatic cSCCs (1:1). The potential refined histopathological variables were selected based on a literature review. A dermatopathologist revised the histopathologic slides. Analyses were conducted using conditional logistic regression.
Results 217 metastatic cSCCs and 217 non-metastatic controls were included. Univariable analysis showed no association between metastatic risk and desmoplastic cSCC (OR 1.1, 95%CI 0.41-3.17) , peritumoral lymphocyte infiltration (OR 0.85, 95%CI 0.58-1.26), and solar elastosis (0.99 OR 95%CI 0.67-1.45). Tumor budding (OR 1.29 95%CI 1.09-1.53) and mitotic rate (1.40, 95%CI 1.18-1.65) were associated with metastasis. However, none of these refined histopathological variables were selected in the multivariable conditional logistic regression model using backward selection.
Conclusion The inclusion of refined histopathological variables does not provide added value in predicting metastasis compared to routinely used parameters.

18 – CHRISTOS DIAMANTIDIS
AUTOMATED DETECTION AND SEGMENTATION OF SUPERFICIAL BASAL CELL CARCINOMA ON OPTICAL COHERENCE TOMOGRAPHY

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Background Superficial basal cell carcinoma (sBCC) represents approximately 30% of all basal cell carcinomas (BCCs), the latter being the most common type of cancer. The gold standard for diagnosing BCC is the histological examination of a biopsy, an invasive and painful procedure. Optical coherence tomography (OCT) has been used to noninvasively diagnose BCC, expediting treatment and reducing healthcare costs. Deep learning algorithms applied to OCT could support assessors by providing data-driven insights regarding tumor presence and location.
Objective To develop and evaluate the performance of a deep learning model for the automated detection and segmentation of sBCC in OCT scans.
Methods A 2D nnUNet-based model was trained on 51 sBCC scans, with tumor nests annotated by a trained OCT assessor. Detection was evaluated on a test set on 20 sBCC and 80 non-BCC scans of histologically verified lesions suspect of non-melanoma skin cancer. The model's segmentation performance was evaluated in 2D and 3D on a test set of 20 sBCC scans.
Results A sensitivity of 80.0% (95% CI: 56.3%-94.3%) and a specificity of 71.3% (95% CI: 60.5%-80.2%) were achieved for sBCC detection. Regarding segmentation performance, a median 2D Dice score of 0.42 (IQR: 0.73) and a median 3D Dice score of 0.31 (IQR: 0.36) were achieved.
Conclusion Our prototype deep learning model serves as a proof of concept for our approach, paving the way for its extension to the other BCC subtypes. Training on a larger dataset to improve its performance will be instrumental in transitioning it to clinical use.

19 – CLARA HARRS
UNRAVELLING THE AGGRESSIVE BEHAVIOUR OF CUTANEOUS SQUAMOUS CELL CARCINOMA IN EPIDERMOLYSIS BULLOSA: EVALUATION OF SOX2 AS A POTENTIAL PROGNOSTIC AND THERAPEUTIC BIOMARKER

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Background A serious complication in epidermolysis bullosa (EB) is the development of aggressive cutaneous squamous cell carcinoma (cSCC) with a high risk for metastasis and poor survival outcomes. There is an urgent demand for safe and effective disease control, particularly with curative and preventive intention. Moreover, little is known about genetic drivers specific for cSCC in EB (EB-cSCc). Information about the molecular profile of EB-cSCC could lead to novel insights about the pathogenesis and could help to detect biomarkers for better risk stratification and novel treatment options.
Objective Analysing the expression profile of cancer and immune-response-related genes in EB-cSCC and identifying prognostic and therapeutic biomarkers.
Methods NanoString mRNA expression analysis was performed on formalin-fixed paraffin-embedded (FFPE) tissues of EB-cSCC. As a control group, cSCC of elderly individuals from the OncoLifeS data-biobank were selected. Differential expression analysis was conducted comparing quantitative changes in expression levels of target genes. Thereafter, immunohistochemistry (IHC) staining of antibodies targeting the protein product of these genes were used evaluating protein expression between both experimental groups.
Results mRNA expression analysis was performed on 26 FFPE tissues of both groups. The expression of the gene SRY-box 2 (SOX2) was significantly increased in the EB-cSCC relative to the control group (log2 fold change: 3.02; P-value <0.05). IHC showed SOX2 expression in the EB-cSCC, whereas no expression was seen in the control group.
Conclusion SOX2 could play a pivotal role in the development of EB-cSCC and could be an important prognostic biomarker and an attractive anticancer target in the future.

20 – CATHERINE ZHOU
THE IDENTIFICATION OF A PROGNOSTIC IMMUNE LANDSCAPE FOR DISTANT METASTASES IN EARLY-STAGE MELANOMA: RNA SEQUENCING RESULTS FROM A MATCHED CASE-CONTROL COHORT

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Background Predicting disease progression in early-stage cutaneous melanoma remains challenging, primarily due to limited research on early-stage primary tumors with sufficient data on distant metastatic events.
Objective To analyze the association between immune cell profiles and the occurrence of distant metastases in early-stage melanoma.
Methods We conducted a matched case-control study involving patients with stage I or II melanoma, utilizing data from the Netherlands Cancer Registry and the Dutch nationwide histopathology network. Matching criteria included age, sex, Breslow thickness, ulceration status, and follow-up duration. Exome-enrichment RNA sequencing of formalin-fixed paraffin-embedded tumor specimens was performed to examine immune cell profiles and T-cell and B-cell receptor (TCR/BCR) repertoires. Hierarchical clustering and multiscale bootstrap resampling was performed to identify immune response patterns.
Results The study included 178 matched cases and 178 controls. No differences were observed in overall immune cell distributions (p = 0.19), hierarchical clusters (p = 0.61), TCR repertoire richness (p = 0.98), evenness (p = 0.60) and Shannon Entropy (p = 0.79) between cases and controls. Variations were observed concerning ulceration status (median relative immune cell abundance in ulcerated vs. non-ulcerated tumors: 1.41 [IQR 0.87-2.79] vs. 1.32 [IQR 0.82-2.44], p = 0.037), highlighting the importance of matching on this variable when identifying new predictors.
Conclusion This unique and extensive matched case-control study of primary cutaneous melanoma did not reveal significant associations between relative immune cell distributions and the occurrence of distant metastases based on RNA sequencing. Spatial relationships between immune cells and tumor cells might provide more prognostic insights.

21 – WOUTER OUWERKERK
BIOMARKERS MEASURED AT START OF TREATMENT TO PREDICT RESPONSE TO TREATMENT IN PATIENTS WITH NON-SEGMENTAL VITILIGO

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Background Treatment of non-segmental vitiligo (NSV) remains a challenge. Aside from a delay in visible repigmentation during therapy, it is uncertain whether a patient will ultimately respond to treatment. Predictive biomarkers could help to assist in monitoring response to therapy.
Objective The aim of this study was to test whether we can predict response during to standard of care treatment using cellular and protein biomarkers measured at start of treatment.
Methods This prospective exploratory study was conducted in 30 previously untreated NSV patients treated with topical therapy with or without narrowband UVB phototherapy. Response was defined as a decrease in Vitiligo Extent Score between baseline and 6 months after starting therapy. We evaluated various immune cell types and large proteomic screens in blood and blister fluid samples at baseline.
Results Will be discussed at the annual meeting of the NVED 2024
Conclusions Will be discussed at the annual meeting of the NVED 2024

22 – SARAH THOMAS
SWITCHING TO IL-23 INHIBITORS AFTER USTEKINUMAB FAILURE: EVALUATING REAL-WORLD OUTCOMES IN PSORIASIS TREATMENT

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Background The interleukin (IL)-12/23-inhibitor (IL-12/23i) ustekinumab has proven to be highly efficacious in psoriasis treatment. In case of incomplete response to ustekinumab, switching to one of the newer generation IL-23-inhibitors (IL-23i) is a possibility, but little is known about their effectiveness after unsuccessful ustekinumab treatment.
Objective To investigate drug survival, effectiveness, and dosing of IL-23i following ustekinumab discontinuation due to ineffectiveness in patients with psoriasis, and to compare outcomes to IL-23i in ustekinumab-naïve patients.
Methods A prospective, multicenter, real-world study was performed using data from the BioCAPTURE registry. Adult

patients with psoriasis treated with guselkumab, risankizumab or tildrakizumab after ineffectiveness of ustekinumab were included. Drug survival analyses were conducted to assess two-year drug survival rates. For effectiveness, first-year quarterly PASI-scores were analysed. Results were compared to patients on IL23i without previous ustekinumab therapy, using confounder-correction.

Results We included 68 patients with prior ineffectiveness to ustekinumab treatment and 91 patients without ustekinumab treatment history, all receiving IL-23i afterwards. Patients with a history of ustekinumab failure exhibited a trend towards lower drug survival rates and PASI-scores compared to those without prior ustekinumab exposure. For drug survival, this difference was not present anymore after confounder correction; for PASI, the difference remained statistically significant at 6 months, but not at 12 months.

Conclusion Previous failure of ustekinumab seems not to be the determining factor in the success of IL-23i treatment. Our data show that IL-23i are effective despite previous ustekinumab ineffectiveness in the treatment of psoriasis in a substantial part of patients.

23 – CHARLOTTE VAN RIEL
BASELINE CHARACTERISTICS OF THE BENEBIO STUDY: DOSE REDUCTION OF THE NEWEST GENERATIONS BIOLOGICS (IL-17 AND IL-23 INHIBITORS) IN PSORIASIS: A PRAGMATIC, MULTICENTER, RANDOMIZED, CONTROLLED, NON-INFERIORITY STUDY

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Background Biologics for psoriasis are highly effective but expensive. Dose reduction (DR) of the first-generation biologics has proven to be safe and (cost-)effective. However, data on DR of the newest biologics is scarce.

Objective This pragmatic non-inferiority study evaluates whether controlled DR of IL-17 and IL-23 inhibitors in psoriasis patients with low disease activity is non-inferior to usual care (UC).

Methods A total of 244 patients, receiving UC of IL-17/IL-23 inhibitors with Psoriasis Area and Severity Index (PASI) ≤5 for at least 6 months, and PASI and Dermatology Life Quality Index (DLQI) ≤5 at inclusion, were randomized 2:1 to DR (interval prolongation to 66% and 50% of UC) or UC. Outcomes: difference in cumulative incidence of persistent flares (PASI >5 for ≥3 months) (primary) and proportion of patients with successful DR, course of PASI and DLQI, safety, costs, and pharmacokinetic profile (secondary).

Results In August 2023, 244 patients (100%) were included: 14% used secukinumab, 25% ixekizumab, 6% brodalumab, 1% bimekizumab, 30% guselkumab, 21% risankizumab, and 3% tildrakizumab. Mean age was 51 years, mean BMI 27.5, 67% was male, 14% had concomitant psoriatic arthritis, median disease duration was 21 years (IQR 20), 47% was biologic naive, and median PASI and DLQI were 0.0 (IQR 1.1 and 1.0, respectively).

Conclusion The baseline characteristics highlight a very low PASI and DLQI (both median 0) at inclusion while the threshold was PASI and DLQI ≤5, a relatively low mean BMI compared to general biologic cohorts, and a well-balanced proportion of biologic naivety vs. non-naivety.

