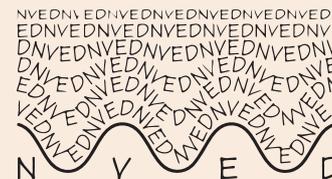


DE AVOND VOORDAT DIT NUMMER NAAR DE DRUKKER GING, IS BESLOTEN HET CONGRES TE VERPLAATSEN NAAR 23-24 JUNI 2022. GELIEVE DIT NUMMER DUS GOED TE BEWAREN.



Thursday 23 June 2022

- 09.30 - 10.15 **Registration and welcome with coffee/tea**
- 10.15 - 10.25 **Opening by the chair of the NVED**
- 10.25 - 11.25 **Session I: Epidermal structure and function**
Session chair: Peter van den Akker (*UMCG*), Hanna Niehues (*Radboudumc*)
1. Marike van Gisbergen *Maastricht UMC+* Novel FAM83G mutations display deficient CK1a- binding in palmoplantar keratoderma.
 2. Felicitas Pardow *Radboudumc* Regulation of keratinocyte differentiation through aryl hydrocarbon receptor signaling involves the transient activation of TFAP2A.
 3. Auke Otten *Amsterdam UMC* A genome-wide long noncoding RNA CRISPRi screen identifies PRANCR as a novel regulator of epidermal homeostasis.
 4. Jos Smits *Radboudumc* CRISPR-Cas9 editing of human keratinocytes to resolve or confirm gene function: A showcase study for filaggrin null phenotype.
- 11.25 - 12.10: **Marcel Jonkman lecture by dr. Joost Meijer, UMCG**
- 12.10 - 13:15 **Lunch**
- 13.15 - 14.15 **Session II: Multi-omic approaches for investigative dermatology**
Session chair: Remco van Doorn (*LUMC*) + Klara Mosterd (*Maastricht UMC+*)
5. Safa Najidh *LUMC* Improved Sézary cell detection and novel insights into immunophenotypic and molecular heterogeneity in Sézary syndrome.
 6. Elisabetta Michielon *Amsterdam UMC* Cellular cross-talk-induced secretion of interleukin-10 (IL-10) in an organotypic human melanoma-in-skin model skews monocyte differentiation towards an M2-like phenotype.
 7. Inger Kreuger *LUMC* Multi-omics analysis of mutant NRAS-induced senescence in human melanocytes.
 8. Wouter Ouwerkerk *Amsterdam UMC* Genetic association between vitiligo genetic susceptibility and response to immune checkpoint inhibitor therapy in advanced melanoma patients: early results of the IO-GEM consortium.
- 14.15 - 14.30 **Break (stretch your legs)**
- 14.30 - 15.30 **Session III: Diagnostics in dermatology**
Session chair: Marcel Bekkenk (*Amsterdam UMC*) + Emőke Rácz (*UMCG*)
9. Tobias Sangers *ErasmusMC* Limited impact of diagnostic delay due to COVID-19 on melanoma and squamous cell carcinoma tumor characteristics in the Netherlands: A nationwide pathology registry analysis.
 10. Fieke Adan *Maastricht UMC+* Optical coherence tomography versus punch biopsy for diagnosis of basal cell carcinoma: a randomized diagnostic trial.
 11. Anna Smak Gregoor *ErasmusMC* The impact of an artificial intelligence (AI) based mobile health application on dermatological care consumption in the Netherlands: a retrospective cohort study.
 12. Bertine Huisman *CHDR Leiden* Integrin $\alpha v \beta 6$ as a target for tumor-specific imaging of vulvar squamous cell carcinoma and adjacent premalignant lesions.

Poster presentations and networking session I (with coffee and tea)

(selection for poster walks by jury)

- P1. Mehran Aghdam (*UMCU*) Recombinant human C1 esterase inhibitor as prophylactic treatment of idiopathic non-histaminergic angioedema: A phase 1 trial and follow-up.
- P2. Joline Bogaard (*Amsterdam UMC*) Saliva as potential treatment for burns: Assessing antimicrobial properties of saliva and donor variation of burn patients.
- P3. Sven van Egmond (*ErasmusMC*) Telehealth for older adults with skin disease: A qualitative exploration of Dermatologists' experiences & recommendations for improving care.
- P4. Andrew Morrison (*Amsterdam UMC*) A 3D organotypic model to study human lymph node FRC-DC interactions.
- P5. Noa van den Brink (*Radboudumc*) Local dermatitis upon tapestripping and vaseline treatment of healthy human skin is attenuated by coal tar: Insights into AHR-targeting therapies for inflammatory skin diseases.
- P6. Lin Shang (*Amsterdam UMC*) Dynamic host-microbiome interactions in reconstructed human oral mucosa with representative oral biofilms.
- P7. Willem Zoutman (*LUMC*) Diagnosing early cases of Sézary syndrome: Digital improvements in detection of DNA methylation biomarkers.
- P8. Rosanne Ottevanger (*LUMC*) Incidence of mycosis fungoides and Sézary syndrome in the Netherlands between 2000 and 2020.
- P9. Britt van der Leeden (*Amsterdam UMC*) METs and NETs are present in burn wound tissue and coincide with a procoagulant phenotype.
- P10. Clara Harrs (*UMCG*) Unravelling the aggressive behaviour of squamous cell carcinoma in epidermolysis bullosa: Analysis of clinical outcome and tumour characteristics in the Dutch EB Registry.
- P11. Jonas Jäger (*Amsterdam UMC*) Metabolically active, tri-layered reconstructed human skin.
- P12. Daphne van der Hout (*LUMC*) Epidemiology of Mycosis fungoides and Folliculotropic mycosis fungoides from 2000-2018.
- P13. Michelle Meertens (*UMCU*) First and second omalizumab treatment episode in chronic urticaria patients.
- P14. Reineke Soegiharto (*UMCU*) Clinical profile of adult patients with idiopathic angioedema.
- P15. Mirjam Schaap (*Radboudumc*) Challenges in noninvasive skin biomarker measurements in daily practice: A longitudinal study on skin surface protein detection by the transdermal analysis patch in pediatric psoriasis.
- P16. Nicoline Post (*Amsterdam UMC*) Does autoimmune vitiligo protect against COVID-19 disease?
- P17. Lisa Pagan (*CHDR Leiden*) A systematic review of the vulvar microbiome in health and disease.
- P18. Jannik Rousel (*CHDR Leiden*) Results of a double-blind, randomized, placebo-controlled clinical trial with ketoconazole and placebo in seborrheic dermatitis.
- P19. Catharine Zhou (*ErasmusMC*) Primary melanoma characteristics of metastatic disease: a nationwide cancer registry study.
- P20. Celeste Eggermont (*ErasmusMC*) Nationwide data on patient profiles and patterns of care of patients with advanced cutaneous squamous cell carcinoma in The Netherlands.
- P21. Lieke van Delft (*Maastricht UMC+*) A patient decision aid for patients with a superficial basal cell carcinoma: hype or valuable?
- P22. Tamara van Hal (*Sint Maartenskliniek Nijmegen*) Discovery of arthritis in psoriasis for early rheumatologic referral (DAPPER): a cross-sectional study.
- P23. Elke ter Haar (*Radboudumc*) Drug survival and tolerability of biologics in older adult patients with psoriasis, a comparison with younger patients.
- P24. Yann Hoogland (*LUMC*) A nation-wide study to determine the tumour profile and risk in patients with the CDKN2A mutation.
- P25. Estella de Jong (*LUMC*) Cumulative incidence and risk factors for cutaneous squamous-cell carcinoma metastases in organ transplant recipients: the SCOPE-ITSCC metastases study.
- P26. Anna Zwanenburg (*Netherlands Cancer Institute, Amsterdam*) Predictors for recurrence, metastasis and mortality in primary cutaneous squamous cell carcinoma: a systematic review and meta-analysis.
- P27. Lara van der Schoot (*Radboudumc*) Implementation of a tightly controlled dose reduction strategy of adalimumab, etanercept and ustekinumab for psoriasis in daily clinical practice: a pilot study.
- P28. Celeste Boesjes (*UMCU*) Daily practice experience of baricitinib in patients with moderate to severe atopic dermatitis: a 16-week evaluation of clinical efficacy and safety.
- P29. Anouk Nouwen (*ErasmusMC*) Natural Moisturizing Factor as a clinical marker in atopic dermatitis.
- P30. Annelie Musters (*Amsterdam UMC*) COVID-19 outcomes in patients with atopic dermatitis: results from

the global SECURE-AD physician registry.

- P31. Marjolijn Haisma (*UMCG*) Association of frailty and life expectancy with guideline deviation and clinical outcome, including quality of life in elderly patients with cutaneous squamous cell carcinoma of the head and neck.
- P32. Selinde Wind (*CHDR Leiden*) Topical bimiralisib, a dual pan-class PI3K/mTOR inhibitor, shows meaningful cutaneous drug levels in healthy volunteers and mycosis fungoides patients but no clinical activity.
- P33. Alet Leus (*UMCG*) Age-related differences in tumor characteristics and prognostic factors for disease progression in cutaneous squamous cell carcinoma of the head and neck.
- P34. Julia Clabbers (*Maastricht UMC+*) Alitretinoin as alternative treatment for inherited diseases of keratinization in childbearing age women – a case series and literature review.

16.45 - 17.30: **Guest Lecture by dr. Frank de Gruijl, LUMC**

17.30 - 20.00 **Drinks and Dinner**

20.00 - 20.45 **22th general assembly of the NVED**

20.45 - 01.00 **Party? Having fun together?**

Friday 24 June 2022

09.00 - 10.00 **Session IV: Skin immunity and inflammation**

Session chair: Ibrahim Korkmaz (*Amsterdam UMC*) + Femke van Wijk (*UMCU*)

13. Jasper Koning *Amsterdam UMC* A multi-organ-on-chip approach to investigate how oral exposure to metals can cause systemic toxicity leading to Langerhans Cell activation in skin.
14. Yixin Luo *LUMC* Assessment of Socs1 deletion in CD4+ T cells of chronically inflamed mouse skin to develop a pathogenic model of MF.
15. Luca Meesters *Radboudumc* Untangling the complex cytokine milieu in psoriasis and atopic dermatitis through in vitro epidermal models.
16. Jill Olydam *ErasmusMC* EASI p-EASI: predicting disease severity in atopic dermatitis patients treated with tralokinumab.

10.00 - 11.15 **Poster walks (selected for poster prize) and networking session II (with coffee and tea)**

11.15-12.30 **Session V: Biologicals in dermatological practice**

Session chair: Juul vd Reek (*Radboudumc*) + Ly Nguyen (*LUMC*)

17. Marloes van Muijen *Radboudumc* Guselkumab drug survival is high in patients with psoriasis treated in real-world practice.
18. Roselie Achten *UMCU* Ocular surface disease is a common finding in moderate-to-severe atopic dermatitis patients.
19. Sarah Tomas *Radboudumc* 'Happy drug survival 2.0': drug survival combined with patient reported outcomes in psoriasis patients on biologics: results of the BioCAPTURE registry.
20. Lotte Spekhorst *UMCU* Successful tapering of dupilumab in patients with well-controlled AD.
21. Vanya Rossel *Maastricht UMC+* Expanding the spectrum of mutations for PNPLA1 and NIPAL4 in ichthyosis and evaluation of novel therapeutic interventions.

12.30 - 13.30 **Lunch**

13.30 - 14.15 **Guest Lecture by dr. Hendri Pas, UMCG**

14.15 – 15.30

Session VI: Novel therapeutic strategies and treatment effects

Session chair: Abdoel El-Ghalbzouri (*LUMC*) + Antoni Gostyński (*Maastricht UMC+*)

22. Shidi Wu *LUMC* Application of doxorubicin-loaded PLGA nanoparticles targeting both tumor cells and cancer-associated fibroblasts on human skin equivalents mimicking melanoma and cutaneous squamous cell carcinoma.
23. Babette Verkouteren *Maastricht UMC+* Eight years of experience with vismodegib for advanced and multiple basal cell carcinoma patients in the Netherlands.
24. Shima Ahmady *Maastricht UMC+* Risk of cutaneous squamous cell carcinoma after four different treatments for actinic keratosis: long-term results of a randomized controlled trial.
25. Maaïke Waasdorp *Amsterdam UMC* Adipocytes reduce scar formation but delay re-epithelialization in in vitro reconstructed human skin.
26. Nicoline Post *Amsterdam UMC* Meek micrografting: A novel surgical technique for the treatment of depigmentation.

15.30 - 15.40

Awards for best presentation and poster; selection breaking news

15.40

Closure

Meeting Location:

Congress hotel 'De Werelt'
Westhofflaan 2
6741 KH Lunteren
Tel: 0318-484641

Program committee:

Michel van Geel (*Maastricht UMC+*), Ellen van den Bogaard (*Radboudumc*), Gilles Diercks (*UMCG*), Luba Pardo (*Erasmus MC*), Walbert Bakker (*Amsterdam UMC*), Judith Thijs (*UMCU*), Abdoel El-Ghalbzouri (*LUMC*)

Jury for presentation prize: Daphne Bakker (*UMCU*), Robert Rissmann (*CHDR*), Hanna Niehues (*Radboudumc*)

Jury for poster prize: Juul vd Reek (*Radboudumc*), Loes Hollestein (*Erasmus MC*), Jeroen Bremer (*UMCG*)

NVED board:

Sue Gibbs (president, *Amsterdam UMC/ACTA*), Marcel Bekkenk (secretary, *Amsterdam UMC*), DirkJan Hijnen (representative in NVDV 'Commissie Nascholing', *Erasmus MC*), Antoni Gostynski (treasurer, *Maastricht UMC+*), Patrick Zeeuwen (*Radboudumc*)

1 - NOVEL FAM83G MUTATIONS DISPLAY DEFICIENT CK1A-BINDING IN PALMOPLANTAR KERATODERMA.

Marika W. van Gisbergen^{1,2}, Vanya S.V.J. Rossel^{1,2}, Tom E.J. Theunissen^{1,2}, Renske Janssen^{1,2}, Jasper J. van der Smagt³, Peter M. Steijlen^{1,2}, Maaïke Vreeburg⁴, Antoni H. Gostynski^{1,2}, Michel van Geel^{1,2,4}

1) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; 2) GROW School for Oncology and Developmental Biology, Maastricht University Medical Center+, Maastricht, The Netherlands; 3) Department of Clinical Genetics, University Medical Center Utrecht, The Netherlands; 4) Department of Clinical Genetics, Maastricht University Medical Center+, Maastricht, The Netherlands.

Background: Hereditary palmoplantar keratoderma (hPPK) is a heterogeneous group of inherited disorders characterized by abnormal thickening of the palmoplantar epidermis. hPPK may be explained by pathogenic variants in many different genes. Recently, FAM83G was described to be involved in a hPPK phenotype in humans and different animal species.

Objective: Here, we identified two additional patients with a hPPK phenotype, homozygous for variations in FAM83G, and investigated the binding capacity of aberrant FAM83G to Casein Kinase 1α (CK1α) to functionally prove causality.

Methods: Previously reported mutations c.697A>T p.(R233*) in the wooly mouse, c.155G>C p.(R52P) in dogs and c.101C>A p.(A34E) in humans, were investigated alongside by WES analysis newly identified homozygous variations. All variants were introduced by site-directed mutagenesis in a pCMV5-FLAG vector containing FAM83G and transfected into HEK-293 cells. CK1α protein interactions for FAM83G were evaluated by immunoprecipitation and Western blotting.

Results: We identified 2 patients having a potential causative mutation for hPPK in the FAM83G gene. We observed that the mutated FAM83G indeed showed reduced binding capacity to CK1α, as was also shown for all other known mutations.

Conclusion: Causality of novel mutations in FAM83G was proven in the second and third patient known worldwide with a specific hPPK phenotype, by showing deficient binding to CK1α. FAM83G interaction with CK1α is key in regulating the WNT/β-catenin signaling cascade and controlling proliferation in palmoplantar epidermal skin.

2 - REGULATION OF KERATINOCYTE DIFFERENTIATION THROUGH ARYL HYDROCARBON RECEPTOR SIGNALING INVOLVES THE TRANSIENT ACTIVATION OF TFAP2A

Felicitas Pardow¹, Jos P.H. Smits¹, Jieqiong Qu², Diana Rodijk-Olthuis¹, Ivonne M.J.J. van Vlijmen-Willems¹, Simon J. van Heeringen², Huiqing Zhou², Ellen H. van den Bogaard¹

1) Department of Dermatology, Radboud Institute for Molecular Life Sciences (RIMLS), Radboud University Medical Center, Nijmegen, The Netherlands; 2) Department of Molecular Developmental Biology, Faculty of Science, RIMLS, Radboud University, Nijmegen, The Netherlands. *These authors contributed equally.

Background: Terminal differentiation of epidermal keratinocytes is essential for skin barrier development and tightly coordinated by a complex network of interacting transcription factors. Previous work identified the aryl hydrocarbon receptor (AHR), a ligand-activated transcription factor and environmental sensor, to orchestrate epidermal differentiation through transient activation of putative downstream transcription factors, amongst others TFAP2A.

Objective: With this study we aim to investigate the role of TFAP2A in AHR-mediated keratinocyte differentiation to understand the contribution of AHR signaling to skin barrier formation and function.

Methods: We utilized siRNA-mediated TFAP2A knockdown in primary keratinocytes and CRISPR-Cas9 induced TFAP2AKO in N/TERT keratinocytes combined with transcriptomic analysis and organotypic modelling of the epidermis.

Results: Keratinocyte-specific ablation of TFAP2A negatively impacted epidermal development resulting in disorganized stratification, aberrant differentiation and reduced barrier function (by transepithelial resistance) in organotypic TFAP2AKO epidermis. Furthermore, TFAP2A deficiency impeded the AHR ligand-mediated induction of terminal differentiation gene expression (e.g. HRNR, DSC1, S100A8, MMP1).

Conclusion: We conclude that TFAP2A is an essential transcription factor for human keratinocyte differentiation and epidermal development and that AHR regulates epidermal differentiation through transient activation of a specific panel of key transcription factors, as herein illustrated by TFAP2A. Identification of this AHR-TFAP2A axis provides further insights into the complex regulatory network driving epidermal differentiation in response to environmental cues and prompts new avenues for the treatment of barrier dysfunction related diseases by targeting AHR's partners in crime.

3 - A GENOME-WIDE LONG NONCODING RNA CRISPRi SCREEN IDENTIFIES PRANCR AS A NOVEL REGULATOR OF EPIDERMAL HOMEOSTASIS.

Auke B.C. Otten^{1,2}, Penfei Cai³, Binbin Cheng², Mitsuhiro A. Ishii², Kun Qu³, Bryan K. Sun²

1) Department of Physiology, Amsterdam University Medical Centers, location VUmc; 2) Department of Dermatology, University of California–San Diego; 3) School of Life Sciences, University of Science and Technology of China.

Background: Genome-wide association studies indicate that many human skin disease susceptibility reside in non-protein-coding regions of the genome. Long noncoding RNAs (lncRNAs) make up a large proportion of the noncoding genome, but their biological impacts in are poorly understood.

Objective: Based on observation that some lncRNAs (TINCR, WAKMAR1) regulate epidermal homeostasis and the high number of annotated human lncRNAs, we hypothesized that additional epidermally-relevant lncRNAs exist, and it is our objective to identify them.

Methods: We performed a CRISPR interference (CRISPRi) proliferation screen on 2.263 epidermis-expressed lncRNAs and characterized a top-candidate using RNA interference-me-

diated knockdown and phenotypic analysis in organotypic epidermal tissue.

