21th Annual scientific meeting of the Nederlandse Vereniging voor Experimentele Dermatologie 30 and 31 January 2020

Programme

At the 21th annual scientific meeting of the NVED the ongoing scientific research in dermatology in the Netherlands will be presented.

Programme summary

Thursday 30 January 2020

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: Experimental models, therapeutics and co-morbidities in inflammatory disease
11.25	-	12.10	Session II: Insights into melanoma from clinical studies and experimental models
12.10	-	13:15	Lunch
13.15	-	14.00	Guest Lecture by **Prof. dr. Manfred Kayser** (Erasmus MC)
14.00	-	15.15	Session III: Skin microbiome: from association to causality
15.15	-	16.15	Poster and networking session I (with coffee and tea)
16.15	-	17.15	Session IV: Burns, wound healing and regenerative medicine
17.15	-	20.00	Drinks and Dinner
20.00	-	20.45	21th general assembly of the NVED
20.45	-	01.00	Pub Quiz

Friday 31 January 2020

09.00	-	10.00	Session V: Experimental models, therapeutics and co-morbidities in inflammation
10.00	-	11.00	Poster and networking session II, including poster walk and presentation of selected posters (with coffee and tea)
11.00	-	11.40	Guest Lecture by **Prof. dr. Andre Knulst** (UMCU).
11.40	-	12.50	Lunch
12.50	-	14.05	Session VI: Epidemiology and clinical studies of patients with non-melanoma skin cancer
14.05	-	14.20	Break (stretch your legs)
14.20	-	15.05	Session VII: Pathophysiology and diagnosis of blistering skin diseases
15.05	-	15.15	Awards for best presentation and poster; selection breaking news
15.15			Closure

Full programme

THURSDAY 30 JANUARY 2020

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: Experimental models, therapeutics and co-morbidities in inflammatory disease**
Session chairs: Marie-Louise Schuttelaar (*UMCG*), Rosalie Luiten (*Amsterdam UMC*)

1.	Annelie Musters *(Amsterdam UMC)*	Adding methotrexate to adalimumab therapy in psoriasis is a valuable and cheap option to decrease immunogenicity: first year outcomes of a randomized controlled trial.
2.	Finola Bruins *(Radboudumc)*	Time from psoriasis onset until discontinuation of topical therapy and switch to systemic treatment – results from the Child-CAPTURE registry.
3.	Angelique Rondags *(UMCG)*	Identification of clinical categories in hidradenitis suppurativa based on patient characteristics: results from a cluster analysis.
4.	Jade Logger *(Radboudumc)*	Value of reflectance confocal microscopy for monitoring Demodex, inflammation and vascularity in rosacea patients using topical ivermectin.

11.25 - 12.10 **Session II: Insights into melanoma from clinical studies and experimental models**

5.	Elisabetta Michielon *(Amsterdam UMC)*	Microenvironmental cross-talk in an organotypic human melanoma-in-skin model directs M2-like monocyte differentiation via IL-10.
6.	Marcella Willemsen *(Amsterdam UMC)*	Melanoma progression coincides with increased T cell infiltration and PD-1 expression on skin-resident memory T cells.
7.	Darryl Tio *(Amsterdam UMC)*	Patient characteristics and oncogenic mutations of metastasized lentigo maligna melanoma: results from the Dutch Melanoma Treatment Registry.

12.10 - 13:15 **Lunch**

13.15 - 14.00 **Guest Lecture by Prof. dr. Manfred Kayser (*Erasmus MC*) - "CSI Rotterdam: facts no fiction"**

14.00 - 15.15 **Session III: Skin microbiome: from association to causality**
Session chairs: Patrick Zeeuwen (*Radboudumc*), Maaike Waasdorp (*Amsterdam UMC*)

8.	Luba Pardo *(Erasmus MC)*	Composition of cutaneous bacterial microbiome in seborrheic dermatitis patients.
9.	Danique vd Krieken *(Radboudumc)*	Gram-positive anaerobic *cocci* guard epidermal homeostasis by regulating host defense mechanisms.
10.	Minke van Mierlo *(Erasmus MC)*	Spa-typing of the *Staphylococcus aureus* populations from nose and skin in adult patients with atopic dermatitis.
11.	Lin Shang *(Amsterdam UMC)*	Differential influence of *Streptococcus mitis* on host response to metals in reconstructed human skin and mucosa.
12.	Gijs Rikken *(Radboudumc)*	Development of a 3D skin microbiome model to study host-microbe interactions.