24 – REINEKE SOEGIHARTO
REAL-WORLD OMALIZUMAB PERFORMANCE IN PATIENTS WITH CHRONIC INDUCIBLE URTICARIA: DATA FROM THE DRUSO-CU UCARE STUDY

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Background Treatment of chronic inducible urticaria (CIndU)

is currently limited to H1-antihistamines and omalizumab is not globally licensed for CIndU. Case-series and small cohort studies demonstrated the effectiveness and safety of omalizumab for different CIndU types, but long-term data on a large population is lacking.
Objective To evaluate the long-term effectiveness, safety, time on omalizumab and predictors thereof in a large international CIndU cohort.
Methods Fourteen UCAREs included all CIndU patients that have ever received omalizumab since 2009. Time on omalizumab, reasons and predictors of omalizumab discontinuation were investigated by drug survival analysis and Cox regression analysis.
Results 234 CIndU patients (55% female; mean age 37 years) were included, of which 178 (76%) had CIndU as sole diagnosis (CindU-only) and 56 (24%) had mainly CIndU combined with subordinary minor spontaneous urticaria and/or angioedema (CindU-mainly). Most CIndU patients (n=145, 73%) had complete or good response to omalizumab at the end of follow-up, and were continuously treated with omalizumab without discontinuation (n=172, 74%). Omalizumab was discontinued by 62 (26%) patients, of which 29 (47%) discontinued due to well-controlled disease, 37% (n= 23) and 6% (n=4) due to ineffectiveness and side effects, respectively. Omalizumab survival rates associated with well-controlled disease, ineffectiveness and side effects after 5 years were 69%, 85% and 97%, respectively. Predictors of omalizumab discontinuation in CIndU will be presented in detail at the conference.
Conclusion This large multi-centre real world study demonstrates the high effectiveness and safety of omalizumab in CIndU patients with relatively long drug survival.

25 – LISA PAULIEN VAN DER RIJST
THREE-YEAR DRUG SURVIVAL OF DUPILUMAB, CYCLOSPORINE A AND METHOTREXATE IN A LARGE MULTICENTER COHORT OF PEDIATRIC ATOPIC DERMATITIS PATIENTS

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Background Systemic treatment options, including cyclosporine A (CsA), methotrexate (MTX) and dupilumab, are valuable treatments in pediatric AD. Yet, comparative data of these systemic treatments in pediatric patients are scarce.
Objective To evaluate the drug survival of dupilumab, CsA and MTX in a long-term multicenter daily practice cohort of pediatric AD patients.
Methods This study included pediatric AD patients treated with dupilumab, CsA, or MTX at one of five tertiary centers in the Netherlands from 2012 to 2022. Data were extracted from electronic medical records. Kaplan-Meier curves were used to analyze drug survival. The log-rank test was used to test for differences in drug survival. Sub-analyses of CsA and MTX drug survival were performed before and after dupilumab approval.
Results A total of 502 treatment episodes in 362 unique patients, comprising 192 dupilumab episodes, 216 CsA episodes, and 94 MTX episodes were included. Three-year drug survival rates for dupilumab, MTX and CsA were 59.2%, 25.8%, and 10.8%, respectively (p<.001). Ineffectiveness was the most frequent reason for discontinuation in all treatments (36.9%), followed by side-effects (19.3%). Median survival for both CsA and MTX was longer before dupilumab approval compared to after approval (1.2 (95%CI 1.0-1.5) years vs. 0.7 (95%CI 0.6-0.8) years); p<.001).
Conclusion This study shows superior 3-year overall drug survival of dupilumab compared to CsA and MTX in pediatric AD patients. These results provide insight in long-term tolerability of these systemic treatment options and may help clinicians in the decision-making process when choosing treatment options for pediatric AD patients.

26 – ELLEN VAN DEN BOGAARD
NEXT GENERATION IMMUNODERMATOLOGY (NGID): FROM ONE-SIZE-FITS-ALL TO HIGH-TECH PERSONALIZED SKIN CARE

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The development of new therapeutics and therapies in dermatology has been neglected for decades, resulting in the current 'one size fits all' nature of care. Only recently this concept is changing and the unmet needs of patients are slowly starting to be addressed by pharmaceutical and biotech companies

entering the dermatological market. The focus is shifting to identifying disease biomarkers: characteristics that can be objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention. The latest developments in dermatological technologies and methodologies bring individualized, highly effective treatment of chronic inflammatory skin diseases within reach. In the coming six years, a nationwide consortium called: Next-Generation Immuno-Dermatology (NGID) will capitalize on current advances to construct individual signatures (biomarker profiles) allowing for individual characterization of a patient's immune disbalance and to develop targeted and personalised care for the right patient, at the right time. NGID involves a wide range of disciplines required to make a change in dermatological care, by 1) advanced understanding of the pathophysiological mechanisms of immuno-dermatological diseases, 2) technological advancements for ultra-deep, ultra-high resolution skin characterization, 3) identification of novel biomarkers for disease subtyping, monitoring and treatment, 4) design of tailor-made, animal-free translational human (disease) models, 5) insights into the influence of psychological and behavioural factors on disease outcomes, and 6) novel data fusion, data analysis and machine learning technologies for biomedical data. Thereby NGID offers a prospect to define the most effective and the most rational care for each individual patient with a chronic inflammatory skin disease, providing adequate long-term disease control and prevention of disease progression and later-in-life comorbidities.

27 – COCO DEKKERS
ADULT ATOPIC DERMATITIS PATIENTS WITH TYPE 2 DOMINANT ENDOTYPE DO NOT RESPOND BETTER TO DUPILUMAB TREATMENT THAN PATIENTS WITH TYPE 2 NON-DOMINANT ENDOTYPE

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Background Increased understanding of the pathophysiology of atopic dermatitis (AD) has led to the development of new targeted therapies. Endotyping of patients with AD may be important to better inform clinicians which patients are most likely to benefit from specific targeted therapies.
Objective To investigate serum protein profiles in AD patients with different responses to dupilumab treatment and to assess the role of the measured proteins in predicting response to dupilumab treatment.
Methods All patients were categorized based on their response to dupilumab treatment at week 16 compared to baseline by using the Eczema Area and Severity Index (EASI). For each patient, the concentrations of 60 proteins were measured in serum. Cluster analysis was performed, and the different response groups were compared.
Results A total of 127 patients were selected, with 47 patients reaching EASI≥90, 49 patients reaching EASI-75 and 31 patients reaching EASI<50 after 16 weeks of treatment. None of the proteins were identified as predictive for treatment response. Based on the expression pattern of the measured proteins, a type 2 dominant and a type 2 non-dominant cluster were identified. The clusters were not associated with response to treatment.
Conclusion Our results demonstrate that patients with type 2 dominant endotype do not respond better to dupilumab treatment than patients with type 2 non-dominant endotype.

28 – CELESTE BOESJES
DIFFERENTIAL DYNAMICS OF TARC DURING JAK-INHIBITOR THERAPY COMPARED TO BIOLOGICAL THERAPIES TARGETING TYPE 2 INFLAMMATION

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Background Serum thymus and activation-regulated chemokine (TARC, CCL17) is the most commonly used disease severity biomarker in atopic dermatitis (AD) and previous research demonstrated its use in evaluating therapeutic response, including treatment with biologicals. No data is yet available on the effect of Janus kinase (JAK)-inhibitor (JAKi) treatment on serum TARC levels in AD patients.
Objective To evaluate the effect of JAKi treatment on serum TARC levels in AD patients in context of clinical response.
Methods This observational study included adult AD patients with baricitinib, upadacitinib or abrocitinib treatment, and for comparison dupilumab or tralokinumab treated patients. Eczema Area Severity Index (EASI) and serum TARC levels were evaluated at baseline and week 4, 8 and 16 of treatment. In a JAKi (n=10) and dupilumab subgroup (n=5) both plasma and serum TARC levels were measured at baseline and one follow-up visit.
Results Ninety-five JAKi, 622 dupilumab and 60 tralokinumab treated patients were included. In JAKi patients the median EASI decreased during 16-weeks of treatment, but, in contrast to dupilumab or tralokinumab treated patients, median TARC levels remained relatively unchanged or even tended to increase during treatment. Serum/plasma TARC ratios were stable during follow-up, excluding a selective effect of JAKi on TARC containing platelets.

Conclusion Persistently high and increased TARC levels were found in AD patients treated with baricitinib, upadacitinib or abrocitinib despite a good clinical response, implicating a limited use of serum TARC as biomarker in AD patients with JAKi treatment and warranting further investigation on the potential persistent biological effects.

29 – FIEKE ROSENBERG
TRANSCRIPTOMICS AND GENOMICS-GUIDED DRUG REPURPOSING FOR THE TREATMENT OF VESICULAR HAND ECZEMA

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Background Vesicular hand eczema (VHE), a clinical subtype of hand eczema (HE), has shown limited responsiveness to alitretinoin, which is the only approved systemic treatment for severe chronic HE. This emphasizes the need for alternative treatment approaches.
Objective to identify drug repurposing opportunities for VHE based on transcriptomics and genomics data.
Methods We constructed a causal network by combining 52 differentially expressed genes (DEGs) in healthy and VHE skin samples, and three quantitative trait locus (QTL) genes at locus 20q13.33 associated with hand eczema. Through network analysis, clustering, and functional enrichment analyses, we analyzed the underlying mechanisms of our network. We leveraged drug-gene interactions in the DrugBank database to identify drug repurposing opportunities. We also retrieved pharmaco-transcriptomics data to identify drugs that could reverse the VHE transcriptomic profile to a healthy status.
Results Our (V)HE network comprised of 78 genes, including 52 VHE DEGs, three HE QTL genes and 23 linker genes. Functional enrichment analyses showed that keratinization, cornified envelope formation, and immune response were among the most significant findings. The drug-gene interaction search together with pharmaco-transcriptomic lookups revealed a total of 123 unique drugs. Spectral network clustering revealed 11 modules with general functions, such as immune response, and their interacting drugs.
Conclusions Our study revealed several potential drug repurposing opportunities that might be effective in treating VHE. Future studies should evaluate the efficacy of these drugs in VHE patients and explore transcriptomics and drug repurposing studies in various HE subtypes, paving the way for more optimal and personalized treatments.

30 – LUCA MEESTERS
TH2 AND TH17 DRIVEN EPIDERMAL PATHOPHYSIOLOGY IN ATOPIC DERMATITIS

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Background We previously discovered specific inflammatory signatures to drive epidermal morphological hallmarks of atopic dermatitis (AD).
Objective To elucidate the contribution of AD-associated cytokines to the AD epidermal transcriptome and identify an optimal cytokine cocktail to mimic AD in vitro.
Methods Normal human epidermal keratinocyte and immortalized N/TERT-2G-derived human epidermal equivalents (HEEs), stimulated with Th2 cytokines IL-4 and IL-13 with and without IL-17A or IL-22, were analyzed by RNA-sequencing and spatial transcriptomics and compared to AD epidermis.
Results The HEE transcriptome was altered upon Th2 cytokine stimulation, including induction of inflammation (CCL2, IL33) and proliferation (MKI67). Combination of Th2 cytokines with IL-17A or IL-22 showed a more drastically changed transcriptome, including deregulation of skin barrier genes (FLG, IVL, CLDN4), and induction of I–kappaB kinase/NF–kappaB-, intrinsic apoptotic-, and macroautophagy-signaling. As compared to in vivo, the Th2 condition mimicked 21% of upregulated and 12% of downregulated genes, Th2 + IL-17A respectively 35% and 28%, and Th2 + IL-22 respectively 43% and 38%. Next to the better resemblance, pathway analysis indicated that in vivo interferon signaling (STAT1, CXCL10) and TGF-beta upregulation were not recapitulated in vitro upon Th2 + IL-22 stimulation.
Conclusion Transcriptomic profiling of in vitro AD models revealed the importance of Th17 cytokines and specifically IL-22 in AD pathophysiology, synergizing with Th2-mediated inflammation. We could account epidermal hyperproliferation to Th2 cytokines, while deregulated skin barrier gene expression was driven by IL-17A or IL-22. This improves our understanding of drivers and targets of epidermal defects and help to refine organotypic AD models.