Results: Statistical evaluation of the CRISPRi screen resulted in the identification of nine novel candidate lncRNAs regulating keratinocyte proliferation. Characterization of a top hit from the screen, showed a regulatory role for this lncRNA in keratinocyte cell cycle progression, clonogenicity and in vitro wound healing. Therefore, we named this lncRNA progenitor renewal associated noncoding RNA (PRANCR). PRANCR-deficient epidermis displayed impaired stratification with reduced expression of disease-relevant differentiation genes, including keratins 1, 10, filaggrin and loricrin. Transcriptome analysis showed that PRANCR controls the expression of 1.136 genes, with strong enrichment for late cell cycle genes containing a CHR promoter element. PRANCR-knockdown also led to increased levels of CDKN1A (p21), known to govern keratinocyte senescence and differentiation.

Conclusion: Collectively, we identified novel lncRNA candidates, including PRANCR, that (potentially) regulate epidermal homeostasis. Future endeavors are aimed to further unravel (molecular) function of PRANCR and other lncRNAs during skin wound healing.

4 - CRISPR-CAS9 EDITING OF HUMAN KERATINOCYTES TO RESOLVE OR CONFIRM GENE FUNCTION: A SHOWCASE STUDY FOR FILAGGRIN NULL PHENOTYPE.

J.P.H. Smits¹, N.J.M. van den Brink¹, L.D. Meesters^{1,2}, I.M.J.J. van Vlijmen-Willems¹, C. Evrard³, Y. Poumay³, M. van Geel^{4,5,6}, W.J.A.J. Hendriks⁷, P.L.J.M. Zeeuwen¹, E.H. van den Bogaard¹

1) Department of Dermatology, Radboud Institute for Molecular Life Sciences (RIMLS), Radboudumc, Nijmegen, The Netherlands; 2) Department of Molecular Developmental Biology, RIMLS, Radboudumc; 3) Research Unit for Molecular Physiology, NARILIS, University of Namur, Namur, Belgium; 4) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; 5) GROW School for Oncology and Developmental Biology, Maastricht University Medical Center+ The Netherlands; 6) Department of Clinical Genetics, Maastricht University Medical Center+ The Netherlands; 7) Department of Cell Biology, RIMLS, Radboudumc The Netherlands.

Background: Ever since the association of filaggrin (FLG) loss of function mutations to ichthyosis vulgaris and atopic dermatitis disease onset, studies were performed to understand the role of FLG in epidermal structure and function. Intra-individual genomic predisposition and immunologic confounders complicate the clear-cut comparison between FLG genotypes and identifying causal effects thereof. CRISPR-Cas9 enables the precise altering of any gene of interest and to meticulously dissect and study the consequential phenotypes.

Objective: To generate FLG knockout (Δ FLG) keratinocytes and study their behavior using organotypic epidermal equivalent culture model system.

Methods: Using electroporation of RNP complexes containing sgRNAs and Cas9, N/TERT-2G immortalized human keratinocytes were efficiently modified to generate a Δ FLG cell pool.

After clonal expansion, organotypic human Δ FLG epidermal equivalents (Δ FLG-HEE) were generated. To validate the causality of the FLG knockout, FLG expression in Δ FLG cells was restored by correcting the FLG gene using CRISPR-Cas9-induced homology-directed repair.

Results: FLG deficiency was accompanied by (partial) loss of structural and functional proteins, such as involucrin, hornerin, and transglutaminases. Consequently, transepithelial electrical resistance (TEER) indicated a decreased barrier function in Δ FLG-HEEs. Repair of the Δ FLG clonal lines reinstated FLG protein expression and the concomitant expression of the aforementioned epidermal differentiation proteins in FLG-restored HEEs.

Conclusion: The phenotypical consequences of FLG deficiency in cell lines with an identical genetic background indicate a functional role for FLG – not only in epidermal barrier function – but also in epidermal barrier development which provides new insights into the disease pathogenesis of atopic dermatitis and ichthyosis vulgaris.

5 - IMPROVED SÉZARY CELL DETECTION AND NOVEL INSIGHTS INTO IMMUNOPHENOTYPIC AND MOLECULAR HETEROGENEITY IN SÉZARY SYNDROME.

Safa Najidh¹, Cornelis P. Tensen¹, Alita J. van der Sluijs-Gelling², Cristina Teodosio², Davy Cats³, Hailiang Mei³, Thomas B. Kuipers³, Jacoba J. Out-Luijting¹, Willem H. Zoutman¹, Thorbald van Hall⁴, Alberto Orfao⁵, Julia Almeida⁵, Jacques J.M. van Dongen², Maarten H. Vermeer¹

1) Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; 2) Department of Immunology, Leiden University Medical Center, Leiden, The Netherlands; 3) Sequencing Analysis Support Core, Leiden University Medical Center, Leiden, The Netherlands; 4) Department of Medical Oncology, Oncode Institute, Leiden University Medical Center, Leiden, The Netherlands; 5) Translational and Clinical Research Program, Centro de Investigación del Cáncer and IBMCC (CSIC – University of Salamanca); Cytometry Service, NUCLEUS; Department of Medicine, University of Salamanca (USAL) and IBSAL, Salamanca. CIBERONC (CB16/12/00400), Spain.

Background: Sézary syndrome (SS) is an aggressive leukemic form of Cutaneous T-cell Lymphoma with neoplastic CD4+ T cells present in skin, lymph nodes, and blood. The detection of these so-called Sézary cells and the assessment of tumor burden in blood mostly rely on flow cytometry (FC) technique. Nevertheless, FC protocols lack standardization and are hampered by the profound diversity in Sézary cell immunophenotypic characteristics.

Objectives: We aimed to define the immunophenotypic profiles of Sézary cells and perform an in-depth characterization of SS cellular identity, evaluate potential immunophenotypic changes over time, study the transcriptome of phenotypically distinct Sézary cell subsets, and discover novel Sézary-specific markers.

Methods: We applied highly sensitive and standardized EuroFlow-based multiparameter FC (MFC) on 37 SS samples

combined with fluorescence-activated cell sorting (FACS) and RNA sequencing (RNA-seq) on purified immunophenotypically distinct Sézary and matched normal CD4+ T-cell subsets of the same patients and healthy controls.

Results: By applying MFC, we accurately identified, quantified, and characterized Sézary cells in all SS samples. We observed substantial inter- and intra-patient heterogeneity and immunophenotypic changes over time. Our RNA-seq data confirmed pure mono-clonality of isolated immunophenotypically aberrant CD4+ T-cell subsets and revealed the transcriptional profiles of different FACS-sorted CD4+ T-cell populations thereby identifying novel Sézary-specific signature genes that were consistently and exclusively perturbed across Sézary cell subsets.

Conclusion: Together, these findings further unravel the heterogeneity of Sézary cell subpopulations within and between patients. These new data will support improved diagnosis, disease monitoring, therapy, and prognosis.

6 - CELLULAR CROSS-TALK-INDUCED SECRETION OF INTERLEUKIN-10 (IL-10) IN AN ORGANOTYPIC HUMAN MELANOMA-IN-SKIN MODEL SKEWS MONOCYTE DIFFERENTIATION TOWARDS AN M2-LIKE PHENOTYPE.

Elisabetta Michielon¹, Marta López González², Judith L.A. Burm¹, Taco Waaijman¹, Ekaterina S. Jordanova³, Tanja D. de Grijpl², Susan Gibbs^{3,4}

1) Department of Molecular Cell Biology and Immunology, Amsterdam UMC, Vrije Universiteit, Amsterdam, The Netherlands; 2) Department of Medical Oncology, Amsterdam UMC, Vrije Universiteit, Cancer Center Amsterdam, Amsterdam Infection & Immunity Institute, Amsterdam, The Netherlands; 3) Center for Gynecologic Oncology Amsterdam (CGOA), Amsterdam UMC, Vrije Universiteit, Amsterdam, The Netherlands; 4) Department of Oral Cell Biology, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit, Amsterdam, The Netherlands.

Background: The melanoma-induced microenvironment promotes immune-escape and tumor progression, contributing to ineffectiveness of anti-melanoma therapies in a large group of treated patients. While two-dimensional cultures lack tissue context, animal models poorly predict human immune responses. This highlights a pressing need for more physiological human melanoma models.

Objective: To establish an in vitro human melanoma model mimicking tumor progression and immunosuppression.

Methods: Reconstructed human melanoma-in-skin (Mel-RhS) models were constructed by co-seeding melanoma cells (SK-MEL-28) and keratinocytes onto a collagen-based fibroblast-populated dermal equivalent. Immunohistochemistry was used to identify tumor cells. Culture supernatants were used to detect cytokine secretion (ELISA) and assess changes in expression of surface markers during monocyte to monocyte-derived dendritic cell (mo-DC) differentiation (FACS).

Results: Tumor nests developed over time and spread towards the dermis. While SK-MEL-28 monolayers did not produce detectable levels of interleukin-10 (IL-10), the cellular cross-

talk in the three-dimensional (3D) model led to IL-10 expression by the melanoma cells, as well as by the surrounding keratinocytes and fibroblasts. This resulted in increased IL-10 secretion in Mel-RhS compared to healthy controls. Indeed, Mel-RhS-derived culture supernatants interfered with monocyte to mo-DC differentiation, leading to the development of M2-like macrophages, which was partly prevented upon antibody-mediated IL-10 blockade.

Conclusion: Features of the Mel-RhS resemble the initial stages of melanoma invasion. The 3D configuration of the Mel-RhS model revealed a role for IL-10 in immune escape through misdirected myeloid differentiation, demonstrating the potential of the Mel-RhS in research on melanoma development and invasion in the setting of an immune competent model.

7 - MULTI-OMICS ANALYSIS OF MUTANT NRAS-INDUCED SENEESCENCE IN HUMAN MELANOCYTES.

I.Z.M. Kreuger¹, R.C. Slieker², G.M.C. Janssen³, E. Sánchez López³, P.A. van Veelen³, M.A. Giera³, T.J.B. van Groningen^{*}, R. van Doorn^{*}

1) Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; 2) Department of Cell and Chemical Biology, Leiden University Medical Center, Leiden, The Netherlands; 3) Center of Proteomics and Metabolomics, Leiden University Medical Center, Leiden, The Netherlands. *These authors contributed equally.

Background: Melanocytic nevi consist of melanocytes that have entered a state of growth arrest known as oncogene-induced senescence (OIS). Accumulation of mutations can lead to OIS bypass and development of melanoma. Therapeutic targeting of nevus precursor lesions constitutes a potential strategy to prevent melanoma, in particular in patients with congenital nevus or hereditary melanoma susceptibility.

Objective: In this study, we want to characterize in depth an NRASQ61R OIS state in melanocytes. Understanding the differences between normal and OIS melanocytes may lead to the identification of therapeutic vulnerabilities, which can be targeted to specifically eliminate nevus cells.

Methods: We generated human melanocytes with inducible overexpression of NRASWT as control and NRASQ61R as a model for OIS. Senescence was verified by SA- β GAL assays, western blot, qPCR and proliferation analysis. Inducible NRASQ61R melanocytes were subjected to a multi-omics pipeline, including RNA-seq, metabolomics, lipidomics and immune precipitation of p16 followed by mass-spectrometry.

Results: Inducible overexpression of NRASQ61R, but not NRASWT, induced an OIS phenotype in human melanocytes. Transition of normal melanocytes towards an OIS phenotype has been recorded with RNA-seq, lipidomics and metabolomics. In addition, p16 pull-down data uncovers interactors in normal and OIS melanocytes.

Conclusion: Mutant NRAS-induced senescence is associated with profound changes in the transcriptome and metabolome. Additionally, further exploration of the p16 interactome may reveal novel functions of p16 in OIS melanocytes. Overall,

multi-omics analysis will advance our understanding of the OIS melanocytic state, which may lead to the identification of novel therapeutic vulnerabilities.

8 - GENETIC ASSOCIATION BETWEEN VITILIGO GENETIC SUSCEPTIBILITY AND RESPONSE TO IMMUNE-CHECKPOINT INHIBITOR THERAPY IN ADVANCED MELANOMA PATIENTS: EARLY RESULTS FROM THE IO-GEM CONSORTIUM

W. Ouwerkerk^{1,2}, S. Chielie¹, M.W. Bekkenk¹, R. van Doorn³, D. Schadendorf⁴, C.U. Blank⁵, J.B.A.G. Haanen⁵, G.A.P. Hospers⁶, K.F. Bol^{7,8}, T. Kirchhoff⁹, R.M. Luiten¹

1) Department of Dermatology and Netherlands Institute for Pigment Disorders, Amsterdam University Medical Centers, University of Amsterdam, Cancer Center Amsterdam, Amsterdam Infection & Immunity Institute, Amsterdam, The Netherlands; 2) National Heart Centre Singapore, Singapore; 3) Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; 4) Skin Cancer Unit, German Cancer Research Center, Heidelberg, Germany; 5) Department of Medical Oncology, Netherlands Cancer Institute-Antoni van Leeuwenhoek, Amsterdam, The Netherlands; 6) Department of Medical Oncology, University of Groningen, University Medical Center Groningen, The Netherlands; 7) Department of Tumor Immunology, Radboud Institute for Molecular Life Sciences, Nijmegen, The Netherlands; 8) Department of Medical Oncology, Radboud University Medical Center, Nijmegen, The Netherlands; 9) Perlmutter Cancer Center, New York University School of Medicine, New York, NY, USA.

Background: Only ~ 50% of melanoma patients shows objective response to immune checkpoint inhibitor (ICI) therapy. Currently, there are no reliable predictive biomarkers explaining ICI response heterogeneity. Patients who develop vitiligo upon ICI show better prognosis. The genetic basis of vitiligo is found using multiple large GWAS studies. These vitiligo genes are also associated with other autoimmune diseases and melanoma.

Objective: To test if the germline genetic risk to vitiligo predicts ICI response in patients with advanced melanoma.

Methods: From the ongoing effort of the IO-GEM international consortium that is set to pool a large resource of ICI treated advanced stage melanoma patients, we have identified a subset of patients from four IO-GEM centers, to be analyzed in this study. DNA was extracted from blood or saliva and genotyped. We developed a polygenetic vitiligo-risk score from a pre-defined set of vitiligo-associated single nucleotide polymorphisms (SNPs) and associated this score with overall survival. We also determined the combination of vitiligo risk SNPs most significantly associated with mortality.

Results: Results will be discussed.

Conclusion: These first results suggest that the genetic susceptibility to vitiligo may be associated with more favorable survival outcome in melanoma patients treated with ICI. Additional analyses in the expanded data from IO-GEM is warranted to validate these associations.

9 - LIMITED IMPACT OF DIAGNOSTIC DELAY DUE TO COVID-19 ON MELANOMA AND SQUAMOUS CELL CARCINOMA TUMOR CHARACTERISTICS IN THE NETHERLANDS: A NATIONWIDE PATHOLOGY REGISTRY ANALYSIS.

T.E. Sangers¹, M. Wakkee¹, E.C. Kramer-Noels², T. Nijsten¹, M.W.J. Louwman³, E.H. Jaspars⁴, L. Hollestein¹

1) Department of Dermatology, Erasmus MC Cancer Institute, University Medical Center Rotterdam, The Netherlands; 2) Dutch Society of Dermatology and Venereology, Utrecht, The Netherlands; 3) Netherlands Comprehensive Cancer Organization, Utrecht, The Netherlands; 4) Department of Pathology, Amsterdam UMC, Amsterdam, The Netherlands.

Background: The COVID-19 pandemic has resulted in a delay of skin cancer diagnoses, potentially causing a progression to unfavorable tumor stages. Population-based studies demonstrating an effect on tumor characteristics are lacking.

Objective: To identify the impact of delayed diagnostics on melanoma and cutaneous squamous cell carcinoma (cSCC) tumor characteristics in the Netherlands.

Methods: Histopathology reports of primary invasive cutaneous melanoma and cSCCs between 01-01-2018 and 22-7-2021 were obtained from the nationwide histopathology registry in the Netherlands. Cases were stratified in five time periods: (i) pre-COVID, (ii) first lockdown, (iii) between first and second lockdown, (iv) second lockdown, and (v) after second lockdown. Breslow thickness was compared using an independent t-test. Tumor stage groups were compared using a χ^2 -test. Outcomes were corrected for multiple testing using the false discovery rate.

Results: Melanoma The mean primary melanoma Breslow thickness of pre-pandemic era (i) and the following time periods (ii-v) showed no significant difference. A small shift was found towards unfavorable T-stages during the first lockdown compared to the pre-COVID period: T1 55.9% vs. 61.9%; T2 20.2% vs. 18.8%; T3 14.1% vs. 11.6%; T4 9.7% vs. 7.7% (p=0.001). No relevant changes were seen in subsequent periods. cSCC No significant change in tumor stage distribution was observed between the pre-COVID (i) and COVID-affected periods (ii-v) for primary cSCCs.

Conclusion: Besides a small and short effect on tumor stage distribution for melanoma, COVID-19 had no major or ongoing impact on the stage distribution of melanoma or cSCC.

10 - OPTICAL COHERENCE TOMOGRAPHY VERSUS PUNCH BIOPSY FOR DIAGNOSIS OF BASAL CELL CARCINOMA: A RANDOMIZED DIAGNOSTIC TRIAL.

Fieke Adan¹, Patty J. Nelemans², Tjinta Brinkhuizen^{1,3}, Sharon R.P. Dodemont³, Janneke P.H.M. Kessels⁴, Patricia J.F. Quaedvlieg⁴, Gert-Jan Dermont¹, Veronique J.L. Winnepenninckx⁵, Myrurgia Abdul Hamid⁵, Brigitte A.B. Essers⁶, Nicole W.J. Kelleners-Smeets¹, Klara Mosterd¹

1) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; GROW Research Institute for Oncology and Developmental Biology, Maastricht University, Maastricht, The Netherlands; 2) Department

of Epidemiology, Maastricht University, Maastricht, The Netherlands; 3) Department of Dermatology, Catharina Hospital, Eindhoven, The Netherlands; 4) Department of Dermatology, Zuyderland Medical Center, Heerlen, The Netherlands; 5) Department of Pathology, Maastricht University Medical Center+, Maastricht, The Netherlands; 6) Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht, The Netherlands.

Background: Basal cell carcinoma (BCC) is the most common form of cancer in Caucasians. Currently, the gold standard for diagnosis and subtyping of BCC is a punch biopsy. Recently, imaging methods such as optical coherence tomography (OCT), have become available for non-invasive diagnosis of skin lesions. Use of OCT to diagnose BCC may obviate the need for biopsy, resulting in more efficient, patient friendly and potentially cost-saving patient care.

Objective: The objective of this study is to evaluate whether use of OCT results in an effective, more efficient and patient friendly approach in patients with clinical suspicion of BCC without compromising efficacy of treatment.

Methods: We conducted a multi-centre randomized non-inferiority trial in three Dutch hospitals. Patients with an indication for biopsy of a lesion with BCC in the differential diagnosis were randomized to OCT-guided diagnosis and treatment or to regular care, in which diagnosis and treatment is always based on a biopsy.

The main endpoint was the proportion of patients with a recurrent or residual (pre-)malignant lesion 12 months after treatment. Secondary outcomes were the proportion of patients in whom biopsy could be avoided, the frequency of misclassifications and diagnostic accuracy of high confidence OCT diagnosis.

Results and Conclusion: will be discussed.