15.15 - 16.15 **Poster and networking session I (with coffee and tea)**

P1. Fieke Adan (*MUMC*) - Topical application of glycerol for increasing Penetration depth in diagnosis of basal cell carcinoma with optical coherence tomography.
P2. Melvin Frie (*UMCG*) - Patient-reported quality of life in solid organ transplant recipients with keratinocyte carcinoma.
P3. Marieke van Winden (*Radboudumc*) - Treatment burden in older adults with high-risk basal cell carcinoma.
P4. Christina Yfanti (*CHDR Leiden*) - High treatment adherence in clinical trials with the use of a mobile e-diary application.
P5. Nynke de Vos (*UMCU*) - Incidence rates of pemphigoid diseases, pemphigus diseases, and dermatitis herpetiformis in the Netherlands during the 1991-2018 period.
P6. Vidhya Narayan (*Amsterdam UMC*) - Patients' perspective on current treatments and demand for novel treatments for vitiligo.
P7. Shima Ahmady (*MUMC*) - The effect of four treatment approaches for actinic keratosis on the Quality of Life, assessed by Skindex-29 and AKQoL.
P8. Marcella Willemsen (*Amsterdam UMC*) - Effect of cytokines on PD-L1 expression on melanoma cells and T cell effector function.
P9. Salma Assil (*CHDR Leiden*) - Characterization of skin inflammatory models in healthy volunteers.
P10. Rosalie Baardman (*UMCG*) - IgM-mediated bullous pemphigoid: an enigma.
P11. Elke de Jong (*Radboudumc*) - Medical history of patients with psoriasis treated with apremilast in the Netherlands: interim results from 145 patients in the prospective, multicenter, real-world APRIL study.
P12. Aniek Lamberts (*UMCG*) - Gene expression profile of lesional skin in bullous and nonbullous pemphigoid: an explorative pilot study.
P13. Julie Tutein Olthenius (*MUMC*) - External validation: a clinical prediction model for surgical site infection in dermatologic surgery.
P14. Jart Oosterhaven (*UMCG*) - Interpretability of the Quality Of Life in Hand Eczema Questionnaire (QOLHEQ).
P15. Lisette Prens (*UMCG*) - Hidradenitis Suppurativa has a clear impact on work productivity and activity impairment.
P16. Klaziena Politiek (*UMCG*) - Quality of life, treatment satisfaction and adherence to treatment, in patients with recurrent vesicular hand eczema – a cross sectional study.

P17. Vanya Rossel (*MUMC*) - Genotype-phenotype correlation and effectiveness of ustekinumab in CARD14-associated papulosquamous eruption.
P18. Wouter ten Voorde (*CHDR Leiden*) - Intradermal microneedle delivery compared to subcutaneous administration of adalimumab: pharmacokinetics and pain.
P19. Hanan Rashid (*UMCG*) - European evidence and consensus-based (S3) guideline for the diagnosis and treatment of mucous membrane pemphigoid.
P20. Hanan Rashid (*UMCG*) - Assessment of diagnostic strategy in mucous membrane pemphigoid.
P21. Tamara van Hal (*Radboudumc*) - Discovery of arthritis in psoriasis for early rheumatologic referral (DAPPER): a cross-sectional study.
P22. Frank van Leersum (*MUMC*) - Topical pathogenesis-based therapy in Conradi-Hunermann-Happle syndrome.
P23. Angelique Voorberg (*UMCG*) - Observational study on the effect of Dupilumab on hand eczema in patients with atopic dermatitis: an update.
P24. Noa van den Brink (*Radboudumc*) - 3D human epidermal equivalents for drug positioning: an unbiased approach illustrated by AHR agonists for atopic dermatitis treatment.
P25. Cynthia van Amerongen (*UMCG*) - The expression pattern of N-acetyltransferase 1 in healthy human skin.
P26. Marloes van Muijen (*Radboudumc*) - Personal treatment goals in psoriatic patients with a stable low disease activity.
P27. Estella de Jong (*LUMC*) - The SCOPE-ITSCC Metastases study.

16.15 - 17.15 **Session IV: Burns, wound healing and regenerative medicine**
Session chairs: Magda Ulrich (*Amsterdam UMC*), Sue Gibbs (*Amsterdam UMC*)

13.	H. Ibrahim Korkmaz (*Amsterdam UMC*)	NOX2 expression is increased in keratinocytes after burn injury.
14.	Judith Burm (*Amsterdam UMC*)	Innovation in burn wound treatment - an approach aiming at development and implementation of tissue-engineered, autologous skin constructs.
15.	Feeke Linders (*CHDR Leiden*)	Objective quantification of mean grayscale value using Optical Coherence Tomography in cutaneous wound healing.
16.	Maaike Waasdorp (*Amsterdam UMC*)	Assessing the therapeutic potential of human saliva using in vitro wound healing models.