31 – LISA PAGAN
THE VULVAR MICROBIOME IN LICHEN SCLEROSUS AND HIGH-GRADE INTRAEPITHELIAL LESIONS

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Background The role of the vulvar microbiome in the development of (pre)malignant vulvar disease is scarcely investigated.
Objective The aim of this exploratory study was to analyse vulvar microbiome composition in lichen sclerosus (LS) and vulvar high-grade squamous intraepithelial lesions (HSIL) compared to healthy controls.
Methods Women with vulvar lichen sclerosus (n=10), HSIL (n=5) and healthy controls (n=10) were included. Swabs were collected from the vulva, vagina and anal region for microbiome characterization by metagenomic shotgun sequencing. Both lesional and non-lesional sites were examined.
Results Compared to the healthy vulvar skin, vulvar microbiome composition of both LS and vulvar HSIL patients was characterized by significantly higher proportions of respectively Papillomaviridae (p=0.045) and Alphapapillomavirus (p=0.002). In contrast, the Prevotella genus (p=0.031) and Bacteroidales orders (p=0.038) were significantly less abundant in LS, as was the Actinobacteria class (p=0.040) in vulvar HSIL. Fungal and archaeal taxa were scarcely observed.
Conclusion This study is the first to examine the vulvar microbiome through metagenomic shotgun sequencing in LS and HSIL patients. Diseased vulvar skin presents a distinct signature compared to healthy vulvar skin with respect to bacterial and viral fractions of the microbiome. Key findings include the presence of papillomaviruses in LS as well as in vulvar HSIL, although LS is generally considered an HPV-independent risk factor for vulvar dysplasia. This exploratory study provides clues to the aetiology of vulvar premalignancies and may act as a steppingstone for expanding the knowledge on potential drivers of disease progression.

POSTERS

P1 – SELINDE WIND
CLINICAL VALIDATION OF NON-INVASIVE DIGITAL BIOMARKERS FOR SEVERITY SCORING IN EARLY-STAGE MYCOSIS FUNGOIDES COMPARED TO CAILS

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Background The Composite Assessment of Index Lesion Severity (CAILS) score is widely used in clinical trials of Mycosis Fungoides to i) assess lesion severity and ii) evaluate response to treatment. However, CAILS is subjected to substantial inter-rater variability and limited sensitivity.
Objective Therefore, we aimed to explore the performance of novel non-invasive imaging techniques to enable digital disease monitoring in CTCL-MF.
Methods An explorative, open-label study was performed in 21 patients with early-stage CTCL-MF, administering chlormethine gel 0.016% for 16 weeks. Lesional and non-lesional skin were characterized on week -6 and 0 (observational), week 4, 8, 12 and 16 (on treatment) by a trained physician clinically scoring CAILS and using multiple devices for objective quantification of the subjective individual CAILS parameters (erythema, desquamation, hypo- or hyperpigmentation, plaque elevation).
Results At baseline significant differences were observed between lesional and non-lesional skin in skin erythema ($p<0.05$), hemoglobin average level ($p<0.01$) by means of multispectral imaging and by colorimetry (DSMIII) quantifying erythema ($p<0.01$) and for melanin index by automated total body mapping (ATBM) quantifying skin pigmentation ($p<0.05$). In addition, cutaneous microcirculation was significantly more abundant in lesions by laser speckle contrast imaging (LSCI). The test-retest variability of the digital assessments was excellent with CVs of <10% for all parameters and ICCs >0.84. In general, CAILS score showed moderate concordance to the lesional digital assessments.
Conclusion Easy-to-use handheld devices are able to reliably quantify individual CAILS parameters in CTCL-MF patients and can be very valuable for disease severity evaluation and monitoring treatment response.

P2 – JANNIK ROUSSEL
THE TREATMENT RESPONSE TOWARDS THE ANTI-INTERLEUKIN-23 INHIBITOR GUSELKUMAB IN MILD PSORIASIS PATIENTS

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Background Moderate-to-severe psoriasis can be increasingly well-managed as safe and efficacious therapeutics have become readily available. However, this results in fewer patients eligible for clinical trials which negatively impacts the development of new therapies. Contrarily, mild psoriasis patients are generally not systemically treated and might therefore present a suitable alternative population presuming treatment responses can be demonstrated.
Objective To characterize the treatment effect of guselkumab in mild psoriasis patients with a moderate target plaque.
Methods A randomized, double blind controlled trial was performed in 20 mild and 6 moderate-to-severe patients based on a Psoriasis Area and Severity Index (PASI) of ≤5 and ≥10, respectively. Patients were randomized to standard-of-care Guselkumab 100 mg or placebo (3:1) and treatment response monitored for 24 weeks by clinician-reported outcomes and scoring of a single lesion reinforced with multispectral imaging, optical coherence tomography and laser speckle contrast imaging as digitalized endpoints.
Results PASI scores showed a significant decrease in clinical scoring compared to placebo in both the mild ($p=0.009$) and moderate-to-severe treatment group ($p<0.0001$). Focusing on a single target lesion, target severity scores significantly decreased during treatment ($p<0.004$). Objective modalities demonstrated concomitant significant decreases in erythema ($p<0.009$), cutaneous perfusion ($p<0.001$) and epidermal thickness ($p<0.002$) in both guselkumab-treated groups.
Conclusions Total body clinical scoring and target lesion monitoring enable the detection of a treatment effect in mild psoriasis patients. Although this trial was not powered to demonstrate equivalence between severity groups, results indicate treatment responses follow the same trend in mild and moderate-to-severe patients.

P3 – DIGNA DE BRUIN
AN EXPLORATORY SINGLE-CENTER, TWO-PART STUDY TO CHARACTERIZE CUTANEOUS LUPUS ERYTHEMATOSUS AND INVESTIGATE THE EFFECT ON AN IMMUNE CHALLENGE BY COMPARING CLE PATIENTS WITH HEALTHY VOLUNTEERS

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Background Cutaneous lupus erythematosus (CLE) is a rare immune mediated inflammatory disease that includes various subtypes. Given the heterogenous character and limited knowledge on the pathogenesis and pathophysiology of the disease, identification of biomarkers for disease stratification and new drug targets is needed. This study is part of the Next Generation Immuno-Dermatology consortium SKINERGY trials.
Objective The main objective is to characterize objectively measured disease characteristics and to detect novel biomarkers for CLE(-subtypes) using a deep phenotyping approach. To specifically study the role of TLR7 activation in the pathophysiology of the various clinical subtypes of CLE, an ex vivo and in vivo immune challenge with a TLR7 agonist will be performed.
Methods This is a single-center, two-part, exploratory study in CLE patients and healthy volunteers. Up to 30 patients with subacute cutaneous LE, chronic discoid cutaneous LE, or lupus tumidus without systemic manifestations will be included. As a comparison, 10 healthy volunteers will be included. A subset of patients will undergo the optional in vivo immune challenge with topical imiquimod under occlusion. Invasive (skin biopsies, suction blisters, and blood sampling) and non-invasive (imaging, tape stripping, skin swabs, fecal collection, and questionnaires) assessments will be performed to identify disease characteristics and to evaluate the response to the imiquimod challenge.
Conclusion Identifying specific characteristics of CLE and a deeper understanding of the mechanisms involved in the pathophysiology of CLE can potentially lead to better stratification between and possibly within the clinical subtypes and support the development of innovative targeted therapies.

P4 – ANNE VAN HUIJSTEE
IMPROVED CLINICAL EFFECTIVENESS OF ADALIMUMAB WHEN INITIATED WITH CLINDAMYCIN AND RIFAMPICIN IN HIDRADENITIS SUPPURATIVA

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Background Adalimumab monotherapy for hidradenitis suppurativa (HS) is often insufficient with a maximum clinical efficacy of 60% in Hidradenitis Suppurativa Clinical Response (HiSCR) and limited effect on draining tunnels. Data suggest that adalimumab therapy could be improved by concomitant antibiotics.
Objective To compare the clinical effectiveness of adalimumab with clindamycin and rifampicin versus adalimumab monotherapy after 12 weeks.

Methods This retrospective study included patients who started adalimumab with additional clindamycin and rifampicin and patients treated with adalimumab monotherapy, matched on sex and refined Hurley score. The primary outcome measure was the difference in change in the International Hidradenitis Suppurativa Severity Score System (IHS4) at 12 weeks.
Results In total, 62 patients were included in the combination therapy group (n=31) and adalimumab monotherapy group (n=31), showing comparable IHS4 scores; 32.5 vs 29, P=0.87 at baseline respectively. The combination therapy demonstrated greater clinical effectiveness expressed in median IHS4 improvement (-20 vs -9, P<0.001), IHS4-55 (74% vs 36%, P=0.002), median draining tunnel reduction (-4 vs -2, P<0.001) and pain response (47% vs 27%, P=0.02).
Conclusion Adalimumab initiated with clindamycin and rifampicin shows greater clinical effectiveness than adalimumab monotherapy. An important difference in effect was observed in the decrease of draining tunnels, addressing a serious limitation of adalimumab monotherapy.

P5 – MALAK AL-GAWAHIRI
THE CURRENT LIFESTYLE OF PSORIASIS PATIENTS AND THEIR MOTIVATION TO CHANGE

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Background Knowledge about the current lifestyle of patients with psoriasis and the motivation to change their lifestyle enhances development of targeted lifestyle interventions.
Objective To assess the motivation of psoriasis patients to change their lifestyle, to assess current lifestyle in six lifestyle domains, and to compare the lifestyle of patients who are motivated with patients who are unmotivated to change their lifestyle.
Methods A web-based survey among Dutch psoriasis patients ≥16 years was conducted, addressing patients' motivation to change lifestyle, their current lifestyle within the domains physical activity, smoking, alcohol, diet, stress and sleep, and their preferred domains to change lifestyle.
Results Of 448 included patients, most were motivated (48.5%) or possibly motivated (36.8%) to change their lifestyle, whereas 5.1% of patients was unmotivated and 9.6% was uncertain. Motivated or possibly motivated patients were most willing to change physical activity and dietary habits. Only one third of 298 motivated and unmotivated patients answering questions on current lifestyle complied to the recommended Dutch physical activity and dietary guidelines. Unmotivated patients used systemic- or phototherapy more often than motivated patients(p=0.024), met physical activity guidelines less often (p=0.047), were more often smokers (p=0.029) and had a lower vegetable intake than motivated patients (p=0.026).
Conclusion The majority of patients was motivated to change their lifestyle, with exercise and diet being the most popular lifestyle domain targets. There is potential for improvement of lifestyle in both motivated and unmotivated patients. Interventions aiming at incitement of more physical activity and a healthier diet seem most promising.

P6 – NIKI HENCKENS
MULTI-TREATMENT RESISTANCE IN BIOLOGICAL TREATMENT FOR PSORIASIS PATIENTS: DEFINITIONS AND IMPLICATIONS

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Background Although many psoriasis patients respond well to biologic treatment, a small subgroup remains for whom treatment with multiple biologics is unsuccessful, mostly due to ineffectiveness. In literature, a standardized classification for 'multi-treatment resistance' (MTR) is not yet defined.
Objective To explore the various definitions currently used in literature. To assess the implications of these different definitions by determining the magnitude of the prevalence of MTR in a prospective real-world practice cohort (BioCAPTURE).
Methods A literature search, merging synonyms for MTR, psoriasis and currently used biologics in psoriasis treatment was conducted. BioCAPTURE data was used to assess the point-prevalence of MTR by using different definitions for MTR.
Results A total of 53 articles were identified, of which four formed a strict definition for MTR. Definitions found in literature included: discontinuation due to ineffectiveness on ≥4 different biologics, the use of ≥3 biologics regardless of the reason of discontinuation, failure due to ineffectiveness in ≥2 distinct biologic pathways to ≥2 biologics, and failure due to ineffectiveness in ≥2 distinct biologic pathways to ≥3 biologics. The prevalence of MTR for multiple thresholds of biologic failure was assessed using BioCAPTURE data(n=1335 patients) and will be presented in detail.
Conclusion No fixed definition for multi-treatment resistance is available in literature. Depending on definition, the prevalence of MTR differed substantially in real-world practice. It is recommended that a definition is established, considering number and time-span of failures, as well as failure to different working mechanisms of biologics. Through a Delphi approach, consensus can be obtained.