11 - THE IMPACT OF AN ARTIFICIAL INTELLIGENCE (AI) BASED MOBILE HEALTH APPLICATION ON DERMATOLOGICAL CARE CONSUMPTION IN THE NETHERLANDS: A RETROSPECTIVE COHORT STUDY.

A.M. Smak Gregoor, T.E. Sangers, T.E.C. Nijsten, L.M. Hollestein, M. Wakkee

Department of Dermatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands.

Background: AI-based algorithms that can recognize skin cancer have been implemented in mobile phone applications. The actual impact of such apps on dermatological care has not been investigated.

Objective: To describe the impact of an AI-based mHealth application on dermatological healthcare consumption.

Methods: In 2019, all adults insured at a large Dutch health insurer were invited to use an AI-based mHealth app to recognize skin cancer. We conducted a retrospective analysis on claims of the mHealth users. Dermatological claims were categorized into benign skin lesions, pre-malignancies, malignancies and claims unrelated to suspicious skin lesions. The difference in proportions of different types of claims before

(2018) and after the introduction (2019) of the mHealth app was compared using z-tests.

Results: A total of 22,808 adults used the mHealth app. 74,452 assessments were made, of which the algorithm rated 20.6% as high-risk. Results on the difference in dermatological claims will be discussed.

Conclusion: This study provides a first glance on the impact of population wide implementation of an mHealth application on dermatological care consumption for (pre-)malignant and benign skin lesions.

12 - INTEGRIN α V β 6 AS A TARGET FOR TUMOR-SPECIFIC IMAGING OF VULVAR SQUAMOUS CELL CARCINOMA AND ADJACENT PREMALIGNANT LESIONS.

Bertine W. Huisman^{1,2}, Merve Cankat¹, Tjalling Bosse³, Alexander L. Vahrmeijer⁴, Robert Rissmann^{1,5}, Jacobus Burggraaf^{1,4,5}, Cornelis F.M. Sier^{4,6*}, Mariette I.E. van Poelgeest^{1,2*}

1) Center for Human Drug Research, Leiden, The Netherlands; 2) Department of Gynecology, Leiden University Medical Center, Leiden, The Netherlands; 3) Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands; 4) Department of Surgery, Leiden University Medical Center, Leiden, The Netherlands; 5) Leiden Academic Center for Drug Research, Leiden University, Leiden, The Netherlands; 6) Percuro BV, Leiden, The Netherlands. *Shared last authors.

Background: Surgical treatment of vulvar squamous cell carcinoma (VSCC) is associated with significant morbidity and high recurrence rates. This is at least partially related to the limited ability to distinguish (pre)malignant from normal vulvar tissue. Illumination of neoplastic tissue based on fluorescent tracers, known as fluorescence-guided surgery (FGS), could help resect involved tissue and decrease ancillary mutilation.

Objective: To evaluate potential targets for FGS in VSCC.

Methods: Immunohistochemistry was performed on pre-malignant (high grade squamous intraepithelial lesion and differentiated vulvar intraepithelial neoplasia) and (human papillomavirus (HPV) -dependent and -independent) VSCC tissue sections with healthy vulvar skin as controls. Sections were stained for integrin α v β 6, CAIX, CD44v6, EGFR, EpCAM, FR α , MRP1, MUC1 and uPAR. Marker expression was quantified using digital image analysis. H-scores were calculated, and percentages positive cells, expression pattern, and biomarker localization were assessed. In addition, tumor-to-background ratios (TBR) were established.

Results: Upregulated homogeneous α v β 6 expression was observed in VSCCs compared to surrounding stromal tissue and normal squamous epithelium. α v β 6 showed promising TBRs in 78% of HPV-independent and 30% of HPV-dependent VSCC patients. Other markers were assessed not potential, based on: EpCAM, MRP1 and FR α showed no or low expression in vulvar malignant tissues; CD44v6 and EGFR showed an overall high expression in all tissues, including normal squamous epithelium; MUC1 and uPAR showed a heterogenous or patchy expression pattern in vulvar malignant tissue.

Conclusion: Integrin $\alpha\beta6$ allowed for most robust discrimination of VSCCs and adjacent premalignant lesions compared to surrounding healthy tissue in immunohistochemically stained tissue sections. The use of an $\alpha\beta6$ targeted probe for FGS of vulvar (pre)malignancies should be evaluated in future studies.

13 - A MULTI-ORGAN-ON-CHIP APPROACH TO INVESTIGATE HOW ORAL EXPOSURE TO METALS CAN CAUSE SYSTEMIC TOXICITY LEADING TO LANGERHANS CELL ACTIVATION IN SKIN.

Jasper J. Koning¹, Charlotte T. Rodrigues Neves^{1*}, Katharina Schimek³, Maria Thon¹, Sander W. Spiekstra¹, Taco Waaijman¹, T. de Gruijl⁴, Susan Gibbs^{1,2}

1) Department of Molecular Cell Biology and Immunology, Amsterdam University Medical Center, Amsterdam Infection and Immunity Institute, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; 2) Department of Oral Cell Biology, Academic Centre for Dentistry (ACTA), University of Amsterdam and Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; 3) TissUse GmbH, Berlin, Germany; 4) Department of Oncology, Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands. *These authors contributed equally.

Background: Topical exposure of oral mucosa to metals which are known to activate the immune system may result in skin inflammation in susceptible individuals. Investigating systemic immuno-toxicity in vitro is still a huge challenge.

Objective: The aim of this study is to showcase a new method for investigating systemic immuno-toxicity in a multi-organ on chip setting.

Methods: Reconstructed human gingiva (RHG) and reconstructed human skin containing MUTZ-3 derived Langerhans Cells in the epidermis (RHS-LC) were incorporated into a HUMIMIC Chip3plus, connected by dynamic flow and cultured for a total period of 72 hours. Three independent experiments were performed each with an intra-experiment replicate in order to assess donor and technical variation. After an initial culture period of 24 hours, nickel sulphate was applied topically to RHG for 24 hours and LC activation (maturation and migration) was determined in RHS-LC after an additional 24 hour incubation time.

Results: Stable dynamic culture of RHG and RHS-LC was achieved as indicated by assessment of glucose uptake, lactate production and lactate dehydrogenase release into the microfluidics compartment. Nickel exposure resulted in no major histological changes within RHG or RHS-LC, or cytokine release into the microfluidics compartment, but did result in increased activation of LC as observed by increased mRNA levels of CD1a, CD207, HLA-DR and CD86 in the dermal compartment.

Conclusion: This first study to describe systemic toxicity and immune cell activation in a multi-organ setting can provide a framework for applying to other organoids in the future.

14 - ASSESSMENT OF SOCS1 DELETION IN CD4+ T CELLS OF CHRONICALLY INFLAMED MOUSE SKIN TO DEVELOP A PATHOGENIC MODEL OF MF.

Y. Luo, M.H. Vermeer, T. van. Hall, F.R. de. Gruijl, E. Vreugdenhil, C.P. Tensen

Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands. (Correspondence should be addressed to C.P. Tensen: C.P.Tensen@lumc.nl)

Background and Objective: Mycosis fungoides (MF) is the most common type of Cutaneous T cell Lymphoma, a highly heterogeneous group of extranodal non-Hodgkin Lymphomas that first present in the skin. The oncogenic Janus kinase (JAK)-signal transducer and activator of transcription (STAT) signaling is of great importance to MF pathogenesis. SOCS1, an endogenous inhibitor of the JAK/STAT signaling pathway, was identified recurrently deleted in MF. This study aimed at validating and characterizing the functions of the Socs1 deletion in the early stage of MF pathogenesis in vivo.

Methods: Oxazolone was used to introduce chronic skin inflammation, and 4-hydroxy tamoxifen (4HT) was applied to the inflamed skin of transgenic mice to knockout Socs1 locally in Cd4 T cells. Flow cytometry on blood samples quantified cells carrying murine Cd3, Cd19, Cd4, Cd8 or human CD4. Hematoxyline & Eosin and immunohistochemical (IHC) stainings were performed on skin samples; IHC staining for same markers as before complemented with F4-80 and p-Stat3.

Results: Stat3 was successfully activated in 4HT-activated transgenic skin. Also, the thickness of the epidermis in 4HT-activated transgenic skin was increased in comparison to controls, and 4HT-activated transgenic skin with double Socs1 knockout Cd4 T cells has the thickest epidermis. Macrophages were more abundant in 4HT-activated transgenic skin with double Socs1 knockout Cd4 T cells than in all other skin.

Conclusion: We demonstrate that Socs-1 knockout in Cd4 T cells of transgenic mice can activate Stat3 and thus clearly increase skin inflammation, which could lead up to a proper pathogenic model of MF.

15 - UNTANGLING THE COMPLEX CYTOKINE MILIEU IN PSORIASIS AND ATOPIC DERMATITIS THROUGH IN VITRO EPIDERMAL MODELS.

L.D. Meesters^{1,2}, H. Niehues¹, D. Rodijk-Olthuis¹, I.M.J.J. van Vlijmen-Willems¹, H. Zhou^{2,3}, E.H.J. van den Bogaard¹

1) Department of Dermatology, Radboud university medical center (Radboudumc), Radboud Institute for Molecular Life Sciences (RIMLS), Nijmegen, The Netherlands; 2) Department of Molecular Developmental Biology, Faculty of Science, RIMLS, Radboud University, Nijmegen, The Netherlands; 3) Department of Human Genetics, RIMLS, Radboudumc, Nijmegen, The Netherlands.

Background: In psoriasis (PSO) and atopic dermatitis (AD), the complex inflammatory milieu drives epidermal disease hallmarks that are associated to skin inflammation. The current lack in understanding on how this, often patient-specific,

inflammatory signature translates to disease endotypes hampers the development of translational models and the personalized use of targeted drugs.

Objective: We aimed to identify optimal cytokine combinations to mimic disease phenotypes in human epidermal equivalents (HEEs) and to unravel which disease hallmarks are attributed to specific disease-associated cytokine(s).

Methods: HEEs generated from primary human keratinocytes or N/TERT-2G immortalized keratinocytes were stimulated with single Th17 and Th2 cytokines, and combinations thereof. Morphological features, gene/protein expression, and trans-epidermal resistance (TEER, barrier function) were analyzed.

Results: Specific (combinations of) cytokines induced typical epidermal disease hallmarks. For PSO: loss of the granular layer and hyperplasia upon IL-22 stimulation, hyperproliferation by IL-17, and parakeratosis and PSO marker induction (e.g. beta defensin) upon combined IL-17/IL-22 treatment. AD features were more pronounced after combination of Th2 (IL-4/IL-13) with Th17 (IL-17/IL-22) cytokines, including spongiosis, AD marker gene expression, loss of epidermal differentiation and reduced TEER values. Similar effects were seen in N/TERT-2G keratinocytes showing the potential of immortalized cell lines as alternative and sustainable cell source for developing inflammatory skin models.

Conclusion: Refinement of in vitro epidermal models to better mimic psoriasis and atopic dermatitis phenotypes enables the deconstruction of the cytokine cocktail that drives epidermal inflammation. Subsequent characterization of disease endotypes herein is important for future targeting of the inflammatory signature in a personalized approach.

16 - EASI P-EASI: PREDICTING DISEASE SEVERITY IN ATOPIC DERMATITIS PATIENTS TREATED WITH TRALOKINUMAB.

J. Olydam¹, L. de Wijs¹, W. Dik², M. Røpke³, J. Correa Da Rosa⁴, A. Herath¹, D. Hijnen¹

1) Department of Dermatology, Erasmus University Medical Center, Rotterdam, The Netherlands; 2) Department of Immunology, Laboratory Medical Immunology, Erasmus Medical Center, Rotterdam, The Netherlands; 3) LEO Pharma A/S, Ballerup, Denmark; 4) Department of Dermatology, The Rockefeller University Hospital, The Rockefeller University, New York, NY, USA.

Background: Numerous targeted treatments for atopic dermatitis are currently under investigation. Comparability of effectiveness of new drugs is therefore becoming more important. Serum biomarkers may offer an objective outcome-measure for disease severity in AD. A combination of serum biomarkers TARC, IL-22, and sIL-2R as a signature (predicted-EASI) may offer an objective measurement tool for disease severity in AD patients treated with topical steroids, Cyclosporin A, or dupilumab.

Objective: To validate p-EASI in AD patients treated with tralokinumab in a clinical trial setting.

Methods: Serum samples were collected from 198 patients with moderate-to-severe AD in the ECZTRA 1 (NCT03131648)

trial. Patients were randomized (3:1) to tralokinumab 300mg (n=149), or placebo (n=49) Q2W for 16 weeks. Disease severity was assessed by EASI and serum was collected at baseline and after 16 weeks of treatment. Serum biomarkers TARC, IL-22, and sIL-2R were measured by Luminex.

Results: EASI and predicted-EASI scores highly correlated in tralokinumab treated patients ($r=.59$, $P<.0001$). In patients treated with tralokinumab, median EASI and p-EASI decreased from 30.9 (IQR,22.5-42.3) and 32.9 (IQR,25.6-40.2), respectively, to 13.5 (IQR,6.6-22.5) and 24.8 (IQR,20.6-59.0) after 16 weeks of treatment. In the placebo group, median EASI and p-EASI were 31.1 (IQR,22.5-40.4) and 31.3 (IQR,25.0-37.5), respectively, at baseline; 19.0 (IQR,10.2-29.1) and 29.2 (IQR,25.5-32.5) after 16 weeks.

Conclusion: The biomarker signature p-EASI correlated with disease severity in AD patients treated with tralokinumab. The use of objective biomarkers such as p-EASI may be considered as a tool to objectively assess treatment effect of new drugs for AD.

17 - GUSELKUMAB DRUG SURVIVAL IS HIGH IN PATIENTS WITH PSORIASIS TREATED IN REAL-WORLD PRACTICE.

M.E. van Muijen^{1,2}, S.E. Thomas^{1,2}, D. Vellinga³, K. Bouwman⁴, M.B.A. van Doorn⁵, K. Politiek⁶, M.E. Otero^{1,2}, M.D. Njoo⁷, E.N. Kop⁸, P.M. Ossenkoppele⁷, J.E.M. Körver⁹, S. Dodemont¹⁰, C.J. de Jonge¹¹, R.A. Tupker¹², M.A.M. Berends¹³, P.P.M. van Lümig¹⁴, J.M.M. Groenewoud^{2,15}, J.M.P.A. van den Reek^{1,2}, E.M.G.J. de Jong^{1,2,16}

1) Department of Dermatology, Radboud University Medical Center (Radboudumc), Nijmegen, The Netherlands; 2) Radboud Institute for Health Sciences (RIHS), Radboudumc, Nijmegen, The Netherlands; 3) Department of Dermatology, Alrijne Ziekenhuis, Leiderdorp, The Netherlands; 4) Department of Dermatology, University Medical Center Groningen, Groningen, The Netherlands; 5) Department of Dermatology, Erasmus University Medical Center, Rotterdam, The Netherlands; 6) Department of Dermatology, Medisch Centrum Leeuwarden, Leeuwarden, The Netherlands; 7) Department of Dermatology, Ziekenhuisgroep Twente, Almelo/Hengelo, The Netherlands; 8) Department of Dermatology, Bernhoven Ziekenhuis, Uden, The Netherlands; 9) Department of Dermatology, Amphia Ziekenhuis, Breda, The Netherlands; 10) Department of Dermatology, Catharina Ziekenhuis, Eindhoven, The Netherlands; 11) Department of Dermatology, Utrecht Medisch Centrum, Utrecht, The Netherlands; 12) Department of Dermatology, St. Antonius Ziekenhuis, Nieuwegein, The Netherlands; 13) Department of Dermatology, Slingeland Ziekenhuis, Doetinchem, The Netherlands; 14) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; 15) Department of Health Evidence, Radboudumc, Nijmegen, The Netherlands; 16) Radboud University, Nijmegen, The Netherlands.

Background: Guselkumab was registered as the first IL-23 p19 subunit inhibitor for the treatment of psoriasis. In randomized controlled trials, a favorable efficacy and safety profile has been demonstrated. Drug survival, defined as the time a

patient remains on a specific therapy, can be used as a measure for treatment success in daily practice.

Objective: The primary objective of this observational multi-center study was to evaluate the one- and two-year drug survival of guselkumab in psoriasis patients, split for discontinuation due to ineffectiveness and/or side effects. Furthermore, we aimed to elucidate variables associated with drug survival.

Methods: Drug survival was analyzed using Kaplan-Meier survival curves, split for reasons of guselkumab discontinuation. To assess factors associated with drug survival, univariate Cox regression analyses were performed. Baseline variables with p-values ≤ 0.2 in univariable analysis were entered in a multivariable Cox regression model to identify factors affecting drug survival.

Results: We included 195 patients (29.7% biologic-naïve). Overall 1- and 2-year drug survival rates were 85.5% and 77.8% respectively. Similar 1- and 2-year survival rates were found when discontinuation due to ineffectiveness (92.8% and 88.7%) or side effects (94.3% and 92.1%) were assessed separately. In multivariable Cox regression analyses, diabetes mellitus type 2 and psoriatic arthritis were associated with shorter drug survival due to ineffectiveness or side effects, respectively.

Conclusion: Guselkumab showed high 1- and 2-year drug survival rates in daily practice. Having diabetes mellitus type 2 and psoriatic arthritis were associated with a shorter drug survival.

18 - OCULAR SURFACE DISEASE IS A COMMON FINDING IN MODERATE-TO-SEVERE ATOPIC DERMATITIS PATIENTS.

R.E. Achten¹, C.M. van Luijk², D.S. Bakker¹, N.P.A. Zuithoff¹, M. de Graaf¹, F. van Wijk³, M.M. van der Wal³, J.L. Thijs¹, J.H. de Boer², M.S. de Bruin-Weller¹

1) Department of Dermatology and Allergology, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht, Utrecht, The Netherlands; 2) Department of Ophthalmology, University Medical Center Utrecht, Utrecht, The Netherlands; 3) Center for Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands.

Background: Due to increased rates of ocular surface disease (OSD) reported during dupilumab treatment, more insight into the occurrence of OSD in moderate-to-severe atopic dermatitis (AD) patients is needed.

Objective: To investigate OSD in moderate-to-severe AD patients.

Methods: This prospective study included moderate-to-severe AD patients treated with topical corticosteroids who were examined both dermatologically and ophthalmologically. AD severity was assessed by the Eczema Area and Severity Index (EASI). Clinical ophthalmological characteristics and symptoms of OSD were reported. Conjunctival impression cytology was conducted to measure goblet cell density (GCD), and additionally analysed by flow cytometry.

Results: A total of 70 patients (median EASI 15.0 (IQR) 10.8-20.9) were included. Mild, moderate, and severe OSD were reported in 32/70 (45.7%), 24/70 (34.3%), and 7/70 (10.0%)

patients, respectively. In only 7/70 (10.0%) patients, no OSD was found. Significant differences between patients with no or mild OSD and patients with moderate-to-severe OSD were observed in EASI (11.8 (IQR 9.0-16.7) vs. 17.7 (IQR 13.7-24.9), $p < 0.001$, respectively). Remarkably, only 23/31 patients (74.2%) with moderate-to-severe OSD experienced symptoms of OSD. Median conjunctival GCD was higher in patients without OSD, compared to patients with OSD.

Conclusion: OSD is frequently observed in patients with moderate-to-severe AD (90%), and is associated with lower conjunctival GCD compared to AD patients without OSD. Moderate-to-severe OSD was seen in 44.3% patients and was associated with more severe AD. Clinicians should be aware of the common occurrence of OSD in moderate-to-severe AD patients, and low-threshold referral to an ophthalmologist is recommended.