17.15 - 20.00 **Drinks and Dinner**

20.00 - 20.45 **21th General assembly of the NVED**

20.45 - 01.00 **Pub Quiz**

FRIDAY 31 JANUARY 2020

09.00 - 10.00 **Session V: Experimental models, therapeutics and co-morbidities in inflammation**
Session chairs: Juul van den Reek (*Radboudumc*), Robert Rissmann (*CHDR/LUMC*)

17.	Thomas Buters (*CHDR Leiden*)	Evaluation of the human intradermal LPS challenge model with topical and systemic corticosteroids.
18.	Linde de Wijs (*Erasmus MC*)	Clinical and histopathological characterization of paradoxical head and neck erythema in atopic dermatitis patients treated with dupilumab: a case series.
19.	Jannik Rousel (*CHDR Leiden*)	Altered expression of epidermal enzymes in atopic dermatitis skin is an underlying factor in stratum corneum lipid composition.
20.	Ivo Nagtzaam (*MUMC*)	The clinical and genetic overlap of X-linked ichthyosis with ichthyosis vulgaris in the Dutch population.

10.00 - 11.00 **Poster and networking session II, including poster walk and presentation of selected posters (with coffee and tea)**

11.00 - 11.40 **Guest Lecture by Prof. dr. Andre Knulst (*UMCU*): "New developments in diagnostics and therapy of food allergy"**

11.40 - 12.50 **Lunch**

12.50 - 14.05 **Session VI: Epidemiology and clinical studies of patients with non-melanoma skin cancer**
Session chairs: Marlies Wakkee (*ErasmusMC*), Satish Lubeek (*Radboudumc*)

21.	Selin Tokez (*Erasmus MC*)	Predicting keratinocyte carcinoma in patients with actinic keratosis: development and internal validation of a multivariable risk prediction model.
22.	Eva van Loo (*MUMC*)	Cumulative sum analysis for the learning curve of optical coherence tomography assisted diagnosis of basal cell carcinoma.
23.	Lisa Pagan (*CHDR Leiden*)	External anogenital warts treatment with topical digoxin and furosemide gel: results of a randomized controlled trial.
24.	Babette Verkouteren (*MUMC*)	Molecular testing in metastatic basal cell carcinoma: a case series.
25.	Alet Leus (*UMCG*)	Postoperative radiotherapy for head and neck cutaneous squamous cell carcinoma with microscopic residual disease.

14.05 - 14.20 **Break (stretch your legs)**

14.20 - 15.05 **Session VII: Pathophysiology and diagnosis of blistering skin diseases**
Session chairs: Marieke Bolling (*UMCG*), Antoni Gostynski (*MUMC*)

26.	Farhat Zaheri (*UMCG*)	The autoimmune IgG subclass response defines the IgG deposition pattern in pemphigus patient skin.
27.	Eline Lokermans (*MUMC*)	Expression of hSPCA1 and ultrastructural analysis of the skin before and after laser therapy in Hailey-Hailey disease.
28.	Aniek Lamberts (*UMCG*)	IgE in skin and serum of nonbullous and bullous pemphigoid patients.

15.05 - 15.15 **Awards for best presentation and poster; selection breaking news**

15.15 **Closure**

Meeting Location: Congress hotel '*De Werelt*' | Westhofflaan 2 | 6741 KH Lunteren | T 0318 48 46 41

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Accreditation: The NVDV has awarded 11 points for full participation in this scientific meeting last year; accreditation for 2020 is applied for.

Program committee: Michel van Geel (*MUMC*), Ellen van den Bogaard (*Radboudumc*), Siamaque Kazem (*Amsterdam UMC*), Gilles Diercks (*UMCG*), Luba Pardo (*Erasmus MC*), Walbert Bakker (*Amsterdam UMC*), Judith Thijs (*UMCU*), Abdoelwaheb El Ghalbzouri (*LUMC*)

Jury for presentation prize: Gilles Diercks (*UMCG*), Abdoelwaheb El Ghalbzouri (*LUMC*), Hanna Niehues (*Radboudumc*)

Jury for poster prize: Maud Jansen (*MUMC*), Marcel Bekkenk (Amsterdam *UMC*), Ellen van den Bogaard (*Radboudumc*)