P7 – NICHOLAS SCHRÄDER
THE C4EB STUDY-TRANSVAMIX (10% THC / 5% CBD) TO TREAT CHRONIC PAIN IN EPIDERMOLYSIS BULLOSA: A PROTOCOL FOR AN EXPLORATIVE RANDOMIZED, PLACEBO CONTROLLED, AND DOUBLE BLIND INTERVENTION CROSSOVER STUDY

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Background Patients with the genetic blistering skin condition epidermolysis bullosa (EB) report severe pain as a consequence of skin and mucous membrane lesions including blisters, wounds, and scars. Adequate symptom alleviation is not often achieved using conventional pharmacologic interventions. Finding novel approaches to pain care in EB is imperative to improve the quality of life of patients living with EB. There are several anecdotal reports on the use of cannabinoid-based medicines (CBMs) by EB patients to reduce the burden of symptoms. However, controlled clinical investigations assessing these reported effects are lacking. As the pain quality "unpleasantness" delineates EB pain, we hypothesize the modulation of affective pain processing in the brain by way of intervention with CBMs comprising the cannabinoids Δ-9-tetrahydrocannabinol and cannabidiol-objectified by functional magnetic resonance imaging (fMRI).
Objective The primary outcome is the difference in numeric rating scale pain scores between grouped interventions, using affective descriptors within the Short-form McGill Pain Questionnaire-2. Secondary outcomes include pain self-efficacy, concomitant analgesic medication-use and adverse events. Additionally, fMRI will be employed to assess brain connectivity related to neuroanatomic pain circuits at baseline, placebo and Transvamix® interventions.
Methods The C4EB study is an investigator-initiated, single-centre, randomized, double-blind, placebo-controlled and crossover trial. Adult patients with the diagnosis epidermolysis bullosa, reporting chronic pain will be eligible to participate. Following baseline measurements, participants will be randomized to receive the sublingually administered interventions placebo and Transvamix® in forward or reversed orders, each for two weeks and separated by a washout.

P8 – ESMÉ KAMPHUIS
REAL-WORLD EXPERIENCE OF ABROCITINIB TREATMENT IN PATIENTS WITH ATOPIC DERMATITIS: UP TO 28-WEEK RESULTS FROM THE BIODAY REGISTRY

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Background Abrocitinib has proven to be an effective treatment for patients with atopic dermatitis (AD) in clinical trials. However, limited daily practice data is available.
Objective To evaluate the effectiveness and safety of abrocitinib in patients with AD, including those with previous inadequate response to dupilumab or upadacitinib, in daily practice.
Methods This multicenter prospective observational cohort study includes clinician- and patient reported outcomes on all AD patients treated with abrocitinib.
Results In total, 103 patients from the BioDay registry were included: week 4 (n=95), week 16 (n=61), and week 28 (n=39). Eczema Area and Severity Index (EASI)-50/75/90 was achieved by 81.8%, 57.6%, and 18.2% at week 28, respectively. At week 28, EASI ≤7 was achieved by 66.7%, EASI ≤4 by 51.5%, (almost) clear on the Investigator Global Assessment by 26.5%, Numeric Rating Scale-pruritus ≤4 by 62.9%, Patient-Oriented Eczema Measure ≤7 by 34.8%, Dermatology Life Quality Index ≤5 by 65.2%, and Patient Global Assessment of Disease rating of at least 'good' by 47.8%. Atopic Dermatitis Control Tool <7 was achieved by 56.3% at week 16. The effectiveness of abrocitinib was not significantly different between dupilumab non-responders and dupilumab naïve patients/responders, and between upadacitinib non-responders and upadacitinib naïve patients/responders. Thirty-two patients (31.1%) discontinued treatment due to ineffectiveness (n=17), adverse events (AEs) (n=9) or both (n=3). Most frequently reported AE was nausea (n=28).
Conclusion Abrocitinib is an effective treatment for AD patients and it can be effective for patients with previous inadequate response to dupilumab or upadacitinib.

P9 – REINEKE SOEGIHARTO
TIME ON AND DETERMINANTS OF EFFECTIVENESS OF HIGH DOSE OMALIZUMAB IN CHRONIC URTICARIA PATIENTS

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Background Omalizumab up-dosing up to 600mg/2w is recommended in chronic urticaria (CU) patients with insufficient response to standard dose (SD). Small studies demonstrated the effectiveness of high dose (HD) treatment. Long-term data is lacking.
Objective To investigate time on HD omalizumab, reasons for HD discontinuation and potential predictors of effectiveness in CU patients with insufficient response to SD.
Methods All CU patients with at least one HD omalizumab administration (>300mg/4w) were retrospectively included until September 2022. Time on HD omalizumab was investigated by survival analysis (event=discontinuation of HD). Reasons for HD discontinuation and determinants of HD effectiveness were analyzed.
Results 106 patients (mean age 39.2 years; 76% female) received HD omalizumab, leading to response in 60 patients (57%). At the end of follow-up, 16 patients (15%) continuously received and 88 patients (83.0%) discontinued HD omalizumab. The 1-, 2- and 5-year overall HD survival rate was 44%, 19%, 10% respectively (median time on HD 8 months); mostly determined by well-controlled disease (n=43, 49%) and ineffectiveness (n=35, 40%). Twelve patients (14%) discontinued due to side effects. Initial improvement of disease activity within 3 months SD treatment was associated with higher chance of omalizumab HD effectiveness.
Conclusion This large daily practice study of CU patients with HD omalizumab and long observation period confirmed the success of HD treatment in a substantial part of patients with prior failure on SD. Initial improvement to SD omalizumab may be a relevant factor to select patients that are likely to benefit from omalizumab up-dosing.

P10 – LISA PAULIEN VAN DER RIJST MULTIDISCIPLINARY DIAGNOSIS AND FOLLOW-UP OF COMORBID ASTHMA AND AEROALLERGEN-SPECIFIC IGE LEVELS IN PEDIATRIC ATOPIC DERMATITIS PATIENTS TREATED WITH DUPILUMAB

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Background Atopic dermatitis (AD) is associated with the comorbidities asthma and allergic rhinitis (AR). Dupilumab is an effective treatment for pediatric AD, although the effect on comorbidities remains unknown.
Objective To investigate the prevalence of asthma and AR in pediatric AD patients starting dupilumab treatment, and to evaluate the effect of dupilumab on these comorbidities.
Methods This study included pediatric AD patients treated with dupilumab between 2019 and 2023. Patients were screened at baseline by a pulmonologist for the presence of asthma and AR. Screening included evaluation of medical history and current symptoms, spirometry, Fractional exhaled Nitric Oxide (FeNO), and measurement of aeroallergen-specific IgE levels. In patients diagnosed with comorbid asthma and/or AR, measurements were repeated at week 16 and 52. Likelihood ratio tests were used to identify the primary endpoints: change in FeNO, Forced Expiratory Volume in 1 second (FEV1) and aeroallergen-specific IgE levels during treatment.
Results Eighty-four patients were included. Asthma was diagnosed in 50 patients (59.5%) and AR in 72 patients (85.7%). Baseline FeNO levels were elevated in both patients with (29.0ppb (95%CI 22.0-54.0)) and without asthma (26.0ppb (95%CI 22.0-30.0)). During treatment, FeNO levels decreased (p<.001) and FEV1 scores increased (p<.001) in patients with asthma. In patients with asthma and/or AR., all aeroallergen-specific IgE levels decreased between 61.3% and 89.1% at 52 weeks of treatment.
Conclusion One year of dupilumab treatment, primarily indicated for AD, resulted in a significant improvement in comorbid asthma and a profound decrease in aeroallergen-specific IgE levels in patients with asthma and/or AR.

P11 – LISA PAULIEN VAN DER RIJST DUPILUMAB INDUCES A SIGNIFICANT DECREASE OF FOOD SPECIFIC IGE LEVELS IN PEDIATRIC ATOPIC DERMATITIS PATIENTS

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Background Childhood atopic dermatitis (AD) is strongly associated with the development of food allergy (FA). Dupilumab, an effective treatment for pediatric AD, may also exert an effect on comorbid FA.
Objective This study aimed to assess the effect of dupilumab on food specific IgE (sIgE) levels and patient-reported food allergic symptoms in pediatric AD patients with comorbid FA.
Methods This study included pediatric AD patients (<18 years), with a suggestive clinical history of comorbid FA for peanut, hazelnut, cashew nut, almond, walnut, pistachio, hen's egg, cow's milk, kiwi, or apple, and a corresponding positive sIgE at

the start of dupilumab treatment. sIgE levels were measured every 4-12 weeks during the first year of treatment. A covariance pattern model was used to analyze sIgE levels over time. Patient-reported food allergic symptoms were evaluated during follow-up.
Results Thirty-six patients were included. An estimated percentage decrease of sIgE levels was observed for all food allergens during one year dupilumab treatment, ranging from 70.5% (95%CI:37.1-86.1) to 82.5% (95%CI:75.0-87.7). After one year of treatment, the lowest estimated median sIgE levels were observed in almond (0.8 kU/L, 95%CI:0.5-1.2), while the highest levels were observed in hazelnut (9.8 kU/L, 95%CI:6.0-15.9). Less severe food allergic symptoms were reported in 60% (12/20) of patients who accidentally ingested the culprit food during treatment.
Conclusion Dupilumab treatment resulted in a profound decrease of food sIgE levels for multiple food allergens in pediatric AD patients with comorbid FA, and less severe food allergic symptoms after accidental ingestion in a subset of patients.

P12 – JULIETTE SIMONS
EVALUATING THE DIAGNOSTIC SENSITIVITY OF THE PULSE-CONTROLLED ERGOMETRY TEST FOR CHOLINERGIC URTICARIA

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Background In cholinergic urticaria (CholU), active or passive warming leads to development of pinpoint wheals, erythema and itching. The standardized pulse-controlled ergometry test is a diagnostic tool to confirm CholU and assess exercise thresholds.
Objective To investigate the sensitivity of the pulse-controlled ergometry test and explore factors influencing the diagnostic accuracy.
Methods All (suspected) CholU patients with a pulse-controlled ergometry test between 2021 and 2023 were included in this retrospective study. Patient characteristics, anamnestic exercise-related symptoms (itching, erythema, wheals, sweating and photo-documentation) at baseline and after maximum treatment were analyzed, as well as symptoms and their timing during the ergometry test. Positive ergometry test was defined as occurrence of wheals. Sensitivity/specificity analyses were performed.
Results Twelve patients (91.7% male, median age 22.5 years) were included, of which 10 patients had high suspicion of CholU based on anamnesis and photo-documentation. In 5 patients ergometry test was positive, resulting in a sensitivity of 50%. This indicates that 5 out of 10 CholU patients were false-negatives. Patients with a negative ergometry showed later onset of a positive sweat test compared to patients with a positive ergometry (20 vs. 5 minutes respectively, p=0.055). Wheals occurred in positive ergometry patients within a median of 17.5 (IQR 11.3-23.8) minutes after a positive sweat test.
Conclusion The sensitivity of the pulse-controlled ergometry was low with only 50%. Late positive sweat test was associated with negative ergometry test, possibly explaining negative test results. Whether interventions for earlier sweating are beneficial, needs to be investigated in further studies.

P13 – ALEX ROOKER
THE RISK OF KERATINOCYTE CANCER IN VITILIGO AND THE POTENTIAL MECHANISMS INVOLVED

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Background Light skin types are associated with increased skin cancer risk. Therefore, vitiligo patients might be more at risk for developing skin cancer. However, a lower incidence of both melanoma and nonmelanoma skin cancer (NMSC) has been reported in patients with vitiligo.
Objective This study aimed to evaluate the literature on the risk of developing NMSC in vitiligo patients. Additionally, we proposed a series of hypotheses on the underlying mechanisms.
Methods We performed a systematic review and meta-analysis on the NMSC risk in patients with vitiligo. 9 studies were included in the meta-analyses. A critical appraisal was performed using ROBINS-E analysis and 2 studies were found to have a high risk of bias.
Results The meta-analysis of all KC events in the included studies showed that the overall risk ratio (RR) of developing KC for patients with vitiligo compared with that for healthy controls is 0.60 (95% CI=0.34-1.07; P = 0.0863) in the random effects models.
Conclusion Our meta-analysis demonstrates that patients with vitiligo do not have an increased risk of KC, as may be expected from the increased skin cancer risk observed in light skin types. On the contrary, our meta-analysis indicates a lower KC risk among patients with vitiligo than in healthy controls.