19 - 'HAPPY DRUG SURVIVAL 2.0': DRUG SURVIVAL COMBINED WITH PATIENT REPORTED OUTCOMES IN PSORIASIS PATIENTS ON BIOLOGICS: RESULTS OF THE BIOCAPTURE REGISTRY.

L.J. van Vugt^{1,2*}, S.E. Thomas^{1,2*}, J.M.M. Groenewoud^{2,3}, M.E. Otero^{1,2}, M.D. Njoo⁴, P.M. Ossenkuppele⁴, E.N. Kop⁵, A.L.A. Kuijpers⁶, S. Dodemont⁷, J.E.M. Körver⁸, J.M. Mommers⁹, R.J. Lindhout¹⁰, M.A.M. Berends¹¹, M.I.A. Koetsier¹², R.A. Tupker¹³, B. Peters¹⁴, W.P. Arnold¹⁵, C.J. de Jonge¹⁶, M.M. Kleinpenning¹⁷, P.P. van Lümig¹⁸, M.M.B. Seyger^{1,2}, J.M.P.A. van den Reek^{1,2}, E.M.G.J. de Jong^{1,2,19}

1) Department of Dermatology, Radboud University Medical Center (Radboudumc), Nijmegen, The Netherlands; 2) Radboud Institute for Health Sciences (RIHS), Radboudumc, Nijmegen, The Netherlands; 3) Department for Health Evidence, Radboudumc, Nijmegen, The Netherlands; 4) Department of Dermatology, Ziekenhuisgroep Twente, Almelo/Hengelo, The Netherlands; 5) Department of Dermatology, Bernhoven Ziekenhuis, Uden, The Netherlands; 6) Department of Dermatology, Máxima Medisch Centrum, Eindhoven, The Netherlands; 7) Department of Dermatology, Catharina Ziekenhuis, Eindhoven, The Netherlands; 8) Department of Dermatology, Amphia Ziekenhuis, Breda, The Netherlands; 9) Department of Dermatology, St Anna Ziekenhuis, Geldrop, The Netherlands; 10) Department of Dermatology, Jeroen Bosch Ziekenhuis, 's Hertogenbosch, The Netherlands; 11) Department of Dermatology, Slingeland Ziekenhuis, Doetinchem, The Netherlands; 12) Department of Dermatology, Gelre Ziekenhuizen, Apeldoorn, The Netherlands; 13) Department of Dermatology, St Antonius Ziekenhuis, Nieuwegein, The Netherlands; 14) Department of Dermatology, Ziekenhuis Rijnstate, Arnhem, The Netherlands; 15) Department of Dermatology, Ziekenhuis Gelderse Vallei, Ede, The Netherlands; 16) Department of Dermatology, Utrecht Medisch Centrum, Utrecht, The Netherlands; 17) Department of Dermatology, Canisius-Wilhelmina Ziekenhuis, Nijmegen, The Netherlands; 18) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; 19) Radboud University, Nijmegen, The Netherlands.

Background: Drug survival studies on biologics are important for making well-considered treatment decisions for psoriasis. Patient Reported Outcome Measures (PROMs) can supplement our view on drug survival.

Objectives: (i) To describe and compare the first-year drug survival of all biologics currently used in a daily practice psoriasis cohort. (ii) To evaluate first-year quality of life (measured by DLQI) and treatment satisfaction (measured by TSQM) in psoriasis patients 'on drug'.

Methods: A prospective cohort study was carried out, using BioCAPTURE-registry data collected between 2010-2020. Drug survival analyses and a Cox Proportional Hazards Model with confounder-correction were performed to obtain pairwise comparisons between biologics. DLQI- and TSQM-questionnaires were analysed using a per protocol approach.

Results: We included 1120 treatments from 738 patients on etanercept, adalimumab, ustekinumab, infliximab, secukinumab, ixekizumab, guselkumab, brodalumab, risankizumab, and certolizumab. High first-year, and long-term drug survival, when only taking discontinuation due to ineffectiveness into account, was reported for guselkumab, infliximab, ixekizumab, secukinumab, and ustekinumab compared to adalimumab, and for guselkumab, ixekizumab, and ustekinumab compared to etanercept. At month 12, 54.1% of on drug patients reached a DLQI-score of 0-1, 78.9% a DLQI-score ≤ 5 , and 84.7% a TSQM-score ≥ 65 (high satisfaction with the treatment), compared to 12.4%, 37.3% and 52.1% at start.

Conclusion: In this cohort, including IL17- and IL23-inhibitors, guselkumab, ixekizumab, and ustekinumab had high confounder-corrected first-year and long-term drug survival, combined with low DLQI scores and high treatment satisfaction. Special personalised attention is needed for those patients that did not reach good QoL nor satisfaction with treatment.

20 - SUCCESSFUL TAPERING OF DUPILUMAB IN PATIENTS WITH WELL-CONTROLLED AD.

L. Spekhorst¹, C. Boesjes¹, M. Poelhekkens², G. Romeijn², M. Schuttelaar², M. de Graaf¹, M. de Bruin-Weller¹

1) National Expertise Center of Atopic Dermatitis, Department of Dermatology and Allergology, University Medical Center Utrecht, The Netherlands; 2) Department of Dermatology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.

Background: Dupilumab has been introduced and proven to be effective in the treatment of moderate-to-severe atopic dermatitis (AD). Daily practice data about continuation, dose modification or discontinuation of dupilumab (treat-to-target) is lacking.

Objective: To obtain daily practice data of tapering dupilumab in AD patients with well-controlled disease.

Methods: Adult AD patients treated with dupilumab between October 2017 and May 2020 were included in this prospective observational cohort study of the BioDay Registry. In case of well-controlled disease (Eczema Area and Severity Index (EASI) score < 7) after 12 months of dupilumab treatment with 300mg/2 weeks the dupilumab dosage was tapered by

extending the interval with one week to 300mg/3 weeks. Subsequently, in case of persistent well-controlled disease, the interval was gradually extended by two weeks, resulting in 300 mg every four, six or eight weeks. Physician measured eczema scores, patients reported outcomes (PROMs), biomarkers and dupilumab serum levels were analyzed.

Results: 227 Patients were included of which 149 patients (65.6%) were eligible for tapering of dupilumab. The tapering protocol was implemented in 48.9% of the patients at one year and three months visit. The majority of patients remained well-controlled (EASI < 7) and mean EASI score did not significantly change during tapering of dupilumab. Results of PROMs, Physician measured eczema scores, biomarkers and dupilumab serum levels between October 2017 and October 2021 will be presented.

Conclusion: Tapering of dupilumab by extending dosing interval was successful in majority of AD patients in a daily practice setting. Disease severity scores remained stable while tapering dupilumab.

21 - EXPANDING THE SPECTRUM OF MUTATIONS FOR PNPLA1 AND NIPAL4 IN ICHTHYOSIS AND EVALUATION OF NOVEL THERAPEUTIC INTERVENTIONS.

S.V.J. Rossel^{1,2}, J.M.K. Clabbers^{1,2}, M. Haulez^{1,2}, P.C. van den Akker³, P.I. Spuls⁴, M.A. Middelkamp Hup⁴, M.C. van Maarle⁵, M. Vreeburg⁶, P.M. Steijlen^{1,2}, M. van Geel^{1,2,6}, A. Gostynski^{1,2}

1) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; 2) GROW school for Oncology and Developmental Biology, Maastricht University, Maastricht, The Netherlands; 3) University of Groningen, University Medical Center Groningen, Department of Clinical Genetics, Groningen, The Netherlands; 4) Department of Dermatology, Amsterdam Public Health/Infection and Immunology, University of Amsterdam, Amsterdam University Medical Center, Amsterdam, The Netherlands; 5) Department of Clinical Genetics, Amsterdam University Medical Center, Amsterdam, The Netherlands; 6) Department of Clinical Genetics Maastricht University Medical Center+, Maastricht, The Netherlands.

Background: Autosomal recessive congenital ichthyosis (ARCI) is a group of rare, genetically heterogeneous disorders of keratinization resulting in generalized scaling and erythroderma. So far mutations in ten different genes are responsible for ARCI, including PNPLA1 and NIPAL4. No genotype-phenotype correlation has yet been established.

Objective: To retrospectively investigate the clinical characteristics associated with PNPLA1 and NIPAL4 mutations in Dutch families and to assess the therapeutic effect of novel interventions.

Methods: We performed genodermatosis-specific deep-phenotyping in patients with PNPLA1 and NIPAL4 mutations and ichthyosis area severity index (IASI), investigator global assessment (IGA) and Numeric Rating Scale (NRS) itch (past 24h) were assessed. The therapeutic effect of off-label dupilumab (anti-IL-4/IL-13) in two patients with a PNPLA1 mutation and secukinumab (anti-IL-17A) in two patients with a NIPAL4

mutation was evaluated.

Results: We report six patients from four families with three different recessive PNPLA1 mutations, one with an additional pathogenic variant in FLG. Five unrelated patients displayed three different recessive NIPAL4 mutations (one novel). Both cohorts showed diverse clinical presentations. Results will be discussed during the meeting.

Conclusion: This study adds to the clinical spectrum of ARCI and suggests that (epi-)genetic and environmental factors are involved. Therapy with anti-IL-4/IL-13 and anti-IL-17A is promising in clinical management of these patients.

22 - APPLICATION OF DOXORUBICIN-LOADED PLGA NANOPARTICLES TARGETING BOTH TUMOR CELLS AND CANCER-ASSOCIATED FIBROBLASTS ON HUMAN SKIN EQUIVALENTS MIMICKING MELANOMA AND CUTANEOUS SQUAMOUS CELL CARCINOMA.

S. Wu¹, Y. He², M.H. Rietveld¹, L.J. Cruz², C. Eich², A.E. Ghalbzouri¹

1) Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; 2) Translational Nanobiomaterials and Imaging (TNI) Group, Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands.

Background: Nanoparticles (NPs) have been thoroughly studied in tumour cells for their performance in prolonging retention time and achieving targeted delivery. Recently, few new strategies for NP application have tried to achieve tumour microenvironment modulation by regulating cancer associated fibroblasts (CAFs) in monocultures or in mouse models. Here we developed 3D-human skin equivalents (HSEs) mimicking melanoma and cutaneous squamous cell carcinoma (cSCC) and examined the effectiveness of NP targeting the tumour cells and CAFs simultaneously.

Objective: Study the efficiency of Doxorubicin-loaded PLGA Nanoparticles in HSEs and explore the potential dual NP targeting strategy.

Methods: In monolayer cultures, the NP uptake ability, cell viability and apoptosis in both CAFs and tumor cells were studied. Melanoma and cSCC HSEs were developed and treated with NPs by topical application or dermal injection. The distribution pattern and the uptake ability of NPs and their effects on tumor cell proliferation, invasion and CAF phenotype were analysed.

Results: NPs significantly reduced cell viability and induced apoptosis in monocultures. An increased uptake ability was observed on a time-dependent manner. In HSEs, NPs successfully penetrated through the tumor epidermis into the dermis matrix after topical application and were taken up by CAFs after topical and injected methods, resulting in decreased proliferative tumor cells, a thinner tumor epidermis and less tumor invasion.

Conclusion: The successful dual NP targeting strategies on tumor cells and CAFs in HSEs showed promising outcome on decreasing tumor invasion and CAF phenotype. This paves a new path for future treatment options in skin cancer therapy.

23 - EIGHT YEARS OF EXPERIENCE WITH VISMODEGIB FOR ADVANCED AND MULTIPLE BASAL CELL CARCINOMA PATIENTS IN THE NETHERLANDS.

B.J.A. Verkouteren^{1,2}, M. Wakkee³, A.K.L. Reyners⁴, P. Nelemans⁵, M.J.B. Aarts⁶, E. Racz⁷, J.B. Terra⁸, L.A. Devriese⁹, R.J. Alers¹⁰, E. Kapiteijn¹¹, R. van Doorn¹², M.W. Bekkenk¹³, M.G.H.C. Reinders^{1,2}, K. Mosterd^{1,2}

1) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; 2) GROW School for Oncology and Developmental Biology, Maastricht University Medical Center+, Maastricht, The Netherlands; 3) Department of Dermatology, Erasmus Medical Center Cancer Institute, Rotterdam, The Netherlands; 4) Department of Medical Oncology, University Medical Center Groningen, Groningen, The Netherlands; 5) Department of Epidemiology, Maastricht University, Maastricht, The Netherlands; 6) Department of Medical Oncology, Maastricht University Medical Center+, Maastricht, The Netherlands; 7) Department of Dermatology, University Medical Center Groningen, Groningen, The Netherlands; 8) Department of Dermatology, Isala Dermatologic Center, Zwolle, The Netherlands; 9) Department of Medical Oncology, University Medical Center Utrecht, Utrecht, The Netherlands; 10) Department of Gynecology, Maastricht University Medical Center+, Maastricht, The Netherlands; 11) Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands; 12) Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; 13) Department of Dermatology, Academic Medical Center, Amsterdam, The Netherlands.

Background: Vismodegib has been used for the treatment of locally advanced basal cell carcinoma (laBCC) and metastatic BCC (mBCC) since 2011. Information about the use of vismodegib beyond clinical trials still sparse.

Objectives: To evaluate the effectiveness of vismodegib for the treatment of laBCC, mBCC and basal cell nevus syndrome (BCNS) patients and the tumor characteristics associated with a higher probability of achieving complete response in the Netherlands.

Methods: A retrospective cohort study which included all patients ≥ 18 years with histologically proven BCC that received first dose of vismodegib between July 2011 and September 2019 in the Netherlands.

Results: In total, 48 laBCC, 11 mBCC and 19 BCNS patients were included. Median progression-free survival was 10.3 months (95% confidence interval (CI), 7.5-22.6 months) for laBCC, 11.7 (95% CI, 5.2-17.5 months) for mBCC, and 19.1 (95% CI, 7.4-20.2) for BCNS. Larger laBCCs were associated with a lower probability of complete response (hazard ratio (HR) 0.77 per increase in cm, $p=0.02$). Of all BCNS patients, 63% received two or more treatment sequences with vismodegib; all patients achieved partial response in all following sequences. Main reasons for treatment discontinuation were side effects (51%) and tumor progression (29%). All patients reported at least one side effect, with a median of 4 side effects per patient (range, 1-12).

Conclusion: Half of the aBCC patients progress within 1 year after the start of vismodegib treatment. More research is needed.

ded to investigate other treatment strategies after vismodegib progression and to evaluate long-term effects of repetitive vismodegib treatment.

24 - RISK OF CUTANEOUS SQUAMOUS CELL CARCINOMA AFTER FOUR DIFFERENT TREATMENTS FOR ACTINIC KERATOSIS: LONG-TERM RESULTS OF A RANDOMIZED CONTROLLED TRIAL.

Shima Ahmady^{1,2}, Maud H.E. Jansen^{1,2}, Patty J. Nelemans³, Janneke P.H.M. Kessels⁴, Aimee H.M.M. Arits^{1,2,5}, Michette J.M. de Rooij⁶, Brigitte A.B. Essers⁷, Patricia J.F. Quaedvlieg⁴, Nicole W.J. Kelleners-Smeets^{1,2}, Klara Mosterd^{1,2}

1) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands 2) GROW School for Oncology and Developmental Biology, Maastricht University Medical Center+, Maastricht, The Netherlands; 3) Department of Epidemiology, Maastricht University, Maastricht, The Netherlands; 4) Department of Dermatology, Zuyderland Medical Center, Heerlen, The Netherlands; 5) Department of Dermatology, Catharina Hospital, Eindhoven, The Netherlands; 6) Department of Dermatology, VieCuri Medical Center, Venlo, The Netherlands; 7) Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht University Medical Center+, Maastricht, The Netherlands.

Background: Treatment of actinic keratosis (AK) is aimed at preventing cutaneous squamous cell carcinoma (cSCC). However, whether AK can progress into cSCC is matter of debate and little is known about the effect of treatment on preventing cSCC.

Objective: To evaluate the risk of cSCC and factors that may contribute to increased risk in a broad spectrum of patients with AK who participated in a randomized trial comparing four field-directed treatments of AK.

Methods: Long-term follow-up study of a randomized controlled trial comparing 5% fluorouracil, 5% imiquimod cream, methyl-aminolevulinic acid photodynamic therapy and 0.015% ingenol mebutate gel for the treatment of AK. The primary outcome was the proportion of patients with cSCC in the target area during follow-up. Secondary outcomes were the associations between risk of cSCC and a priori defined potential prognostic factors; type of treatment, severity of AK, history of nonmelanoma skin cancer, and retreatment.

Results and **Conclusion:** will be discussed.

25 - ADIPOCYTES REDUCE SCAR FORMATION BUT DELAY RE-EPITHELIALIZATION IN IN VITRO RECONSTRUCTED HUMAN SKIN.

M. Waasdorp¹, J.P. Boogaard¹, S. Gibbs^{1,2}

1) Molecular Cell Biology and Immunology, Amsterdam UMC location VUmc, Amsterdam, The Netherlands; 2) Department of Oral Cell Biology, Academic Centre for dentistry (ACTA), Amsterdam, The Netherlands.

Background: Fat grafting shows promising results in reducing scar formation. Subcutaneous fat contains adipocytes, adipose

stromal cells (ASCs), growth factors and cytokines that may affect wound healing, but the role of adipocytes in wound healing remains largely unknown.

Objective: By developing a reconstructed human skin construct with and without adipocytes, we aim to study the role of adipocytes in wound healing.

Methods: Donor-matched keratinocytes, fibroblasts and ASCs were isolated from human skin (n=3). ASCs were differentiated into adipocytes. Matriderm[®] was used as a scaffold to reconstruct dermis, epidermis and subcutaneous fat. 4 mm biopsy wounds were made in reconstructed human skin with or without adipocytes and 1, 4, 7 and 14 days after wounding culture supernatant and biopsies were collected for cytokine analysis and histological evaluation.

Results: Presence of a stratified epithelium, basement membrane, fibroblasts, ASCs and adipocytes were confirmed by immunohistochemical staining for Ki10, collagen IV, vimentin and perilipin. Re-epithelialization was significantly reduced with the presence of adipocytes and was accompanied by reduced ITGA5 expression and increased release of chemokines CCL27, CCL5 and CXCL10. Interestingly, VEGF, TIMP1 and CCL2 secretion and α -SMA expression (marker for scar formation) were significantly reduced in the presence of adipocytes.

Conclusion: We developed a reconstructed human skin model including subcutaneous fat layer, that can be used to study deep wound healing. Presence of adipocytes leads to delayed wound closure, but reduces scar formation.

26 - MEEK MICROGRAFTING: A NOVEL SURGICAL TECHNIQUE FOR THE TREATMENT OF DEPIGMENTATION.

V.S. Narayan¹, N.F. Post¹, P.P.M. Van Zuijlen², M.W. Bekkenk¹, A. Wolkerstorfer¹

1) Department of Dermatology, Amsterdam University Medical Centers, Amsterdam, The Netherlands; 2) Burn Center, Red Cross Hospital, Beverwijk, The Netherlands.

Background: There is an unmet need for a simple, reliable and effective transplantation technique for large areas. The Meek micrografting technique was first presented in 1958 by C.P. Meek, and currently, the modification of this method is a milestone in the history of acute burns surgery. However, this technique has never been utilized previously for the treatment of depigmented lesions.

Objective: Assess outcomes of tissue grafting using the Meek technique in the treatment of stable depigmentations.