NVED board: DirkJan Hijnen (president, *ErasmusMC*, representative in NVDV 'Commissie Nascholing'), Marcel Bekkenk (secretary, *Amsterdam UMC*), Antoni Gostyński (treasurer, *MUMC*), Patrick Zeeuwen (representative in Federa, *Radboudumc*), Sue Gibbs (*Amsterdam UMC/ACTA*)

1. ADDING METHOTREXATE TO ADALIMUMAB THERAPY IN PSORIASIS IS A VALUABLE AND CHEAP OPTION TO DECREASE IMMUNOGENICITY: FIRST YEAR OUTCOMES OF A RANDOMIZED CONTROLLED TRIAL

G.E. van der Kraaij[1]*, C.I. Busard[1]*, J. van den Reek[2], S.P. Menting[3], A.H. Musters[1], B. Hutten[4], M.A. de Rie[1], J.S. van Bezooijen[5], E. Prens[5], T. Rispens[6], A. de Vries[7], E.M.G.J. de Jong[2], W. de Kort[8], J.L.W. Lambert[9], M.B.A. van Doorn[5], Ph.I. Spuls[1,10] *These authors contributed equally

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Background: A substantial number of psoriasis patients treated with adalimumab do not respond to treatment or lose initial response over time, possibly due to immunogenicity. It has been shown in rheumatoid arthritis and Crohn disease that concomitant methotrexate (MTX) in adalimumab treatment reduces the formation of anti-drug antibodies (ADAs) and leads to higher adalimumab serum trough concentrations and increased effectiveness. This is the first randomized controlled trial (RCT) to assess the potential advantage of concomitant MTX in psoriasis.
Objective: To assess if addition of low-dose MTX to adalimumab therapy leads to lower ADA titers, higher serum trough concentrations and to increased effectiveness compared to adalimumab monotherapy in the first year of treatment.
Methods: We performed a multicenter assessor blinded RCT comparing adalimumab monotherapy to adalimumab and MTX 10 mg/week in patients with moderate to severe psoriasis. Adalimumab serum trough concentrations, ADA titers, Psoriasis Area and Severity Index (PASI) scores and other clinical parameters were measured at 5 patient visits.
Results: Thirty patients were treated with monotherapy and 31 received combination therapy. In week 49, median adalimumab trough concentrations were 3.9 vs 6.7 mg/L (p=0.03) and ADA formation occurred in 46.7% vs 16.1% (p=0.01) of patients in monotherapy and combination groups, respectively. In the combination group 58.1% of patients achieved PASI75, compared to 31.0% in the monotherapy group (p=0.04).
Conclusion: Addition of low dose MTX to adalimumab treatment of psoriasis leads to significantly less ADA formation, higher adalimumab serum trough levels and improved clinical effectiveness compared to adalimumab monotherapy.

2. TIME FROM PSORIASIS ONSET UNTIL DISCONTINUATION OF TOPICAL THERAPY AND SWITCH TO SYSTEMIC TREATMENT – RESULTS FROM THE CHILD-CAPTURE REGISTRY

F.M. Bruins[1], I. M.G.J. Bronckers[1], H.M.M. Groenewoud[2], E.M.G.J. de Jong[1], M.M.B. Seyger[1]

[1]Department of Dermatology, Radboudumc, Nijmegen; [2]Department for Health Evidence, Radboud University, Nijmegen

Background: Psoriasis can be managed with topical treatments (topical corticosteroids/vitamin D analogues/calcineurin inhibitors) in many patients. If these topical agents are ineffective, day-care dithranol, phototherapy and/or systemic treatments are considered. Little is known about how long topical treatments suffice and about the duration until switch to systemic treatment in young patients.
Objectives: To determine median time from psoriasis onset until i) discontinuation of topical therapy and ii) switch to systemic treatment in young psoriasis patients. Further, iii) to identify patient characteristics associated with switching to systemic treatment.
Methods: Data were obtained from a daily clinical practice cohort of pediatric-onset psoriasis patients that are followed into young adulthood from 2008 until 2018. Median time analyses were conducted through Kaplan Meier survival analyses. Cox regression analysis was used to identify patient characteristics associated with switch to systemic treatment.
Results: Analysis of 448 patients (42.9% male; mean age at psoriasis onset 8.3 [SD 4.0]; median Psoriasis Area Severity Index (PASI) 4.6 [IQR 6.0]) revealed a median time of 3.9 years until topical therapy discontinuation and 10.8 years until switch to systemic treatment. Higher PASI and a (Children's) Dermatology Life Quality Index ((C)DLQI) >5 were identified to be independent characteristics associated with switching to systemic treatment.
Conclusion: In young patients with mild to severe psoriasis, time until discontinuation of solely topical therapy is relatively short. Time until switch to systemic treatment is 10.8 years, with higher PASI and a (C)DLQI >5 being independent characteristics associated with this switch.