P14 – LOAN NGUYÊN
COMPLICATION RATE AND PROGNOSTIC RISK FACTORS AFTER SURGICAL TREATMENT OF LENTIGO MALIGNA (MELANOMA)

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Background Surgical treatment is "the gold standard" for lentigo maligna (melanoma) (LM/LMM). However, in comparison to excision, there is limited awareness about the post-operative complications and the prognostic clinicopathological features after re-excision.
Objective To determine the complication rate after re-excision and patient risk factors in patients with LM/LMM.
Methods Retrospective single-center study of LM/LMM patients who underwent surgical treatment between January 2001 and December 2020.
Results Our study included 400 LM/LMM from 360 patients and showed that both lesions were primarily localized in the head and neck area (62.6%, 199/318, P<0.001 and 52.4%, 43/82, P=0.303) and LMM on woman's lower leg (92.3%, 12/13, P=0.001). Diagnostic shifts from LM in biopsies to LMM/melanoma in excisions occurred in 11.2% of 223 excisions. Complications after re-excision occurred in 8.1% after re-excision in patients with LM/LMM: 9.0% (9/100) of LM and 6.1% (3/49) of LMM (P=0.05), mostly related to wound infection, -dehiscence and postoperative haemorrhage (9/12, 75.0%). Of all 12 complications, 66.7% (6/9) LM required 1.8 mean outpatients visits and 100% (3/3) LMM 5.3 visits (P=0.02). No independent prognostic factors and no confounders were determined.
Conclusion This study showed a higher complication rate after re-excision of 9.0% in LM compared to 6.1% in LMM. Wound infection, -dehiscence and postoperative haemorrhage contained 6.0% (9/149) of the complications after re-excision.

P15 – SHIDI WU
IDENTIFICATION OF INDUSTRIAL COMPOUNDS TARGETING BOTH TUMOR CELLS AND CANCER-ASSOCIATED FIBROBLASTS IN 3D SKIN EQUIVALENTS MIMICKING MELANOMA AND CUTANEOUS SQUAMOUS CELL CARCINOMA

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Background Cancer-associated fibroblasts (CAFs) are a major component of tumor microenvironment (TME) which plays a critical role in skin cancer progression including melanoma and cutaneous squamous cell carcinoma (cSCC). Developing new drugs which target both cancer cells and CAFs emerged as a hopeful subject of cancer therapy.
Objective To explore the therapeutic potential of two compounds (FC1, FC2) received from Chanel in melanoma and cSCC.
Methods The antiproliferative effect of FC1 and FC2 on melanoma (A375, MW1316A) and cSCC (MET2, MET4) cell lines were examined via colony formation assays and growth curve comparison. CAF deactivation was detected by RT-PCR and immunofluorescence staining. 3D full-thickness models (FTMs) mimicking melanoma and cSCC were generated by seeding A375 and MET2 cells respectively on dermal matrix harboring CAFs, then tumor thickness and CAF phenotype in both tumorous models were examined via HE and IHC staining.
Results Compared to the control group, FC2 strongly inhibited the colony formation of all included tumor cell lines whereas FC1 showed mild effect. In CAFs, only FC2 altered the flattened appearance of CAFs into spindle shape which represents normal fibroblasts. The expression of CAF markers including α-SMA, COL11A1, VCAM-1 and POSTN was also significantly reduced after FC2 treatment. In both melanoma and cSCC FTMs, FC2 application greatly thinned the tumor epidermis and downregulated the expression of α-SMA and COL11A1 in the dermis whereas FC1 showed less effect.
Conclusion Our findings suggest FC2 as a promising new anti-tumor reagent for dual modulating tumor cells and CAFs in melanoma and cSCC.

P16 – TOM WOLSWIJK
E-LEARNING FOR TRAINING HEALTHCARE PROFESSIONALS TO DIFFERENTIATE BASAL CELL CARCINOMA FROM NON-BASAL CELL CARCINOMA ON OPTICAL COHERENCE TOMOGRAPHY

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Introduction Optical coherence tomography (OCT) may replace biopsy for diagnosing basal cell carcinoma (BCC) if BCC can be differentiated from non-BCC with high confidence. However, clinical implementation of OCT is limited by an OCT assessor shortage. E-learning may facilitate remote and simultaneous training of new OCT assessors.
Objective To evaluate whether e-learning is suitable for training healthcare professionals in achieving and maintaining an acceptable error rate for differentiating BCC from non-BCC on OCT. Additionally, we explored the diagnostic accuracy for high-confidence BCC diagnoses by newly trained OCT assessors.
Methods The e-learning consisted of a theoretical module and practice cases. Trainee performance was monitored by cumulative sum analysis establishing the sequential diagnostic error rate using histopathology as reference standard. Acceptable and unacceptable error rates were set at 16% and 25%, respectively. After successful completion, newly trained OCT assessors participated in a pilot study to assess their ability to discriminate BCC from non-BCC. Histopathology was used as reference standard. Diagnostic certainty on BCC presence was expressed on a 5-point confidence-scale. Only the highest score was considered a positive OCT test result (high-confidence).
Results Will be discussed at the annual meeting of the NVED 2024

Conclusion Will be discussed at the annual meeting of the NVED 2024

P17 – EMMY CRUTS
PERINEURAL INVASION IN CUTANEOUS SQUAMOUS CELL CARCINOMA: IT IS NOT ONLY THE SIZE THAT MATTERS

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Background In the eight edition of the American Joint Committee on Cancer (AJCC), microscopic perineural invasion (mPNI) in nerves ≥0.1mm is considered a high-risk factor for poor prognostic outcomes in cutaneous squamous cell carcinoma (cSCC). However, little is known on whether other aspects of mPNI besides nerve diameter have prognostic impact.
Objective We aimed to perform a scoping review of the literature to evaluate the association between one or more aspects of mPNI and risk of recurrence and/or metastasis in cSCC.
Methods A systematic literature search was performed using Embase, Pubmed and Web of Science between January and October 2023. Eligible for inclusion were controlled trials and observational studies, which reported on the prognostic impact of one or more aspects of mPNI.
Results Nineteen studies were included. Results will be discussed during the NVED Annual Meeting 2024.
Conclusion The conclusion of this study will be discussed during the NVED Annual Meeting 2024.

P18 – EMMY CRUTS
PATIENT REPORTED OUTCOMES IN THE MULTIDISCIPLINARY TREATMENT OF PATIENTS WITH HIGH-RISK CUTANEOUS SQUAMOUS CELL CARCINOMA IN THE HEAD-NECK AREA: MEASURING DECISIONAL CONFLICT, HEALTH-RELATED QUALITY OF LIFE AND SATISFACTION WITH CARE

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Background Multidisciplinary care pathways improve quality and efficiency of the care provided. To date, it is unknown how multidisciplinary care pathways affect patient-reported outcomes in patients with high-risk cutaneous squamous cell carcinoma in the head-neck area (HR-HNcSCC).
Objective To evaluate the degree of decisional conflict, health-related quality of life (HR-QoL), and satisfaction with care in patients with HR-HNcSCC and the factors of influence on patient-reported outcomes.
Methods Included were patients with a HR-HNcSCC visiting the multidisciplinary head-neck dermatology outpatient clinic at one of the participating tertiary centers. At the start of the care pathway, patients completed a baseline questionnaire, the decisional conflict scale, and the EuroQoL-5D-5L. One month after completing the care pathway, they completed the EuroQol-5D-5L, the Basal and Squamous Cell Carcinoma Quality of Life and the European Organization for Research and Treatment of Cancer Patient Satisfaction questionnaires. Corresponding user manuals and the existing literature were used to interpreted scores.
Results Eighty patients were included. Results will be discussed during the NVED Annual Meeting 2024.
Conclusion The conclusion of this study will be discussed during the NVED Annual Meeting 2024.

P19 – MIKAELLA LOIZOU
DESMOPLASIA, A RISK FACTOR FOR RECURRENCE AND METASTASIS IN CUTANEOUS SQUAMOUS CELL CARCINOMA: INTEROBSERVER AGREEMENT AMONG DERMATOPATHOLOGISTS

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Background Desmoplasia is a histopathological finding that has emerged as a significant risk factor for local recurrence and metastasis in cutaneous squamous cell carcinoma (cSCC). However, the lack of a universally accepted definition and inconsistencies in its inclusion in clinical guidelines have raised concerns regarding its practical assessment by dermatopathologists.
Objective This study aimed to investigate the interobserver agreement among dermatopathologists in the assessment of desmoplasia in cSCC.
Methods Histopathologic slides of 50 cSCCs were independently evaluated by seven dermatopathologists from six, both peripheral and academic, centers. Each pathologist assessed the presence of desmoplasia, the extent of desmoplasia (presence in more than one third of the tumor), the presence of fine branches of tumor cells, and the presence of a surrounding stromal reaction. Based on a literature search and consensus between experts, desmoplasia was defined as fine branches of tumor cells at the periphery and a surrounding stromal reaction. Interobserver agreement was evaluated by

the percentage of agreement and Fleiss' kappa. Secondary outcomes were differences in agreement between experienced (>5 years of experience) and less experienced (≤5 years of experience) dermatopathologists and between those working in academic and peripheral centers.
Results The results of this study will be discussed during the NVED Annual Meeting 2024.
Conclusion The conclusion of this study will be discussed during the NVED Annual Meeting 2024.

P20 – ELLEN OYEN
PRESCRIPTION AND MANAGEMENT PATTERNS OF ACTINIC KERATOSIS IN PRIMARY CARE AND THE IMPLEMENTATION OF THE "SUSPECT SKIN LESIONS" GUIDELINE AMONG GENERAL PRACTITIONERS IN THE NETHERLANDS

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Background Actinic keratosis, the most prevalent epithelial precancerous lesion worldwide, poses a growing healthcare burden for dermatologists and general practitioners. In 2017, a guideline for Dutch general practitioners recommended 5-fluorouracil 5% cream as primary treatment for actinic keratosis field changes, but its adherence and implementation in daily practice remain uncertain.
Objective Our study aims to evaluate the impact of the guideline and a randomized trial on field-directed therapy on the prescription and management practices of Dutch general practitioners for actinic keratosis field changes.
Methods This retrospective cohort study utilized the Research Network Family Medicine database, including patients aged ≥ 18 diagnosed with actinic keratosis from 2016 to 2021. Multilevel logistic regression was employed to analyse trends over the years.
Results 7932 patient records were analysed and an increase in 5-fluorouracil 5% cream prescription between 2016-2017 compared to 2020-2021 (OR 1.42; 95% CI [0,96-2,11]) was found (non-statistically significant). However, there was a statistically significant 209% increase in likelihood of biopsies between 2016-2017 and 2020-2021 (OR 3,09; 95% CI [2,14-4,45]), a significant 92% decrease in curettage (OR 0,08; 95% CI 0,01-0,62), and a significant 25% decrease in referrals to secondary care (OR 0,75; 95% CI 0,58-0,97).
Conclusion No statistically significant difference was observed in the prescription of 5-fluorouracil 5% cream. Nonetheless, a statistically significant increase in biopsies and a decrease in curettage and referrals to secondary care indicate a shift in the actinic keratosis management. These findings align with the recommendations in the guideline. Furthermore, increased effort is required for effective implementation.