Methods: A retrospective cohort study involving 6 patients with stable depigmentations who were treated with the Meek micrografting technique using 1:3, 1:4, 1:6 and 1:9 expansion ratio. A 200 μ m split-thickness skin graft was harvested. The harvested skin was placed onto two square cork plates and cut into 196 small square pieces per cork plate. The micro skin grafts were transferred onto a sterile prefolded expandable gauze. The gauze was manually unfolded. The recipient site was prepared with a CO₂ laser ablating 209 μ m of tissue. Finally, the Meek gauzes and dressing were removed after one week.

Results: Our patients showed remarkably high repigmenta-

tion percentages after 3, 6 and 9 months. A side effect of this treatment seems to be a 'grid-like' pattern of repigmentation in the first months after treatment, although this did improve over time.

Conclusion: The Meek micrografting technique is a novel technique for stable depigmented lesions with a potential benefit, as it is a simple tissue grafting method that potentially reaches high expansion ratios and high repigmentation success rates.

POSTERS

P1 - RECOMBINANT HUMAN C1 ESTERASE INHIBITOR AS PROPHYLACTIC TREATMENT OF IDIOPATHIC NON-HISTAMINERGIC ANGIOEDEMA: A PHASE 1 TRIAL AND FOLLOW-UP.

Mehran A. Aghdam^{1,3}, Zonne L.M. Hofman^{2,3}, Michelle Meertens^{1,3}, Ans Lebens¹, André C. Knulst^{1,3}, Erik C. Hack³, Coen Maas², Heike Röckmann^{1,3}

1) Department of Dermatology/Allergology, University Medical Center Utrecht, Utrecht University, The Netherlands; 2) Laboratory of Clinical Chemistry and Haematology, University Medical Center Utrecht, Utrecht University, The Netherlands; 3) Center for Translational Immunology, University Medical Center Utrecht, Utrecht University, The Netherlands.

Background: Idiopathic non-histaminergic acquired angioedema (InH-AAE) is characterized by antihistamine therapy resistance and normal C4 levels. The bradykinin pathway might also play a role in antihistamine resistant InH-AAE.

Objective: We investigated the efficacy and safety of recombinant human C1-esterase inhibitor (rhC1-INH) for prophylaxis of InH-AAE.

Methods: In this prospective, open-label study, patients with InH-AAE and at least 2 attacks/ month were included. Patients received intravenous rhC1-INH twice weekly for a treatment period of 2 months, preceded and followed by an observational month. The primary endpoint was a reduction in the angioedema activity score (AAS). Disease related biomarkers were measured and post-trial follow-up was evaluated in all patients.

Results: Six patients (four female, mean age 41y) were enrolled. One patient showed significant response, with three attacks during treatment (AAS₂₈: 8 & 21) compared to 19 attacks during the observation period (AAS₂₈: 58 & 175). The other patients showed no significant difference in AAS scores. No major side-effects were reported. No biomarkers were found explaining the treatment response. Post-trial follow-up of the patient with rhC1-INH response showed high effectivity of both pdC1- and rhC1-INH, with treatment intervals of 3 and 5 days respectively. Omalizumab was ineffective. Two patients showed good effect to omalizumab and one to tranexamic acid. Two patients wished to return to antihistamine therapy.

Conclusion: We observed a strong treatment response upon rhC1-INH treatment and pdC1-INH in 1 out of 6 patients with InH-AAE in which omalizumab treatment was ineffective, indicating a role for the bradykinin route in InH-AAE.

P2 - SALIVA AS POTENTIAL TREATMENT FOR BURNS: ASSESSING ANTIMICROBIAL PROPERTIES OF SALIVA AND DONOR VARIATION OF BURN PATIENTS.

J.P. Boogaard¹, M. Waasdorp¹, B.P. Krom², S. Gibbs^{1,3}

1) Department of Molecular Cell Biology and Immunology, Amsterdam Infection and Immunity Institute, Amsterdam UMC location VUmc, The Netherlands; 2) Department of Preventive Dentistry, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit, Amsterdam, The Netherlands; 3) Department of Oral Cell Biology, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit, Amsterdam, The Netherlands.

Background: Most burn wounds lead to hypertrophic scarring, where delayed wound healing and infection are important contributors. Saliva contains thousands of bioactive molecules, among which are growth factors and antimicrobial peptides. Autologous saliva may thus provide an easy therapy for burns. The wound healing properties of saliva from healthy volunteers are well established, but systemic effects of burns might affect these properties. Furthermore, how saliva affects burn wound pathogens is unknown.

Objective: To assess therapeutic properties of saliva from burn patients and its antimicrobial potential.

Methods: Saliva from healthy donors and burn patients was collected and filter sterilized. Age, sex, burn size (%TBSA) and (post)burn day were collected. To assess the effect of donor variation in saliva on wound healing rate, scratch assays with primary human fibroblasts were performed. Using a minimal inhibitory concentration assay, the antimicrobial effect of pooled saliva on strains of the common burn wound pathogens *Staphylococcus aureus* and *Candida albicans* was assessed.

Results: We showed that 5% and 20% saliva significantly increased wound healing rate compared to control. No differences were observed between healthy donors and burn patients. There was no correlation between age, burn wound size or post burn day and closure rate. Furthermore, 50% saliva was able to significantly reduce generation time of some burn wound pathogens.

Conclusion: Saliva can reduce pathogen generation time. Furthermore, saliva of both healthy donors and burn patients stimulate fibroblast migration, and to a similar extent. Autologous saliva is thus a promising cheap therapeutic for treatment of burns.

P3 - TELEHEALTH FOR OLDER ADULTS WITH SKIN DISEASE: A QUALITATIVE EXPLORATION OF DERMATOLOGISTS' EXPERIENCES & RECOMMENDATIONS FOR IMPROVING CARE.

I. de Vere Hunt¹, S. van Egmond^{1,2}, V. Nava¹, R. Khodosh³, J. Lester³, A.S. Chiou⁴, E. Linos¹

1) Program for Clinical Research and Technology, Stanford University, Stanford, USA; 2) Department of Dermatology, Erasmus MC, Rotterdam, The Netherlands; 3) Department of Dermatology, University of California San Francisco, San Francisco, USA; 4) Department of Dermatology, University of California San Francisco, San Francisco, USA.

Francisco, USA; 4) Department of Dermatology, Stanford University, Stanford, USA.

Background: The COVID-19 pandemic accelerated the use of telehealth. Yet, there is little research exploring the implications of telehealth practice for underserved populations such as older adults.

Objective: To explore dermatologists' experiences of using telehealth with older adults, in order to identify and summarise recommendations to improve telehealth care.

Methods: We conducted 23 in-depth, semi-structured interviews over video with dermatologists across the US. We performed an inductive thematic analysis of the interview transcripts to extract themes regarding dermatologists' experience of using telehealth with older adults and recommendations for improving telehealth care.

Results: The following core experience ('E') and recommendation ('R') themes were extracted: E1) beneficial for patient to be able to stay at home; E2) works well for 'stable chronic disease', but concerns about malignant lesions; E3) technology presents a barrier for many, but not all, older adults; E4) can't see the whole patient and feel the skin; and E5) can be more difficult to communicate virtually. Five themes summarising recommendations were identified: R1) don't make assumptions about patient comfort with technology; R2) appropriate appointment triage is crucial; R3) important to manage patient expectations about what can be achieved in a telehealth visit; R4) give comprehensive instructions ahead of time; and R5) need for healthcare providers to make telehealth accessible for all.

Conclusion: Based on our qualitative data analysis, we call for active optimisation of telehealth systems to ensure usability for all, and to prevent exacerbation of healthcare disparities as a result of technological literacy and cost barriers.

P4 - A 3D ORGANOTYPIC MODEL TO STUDY HUMAN LYMPH NODE FRC-DC INTERACTIONS.

Andrew Morrison¹, Sander W. Spiekstra¹, Susan Gibbs^{1,2}, Reina Mebius¹

1) Department of Molecular Cell Biology and Immunology, Amsterdam UMC, Vrije Universiteit, Amsterdam, The Netherlands; 2) Department of Oral Cell Biology, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit, Amsterdam, The Netherlands.

Background: Lymph nodes are secondary lymphoid organs that are fundamental in orchestrating the adaptive immune response and strategically positioned to drain all tissues, including skin. Their highly specialized architecture is regulated by non-hematopoietic Fibroblast Reticular Cells (FRCs) that can shape immune events, such as facilitating T cell and Dendritic Cell (DC) interactions within the T cell zone. The study of human adaptive immune responses arising from allergens and external stimuli requires competent in vitro models that can recapitulate the physiological tissue-microenvironment.

Objective: Here, we aim to create a 3D organotypic in vitro model containing FRCs to study their interaction and influence on MUTZ-3, a cell line that can differentiate into DCs (DC-Sign+CD1a+), following exposure to maturation stimuli and chemical sensitizers.

Methods: Primary human FRCs were co-cultured with either MUTZ-3 progenitors or MUTZ-3 DC, and phenotype was characterized by flow cytometry, histology and 3D imaging.

Results: After 2 weeks in culture, a FRC-network with FRC-DC interaction was observed, which promoted DC survival. Moreover, FRCs influenced the differentiation of progenitors into DCs by skewing their phenotype into DC-Sign+CD1a-, resembling native DCs found in human lymph nodes.

Conclusion: This system should prove useful for further in-depth studies of stroma-immune cell interactions emerging from allergens within skin-draining lymph nodes. As such, this provides a beneficial organotypic modelling platform that could be implemented into future technologies, such as microfluidics and multi-organs on a chip.

P5 - LOCAL DERMATITIS UPON TAPESTRIPPING AND VASELINE TREATMENT OF HEALTHY HUMAN SKIN IS ATTENUATED BY COAL TAR: INSIGHTS INTO AHR-TARGETING THERAPIES FOR INFLAMMATORY SKIN DISEASES.

Noa J.M. van den Brink, Jade G.M. Logger, Tessa A. Kouwenhoven, Jos P.H. Smits, Ellen H. van den Bogaard
Department of Dermatology, Radboud Institute for Molecular Life Sciences (RIMLS), Radboud University Medical Center (Radboudumc), Nijmegen, The Netherlands.

Background: Coal tar therapy, one of the oldest dermatological therapies, exerts its therapeutic effect through activation of the aryl hydrocarbon receptor (AHR), and AHR-targeting molecules show therapeutic efficacy in trials for chronic inflammatory skin diseases. The anti-inflammatory mechanisms of AHR activation in the skin are partially understood, but mostly studied in animal models.

Objective: We aimed to investigate the therapeutic effects of AHR activation by coal tar application on epidermal responses after skin barrier disruption and inflammatory cues in human skin.

Methods: Healthy volunteers (n=9) were treated with pix lithanthracis (5% in vaseline lanette) or vehicle (vaseline lanette) after complete removal of the stratum corneum by tapestripping. Non-invasive biophysical measurements (TEWL, hydration, erythema), stratum corneum tapes (for protein profiling) and skin biopsies were taken during 4 days of treatment.

Results: The application of vaseline lanette on tape-stripped skin led to an acute inflammatory response characterized by increased keratinocyte proliferation and subsequent acanthosis, a dense dermal CD45+ and MPO+ immune cell infiltrate indicative of (neutrophilic) granulocytes and increased levels of human beta-defensin-2 (hBD2). Strikingly, coal tar treated sites clearly showed less immune cell infiltrate, less pronounced acanthosis and hBD2 levels in the stratum corneum were significantly lower than upon vaseline treatment.

Conclusion: This in vivo human acute dermatitis model indicates that activation of AHR signaling reduces the influx of inflammatory cells potentially resulting in less epidermal activation. Further investigations on the inflammatory signaling molecules driving the acute inflammation can provide new insights in the coal tar and AHR-mediated therapeutic effects.

P6 - DYNAMIC HOST-MICROBIOME INTERACTIONS IN RECONSTRUCTED HUMAN ORAL MUCOSA WITH REPRESENTATIVE ORAL BIOFILMS.

L. Shang¹, S. Roffel², E. D'Agostino⁴, V. Slomka⁵, D. Deng¹, B.P. Krom¹, S. Gibbs^{2,3}

1) Department of Preventive Dentistry and 2) Department of Oral Cell Biology, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; 3) Department of Molecular Cell Biology and Immunology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; 4) Unilever Research & Development, Colworth, England, United Kingdom; 5) Unilever Research & Development, Port Sunlight, England, United Kingdom.

Background: Microbes colonize on body barriers (e.g. oral mucosa, skin) and play important roles in host health and disease. Such host-microbiome interactions are complex and dynamic, therefore difficult to investigate – in vivo studies cannot reflect the dynamic interactive process and the current in vitro co-culture models are too simplified to reflect physiological complexity.

Objective: To establish a representative host-microbiome interaction model using reconstructed human oral mucosa (RHOM) and saliva-derived multi-species biofilms.

Methods: RHOM were topically exposed to saliva collected from healthy subjects, with the presence of a gel containing saliva substitute. After 2 or 4 days, microbial viability and compositional profiles were determined by viable counting or 16S rDNA sequencing, respectively. The host response was evaluated by tissue histology, metabolic activity assay, antimicrobial peptide expression and cytokine secretion.

Results: Co-culturing for 2 and 4 days illustrated oral biofilm formation without loss of viability of RHOM. Saliva biofilms were diverse and stable over time, consisting of 3 major genera Haemophilus, Streptococcus and Neisseria normally present abundantly on healthy oral mucosa in vivo. RHOM exerted protective responses by maintaining tissue histology, increasing expression of antimicrobial peptides Elafin and HBD2 and moderately releasing more cytokines IL-6, CXCL1, CXCL8, CCL5 and CCL20.

Conclusion: By dynamic co-culturing of RHOM and saliva microbiome for extended periods, we established a stable and representative oral host-microbiome interaction model, featuring in responsive RHOM and diverse biofilms. This in vitro model resembles oral host-microbiome symbiosis in physiological complexity and dynamics.

P7 - DIAGNOSING EARLY CASES OF SÉZARY SYNDROME: DIGITAL IMPROVEMENTS IN DETECTION OF DNA METHYLATION BIOMARKERS.

W.H. Zoutman¹, S. Najidh¹, R.J. Nell², M. Versluis², P.A. van der Velden², C.P. Tensen¹, M.H. Vermeer¹

1) Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; 2) Department of Ophthalmology, Leiden University Medical Center, Leiden, The Netherlands.

Background: Sézary syndrome (SS) is an aggressive type of cutaneous T-cell lymphoma. Diagnosing SS can be challenging, especially in early stages of disease. Previously, we showed that promoter methylation of PROM1, GoS2, CMTM2, PAM, GNMT and NEXN is frequently observed in late stages of disease, but is not found in benign erythrodermic (BE) cases.

Objective: In this study, we evaluated the diagnostic value of these biomarkers in early stages of disease. Furthermore, we aimed to improve the accuracy, sensitivity, and straightforwardness of biomarker detection by developing and testing novel digital PCR-based assays.

Methods: We collected peripheral blood from 15 early SS and 15 BE patients. The early SS patients had progressive disease and fulfilled disease-specific WHO criteria during follow-up. The methylation status of our biomarker panel was analyzed in blood and enriched cell fractions by using Methylation Specific – Melting Curve Analysis (MS-MCA) and Methylation Sensitive Restriction Enzyme – digital PCR (MSRE-dPCR).

Results: In 87% of early SS patient samples, one or more of the biomarkers was hypermethylated as detected by MS-MCA. With MSRE-dPCR we could accurately and sensitively quantify methylation of these markers, even in less enriched cell fractions.

Conclusion: These data show that analyzing the methylation status of the panel of 6 biomarkers is useful in the early diagnosis of SS which can have beneficial effects on treatment and quality of life. Furthermore, implementing absolute quantification of DNA methylation by using MSRE-dPCR allows precise threshold calling which results in more accurate, sensitive and straightforward diagnosis.

P8 - INCIDENCE OF MYCOSIS FUNGOIDES AND SÉZARY SYNDROME IN THE NETHERLANDS BETWEEN 2000 AND 2020.

R. Ottevanger¹, D.T. de Bruin¹, R. Willemze¹, P.M. Jansen², M.W. Bekkenk³, E.R.M. de Haas⁴, B. Horvath⁵, M.M. van Rossum⁶, C.J.G. Sanders⁷, J.C.J.M. Veraart⁸, M.H. Vermeer¹, K.D. Quint¹

1) Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; 2) Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands; 3) Department of Dermatology, Academic Medical Center, Vrije Universiteit Medical Center, Amsterdam, The Netherlands; 4) Department of Dermatology, Erasmus Medical Center, Rotterdam, The Netherlands; 5) Department of Dermatology, University Medical Center of Groningen, Groningen, The Netherlands; 6) Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; 7) Department of Dermatology, University Medical Center

Utrecht, The Netherlands; 8) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands.

Background: Cutaneous T-cell lymphomas (CTCLs) are a heterogeneous group of non-Hodgkin lymphomas. Previous studies have shown that the incidence of CTCL has tripled between 1970 and 2000 but since then has stabilized. However, data on the incidence of Mycosis Fungoides (MF) and Sezary syndrome (SS) in the Netherlands have never been published.

Objective: The aim of the present study was to estimate the changes in incidence of newly diagnosed MF and SS in the Netherlands over the last 20 years.

Methods: Annual incidence rates were retrieved from the Dutch Cutaneous Lymphoma Registry (DCLR) between January 2000 and December 2019. In all cases, the diagnosis was based on the clinicopathological criteria of the WHO-EORTC classification and confirmed by an expert panel of dermatologists and pathologists.

Results: 1044 patients with MF, including 238 patients with FMF, and 93 patients with SS were included. In 2000, the number of cases of MF was 30 and 79 in 2019. For SS this was 2 in 2000 and 13 in 2019. The overall increase for MF was 2.6-fold and 6.5-fold for SS between 2000 and 2019.

Conclusion: In summary, a significant increase of patients with classical MF, FMF and SS included in the DCLR was seen over the past 20 years. In contrast to previous studies that suggest a stabilization since 2000, this study shows that the incidence of patients with MF and SS in the Netherlands increased over the past two decades.

P9 - METS AND NETS ARE PRESENT IN BURN WOUND TISSUE AND COINCIDE WITH A PROCOAGULANT PHENOTYPE.

Britt van der Leeden^{1,2}, Magda M.W. Ulrich^{2,3,4}, H. Ibrahim Korkmaz^{2,3,4}, Yolanda Ponstein⁵, Paul P.M. van Zuijlen^{3,6,7}, Hans W.M. Niessen^{1,8,9}, Sue Gibbs^{2,9}, Paul A.J. Krijnen^{1,9}

1) Department of Pathology, Amsterdam University Medical Centers (AUMC), Amsterdam, The Netherlands; 2) Amsterdam Infection & Immunity, AUMC, Amsterdam, The Netherlands; 3) Association of Dutch Burn Centers (ADBC), Beverwijk, The Netherlands; 4) Department of Molecular Cell Biology and Immunology, AUMC, Amsterdam, The Netherlands; 5) Pharming Technologies B.V., Leiden, The Netherlands; 6) Burn Center, Red Cross Hospital, Beverwijk, The Netherlands; 7) Department of Plastic, Reconstructive and Hand Surgery, AUMC, Amsterdam, The Netherlands; 8) Department of Cardiac Surgery, AUMC, Amsterdam, The Netherlands; 9) Amsterdam Cardiovascular Sciences, AUMC, Amsterdam, The Netherlands.

Background: Burn wound conversion is a post-burn phenomenon where vital tissue is lost to expansion of necrosis. Loss of perfusion in the burn wound may be an important underlying cause of burn wound conversion and is caused by microvascular damage, persisting inflammation and post-burn coagulopathy. Previously we showed that neutrophils extracellular traps (NETs) are present in microcirculatory thrombosis of burn wounds.

Objectives: We aimed to determine the presence of monocyte extracellular traps (METs) and NETs as well as the pro-coagulant phenotype in burn wounds.

Methods: Eschar was post-operatively obtained from burn wound patients. Herein, coagulation factors tissue factor (TF) and factor XII (FXII) were studied using immunohistochemistry. The presence of NETs and METs was analyzed via immunofluorescence, combining immune cell markers myeloperoxidase (MPO), CD14, CD45 and major basic protein (MPB) together with endothelial cell marker CD31 and extracellular trap (ET) marker Histone 3 citrullin.

Results: Neutrophils are the most numerous cell type of the immune cell infiltrate in eschar compared to monocytes/macrophages. Expression of TF and FXII was found intravascular in all eschar, TF was also found in necrotic parts of the dermis. Both NETs and METs were found extravascular in the dermis as well as in the lumen of the dermal microvasculature in the eschar tissue. NETs were more abundantly present in the eschar than METs.

Conclusion: Although neutrophils are the prominent source of extracellular traps in burn wounds, monocytes also contribute to post-burn ETosis and may thereby contribute to the hyper-coagulatory state after burns and burn wound conversion.

P10 - UNRAVELLING THE AGGRESSIVE BEHAVIOUR OF SQUAMOUS CELL CARCINOMA IN EPIDERMOLYSIS BULLOSA: ANALYSIS OF CLINICAL OUTCOME AND TUMOUR CHARACTERISTICS IN THE DUTCH EB REGISTRY.

C. Harrs^{1,2}, B. Horváth¹, P.C. van den Akker^{1,3}, J.C. Duipmans¹, R. Baardman¹, M.C. Bolling¹, G.F.H. Diercks^{1,2}

1) Department of Dermatology, Center for Blistering Diseases, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; 2) Department of Pathology and Medical Biology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; 3) Department of Genetics, Center for Blistering Diseases, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands. *The last two authors contributed equally.

Background: A serious complication in Epidermolysis bullosa (EB) is the development of aggressive cutaneous squamous cell carcinoma (cSCC). Limited data about EB cSCCs are available, and the cause of their aggressiveness remains poorly understood.

Objectives: To analyse the epidemiology, clinical course, and tumour characteristics of cSCC within the Dutch EB Registry (Dutch-EB-Reg).

Methods: In this retrospective study, all EB-patients with cSCCs registered in the Dutch-EB-Reg from 1988-2020 were included. Patient data were gathered from medical records.

Results: 22 of 578 EB-patients developed cSCCs with the highest frequency detected in severe recessive dystrophic EB (RDEB-severe) with 26.5%. RDEB-severe patients had the lowest median age at cSCC onset with 27.7 years (range: 14.3-42.2). 11 of the EB-patients developed metastases and all died

from metastatic cSCC. Metastasis occurred mostly in RDEB-severe (77.8%), followed by JEB-intermediate (42.9%). In RDEB-severe the median survival after the first cSCC was 41 months (range: 9-199), compared to 228 months in JEB-intermediate (range: 22-302). Most cSCCs had a tumour diameter of \leq 2 cm (62.7%), but did not show other histopathological risk factors.

Conclusion: cSCC is a life-threatening complication in RDEB-severe and JEB-intermediate due to an increased risk of developing metastasis and eventually dying from the consequences. In RDEB-severe this occurs at a young age. The tumours behave aggressively despite the absence of most high-risk features. The development of a large tumour size, facilitated by a tumour-prone environment, seems to be crucial for this aggressive nature. This emphasizes the importance of regular screenings and rapid intervention in EB cSCCs.

P11 - METABOLICALLY ACTIVE, TRI-LAYERED RECONSTRUCTED HUMAN SKIN.

Jonas Jäger¹, Jasper Koning¹, Taco Waaijman¹, Maria Thon¹, Ranjit K. Bhogal² and Susan Gibbs^{1,3}

1) Department of Molecular Cell Biology and Immunology, Amsterdam UMC, Vrije Universiteit, Amsterdam, The Netherlands; 2) Unilever R&D UK, Colworth Science Park, Bedford, United Kingdom; 3) Department of Oral Cell Biology, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit, Amsterdam, The Netherlands

Background: Over the past few years in skin research, animal experiments have been increasingly replaced by in-vitro models. However, despite its importance in testing of actives, little attention has been paid to metabolism in reconstructed human skin (RhS) and a metabolically very active tissue in particular, the adipose layer.

Objective: Here, we developed a tri-layered, metabolically active RhS model with epidermis, dermis and an adipose layer, which we comprehensively characterized and screened for CYP450 expression – one of the most important enzyme families in metabolism.

Methods: Primary human keratinocytes, fibroblasts and differentiated adipose-derived stem cells were co-cultured in a collagen/fibrin scaffold to create a RhS model. After culturing at the air-liquid interface for two weeks, the model was characterized with immunohistochemistry, confocal microscopy, MTT assay, qPCR, RNAseq and ELISA.

Results: Viability and epidermal integrity were maintained in cultures with the adipose layer. Comparing gene expression of conditions with and without the adipose layer, we identified several CYP450 family members being up- and down-regulated in epidermis and dermis of constructs with the adipose layer. These results were verified and extended by RNAseq.

Conclusion: Most metabolic enzymes were up-regulated in tri-layered cultures. Secretion of less pro-inflammatory cytokines (IL-6, IL-8) into the medium indicate a less inflamed ground-state of the model and thereby emphasize the contribution of adipocytes to tissue homeostasis. Overall, our results suggest that this model mimics native human skin more

closely than traditional skin equivalents and hence is a better model to assess skin toxicity of actives in the future.

P12 - EPIDEMIOLOGY OF MYCOSIS FUNGOIDES AND FOLLICULOTROPIC MYCOSIS FUNGOIDES FROM 2000-2018.

R. Ottevanger, D.D.N. van der Hout

Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands.

Background: van Doorn, et al. studied the epidemiology of Mycosis fungoides (MF) from 1985 till 2000, however, there is no current information present on the epidemiology after the year 2000. In this study the epidemiology of MF and Folliculotropic mycosis fungoides (FMF) will be determined from 2000 till 2018 and will demonstrate the most recent findings of these two cutaneous lymphomas.

Objectives: To determine the patient characteristics, disease progression, therapy response and survival of Dutch LUMC-patients with MF or FMF.

Methods: A single-center, 18-year, retrospective cohort analysis performed on patients selected by the Dutch cutaneous lymphoma group (DCLG) at the Dermatology department of the Leiden University Medical Center. Retrospective statistical analysis was performed using SPSS. Specifically, the epidemiology of both MF and FMF was determined using the patients selected by the DCLG. This selection consists of 428 patients with MF or FMF included between 2000 to 2018 with a minimal follow-up period of 12-months. All patients have clinical and histopathological confirmation of the given diagnosis and have received at least one type of treatment for their MF or FMF.

Results: The results maintain to be determined, however, the prediction is that MF patients will have a superior survival rate, a slower disease progression and a better response to therapy than FMF patients.

Conclusion: MF appears to have a more indolent character than FMF, which is characterized by a more aggressive disease course and responds less adequately to treatment. Subsequently, FMF has a worse disease progression and survival rate than MF.

P13 - FIRST AND SECOND OMALIZUMAB TREATMENT EPISODE IN CHRONIC URTICARIA PATIENTS.

M.A.J. Meertens¹, T. Luijck², S. Assil², M. Bergmans², M. Alizadeh Aghdam¹, P.A. Kentie¹, A.C. Knulst¹, M.B.A. van Doorn², H. Röckmann¹

1) Department of Dermatology/Allergology, University Medical Center Utrecht (UMC), Utrecht, The Netherlands; 2) Department of Dermatology, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands. Disclaimer: at the UCARE meeting, multi-center data from University Medical Center Utrecht and Erasmus Medical Center Rotterdam will be presented.

Background: Omalizumab has shown to be highly effective in patients with chronic urticaria (CU). Equal effectiveness

of first and second treatment episodes was reported in small studies at population level.

Objective: To compare effectiveness of the first and second omalizumab treatment episode on patient level.

Methods: All CU patients treated with omalizumab in the UMC Utrecht between February 2012 and May 2021 with minimum follow-up of 15 months were included in this retrospective study. Treatment responses were assessed using the urticaria activity score (UAS7) or by estimation. Treatment intervals and determinants predicting restart were analyzed.

Results: 278 patients were included. In 148 patients (53%) treatment was discontinued, of which 62 patients (42%) restarted. Median treatment free interval was 147 days. Restarters had a significantly higher disease activity at baseline (median UAS7 29 versus 23; $p=0.03$) and showed more often fast response in the first treatment period, shown as different UAS7 at second administration (2.5 versus 12; $p=0.001$), than non-restarters. Mean omalizumab dosing interval was comparable in first and second treatment episode (7.2 versus 7.6 weeks, $p=0.4$). 53 patients (90%) achieved equal effectiveness on patient level in first and second treatment episode. Two patients (3.4%) showed substantial improvement in effectiveness and four (6.8%) showed substantially less effectiveness during the second treatment episode.

Conclusion: The majority of patients (90%) that restarted omalizumab treatment achieved equivalent effectiveness in the second treatment period. High disease activity at baseline and fast initial treatment response were associated with need to restart.

P14 - CLINICAL PROFILE OF ADULT PATIENTS WITH IDIOPATHIC ANGIOEDEMA.

R. Soegiharto, M. Alizadeh Aghdam, A.C. Knulst, H. Röckmann

Department of Dermatology/Allergology, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands.

Background: Idiopathic angioedema (iAE) is characterized by swellings of unknown cause. Clinical characteristics and therapeutic responses have previously been studied in small populations.

Objective: Investigating disease severity profiles in iAE patients by investigating attack frequency, severity and disease control in relation to prophylactic treatment.

Methods: In this retrospective study, records of all patients visiting the UMC Utrecht with diagnosis related to AE between January 2015 and March 2020 were screened. Patients with iAE, including those with subordinary wheals (iAE-w), were included. Patients with mainly urticaria, Hereditary Angioedema, drug hypersensitivity and ACE-inhibitor users were excluded. Attack frequency, attack treatment and disease control due to prophylactic treatment at first-visit and follow-up were compared and related in a profile analysis, presented as heatmaps.

Results: 242 patients with iAE (59.5%) and iAE-w (40.5%) were included. At first-visit, 39.3% patients used prophylactic treatment, 59.5% endured \leq one attack per month and 33.1%

sought urgent care during attack. At follow-up, 5.4% patients sought urgent care during attack and 57.4% used antihistamine monotherapy as prophylactic treatment, of which 69.9% iAE and 57.6% iAE-w patients reported sufficient effect. Add-on treatment including omalizumab was used in 16.1% patients, with good disease control in 35.3% iAE and 31.8% iAE-w patients. 13 (5.4%) patients were considered 'difficult to treat' with no effect on add-on treatment and \leq one attack per month.

Conclusion: We characterised angioedema patients' population profile in which a majority responds sufficiently to antihistamines. 16.1% requires add-on treatment, with no improvement in a third of patients despite add-on treatment.

P15 - CHALLENGES IN NONINVASIVE SKIN BIOMARKER MEASUREMENTS IN DAILY PRACTICE: A LONGITUDINAL STUDY ON SKIN SURFACE PROTEIN DETECTION BY THE TRANSDERMAL ANALYSIS PATCH IN PEDIATRIC PSORIASIS.

Mirjam J. Schaap¹, Noa van den Brink¹, Finola. M. Bruins¹, Kadri Orro^{2,3}, Hans M.M. Groenewoud⁴, Elke M.G.J. de Jong¹, Ellen H. van den Bogaard¹, Marieke M.B. Seyger¹

*1) Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; 2) FibroTx LLC, Mäealuse 4, 12918 Tallinn, Estonia; 3) Tallinn University of Technology, Department of Chemistry and Biotechnology, Estonia; 4) Department for Health Evidence, Radboud University, Nijmegen, The Netherlands. *These authors contributed equally.*

Background: Skin surface proteins are potential biomarkers in psoriasis and are noninvasively measured with the Transdermal Analysis Patch (TAP).

Objective: To assess markers measured by TAP over time, explore their correlation with disease severity in pediatric psoriasis, and compare the TAP and tape stripping detection capability.

Methods: In this prospective observational daily clinical practice study, pediatric psoriasis patients (>5 to <18 years) were followed during one year. Each visit, TAPs were applied on lesional (n=2), perilesional (n=2), and non-lesional (n=1) sites, and disease severity scores were performed. If all lesions cleared, post-lesional skin was sampled. CXCL-1/2, IL-1RA, IL-23, IL-1 α , IL-8, VEGF, hBD-2, CCL-27, IL-4, IL-22, IL-17A, hBD-1, and KLK-5 levels were quantified. TAP and tape stripping detection capability was compared in adult psoriasis patients.

Results: 32 patients were included with a median age of 15.0 years (IQR 10.9-16.9), median PASI score of 5.2 (IQR 3.7-8.7), and mean follow-up of 11.3 (\pm 3.4) months, resulting in 104 visits. Significantly higher IL-1RA, hBD-2, IL-8, VEGF, CXCL-1/2, IL-23, hBD-1, IL-22, CCL-27, and IL-17A levels were found in lesional skin (n=197), whereas IL-1 α was higher in non-lesional (n=104) skin. Intriguingly, post-lesional (n=6) marker levels were equal to or higher (hBD-2 and KLK-5) than lesional levels. Marker levels were variable over time. Markers did not correlate with disease severity, possibly explained by inverse relations between lesional desquamation and marker levels. In adults (n=10), markers were more frequently detected in tape extracts compared to TAPs.

Conclusion: Noninvasive biomarker detection by TAP is hampered by excessive desquamation, which might limit its use in psoriasis.

P16 - DOES AUTOIMMUNE VITILIGO PROTECT AGAINST COVID-19 DISEASE?

Nicoline F. Post¹, Rosalie M. Luiten¹, Albert Wolkerstorfer¹, Marcel W. Bekkenk¹, Markus Böhm²

1) Department of Dermatology and Netherlands Institute for Pigment Disorders, Amsterdam Institute for Infection and Immunity, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands; 2) Department of Dermatology, University of Münster, Münster, Germany.

Background: The SARS-CoV-2 pandemic has evolved to a global health problem with a dramatic mortality rate impacting our daily life and those of many patients. While there is evidence that some diseases are associated with an increased risk for development of a more severe course of COVID-19, little is known on protective conditions. A provocative idea is that some diseases may confer protection against SARS-CoV-2 infection and, more importantly, from COVID-19 manifestation. Non-segmental vitiligo (NSV) is an autoimmune-mediated inflammatory disease. The pathobiology of NSV involves adaptive type 1 immune responses with interferon (IFN)- γ signaling and CD8+ T cells but also innate immune responses. Importantly, clearance of viral infection and protection against disease manifestation crucially depends on functional innate and adaptive immunity and the interferon signaling axis.

Objective: 1. What is the relation between NSV and coronavirus infection risk or COVID-19 disease development? 1a. How does vitiligo affect the severity and mortality of COVID-19 disease? 2. Is disease activity of vitiligo affected by COVID-19 disease?

Methods: In The Netherlands we've started to test our hypotheses by initiating two separate research lines: 1. A mono-center epidemiological study of patient data registry at the Amsterdam UMC. 2. A patient reported outcome questionnaire for vitiligo patients.

Results and Conclusion: Both of the research lines are currently work in progress. We expect to analyze our first results within a month, hence being able to present our first results during the Vitiligo International Symposium. We aim to initiate the international questionnaire study around November this year.

P17 - A SYSTEMATIC REVIEW OF THE VULVAR MICROBIOME IN HEALTH AND DISEASE.

L. Pagan^{1,8}, R.A.M. Ederveen^{2,7}, B.W. Huisman^{1,8}, J.W. Schoones³, R.D. Zwitterink⁴, F.H.J. Schuren⁵, R. Rissmann^{1,6}, J.M.J. Piek⁷, M.I.E. van Poelgeest^{1,8}

1) Centre for Human Drug Research, Leiden, The Netherlands; 2) Maastricht University Medical Center, Maastricht, The Netherlands; 3) Directorate of Research Policy (formerly: Walaeus Library), Leiden University Medical Center, Leiden,

The Netherlands; 4) Center for Microbiome Analyses and Therapeutics, Leiden University Medical Center, Leiden, The Netherlands; 5) Netherlands Organisation for Applied Scientific Research, TNO, Zeist, The Netherlands; 6) Leiden Amsterdam Center for Drug Research, Leiden University, Leiden, The Netherlands; 7) Department of Obstetrics and Gynaecology and Catharina Cancer Institute, Catharina Ziekenhuis, Eindhoven, The Netherlands; 8) Department of Gynecology and Obstetrics, Leiden University Medical Center, Leiden, The Netherlands.

*These authors contributed equally.

Background: The link between cancer and the microbiome is a fast-moving field in research. There is little knowledge on the microbiome in ((pre)malignant) conditions of the vulvar skin.

Objective: This systematic review aims to provide an overview of the literature regarding the microbiome composition of the healthy vulvar skin and in (pre)malignant vulvar disease.

Methods: This study was performed according to the PRISMA statement guidelines and registered in PROSPERO. A comprehensive, electronic search strategy was used to identify original research articles (updated February 2021). The main inclusion criteria were research articles using culture-independent methods for microbiome profiling in tissue or swabs of the vulvar region. The main exclusion criteria were systematic reviews, culture-based studies, animal studies and case reports.

Results: Ten articles were included. The bacterial composition of the vulva consists of several genera including Lactobacillus, Corynebacterium, Staphylococcus and Prevotella, suggesting that the microbiome composition of the vulva shows similarities with the corresponding vaginal milieu. However, the vulvar microbiome generally displayed higher diversity with commensals of cutaneous and fecal origin, giving the vulva a distinctive signature.

Conclusion: This is the first systematic review that investigates the relationship between microbiome and vulvar (pre) malignant disease. We found that there is limited knowledge available, and that the level of evidence is low. There are limitations in study size, population diversity and sequencing methodology. Nevertheless, the vulvar microbiome represents a promising field for exploring potential links for disease etiology and targets for therapy.

P18 - RESULTS OF A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED CLINICAL TRIAL WITH KETOCONAZOLE AND PLACEBO IN SEBORRHEIC DERMATITIS.

J. Rousel^{1,2}, L. Pagan¹, A. Nädäban², M. Saghari¹, T. Niemeyer-van der Kolk¹, T. Gambrah¹, M. de Kam¹, J. Burggraaf^{1,4}, M.B.A. van Doorn^{1,3}, J.A. Bouwstra², R. Rissmann^{1,2}

1) Centre for Human Drug Research, Leiden, The Netherlands; 2) Division of BioTherapeutics, Leiden Academic Centre for Drug Research, Leiden University, Leiden, The Netherlands; 3) Erasmus Medical Center, Rotterdam, The Netherlands; 4) Division of Systems Biomedicine and Pharmacology, Leiden Academic Centre for Drug Research, Leiden University, Leiden, The Netherlands.

Background: Seborrheic dermatitis (SD) is an immunological dermatological disease affecting mainly the scalp and face. While the root cause of the disease is an aberrant immunological response in the skin, dysfunctional cutaneous barrier function and colonization by the pathogenic yeast *Malassezia* are implicated in its pathogenesis.

Objective: Establishing a comprehensive understanding of disease using an established treatment in combination with multimodal assessments.