P21 – ANNA ZWANENBURG
IMAGING IN ADVANCED BASAL CELL CARCINOMA: FINDINGS AND RECOMMENDATIONS

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Background Most basal cell carcinoma's (BCC) can be treated based on histology or clinical examination, but in both locally advanced (laBCC) and metastatic BCC (mBCC) radiologic imaging to determine suitable management might be required. Yet, a comprehensive guideline is missing.
Objective To analyse findings of radiologic imaging in laBCC and mBCC.
Methods A retrospective single center cohort study was conducted over a 32 year period to identify all laBCCs and mBCCs. Imaging information as well as basic patient-, tumour- and treatment characteristics were recorded from electronic patient files. Clinical outcomes were local recurrence, metastasis and survival.
Results Fifty-one patients were included, 34 laBCC and 23 mBCC. Pre-operative locoregional imaging was performed in 45% of all patients and 65% of laBCC. MRI was the most used imaging modality (70%), followed by ultrasound. Imaging showed relevant findings in 74% and changed management in 68%. When pre-operative imaging was performed, 79% of surgeries were radical versus 35% without imaging. Imaging to assess metastases was performed in 78% of all patients. The most common incentive for imaging was re-staging (80%), followed by clinical symptoms (33%), most often palpable lymphadenopathy (89%). Of mBCC patients, 19 had local nodal-, 7 bone-, 5 distant nodal-, 4 subcutaneous- and 3 lung metastases. Interestingly, metastases were first found through clinical examination in 78%.
Conclusion This study shows that pre-operative imaging in advanced BCC often results in management changes and strongly increases the chance of radical primary surgery. In follow-up, clinical symptoms often precede diagnosis of metastatic disease. Subsequently, complete re-staging is advised.

P22 – SOFIE KNIPPING
TRANSLATION AND VALIDATION OF THE DUTCH VERSION OF THE SUN EXPOSURE AND PROTECTION INDEX (SEPI)

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Background Skin cancer numbers are rapidly increasing. To improve primary prevention, individualised prevention strategies may be of interest as this could enhance long-term behavioural change. The Sun Exposure and Protection Index (SEPI), previously validated in multiple languages, could help identify individuals with risky behaviour and tailor interventions to the person's propensity to change.
Objective The aim of this study was to investigate the reliability and validity of a Dutch version of the SEPI for daily clinical practice and research.
Methods Patients were included at primary care and dermatology outpatient settings in a 1:1 ratio. Participants were asked to fill out the SEPI with some baseline characteristics and the previously validated FACE-Q Skin Cancer – Sun Protection module. Construct validity was tested by comparing SEPI part I and the FACE-Q module using Spearman's Rho. Internal consistency was assessed with Cronbach's Alpha. To assess test-retest reliability, the SEPI was again filled out three weeks later. Scores were compared with Cohen's weighted Kappa.
Results Of the 171 participants completing the first questionnaire, 147 (86.0 %) participants also completed the follow-up. Comparison between the corresponding SEPI part I and FACE-Q module questions showed good correlations (correlation coefficients: 0.61–0.85). Internal consistency of SEPI part I was 0.63 and SEPI part II was 0.65. The test-retest analysis indicated reproducibility over time (weighted Kappa: 0.38–0.76).
Conclusion In conclusion, the Dutch version of the SEPI is shown to be a valid and reliable tool for evaluating individual UV exposure and measuring a person's propensity to limit it.

P23 – JOEY KARREGAT
SKIN REACTIONS TO BIOCIDES IN DUTCH AGRICULTURAL WORKERS: AN EXPLORATION

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Background Biocides can be harmful to humans. Effects include skin and respiratory irritation/sensitization, organ damage and systemic toxicity. Additionally, a growing body of evidence suggests that exposure to certain biocides increases the risk of developing Parkinson's Disease (PD). Subpopulations like agricultural workers have elevated risk of exposure. While estimating total biocide exposure is challenging, biocide-induced skin reactions may be used as a proxy for exposure in agricultural workers. Moreover, screening for such skin reactions may yield an incidence approximation of biocide-induced allergic contact dermatitis (ACD).
Objective To explore diagnostic capacity, agricultural safety measures and the incidence of (suspected) biocide-induced dermatoses among Dutch agricultural workers in The Netherlands.
Methods 36 dermatological departments were surveyed on their test capacity for biocide-induced ACD. A report on safety measures and regulations at agricultural companies by the Netherlands Labour Authority was analyzed. A preventive medical questionnaire among 2609 agricultural workers was obtained and screened for suspected biocide-induced skin complications.
Results Out of 36 dermatological departments, only three sporadically test for biocide-induced ACD. Safety measures and regulations are suboptimal at a substantial fraction of 85 surveyed agricultural companies. Various skin complaints were frequently reported by agricultural workers that actively work with biocides, although a definitive cause cannot be determined from available data.
Conclusion Better adherence to safety guidelines may minimize exposure risk for agricultural workers, while increased ACD test capacity and improved screening for skin complications among agricultural workers may help estimating biocide exposure, as well as biocide-induced ACD incidence. Additional research is warranted.

P24 – JULIETTE BOLLEMEIJER
LIFETIME PREVALENCE AND ASSOCIATED FACTORS OF DERMATOLOGICAL ITCH IN THE MIDDLE-AGED AND ELDERLY: A POPULATION-BASED CROSS-SECTIONAL STUDY

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Background Itch, a common symptom in dermatological conditions, is often accompanied by psychological distress and reduced quality of life. However, research on the prevalence and associated factors of dermatological itch in general populations is limited.
Objective This cross-sectional study aimed to determine the lifetime prevalence of dermatological itch and identify its associated factors in middle-aged and elderly individuals.
Methods Participants from the Rotterdam Study, a prospective population-based cohort, were interviewed to assess whether they had ever experienced an itchy skin condition, defining lifetime dermatological itch. Additionally, data on over 20 demographic, lifestyle, dermatological, and non-dermatological factors was collected. Multivariable logistic regression analysis was used to explore associations between these factors and dermatological itch.
Results This study included 5,246 eligible participants (median age: 67 years, female: 56.0%). The lifetime prevalence of dermatological itch was 33.7%. Female sex (OR (95% CI): 1.26 (1.11-1.43)), body mass index (1.02 (1.01-1.03)), self-reported and presence of atopic dermatitis (4.29 (3.74-4.92), and 1.97 (1.60-2.43)), self-reported and presence of psoriasis (2.31 (1.77-3.01), and 2.11 (1.55-2.87)), self-reported dry skin (1.95 (1.73-2.29)), asthma (1.40 (1.08-1.83)), renal impairment (1.45 (1.17-1.79)), and clinically relevant depressive and anxiety symptoms (1.85 (1.52-2.25), and 1.36 (1.11-1.66)) were significant factors associated with dermatological itch.
Conclusion This study reveals that a substantial one-third of middle-aged and elderly individuals experience dermatological itch during their lifetimes. Various lifestyle, demographic, dermatological, and non-dermatological factors were found to be associated with dermatological itch. These findings provide an important foundation for future research to better understand the development and burden of itch.

P25 – WILLEMIJN WITKAM
ASSOCIATION OF AIR POLLUTANT EXPOSURE WITH ACNE SEVERITY IN A MULTI-ETHNIC ADOLESCENT COHORT IN ROTTERDAM, THE NETHERLANDS

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Background Acne vulgaris is a prevalent multifactorial inflammatory skin condition. Recent evidence suggests that exposure to air pollutants might aggravate acne symptoms by altering sebum production and damaging the skin barrier. However, a large population-based study exploring the effect of air pollutants on acne severity is currently lacking.
Objective To examine the association between air pollution exposure and acne severity in adolescents.
Methods This study was embedded in the Generation R study from Rotterdam, the Netherlands. Adolescents with available data on air pollution exposure and physician-graded acne severity were included (N=4422). Average exposure levels of six pollutants (particulate matter and nitrogen oxides) at participants' home addresses three months prior to acne evaluation were estimated using land-use regression models. Acne severity was graded using the Global Evaluation of Acne severity score and subdivided into three ordinal categories: (almost) clear, mild and moderate/severe. Outcomes were adjusted for socio-economic status, ethnicity and maternal smoking exposure and corrected for multiple testing using the effective number of tests (Galwey method). Adjusted odds ratios (AORs) were obtained from single-pollutant ordinal logistic regression.
Results Mild/severe acne was present in 53% of the adolescents (median age 13.5). Exposure to one air pollutant was associated with a smaller AOR for acne severity: 0.97(99%CI 0.95-0.99) for exposure to PM10. Exposure to PM2.5, PM25abs, PMCOARSE, NO2 or NOx was not associated with acne severity.
Conclusion Exposure to higher levels of air pollution was not associated with more severe acne. Observed protective effects are likely due to chance or residual confounding.

P26 – ROSANNE OTTEVANGER
ASSOCIATED MALIGNANCIES IN PATIENTS WITH MYCOSIS FUNGOIDES: A DUTCH NATIONWIDE RETROSPECTIVE COHORT STUDY

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Background Recent evidence shows a higher incidence of other primary malignancies (OPMs) in MF patients.
Objective Investigate the incidence of OPMs in MF patients in

the Netherlands compared to the Dutch population.
Methods A retrospective, nationwide, population-based cohort study was performed with data from the Dutch Cutaneous Lymphomas Registry (DCLR) including patients with a diagnosis of MF between January 2000 and January 2020. All histopathology reports were requested from the Nationwide Network and Registry of Histo- and Cytopathology in the Netherlands (PALGA) and screened for diagnoses of OPMs. Life-long incidence rates were used to compare the incidence of malignancies in MF patients and the general population based on data from the Netherlands Cancer Registry(NCR) and Statistics Netherlands(CBS).
Results 1024 patients were included. A total of 294 cases of other primary malignancies were found with 28% of the MF patients developing at least one OPM. Cutaneous (OR 2.54 (CI 2.0-3.2) and hematological malignancies (OR 2.62 (CI 2.00-3.42) had a statistically significant higher incidence than the Dutch population. For cutaneous malignancies there was a significantly increased risk of developing melanomas (OR 2.76; CI 2.11-3.59) and cutaneous squamous cell carcinomas (OR 2.34; CI 1.58-3.45). For hematological OPMs Lymphomatoid papulosis and Hodgkin lymphoma were more frequently found, with respective ORs of 76.22 (CI 50.35-115.32) and 6.28 (CI 2.02-19.55).
Conclusion MF patients are significantly at risk for developing other hematological and cutaneous malignancies. Clinicians should be aware of this increased risk and could conduct regular screening of MF patients with frequent total body skin inspections.

P27 – JULIETTE KERSTEN
LESIONAL BSA CUTOFFS AND PROGNOSIS IN EARLY STAGE MYCOSIS FUNGOIDES: A RETROSPECTIVE ANALYSIS

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Background The prognostic significance of the 10% lesional body surface area (BSA) cutoff, differentiating between mycosis fungoides (MF) stages IA/IB, remains uncertain despite its use in the International Society for Cutaneous Lymphomas (ISCL)/European Organisation for Research and Treatment of Cancer (EORTC) criteria.
Objective To investigate the prognostic impact of varying lesional BSA cutoffs on disease-specific survival in early stage MF patients.
Methods In this retrospective single-center cohort study, 313 early stage MF patients (January 2000 to December 2018) were assessed. Lesional BSA categories (<10%, 10-29%, ≥30%) were determined from clinical images by two independent observers, with discrepancies resolved by a third observer. Disease-specific survival was the primary endpoint, calculated using univariate and multivariate hazard rate models.
Results Patients were grouped by lesional BSA: BSA <10% (n=173 [55%]), BSA 10-29% (n=103 [33%]) and BSA ≥30% (n=17 [5%]). The median follow-up was 74 months (IQR 54–109). The 5- and 10-year disease-specific survival rates were similar between BSA <10% group (99% and 94%) and BSA 10-29% group (97% and 91%; p=.442), yet significantly different between BSA <10% and BSA ≥30% group (81% and 72%; p<.001). Significantly higher hazard rates were found for patients with BSA ≥30% compared to BSA <10%, hazard ratio 8.5 (95% CI 2.5–29.1; p=.004), but not for BSA 10-29% compared to BSA <10%, with a hazard rate of 0.8 (95% CI 0.1–4.5; p=.820).
Conclusion Patients with lesional BSA <10% and BSA 10-29% had comparable disease-specific survival. These results advocate for adjusting the early stage MF cutoff to BSA ≥30%.