Methods: Mild-to-moderate SD patients were treated with the standard of care ketoconazole (n=12) or placebo (n=12) twice daily over 4 weeks. Conventional clinical scoring was complemented by several non-invasive and novel readouts such as optical coherence tomography, skin barrier measurements, superficial barrier markers and the cutaneous micro- and mycobial composition.

Results: In patients randomized to ketoconazole a significant decrease ($p < 0.01$) was observed in all clinical scores such as the lesion severity score after 4 weeks of treatment compared to the placebo group. This clinical effect was in alignment with a significant decrease in epidermal thickness ($p < 0.05$) and increased skin barrier function ($p < 0.01$). Noteworthy, a baseline increase in the abundance of *Staphylococcus* on lesional skin did not translate into an apparent treatment effect. A significant fungicidal effect was observed in the ketoconazole group based on an increased mycobial diversity index and decreased abundance of *Malassezia*.

Conclusion: The results indicate that the antifungal properties of ketoconazole are inducing disease regression and highlight the pathogenic importance of *Malassezia* in SD. Our comprehensive methodology to assess dermatological conditions is promising for use in clinical development of therapies for SD and other dermatoses.

P19 - PRIMARY MELANOMA CHARACTERISTICS OF METASTATIC DISEASE: A NATIONWIDE CANCER REGISTRY STUDY.

C. Zhou¹, M.W.J. Louwman², M. Wakkee¹, A.M.M. van der Veldt³, D.J. Grünhagen⁴, C. Verhoef⁴, A.L. Mooyaart⁵, T.E.C. Nijsten¹, L.M. Hollestein^{1,2}

1) Department of Dermatology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands; 2) Department of Research and Development, Netherlands Comprehensive Cancer Organization, Utrecht, The Netherlands; 3) Department of Medical Oncology and Radiology & Nuclear Medicine, Erasmus MC Cancer Institute, Rotterdam, The Netherlands; 4) Department of Surgical Oncology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands; 5) Department of Pathology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands.

Background: In most studies on disease progression of melanomas, the progression pattern is not described in relationship to patient- and tumour characteristics. It is essential to gain more insight into this pattern based on primary tumour- and patient characteristics, to be able to identify patients with early-stage cutaneous melanoma who are at high risk for progression.

Objective: Our aim was to investigate the characteristics and disease patterns of primary stage I and II cutaneous melanomas that progress to stage III or IV disease based on data from the Netherlands Cancer Registry (NCR). Methods Data on stage III or IV melanomas at first diagnosis or during follow-up between 2017 and 2019 were retrieved. Patient and primary tumour characteristics were investigated in relation to time to disease progression and the number of organ sites with metastatic disease using regression models.

Results: In total, 2763 patients were included, of whom 1613 were diagnosed with stage IV disease. Among the patients with stage IV disease, 60% (n = 963) were initially diagnosed with stage I or II disease. Among patients with stage IV disease, lung metastases were most often detected as the first metastatic site and females presented with more metastatic sites than males. Most patient and primary tumour characteristics were not associated with the distant metastatic organ site, except melanoma localisation in the lower extremities and the head or neck.

Conclusion: Our observation that most stage IV patients were initially diagnosed with early-stage disease highlights the need for more accurate risk prediction models.

P20 - NATIONWIDE DATA ON PATIENT PROFILES AND PATTERNS OF CARE OF PATIENTS WITH ADVANCED CUTANEOUS SQUAMOUS CELL CARCINOMA IN THE NETHERLANDS.

R.E. Achten¹, C.M. van Luijk², D.S. Bakker¹, N.P.A. Zuithoff¹, M. de Graaf¹, F. van Wijk³, M.M. van der Wal³, J.L. Thijs¹, J.H. de Boer², M.S. de Bruin-Weller¹

1) Department of Dermatology and Allergology, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht, Utrecht, The Netherlands; 2) Department of Ophthalmology, University Medical Center Utrecht, Utrecht, The Netherlands; 3) Center for Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands.

Background: The Netherlands Cancer Registry (NCR) registers the incidence of cutaneous squamous cell carcinoma (cSCC), but nationwide longitudinal data on advanced cSCC (i.e. locally advanced, recurrent and metastatic) is lacking, but highly needed to improve patient care.

Objective: To develop a nationwide longitudinal registry of cSCC.

Methods: From the nationwide pathology database (PALGA), patients with advanced cSCC in 2018/2019 were identified based on PALGA codes and free text. After linkage with the NCR, follow-up records of 204 patients were registered. Data on patient characteristics, tumor characteristics and treatment of advanced cSCC were retrieved from the electronic patient records by registrars.

Results: We included 204 patients with advanced cSCC of which 159 presented with an advanced primary cSCC and 45 patients who presented with stage I/II cSCC and progressed during follow-up. Of the 159 advanced primary cSCCs, 102 had high risk features, such as invasion depth >6 mm (16%), invasion beyond the subcutaneous fat (21%) or perineural invasion (28%). A total of 132 patients underwent surgical excision of

the primary tumor of which 33 (25%) had positive final margins. Three of those patients (9%) were directly treated with adjuvant radiotherapy. In total, 107 out of 204 patients with advanced cSCC developed disease progression (29 local recurrences, 49 regional nodal metastasis and 29 distant metastasis) after a median of 216 days.

Conclusion: The results of this nationwide registry will be used to identify opportunities to improve patient care and develop prediction models for the prognosis of advanced cSCC patients.

P21 - A PATIENT DECISION AID FOR PATIENTS WITH A SUPERFICIAL BASAL CELL CARCINOMA: HYPE OR VALUABLE?

Lieke C.J. van Delft^{1,2}, Brigitte A.B. Essers³, Patty J. Nelemans⁴, Klara Mosterd^{1,2}, Marieke van Winden⁵, Ine Romaen⁶, Sean Retra⁵, Aimee H.M.M. Arits^{1,6}, Peter S. Steijlen^{1,2}, Satish F.K. Lubeek⁵, Nicole W.J. Kelleners-Smeets^{1,2}

1) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; 2) GROW Research Institute for Oncology and Developmental Biology, Maastricht University, The Netherlands; 3) Department of Clinical Epidemiology & Medical Technology Assessment, Maastricht University Medical Center+, Maastricht, The Netherlands; 4) Department of Epidemiology, Maastricht University, Maastricht, The Netherlands; 5) Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; 6) Department of Dermatology, Catharina Hospital, Eindhoven, The Netherlands.

Background: Patients with a superficial basal cell carcinoma (sBCC) may choose between several treatment options with different advantages and disadvantages. A patient decision aid (PDA) might facilitate in making a personalized decision.

Objective: This study evaluates whether the use of a PDA results in a decreased level of decisional conflict, improved satisfaction with the treatment decision, and increased knowledge on prevention, recognition of BCC, and treatment options.

Methods: A prospective multicentre pre- and post-implementation study was performed amongst patients with a newly diagnosed sBCC to compare a group that did not use the PDA with a group that did. The primary outcome was the level of decisional conflict measured by the total mean score on the 'decisional conflict scale' (DCS) before treatment. Knowledge of disease and treatment options was also evaluated.

Results: 120 patients were included before implementation of the PDA, and 155 patients after implementation. The results of this study will be discussed during the NVED meeting.

Conclusion: The conclusion of this study will be discussed during the NVED meeting.

P22 - DISCOVERY OF ARTHRITIS IN PSORIASIS FOR EARLY RHEUMATOLOGIC REFERRAL (DAPPER): A CROSS-SECTIONAL STUDY.

T.W. van Hal¹, M.L.M. Mulder¹, M.H. Wenink¹, M.C. Pasch², J.M.P.A. van Reek², E.M.G.J. de Jong²

1) Department of Rheumatology, Sint Maartenskliniek, Nijmegen, The Netherlands; 2) Department of Dermatology, Radboudumc, Nijmegen, The Netherlands.

Background: One in three patients with psoriasis (Pso) will develop psoriatic arthritis (PsA). When untreated, this can lead to irreversible joint damage. Current screening methods aimed at discovering PsA in psoriasis patients are based on questionnaires, but these lack specificity and sensitivity. Thus, a portion of PsA patients remains undetected.

Objective: Our main objective was to ascertain the prevalence of PsA in a large Pso cohort at a dermatology outpatient clinic. Secondary, we examined clinical characteristics which may help the dermatologist to discover the presence of PsA.

Methods: Pso patients, stratified for current skin therapy (topical, systemic non-biologic, biologic), were screened by a rheumatology resident for PsA signs and symptoms. When PsA was suspected, patients were referred to a rheumatology center for confirmation. Clinical characteristics were gathered at the screening visit.

Results: 303 patients with Pso were included, of which 79 (26.1%) also had PsA. When compared to patients with only Pso, Pso+PsA patient more often had physical trauma in the past year (Pso vs PsA: 33 vs 37%), or dithranol therapy (82 vs 86%, 34 vs. 41%), nail psoriasis (65 vs. 82%), and a lower age of onset of skin disease (30.0 vs 25.6 years), UV. Notably, body mass index, family history or presence of Koebner phenomenon did not differ between Pso and Pso+PsA patients.

Conclusion: Several disease related markers, such as age of onset nail disease, are associated with the presence of PsA in Pso patients. We will use these results to develop a referral tool for dermatologists.

P23 - DRUG SURVIVAL AND TOLERABILITY OF BIOLOGICS IN OLDER ADULT PATIENTS WITH PSORIASIS, A COMPARISON WITH YOUNGER PATIENTS.

E.L.M. ter Haar^{1,2}, S.E. Thomas^{1,2}, J.M.M. Groenewoud^{2,3}, M.E. Otero^{1,2}, M.D. Njoo⁴, P.M. Ossenkuppe⁴, E.N. Kop⁵, S. Dodemont⁶, J.E.M. Körver⁷, A.L.A. Kuijpers⁸, R.J. Lindhout⁹, R.A. Tupker¹⁰, J.M. Mommers¹¹, M.A.M. Berends¹², M.I.A. Koetsier¹³, M.S. de Bruin-Weller¹⁴, B. Visch¹⁵, W.P. Arnold¹⁶, P.P. van Lümig¹⁷, M.M. Kleinpenning¹⁸, J.M.P.A. van den Reek^{1,2}, E.M.G.J. de Jong^{1,2,19}, S.F.K. Lubeek^{1,2}

1) Department of Dermatology, Radboud University Medical Center (Radboudumc), Nijmegen, The Netherlands; 2) Radboud Institute for Health Sciences (RIHS), Radboudumc, Nijmegen, The Netherlands; 3) Department for Health Evidence, Radboudumc, Nijmegen, The Netherlands; 4) Department of Dermatology, Ziekenhuisgroep Twente, Almelo/Hengelo, The Netherlands; 5) Department of Dermatology, Bernhoven Ziekenhuis, Uden, The Netherlands; 6) Department of Dermatology, Catharina Ziekenhuis, Eindhoven, The Netherlands; 7) Department of Dermatology, Amphia Ziekenhuis, Breda, The Netherlands; 8) Department of Dermatology, Máxima Medisch Centrum, Eindhoven, The Netherlands; 9) Department of Dermatology, Jeroen Bosch Ziekenhuis, 's Hertogenbosch, The Netherlands; 10) Department

of Dermatology, St Antonius Ziekenhuis, Nieuwegein, The Netherlands; 11) Department of Dermatology, St Anna Ziekenhuis, Geldrop, The Netherlands; 12) Department of Dermatology, Slingeland Ziekenhuis, Doetinchem, The Netherlands; 13) Department of Dermatology, Gelre Ziekenhuizen, Apeldoorn, The Netherlands; 14) Department of Dermatology, Utrecht Medisch Centrum, Utrecht, The Netherlands; 15) Department of Dermatology, Ziekenhuis Rijnstate, Arnhem, The Netherlands; 16) Department of Dermatology, Ziekenhuis Gelderse Vallei, Ede, The Netherlands; 17) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; 18) Department of Dermatology, Canisius-Wilhelmina Ziekenhuis, Nijmegen, The Netherlands; 19) Radboud University, Nijmegen, The Netherlands.

Background: Psoriasis is a common inflammatory disease that also affects older adults (>65 years). Since older adults are often excluded from clinical trials, only little data regarding safety and effectiveness is available in this growing patient group.

Objective: With this observational study we aim to give insight in the drug survival and tolerability of biologics in older adults with psoriasis.

Methods: Data were extracted from the prospective BioCAPTURE-registry. Patients were divided into two age groups: >65 and <65 years. Reasons of treatment discontinuation were analysed using Kaplan–Meier survival curves. All adverse events (AEs) that led to discontinuation were classified in categories according to the MedDRA classification system, and described per age group.

Results: A total of 890 patients were included, of which 102 (11.4%) were >65 years. BMI, gender, and distribution of biologic classes (e.g. TNF α , IL12-23) were not significantly different between age groups. Five-year overall drug survival for all biologics combined was 32.4% in older patients versus 42.1% in younger patients (Log-Rank test, $p=0.144$). Regarding discontinuation due to ineffectiveness, drug survival was lower for older than for younger patients (44.5% vs. 60.5%; Log-Rank test, $p=0.006$). Discontinuation due to AEs was low in both groups and mostly due to infections. AE related drug survival rates were 82.1% vs. 79.5% (Log-Rank-test, $p=0.913$).

Conclusion: In this cohort, older patients were found to discontinue their biologic earlier due to ineffectiveness, compared to younger patients. Reassuringly, in older patients, discontinuation of biologics due to AEs was low and comparable to a younger population.

P24 - A NATION-WIDE STUDY TO DETERMINE THE TUMOUR PROFILE AND RISK IN PATIENTS WITH THE CDKN2A MUTATION.

Y.P.M. Hoogland¹, T.P. Potjer², E.I. Plasmeijer^{1,3}, A.M.R. Schrader⁴, R. van Doorn¹

1) Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; 2) Department of Clinical Genetics, Leiden University Medical Center, Leiden, The Netherlands; 3) Department of Dermatology, Netherlands

Cancer Institute Antoni van Leeuwenhoek, Amsterdam, The Netherlands; 4) Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands.

Background: Familial atypical multiple mole melanoma (FAMMM) syndrome is a hereditary cancer syndrome caused by germline mutations in the CDKN2A gene. Patients with this mutation have an approximate 70% life-time risk of developing melanoma and a 20% risk of pancreatic cancer. Several smaller studies have pointed at increased risk of other cancer types, including head and neck cancer, but the exact tumour spectrum and risk profile of these patients is unclear.

Objective: To evaluate the occurrence of malignant tumours in established carriers of pathogenic CDKN2A mutations in a nation-wide study. With the outcome we intend to make recommendations for surveillance to improve early diagnosis and prevention of additional tumour types patients with this condition.

Methods: An observational retrospective study analysing data from 700 patients with genetically confirmed CDKN2A mutation, provided by the pathological anatomy national automated archive (PALGA). Statistical analysis was performed to determine the relative incidence of the different tumor types, the age of onset and patient survival.

Results: In addition to melanoma and pancreatic cancer, patients with FAMMM syndrome due to CDKN2A mutation are at increased risk to develop head and neck cancer, lung cancer and breast cancer. Our results also suggest an increased prevalence of other types of cancer such as stomach cancer and sarcoma.

Conclusion: The excess risk of multiple tumour types could signify that carriers of germline CDKN2A mutations might benefit from more extensive oncological surveillance using imaging or endoscopy.

P25 - CUMULATIVE INCIDENCE AND RISK FACTORS FOR CUTANEOUS SQUAMOUS-CELL CARCINOMA METASTASES IN ORGAN TRANSPLANT RECIPIENTS: THE SCOPE-ITSCC METASTASES STUDY.

Estella de Jong, Roel Genders, Jan Nico Bouwes Bavinck
Department of Dermatology, Leiden University Medical Center (LUMC), Leiden, The Netherlands.

Background: Organ transplant recipients (OTR) have an increased risk of cutaneous squamous cell carcinoma (cSCC). Metastases of cSCC can occur, however reliable data in OTR are still missing. Also, little is known about the cSCC metastatic risk of specific immunosuppressive regimens relative to each other.

Methods: Between 2013 and 2018, patient, tumor and treatment characteristics were registered in a standardized questionnaire when OTR visited the outpatient clinic with a cSCC. Two years after diagnosis, the clinical outcome of the cSCC was recorded. Cumulative incidence of metastases were calculated by Kaplan Meier analyses. Multivariable Cox proportional hazard analyses were used for determining risk factors for metastases.

Results: A total number of 514 OTR with 623 primary cSCCs were included in 19 centers. 37 OTR developed metastases with a 2-year patient-based cumulative incidence of 6.2%, whereas in the general population this percentage ranges between 2 and 4%. Well-known clinical and histological risk factors for metastases were confirmed. Drug regimens with tacrolimus alone were associated with a 4.5 (95% CI: 1.7;11.6), mTOR inhibitors alone with a 4.5 (95% CI: 1.2-16.9) and the combination of tacrolimus and mTOR inhibitors with a 8.5 (95% CI: 2.8;26.2) increased risk of cSCC metastases.

Conclusion: OTR have an increased risk of cSCC metastases. These results suggest that immunosuppressive therapy with tacrolimus is associated with cSCC metastases. Conversion to mTOR inhibitors did not decrease this risk and it cannot be excluded that mTOR inhibitors by themselves are also responsible for an increased cSCC metastases risk.

P26 - PREDICTORS FOR RECURRENCE, METASTASIS AND MORTALITY IN PRIMARY CUTANEOUS SQUAMOUS CELL CARCINOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Anna A.J.H. Zwanenburg^{1,2}, Thomas Boere³, Winan J. van Houdt², Michel W. Wouters², Elsemieke Plasmeijer¹

1) Department of Dermatology, The Netherlands Cancer Institute, Amsterdam, The Netherlands; 2) Department of Surgical Oncology, The Netherlands Cancer Institute, Amsterdam, The Netherlands; 3) Department of Head and Neck Surgery, The Netherlands Cancer Institute, Amsterdam, The Netherlands.

Background: The incidence of cutaneous squamous cell carcinoma (cSCC) is increasing worldwide. Determining which cSCC are aggressive is necessary to assign more rigorous therapy and follow-up to those patients that need it.

Objective: To perform a systematic review and meta-analysis of published studies on predictors in patients with primary cSCC lesions on the outcomes recurrence free survival (RFS), metastasis free survival (MFS), disease specific survival (DSS) or overall survival (OS).

Methods: A systematic search of multiple databases was performed. Studies with at least 10 adult patients with primary cSCC were included. Meta-analysis was performed through a random-effects model of reported hazard ratio's.

Results: 49 studies were included. Most important predictors for RFS were: diameter >20mm (pHR; 3.16, 2.12–4.69), tumor thickness >6mm (pHR; 2.58, 1.18–5.65), invasion beyond subcutaneous fat (pHR; 4.74, 1.95–11.50), perineural invasion (pHR; 2.94, 1.92–4.52), lymphovascular invasion (pHR; 2.88, 1.75–4.73), and poor differentiation (pHR; 5.13, 1.81–14.55). For MFS: diameter >20mm (pHR; 4.65, 2.51–8.61), thickness >6mm (pHR; 4.27, 2.61–6.97), invasion beyond subcutaneous fat (pHR; 9.46, 4.88–18.33), perineural invasion (pHR; 5.84, 3.73–9.14), lymphovascular invasion (pHR; 3.82, 1.52–9.59), poor differentiation (pHR; 10.89, 3.45–34.35), and location on the ear (pHR; 3.20, 2.00–5.12). For DSS: invasion beyond subcutaneous fat (pHR; 6.18, 1.74–21.95), lymphovascular invasion (pHR; 2.97, 1.47–6.01), and immunosuppression (pHR; 2.75, 2.04–3.71). For OS immunosuppression was the most important predictor

(pHR; 2.58, 1.74–3.81).

Conclusion: Tumor diameter, tumor thickness, invasion beyond the subcutaneous fat, perineural invasion and poor differentiation were the most important predictors for RFS and MFS. For DSS, the most important predictor was invasion beyond the subcutaneous fat.

P27 - IMPLEMENTATION OF A TIGHTLY CONTROLLED DOSE REDUCTION STRATEGY OF ADALIMUMAB, ETANERCEPT AND USTEKINUMAB FOR PSORIASIS IN DAILY CLINICAL PRACTICE: A PILOT STUDY.

L.S. van der Schoot^{1,2}, M.T. Bastiaens³, A. de Boer-Brand⁴, C. Christiaansen-Smit³, D.N.H. Enomoto⁵, R. Hovingh³, R.A. Tupker⁴, J.M.P.A. van den Reek^{1,2}, E.M.G.J. de Jong^{1,6}

1) Department of Dermatology, Radboud University Medical Center, Nijmegen, The Netherlands; 2) Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, The Netherlands; 3) Department of Dermatology, Elisabeth-TweeSteden Ziekenhuis, Tilburg, The Netherlands; 4) Department of Dermatology, St Antonius Ziekenhuis, Nieuwegein, The Netherlands; 5) Department of Dermatology, Dermatologisch Centrum Isala, Zwolle, The Netherlands; 6) Radboud University, Nijmegen, The Netherlands.

Background: Dose reduction (DR) of biologics for psoriasis patients seems a promising way for more efficient use. For further implementation of DR, evaluation of implementation itself is needed. **Objective:** We propose a pilot implementation strategy, in order to guide dermatologists and psoriasis patients towards DR of adalimumab, etanercept, and ustekinumab.

Methods: A pilot implementation study will be performed in 3 general hospitals. The pilot consists of 1) testing the implementation strategy focusing on feasibility, and 2) effect evaluation of the implemented biologic DR strategy. A multicomponent implementation strategy was developed, consisting of 4 meetings and development of local protocols. DR is aimed at patients with stable low disease activity on adalimumab, etanercept and ustekinumab in a standard dose, and is achieved by interval prolongation in 2 steps (decrease of 33% and 50% of the standard dose) when disease activity (PASI) and impact on quality of life (DLQI) remain low (scores ≤5). Process evaluation of the implementation strategy will be performed focusing on barriers and facilitators. Effect evaluation of DR outcomes will be performed after 6 months. Outcomes will be collected retrospectively and analysed using descriptive statistics.

Results: All participating hospitals started with the implementation of the DR strategy in July 2021. Evaluation will take place after 3 and 6 months. At the NVED Annual Meeting 2022, first preliminary results will be presented.

Conclusion: Results of this pilot might contribute to further implementation of biologic DR in national daily practice.

P28 - DAILY PRACTICE EXPERIENCE OF BARICITINIB IN PATIENTS WITH MODERATE TO SEVERE ATOPIC DERMATITIS: A 16-WEEK EVALUATION OF CLINICAL EFFICACY AND SAFETY.

C.M. Boesjes¹, M. Poelhekkens², M. de Graaf¹, M.L.A. Schuttelaar², M.S. de Bruin-Weller¹

1) Department of Dermatology and Allergology, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht, Utrecht, The Netherlands; 2) Department of Dermatology, University of Groningen, University Medical Center Groningen, The Netherlands.

Background: Baricitinib, an oral selective Janus kinase 1/2 inhibitor, is one of the new advanced systemic treatments for moderate to severe atopic dermatitis (AD). Clinical trials showed that baricitinib effectively reduces AD symptoms, however daily practice data are lacking.

Objective: To assess clinical efficacy and safety of baricitinib in patients with moderate to severe AD after 16-week treatment in daily practice.

Methods: Patients with moderate to severe AD treated with baricitinib were included from the BioDay registry, a prospective multicenter registry. Clinical response was defined by achieving EASI-50 (Eczema Area and Severity Index), EASI-75 or IGA-clear/almost clear (Investigator Global Assessment), as well as patient reported outcome measures (PROMs). Side effects during baricitinib treatment were evaluated and laboratory tests were performed at baseline and after 4, 8 and 16 weeks (blood count, liver enzymes, serum creatinine, creatinine kinase, lipid status, TARC).

Results: The results of approximately 40 patients will be presented. Almost 50% of the patients failed on dupilumab treatment. In total, 11 (27.5%) patients discontinued treatment due to ineffectiveness or side effects (53.6% vs. 36.4%). Preliminary results based on 15 patients show a median percentage change in EASI at week 16 of 46%. EASI-50 was achieved by 9 patients (60%), EASI-75 by 2 patients (13.3%) and an IGA-clear/almost clear by 4 patients (26.7%). Secondary outcomes relate to the PROMs and safety analysis.

Conclusion: Efficacy of baricitinib showed to be heterogeneous in our cohort. Approximately one third discontinued treatment due to side effects or ineffectiveness. Safety analysis showed no new findings.

P29 - NATURAL MOISTURIZING FACTOR AS A CLINICAL MARKER IN ATOPIC DERMATITIS.

A.E.M. Nouwen², D. Karadavut², S.G.M.A. Pasmans², N.J. Elbert¹, L.D.N. Bos¹, T.E.C. Nijsten¹, N.J.T. Arends³, M.W.H. Pijnenburg³, S. Koljenović⁵, G.J. Puppels^{4,6}, P.J. Caspers^{4,6}

1) Department of Dermatology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands; 2) Department of Dermatology, Erasmus MC-Sophia Children's Hospital-Kinderhaven, Rotterdam, The Netherlands; 3) Department of Pediatrics, Paediatric Respiratory Medicine and Allergology, Erasmus MC-Sophia Children's Hospital-Kinderhaven, Rotterdam, The Netherlands; 4) Center for Optical Diagnostics

and Therapy, Department of Dermatology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands; 5) Department of Pathology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands; 6) RiverD International B.V., Rotterdam, The Netherlands. *These authors contributed equally.

Background: A decreased Natural Moisturizing Factor (NMF) concentration in the stratum corneum is a phenotypic marker for filaggrin (FLG) null mutations, which have been linked to early-onset atopic dermatitis (AD) with a more severe disease course. To date, NMF has not been used for stratification of AD-patients.

Objective: We aimed to examine the association of NMF values with several clinical parameters in children, among which disease severity, onset of AD \leq 6 months, food allergy, asthma, and allergic rhinitis.

Methods: We conducted a retrospective, single-center study in AD patients between 0 and 18 years. NMF values in the palmar stratum corneum were measured in vivo using Raman spectroscopy. Clinical parameters were obtained retrospectively from electronic patient files. Univariate and multivariate logistic regression models were used to examine the associations between binary NMF-value (decreased or normal) and the abovementioned clinical parameters.

Results: 207 patients were included in the analysis. In the logistic regression models adjusted for age and gender decreased NMF values were associated with increased odds for severe AD, 2.12 (95%CI 1.02 - 4.43), sensitization for food allergens, OR 2.27 (95%CI 1.21 - 4.23), sensitization for inhalation allergens, 2.22 (95%CI 1.13 - 4.34) and food allergy, 2.79 (95% CI 1.33 - 5.86).

Conclusion: Clinically measured NMF in the skin is associated with AD disease severity, sensitization for food and inhalation allergens and food allergy. These results support the usability of NMF as a clinical marker for stratification of patients with AD.

P30 - COVID-19 OUTCOMES IN PATIENTS WITH ATOPIC DERMATITIS: RESULTS FROM THE GLOBAL SECURE-AD PHYSICIAN REGISTRY.

A.H. Musters¹, C. Broderick², D. Prieto-Merino^{3,4}, B. Arents⁵, T. Burton⁶, Angela L. Bosma¹, E.F. de Monchy¹, G. Fletcher⁷, C.C. Chi⁸, A.M. Drucker⁹, K. Kabashima¹⁰, D. Wall¹¹, A.D. Irvine¹², P.I. Spuls¹, C. Flohr²

1) Department of Dermatology, Amsterdam UMC, location Academic Medical Center, University of Amsterdam, Amsterdam Public Health, Infection and Immunity, The Netherlands; 2) Unit for Population-Based Dermatology Research, Guy's and St Thomas' NHS Foundation Trust and King's College London, London, UK; 3) Faculty of Epidemiology & Population Health, London School of Hygiene & Tropical Medicine, London, UK; 4) Applied Statistical Methods in Medical Research Group, Universidad Católica San Antonio de Murcia (UCAM), Murcia, Spain; 5) Dutch Association for People with Atopic Dermatitis, Nijkerk, The Netherlands; 6) Independent patient representative; 7) National and

International Skin Registry Solutions (NISR), Charles Institute of Dermatology, University College Dublin, Dublin, Ireland; 8) Department of Dermatology, Drug Hypersensitivity Clinical and Research Center, Chang Gung Memorial Hospital, Taoyuan, Taiwan; 9) Department of Medicine, University of Toronto, Toronto, Canada; Women's College Research Institute, Women's College Hospital, Toronto, Canada; 10) Department of Dermatology, Kyoto University Graduate School of Medicine, Kyoto, Japan; 11) National and International Skin Registry (NISR) Solutions, UCD Charles Institute of Dermatology, Dublin, Ireland; 12) Clinical Medicine, Trinity College Dublin, Ireland.

Background: The effect of Coronavirus Disease 2019 (COVID-19) on patients with atopic dermatitis (AD) treated with systemic immunomodulatory treatments is unknown.

Objective: to investigate the impact of COVID-19 on AD patients and how systemic immunomodulatory treatments affect COVID-19 outcomes.

Methods: Healthcare providers were encouraged to report all cases of COVID-19 in their AD patients in the web-based Surveillance Epidemiology of Corona Virus (COVID-19) Under Research Exclusion for Atopic Dermatitis (SECURE-AD) database.

Results: 402 patients (mean age 36.7 years, 52.2% male) from 24 countries were registered. Of these patients 49.2% received dupilumab monotherapy, 17.9% received conventional immunomodulatory treatments, 2.5% received dupilumab combination therapy (mostly with systemic corticosteroids) and 29.4% were treated with topical treatments only. No deaths were reported and 5.5% were hospitalized. Patients treated with any systemic immunomodulatory treatment had a lower odds of hospitalization, compared to those treated with topical medications (OR 0.57, 95% CI 0.24 to 1.43), but this difference was not statistically significant, including after adjustment for confounding variables. Dupilumab combination therapy was associated with an increased risk of hospitalization (OR 10.22, 95% CI 0.41 – 167.70) and A&E attendance (OR 2.52, 95% CI 0.36 – 13.03), compared to dupilumab monotherapy. Dupilumab monotherapy had significantly lower odds of A&E attendance (OR 0.32 95% CI 0.13–0.85), compared to conventional immunomodulatory treatments.

Conclusion: overall risk of COVID-19 complications appears to be low in AD patients treated with systemic immunomodulatory treatments. Patients treated with dupilumab combined with another systemic immunomodulatory treatment, most frequently systemic corticosteroids, had higher rates of hospitalization.

P31 - ASSOCIATION OF FRAILTY AND LIFE EXPECTANCY WITH GUIDELINE DEVIATION AND CLINICAL OUTCOME, INCLUDING QUALITY OF LIFE IN ELDERLY PATIENTS WITH CUTANEOUS SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK.

Alet J.G. Leus¹, Marjolijn S. Haisma¹, Jorrit B. Terra¹, Grigory Sidorenkov², Suzanne Festen³, Boudewijn E.C. Plaat⁴, Gyorgy B. Halmos⁴, Ernöke Rácz¹

1) University of Groningen, University Medical Center

Groningen, Department of Dermatology, Groningen, The Netherlands; 2) University of Groningen, University Medical Center Groningen, Department of Epidemiology, Groningen, The Netherlands; 3) University of Groningen, University Medical Center Groningen, Department of Geriatric Medicine, Groningen, The Netherlands; 4) University of Groningen, University Medical Center Groningen, Department of Otorhinolaryngology, Head and Neck Surgery, Groningen, The Netherlands. *These authors contributed equally.

Background: Frailty and life expectancy are not reflected by current treatment guidelines in patients with cutaneous squamous cell carcinoma of the head and neck (cSCCHN). Treatment in this region might influence quality of life (QoL). Objectives: To evaluate the influence of frailty and life expectancy on treatment decisions and treatment outcomes such as complications, progression of disease and QoL after treatment of patients with cSCCHN.

Methods: Patients with cSCCHN were prospectively included. Frailty, dependency, mobility and QoL using the Basal and Squamous cell carcinoma Quality of Life (BaSQoL) were assessed at three time points. Life expectancy and comorbidities were assessed at diagnosis.

Results: Will be discussed.

Conclusion: Treatment deviation can be considered in frail patients with a limited life expectancy.

P32 - TOPICAL BIMIRALISIB, A DUAL PAN-CLASS PI3K/MTOR INHIBITOR, SHOWS MEANINGFUL CUTANEOUS DRUG LEVELS IN HEALTHY VOLUNTEERS AND MYCOSIS FUNGOIDES PATIENTS BUT NO CLINICAL ACTIVITY.

Selinde S. Wind^{1,3}, Manon A.A. Jansen¹, Melanie Rijsbergen¹, Michiel J. van Esdonk¹, Dimitrios Ziagos, Wieresh Balak¹, Wingchi Cheng¹, Tessa Niemeijer-van der Kolk¹, John Korsten⁸, Debora Schmitz-Rohmer⁵, David Bonnel², Raphael le Gouffe², Florian Barré², Marcel Bekkenk⁶, Ellen de Haas⁷, Koen D. Quint³, Melanie Rolli⁴, Henk Johan Streefkerk⁴, Jacobus Burggraaf^{3,5}, Maarten H. Vermeer³, Robert Rissmann^{1,3,5}

1) Centre for Human Drug Research, Leiden, The Netherlands; 2) Imabiotech, MS Imaging department, Lille, France; 3) Leiden University Medical Center, Leiden, The Netherlands; 4) PIQUR Therapeutics AG, Basel, Switzerland; 5) Leiden Academic Center for Drug Research, Leiden University, The Netherlands; 6) Amsterdam University Medical Centers, Amsterdam, The Netherlands; 7) Erasmus Medical Center, Rotterdam, The Netherlands; 8) Charles River Laboratories, The Netherlands.

Background: Mycosis fungoides (MF) is a subtype of CTCL with a low incidence and high medical need for novel treatments.

Objective: to evaluate safety, efficacy, cutaneous and systemic pharmacokinetics (PK) of topical bimiralisib in healthy volunteers (HV) and MF patients.

Methods: In this randomized, placebo-controlled, double-blinded, first-in-human trial a total of 6 HVs and 19 early-stage MF patients were treated with 2.0% bimiralisib gel and/or

placebo. Drug efficacy was assessed by the CAIS score, supported by objective measuring methods to quantify lesion severity. PK blood samples were collected frequently and in the MF patients cutaneous PK was investigated in skin punch biopsies at the last day of treatment.

Results: Local distribution of bimiralisib in HVs showed a mean exposure of 2.54 µg/g in the epidermis. A systemic concentration was observed after application of a target dose of 2 mg/cm² on 400cm², with a mean Cavg of 0.96 ng/mL. Systemic exposure of bimiralisib was reached in all treated MF patients and normalized plasma concentrations showed a 144% increased exposure compared to HV, with an observed mean Cavg of 4.49 ng/mL and a mean cutaneous concentration of 5.3 µg/g. In general, the treatment was well tolerated in terms of local reactions as well as systemic adverse events.

Conclusion: topical bimiralisib treatment leads to meaningful cutaneous drug levels, well-tolerated systemic drug exposure in MF patients and a lack of clinical efficacy, in need of further exploration due to numerous unknown factors, before amortization of topical bimiralisib as a novel therapeutic drug for CTCLs.

P33 - AGE-RELATED DIFFERENCES IN TUMOR CHARACTERISTICS AND PROGNOSTIC FACTORS FOR DISEASE PROGRESSION IN CUTANEOUS SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK.

Alet J.G. Leus¹, Marjolijn S. Haisma¹, Jorrit B. Terra¹, Gilles F.H. Diercks⁴, Marloes S. van Kester¹, Gyuri B. Halmos³, Emöke Rác², Boukje A.C. van Dijk^{2,5}, Boudewijn E.C. Plaat³

1) University of Groningen, University Medical Center Groningen, Department of Dermatology, Groningen, The Netherlands; 2) University of Groningen, University Medical Center Groningen, Department of Epidemiology, Groningen, The Netherlands; 3) University of Groningen, University Medical Center Groningen, Department of Otorhinolaryngology, Head and Neck Surgery, Groningen, The Netherlands; 4) University of Groningen, University Medical Center Groningen, Department of Pathology, Groningen, The Netherlands; 5) Department of Research and Development, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, The Netherlands.

Background: Guidelines for cutaneous squamous cell carcinoma of the head and neck (cSCCHN) do not take the age of the patient into account, assuming equal tumour characteristics and prognostic factors for poor outcome in younger and elderly patients. We hypothesized that cSCCHNs in elderly patients might have different characteristics from tumors in younger patients.

Objective: To compare tumor characteristics of younger (<75 years) and elderly (≥75 years) patients and identify age-specific risk factors for progression of disease (POD), comprising local recurrence, nodal metastasis and distant metastasis.

Methods: Patient and tumor characteristics were compared using a chi-squared or Fisher's exact test. Multivariable competing risk analyses were performed to compare risk factors for POD, incorporating the risk of dying before developing POD.

Results: Will be discussed.

Conclusion: High-risk tumor characteristics and POD are more common in elderly patients. Risk factors for POD differ between younger and elderly patients. It needs to be evaluated in future studies whether these differences are due to a diagnostic delay or represent true biological differences.

P34 - ALITRETINOIN AS ALTERNATIVE TREATMENT FOR INHERITED DISEASES OF KERATINIZATION IN CHILDBEARING AGE WOMEN – A CASE SERIES AND LITERATURE REVIEW.

J.M.K. Clabbers¹, E.J. van Oosten², M. Vreeburg³, M. van Geel^{1,3}, A. Gostyński¹

1) Department of Dermatology, Maastricht University Medical Center+, Maastricht, The Netherlands; 2) Department of Dermatology, Meander Medical Centre, Amersfoort, The Netherlands; 3) Department of Clinical Genetics, Maastricht University Medical Center+, Maastricht, The Netherlands.

Background: Acitretin is the most studied and widely used oral retinoid for inherited disorders of keratinization. Its major disadvantage is the need for contraceptive measures three years after discontinuation. An alternative is needed for women in childbearing age. With alitretinoin, pregnancy is safe one month after discontinuation.

Objective: Share our experience with alitretinoin for inherited disorders of keratinization in women in childbearing age, and review the literature on this subject.

Methods: A case series was performed with patients from our database, currently or previously using alitretinoin for an inherited disorder of keratinization of the skin. The Ichthyosis Area Severity Index and Investigator Global Assessment were used by three independent physicians to score treatment efficacy, based on photo documentation before and after treatment. Statistical analysis was done with a paired samples t-test. To review the current literature about alitretinoin for inherited disorders of keratinization of the skin, a PubMed search was conducted.

Results: Results will be discussed during the meeting.

Conclusion: Alitretinoin is effective to mitigate the symptoms of the inherited keratinization disorders in women in childbearing age, and is a suitable alternative to acitretin.