P28 – LIANA BARENBRUG
EXPLAINING THE DIFFERENCE IN DRUG SURVIVAL OF BIOLOGICS BETWEEN FEMALE AND MALE PSORIASIS PATIENTS

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Background Drug survival of biologics for psoriasis treatment has reported to be lower in females than males for the first generation biologics (TNF-alfa and interleukin (IL) 12/23 inhibitors (i)), but studies investigating this difference for the newer biologics (IL17i and IL23i) are scarce. Importantly, we lack insight which factors explain this difference.
Objective To assess differences in drug survival rates between females and males in first and second generation biologics, and to assess sex-differences in disease activity (Psoriasis Area and Severity Index (PASI)), safety outcomes, treatment satisfaction (Treatment Satisfaction Questionnaire for Medication (TSQM)) and health-related quality of life (HR-QoL) (Dermatology Life Quality Index (DLQI).
Methods Data of patients with psoriasis treated with a biologic were obtained from the prospective, multicenter, daily-practice BioCAPTURE registry. Drug survival, split for different reasons of discontinuation, and adverse events leading to treatment discontinuation were compared for females and males. Advanced statistical modelling was performed to compare the course of PASI, DLQI and TSQM scores between females and males.
Results Drug survival of biologics was generally lower in females than males for biologics, including most of the newer IL17i and IL23i. Females more often discontinued treatment due to, and with other, adverse events than males. Baseline PASI score was significantly higher in males, but differences disappeared during treatment. Females were less satisfied with their biologic treatment, and reported a lower HR-QoL.
Conclusion A different safety profile, HR-QoL and treatment satisfaction with biologics for females versus males might explain earlier discontinuation of biologics in females.

P29 – LEIS BECIRI
BEYOND THE SKIN: PREVALENCE OF JOINT COMPLAINTS IN NON-SYNDROMIC CONGENITAL ICHTHYOSIS

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Background Congenital ichthyosis (CI), a heterogeneous group of rare scaly skin disorders caused by abnormal keratinization, has a profound impact on the quality of life (QoL). Recent studies showed psoriasis-like immune dysregulations in CI, characterized by increased levels of cytokines such as interleukin-17 and interleukin-23, which are also essential in psoriatic arthritis. This, combined with concerns about joint issues reported by patients in the latest qualitative interview study on QoL in CI, resulted in questions about joint complaints in patients with CI. Until now, prevalence and potential causality of joint complaints in patients with CI have not been investigated.
Objective To identify the prevalence of joint complaints in patients with non-syndromic CI based on patient-reported outcomes.
Methods Patients with a genetically confirmed ichthyosis from the Maastricht UMC+ genodermatology database and via the Dutch ichthyosis patient organization were included. No distinctions were made regarding the presence or absence of joint complaints. By using a digital questionnaire based on rheumatologists', general practitioners', and dermatologists' screening tools for early arthritis, psoriatic arthritis, as well as musculoskeletal complaints from the Maastricht study, we collected patient-reported outcomes.
Results Recruitment is ongoing. First data analysis is planned for December 2023.
Conclusion This study aims to explore the prevalence of joint complaints in CI, which may be useful in the management and prognosis of ichthyoses. We would like to present the first results during the 2024 Annual Meeting of the NVED.

P30 – EMMA HOLTAPPELS
THE EXPRESSION AND FUNCTION OF JAK3 AND TEC FAMILY KINASES IN THE PATHOGENESIS OF VITILIGO

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Background Vitiligo is an autoimmune disease in which the skin melanocytes are destroyed, leading to depigmented skin lesions. Current therapies have limited efficacy, causing a decreased quality of life. JAK and TEC family kinases, involved in cytokine signaling, play an important role in the pathogenesis of vitiligo.
Objective Broad JAK/TEC inhibitors have been shown effective in the treatment of vitiligo in mice and patients. However, after treatment cessation, a rapid relapse is often reported. Therefore, a better understanding is required of the precise molecular and cellular actions of these inhibitors.
Methods Two recently published scRNAseq datasets obtained from vitiligo patients and healthy controls were used in the R2 Genomics Analysis and Visualization Platform to analyze the RNA expression of JAK3/TEC kinases. Multiplex immunohistochemistry will be used to validate the expression of these kinases at the protein level in specific immune and non-immune cells in vitiligo skin. Using a human vitiligo skin explant model, we will next investigate the cellular effects of JAK3 and TEC family kinase inhibition ex vivo.
Results High expression levels of JAK/TEC kinases were found in lesional vitiligo skin, compared to non-lesional and healthy skin. JAK3/TEC kinases were predominantly expressed by infiltrating immune cells, like T cells, macrophages and dendritic cells, but surprisingly also by melanocytes. Low expression levels were also found in fibroblasts and keratinocytes.
Conclusion The expression pattern of JAK3/TEC kinases highlights their role in the vitiligo pathogenesis. The analyses that will be performed could lead to a more effective and durable therapy.

P31 – VEERLE MERKUS
THE DEVELOPMENT OF AN IMMUNE LANDSCAPE PANEL FOR IMAGING MASS CYTOMETRY (IMC) FOR CUTANEOUS T CELL LYMPHOMA'S (CTCL) PATIENTS

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Background Previous studies in cutaneous T-cell lymphoma (CTCL) suggest that interactions of tumor cells with the tumor microenvironment (TME), (including CD8+ T-cells and NK-cells) are important in controlling early stages of disease. A comprehensive analyses of the architecture and composition of the TME in CTCL could give insight in the anti-tumor response and provide clues on therapeutic targets. New histopathological techniques including Imaging Mass Cytometry provide the opportunity of characterizing the TME in detail.
Objective We constructed a CTCL specific immune phenotyping panel with Imaging Mass Cytometry (IMC) to investigate the TME in CTCL on formalin fixed paraffin embedded (FFPE) material. We investigated the expression of immune

checkpoint ligands and its interaction with the surrounding reactive immune cells e.g. subsets of macrophages and dendritic cells. We aim to reveal differences in immune landscapes correlating to disease progression or prognosis.
Methods Biopsies were selected from Mycosis fungoides (MF) patients with (n=6) and without (n=4) progression. The antibodies were initially tested for performance by immunohistochemical staining (IHC) on human skin and tonsil. Subsequently, antibodies with an appropriate signal intensity were conjugated to lanthanide metals.
Results The antibody panel is optimized for 43 markers.
Conclusion The architecture and composition of the TME in MF including spatial organization of immune subsets and expression of checkpoints ligands can be investigated with unprecedented detail using the current IMC panel. We are currently correlating clinical course with immune landscapes to identify critical interactions between tumor cells and the TME.

P32 – NOOR VAN HOUT
EXPANDING THE POSSIBILITIES OF THE STRATUM CORNEUM MODEL FOR BACTERIAL GROWTH

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Background The skin barrier, specifically the stratum corneum, plays a vital role in maintaining skin health and protecting against pathogenic microorganisms. Understanding the interactions between commensal and pathogenic bacteria on the skin's surface is important for our understanding of bacterial dysbiosis as seen in atopic dermatitis.
Objective We focus on exploring the potential of the stratum corneum model, developed within our lab for pathogen testing and the evaluation of biological agents and antibiotics, to investigate microbe-microbe interactions and mimic disease specific environments. In this project, we examine the interplay between S. aureus and C. acnes in the context of atopic dermatitis.
Methods The stratum corneum model utilizes callus as a nutrients source for bacteria, effectively mimicking the stratum corneum. We investigate bacterial growth and survival on the model and explore its customizations by varying agar pH levels, utilizing callus from patients with specific skin mutations, and employing diverse bacterial inoculations combinations and densities.
Results Preliminary findings reveal that the growth and survival of C. acnes on the model appear unaffected by the presence of S. aureus. Intriguingly, as the population of C. acnes diminishes, S. aureus seem to takes this opportunity to use these newfound nutrients, to further enhance its growth.
Conclusion The stratum corneum model demonstrates its potential as a valuable tool for investigating microbe-microbe interactions within disease-specific environments. Our ongoing challenge is to mimic a skin disease within the model, which offers a path for future research.

P33 – MARJOLEIN HIEL
PHENOTYPE SWITCHING IN RELAPSED PEMPHIGUS PATIENTS AFTER RITUXIMAB TREATMENT: A SINGLE CENTRE RETROSPECTIVE COHORT STUDY

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Background Pemphigus is a potentially fatal blistering disease characterized by loss of adhesion of the skin and/or mucosa caused by autoantibodies against the desmosome cadherins; desmoglein (Dsg) 1 and/or Dsg3. Pemphigus can be divided into pemphigus vulgaris (PV) and pemphigus foliaceus (PF). Both are effectively treated with rituximab, a monoclonal antibody targeting CD20 on B-cells. 57% of rituximab-treated pemphigus patients experience relapses after remission, and it has been observed in the clinic they may switch to a different pemphigus phenotype.
Objective This study aims to examine the clinical and immunological features of relapsed rituximab-treated pemphigus patients, to gain further insights into the progression and evolution of the disease.
Methods The medical records of patients with pemphigus who had relapsed after receiving rituximab treatment at a single center between 2017 and 2022 were evaluated retrospectively. We identified the clinical and immunological characteristics of patients with relapsing disease, including mucosal involvement, skin involvement, Dsg1/3 antibody titers, peripheral B-cell count, time to relapse and remission, response to rituximab therapy, and complete remission rates.
Results 52 pemphigus patients who relapsed at least once after treatment with rituximab were identified, 42 PV and 10 PF patients. Preliminary results indicate that about 30% of the patients showed clinical and immunological phenotype switching between PV and PF. Further parameters will be included in the analysis of the phenotype switch of the patients.
Conclusion Further study of the PV and PF phenotype switch could lead to a deeper understanding of pemphigus disease and treatment.

P34 – JOSEFIEN VAN LEENGOED
VEXAS SYNDROME AS AN UNDERLYING CAUSE OF DISEASE IN PATIENTS WITH SWEET SYNDROME: A RETROSPECTIVE COHORT STUDY

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Background VEXAS syndrome (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) is an adult onset autoinflammatory caused by a somatic mutation in the UBA1-gene, leading to severe systemic inflammation and myeloid dysplasia. About 90% of patients have skin involvement, most often presenting as Sweet syndrome-like lesions.
Objective to describe the cohort of patients with Sweet syndrome and potentially risk factors for VEXAS syndrome, to identify VEXAS syndrome as an underlying cause of disease in patients with Sweet syndrome.
Methods retrospective cohort study of patients between 2012 and 2023 with a clinical diagnosis and histopathological affirmation of Sweet syndrome. Chart review included skin and systemic symptoms, laboratory testing, histopathological assessment (skin biopsy and bone marrow), follow-up, and previous genetic testing.
Results 29 patients with Sweet syndrome were identified with a mean age of onset of 57 years and predominantly female (55.2%). Sweet syndrome was attributed to a myeloproliferative disorder in 16 cases, of which 11 were male. Three of these 11 patients were previously tested for VEXAS syndrome, two were found to have the disorder. Retrospective genetic testing is being performed for the remaining cases.
Conclusion Within our cohort of 29 patients with Sweet syndrome, two had a diagnosis of VEXAS syndrome as an underlying cause. A subgroup of eight male patients with a myeloproliferative disorder were considered to have an increased risk for VEXAS syndrome. Genetic testing for mutations in the UBA1-gene is indicated for this high-risk population and may lead to a greater understanding of Sweet syndrome and VEXAS syndrome.

P35 – EMILY KALLEN
ANA O 3: BETTER PREDICTION OF CASHEW NUT ALLERGY THAN CASHEW NUT EXTRACT IN ADULTS

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Background In children, IgE against Ana o 3 predicts cashew nut allergy better than IgE against cashew nut extract (CNE). In adults, the diagnostic value of Ana o 3 and CNE is unknown.
Objective To evaluate the diagnostic value of IgE against Ana o 3 versus that of CNE in adults with suspected cashew nut allergy, and their possible association with symptom severity.
Methods Adult patients that underwent an oral food challenge (OFC) for suspected cashew nut allergy or presented with a history of anaphylaxis to cashew nut were included. Diagnostic value was assessed by receiver operating characteristic curve-analysis.
Results In total, 45 patients were included of which 18 were allergic. IgE against Ana o 3 was statistically significantly superior in predicting cashew nut allergy with an area under the curve of 0.95 (95% CI 0.90-1.00) compared to 0.90 (95% CI 0.80-0.99) for CNE. Using cutoff levels for Ana o 3 with 100% positive predictive value (PPV) (negative predictive value (NPV) 91%), 72% of patients were correctly diagnosed compared to 49% when using the 100% PPV (NPV 94%) cutoff levels for CNE. IgE against Ana o 3 and CNE did not statistically significantly distinguish between patients with mild/moderate and severe symptoms.
Conclusion In adults, IgE against Ana o 3 proved to be a better predictor for cashew nut allergy than CNE, with correct classification in 72% versus 49% in this population. Ana o 3 was not associated with symptom severity.

P36 – LIAN VAN DER GANG
RISK OF INFECTIONS DURING BIOLOGIC OR JAK INHIBITOR THERAPY FOR ATOPIC DERMATITIS: RESULTS FROM THE BIODAY REGISTRY

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Background Real-world evidence comparing infection risk between the different available biologics and Janus kinase (JAK) inhibitors for atopic dermatitis (AD) is scarce.
Objective To assess the differential effect of biologics and JAK inhibitors (JAKi) available for the treatment of AD on the risk of severe infections.
Methods In this registry embedded observational prospective multi-centre study, all treatment-emergent infections reported in the BioDay registry were assessed. Severity was based on the guideline of Common Terminology Criteria for Adverse Events and expert opinion. Incidences rates were standardized in 100 patient-years (PY) per treatment. Negative Binomial Regression (NBR) modelling was used to investigate the risk of infection corrected for confounders. Confounders were identified by a directed acyclic graph.
Results Between 2017 and 2022, 1610 patients with 2047 tre-

atment episodes (total follow-up 3643.1 PY) were included. A total of 487 treatment-emergent infections occurred, of which 244 (49.3%) were moderate and 71 (14.3%) severe. Crude incidence rates of severe infections per 100 PY were 1.5 (95% confidence interval [CI]: 1.0-1.9) for biologics (dupilumab and tralokinumab) and 7.5 (95% CI: 4.3-10.6) for JAKi (abrocitinib, baricitinib, and upadacitinib). Confounder adjusted incidence rates will be presented.

Conclusion Infections were frequently reported in our daily practice cohort. Crude incidence rates of severe treatment-emergent infections were higher for JAKi treated patients compared to patients treated with biologics, consistent with the more immunosuppressive mode of action of JAKi.

P37 – NICOLINE POST
CONSENSUS ON THE SAFETY AND RISKS OF LASER AND INTENSE PULSE LIGHT (IPL) TREATMENTS IN VITILIGO PATIENTS, AN E-DELPHI STUDY

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Background Laser and IPL treatments carry the risk of inducing new vitiligo lesions (Koebner phenomenon). This combined with the absence of guidelines leads to reluctance to administer these treatments in vitiligo patients.

Objective The aim of this study was to achieve consensus on the safety, strategies to minimize risks, and treatment recommendations of laser and IPL treatments in vitiligo patients.

Methods An e-Delphi study, with 51 items, was performed. Consensus was achieved when ≥70% of the participants agreed with the item.

Results Thirty-two items reached consensus (62.8%). We agreed that every laser/IPL treatment, even in ideal circumstances, poses a risk of inducing vitiligo in predisposed patients. Pinpoint-like lesions, the Koebner phenomenon, and hypochromic borders enhance the risk, whereas test-spots are recommended to minimize the risk. Unless there is stability >1 year and absence of activity signs, we advise not to treat. We recommend treating laser/IPL-induced vitiligo like normal vitiligo, and to start early treatment when epidermal damage occurs after a laser/IPL treatment.

Limitations This is an expert opinion-based consensus study, with little evidence available in current literature.

Conclusion Consensus was achieved on the safety, strategies to minimize risks, and treatment recommendations for laser and IPL treatments in vitiligo patients.

P38 – TOM WOLSWIJK
REPEATABILITY OF RADIOMICS FEATURES IN OPTICAL COHERENCE TOMOGRAPHY SCANS OF BENIGN NEVI: A PROSPECTIVE TEST-RETEST STUDY

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Introduction Optical coherence tomography (OCT), a non-invasive imaging modality, is gaining popularity in dermatology as a diagnostic alternative to biopsy. Radiomics is the method of extracting quantitative data from medical images and the identification of highly repeatable handcrafted radiomics features (HRFs) is a crucial step in developing generalizable and accurate predictive, diagnostic, and prognostic radiomics models for OCT which may reduce the need for biopsy.

Objective To evaluate the repeatability of HRFs extracted from OCT images of benign nevi in a test-retest setting.

Methods In this test-retest study, two nevi per healthy volunteer were scanned twice with a ten-minute interval (multi-beam swept-source frequency domain OCT). Nevi on the OCT images were manually delineated (ITK_SNAP) and HRFs were extracted (PyRadiomics). The repeatability of HRFs was evaluated using the concordance correlation coefficient (CCC). A CCC≥ 0.9 was considered indicative of excellent repeatability.

Results Will be discussed at the annual meeting of the NVED 2024

Conclusion Will be discussed at the annual meeting of the NVED 2024

P39 – EVA KORTE
PROTOCOL FOR THE DEVELOPMENT OF CORE DOMAIN SETS FOR EPIDERMOLYSIS BULLOSA CLINICAL TRIALS: A PRACTICAL FRAMEWORK FOR WORKING TOWARDS HARMONIZATION OF OUTCOMES

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Background Epidermolysis bullosa (EB) is a heterogeneous group of rare genetic blistering diseases. The wide variety of treatment outcomes reported in EB clinical trials hinders the acquisition of evidence on the best available treatment options. Core outcome sets are standards of minimum sets of outcomes to measure in clinical trials, thereby enabling uniform measurement and reporting of trial outcomes.
Objective The Core Outcome Sets for Epidermolysis Bullosa (COSEB) initiative aims to develop core outcome sets for use in future EB trials, starting with development of a core domain set (CDS) for the different EB types.
Methods The protocol is based on guidance of the CHORD COUSIN Collaboration (C3), the Harmonizing Outcome Measures for Eczema (HOME) roadmap, and the Core Outcome Measures in Effectiveness Trials (COMET). Involved stakeholders are patient(s) (representatives), EB experts including clinicians, researchers and investigators, methodologists, industry, and regulators. Working groups will be formed to define a list of candidate outcome domains. These domains will undergo evaluation through a three-round e-Delphi study, involving stakeholders from around the world who will rate the importance of the proposed candidate domains. The **Results** of the Delphi studies will serve as the foundation for the final consensus meetings, where the CDSs for the main EB types will be constituted.
Conclusion The final core outcome domains in the CDSs may serve as the minimum set of outcomes to measure in future EB trials, thereby facilitating adequate comparison of treatment effectiveness and safety, and improving the consistency in reporting of outcomes.

P40 – ALEXANDRE MOTTA
A RAPID AND EASY-TO-USE SYSTEM TO EXTRACT SKIN INTERSTITIAL FLUID FOR DERMATOLOGICAL RESEARCH

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Background Skin interstitial fluid (ISF) is a biomarker-rich compartment of high relevance for fundamental and clinical research in dermatology. Yet, skin ISF is understudied mostly due to the difficulty to extract it IMcoMET BV has developed a dual microneedle-based method (M-Duo technology) that allows for the sampling of skin ISF in a localized, rapid, and easy way.
Objective To test the M-Duo technology ex vivo on human full skin explants and melanoma biopsies.
Methods M-Duo needles were assembled as previously described. The needles were inserted in the skin at a depth of 1mm, and 60 microliters of PBS were injected via one needle, while being simultaneously aspirated via the other needle. This system was used on ex vivo human healthy skin, as well as on stage IIB and IIC melanoma biopsies.
Results In the extracts collected, various assays revealed the presence of clinically relevant markers: LDH as measured by enzymatic activity, the cytokines IL-4, IP-10, IL-1b, MCP-1, IL-6, INF-g and TGF-b, measured by CBA assay, tryptophan by metabolomics, and cfDNA of the BRAFwt-gene by digital PCR. Proteomic on samples collected from healthy skin versus melanoma biopsies showed a clear difference with the presence of established melanoma markers like S100B.
Conclusion The M-Duo Technology® allows access to the soluble biomarkers present in skin ISF in a more convenient and quicker way than currently available techniques. It therefore has the potential to be a game changer in dermatological fundamental and clinical research by unlocking novel diagnostics biomarkers and therapeutic approaches.

P41 – CATHERINE MERGEN
STRATUM CORNEUM CERAMIDE PROFILE DIFFERS BETWEEN LESIONAL AND NON-LESIONAL SKIN IN PATIENTS WITH MYCOSIS FUNGOIDES

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Background Mycosis fungoides (MF) is the most common subtype of primary cutaneous T-cell lymphoma, in which malignant T-lymphocytes infiltrate the skin, resulting in patches, plaques, and eventually tumors. Biopsies are used as the current gold standard for monitoring the course of the

disease, but their invasive nature limits their applicability. The ceramide profile of the stratum corneum has previously been shown to be altered in inflammatory skin diseases and normalized upon regression.
Objective We aimed to characterize the ceramide profile of lesional and non-lesional skin in MF patients to assess its potential as a biomarker.
Methods In this study, both lesional and non-lesional skin of 21 MF patients was tape stripped at two different time points for analysis of ceramide composition by liquid chromatography-mass spectrometry (LC-MS). Skin permeability was assessed by measuring transepidermal water loss (TEWL).
Results Principal component analysis (PCA) revealed two distinct populations for lesional and non-lesional skin. More precisely, the ceramide profile of lesional skin was characterized by an increase in CER[NS], a higher degree of unsaturation and a reduction in average carbon chain length. TEWL was significantly increased in lesional skin, but no correlation to ceramide composition could be observed. Sampling of the same sites after 42 days, i.e. test-retest variability without intervention, revealed no significant changes in the ceramide profile, indicating the stability of these compositional changes.
Conclusion The lesional skin of MF patients shows an altered ceramide composition compared to non-lesional skin that is comparable to other skin diseases with a disturbed barrier.

P42 – JONAS JÄGER
TOWARDS NEXT GENERATION RECONSTRUCTED HUMAN SKIN: CONSTRUCTION OF A PERFUSABLE VASCULARIZED DERMIS INSIDE A MULTI-ORGAN-CHIP

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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 Here, we aimed to generate a functional, perfused vascularized dermis in a multi-organ-chip.
Methods A 3D-printed structure was incorporated inside a multi-organ-chip during its fabrication process and the sacrificial, water-dissolvable material used to generate hollow channels in a collagen/fibrin fibroblast-populated hydrogel. Subsequently, these channels were seeded with dermal endothelial cells (ECs) to generate a vasculature. Channels were perfused for 7 days while (co-)culture conditions were monitored for viability and metabolism (lactate, glucose, lactate dehydrogenase). The endothelium was characterized structurally (immunocytochemistry) and functionally (barrier integrity, immune cell transmigration).
Results The sacrificial structure serves as a bio-compatible negative mold to pattern hydrogels. These channels are connected to the on-chip circulation and can be seeded with ECs, aligning in flow and forming a perfusable lumen with barrier properties. Secretion of angiogenesis-associated cytokines are influenced by the collagen/fibrinogen hydrogel composition. EC vessels with dermal fibroblasts remain viable and metabolically active in the chip up to 7 days.
Conclusion We present a method to pattern hydrogels in a commercially available multi-organ-chip platform which allows us to construct a perfused vascularized dermis. In the future, 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.