3. IDENTIFICATION OF CLINICAL CATEGORIES IN HIDRADENITIS SUPPURATIVA BASED ON PATIENT CHARACTERISTICS: RESULTS FROM A CLUSTER ANALYSIS

A. Rondags[1], S. Arends[2], R.J. Volkering[1], I.C. Janse[3], J.L. Blok[4], E. Schoonhoven[1], H. Bootsma[2], A. Spoorenberg[2], B. Horváth[1]

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Background: It is suggested that hidradenitis suppurativa (HS) is a skin disease with a certain phenotypic heterogeneity, which possibly indicates different etiologic, pathophysiologic, and genetic backgrounds that require tailored treatment approaches. Robust description of HS phenotypes does not yet exist.

Objective: To identify distinct clinical sub-categories of HS patients based on associated clinical patient characteristics.
Methods: Cross-sectional study. Cluster analysis was performed on two prospective, longitudinal, observational cohorts including adult HS patients seen in three Dutch centers (2015 - 2017). Used clinical variables were sex, smoking history, body mass index (BMI), and follicular occlusion comorbidities.
Results: Included were 345 HS patients: 72.8% female, mean age 38.3 ± 12.2 years, mean symptom duration 15.4 ± 11.7 years, mean BMI 29.0 ± 6.3 kg/m^2, 82.3 % was ever a smoker. Five distinct clinical sub-categories of HS were revealed: cluster 1. "females with stereotypical HS" (40.0%) are characterized by female smokers with overweight; 2. "females with a single exogenous risk factor for HS" (22.6%) is marked by females that either have a positive smoking history or are overweight; 3. "male HS" (22.0%) represents male patients who have a positive smoking history and/or are overweight; 4. "HS plus follicular occlusion comorbidity" (n=32, 9.2%) is defined by HS patients who are also known with acne conglobata, dissecting cellulitis of the scalp and/or pilonidal sinus; and 5. "limited HS" (6.1%) typifies HS patients without associated risk factors smoking, overweight and follicular occlusion comorbidities.
Conclusion: These clinical sub-categories of HS may help to define sound phenotypes of HS.

4. VALUE OF REFLECTANCE CONFOCAL MICROSCOPY FOR MONITORING DEMODEX, INFLAMMATION AND VASCULARITY IN ROSACEA PATIENTS USING TOPICAL IVERMECTIN

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Department of Dermatology, Radboudumc, Nijmegen

Background: Demodex and immunological factors may play a role in rosacea development. Reflectance confocal microscopy (RCM) allows noninvasive *in vivo* (epi)dermal visualization with high resolution. Topical ivermectin has acaricidal and anti-inflammatory properties, reducing rosacea manifestations.
Objective: To determine the value of RCM to monitor Demodex, inflammation and vascularity in rosacea during anti-inflammatory treatment.
Methods: In 20 patients with moderate-severe facial rosacea, clinical and RCM examination was performed before, during (week 6-12-16) and 12 weeks after a 16-week treatment course with topical ivermectin. RCM 8x8 mm2 mosaics, vertical mappings, and movies were made. Number of mites and inflammatory cells, vascular density and diameter, and epidermal thickness were calculated. RCM features were correlated with clinical assessment.
Results: Treatment resulted in significant reduction of inflammatory lesions, a slight improvement in erythema, but not in telangiectasias. Mites were detected in 80% of patients at baseline, 30% at week 16, and 63% at week 28. Mite number decreased significantly after 16 weeks of treatment; however, individual mite counting was difficult. No changes in inflammatory cells, epidermal thickness and vascular parameters were measured. Correlation between number of inflammatory lesions and mites was low. None of the RCM variables were significant predictors for clinical success.
Conclusion: With RCM, Demodex can be monitored during treatment using a yes/no algorithm, corresponding to clinical symptoms. Unfortunately, quantifying exact mite numbers and inflammatory/vascular characteristics is challenging due to device limitations. Therefore, RCM seems of limited value for noninvasive follow-up of rosacea treatment in daily clinical practice.

5. MICROENVIRONMENTAL CROSS-TALK IN AN ORGANOTYPIC HUMAN MELANOMA-IN-SKIN MODEL DIRECTS M2-LIKE MONOCYTE DIFFERENTIATION VIA IL-10

E. Michielon[1], M. Lopez Gonzalez[2], J.L.A. Burm[1], T. Waaijman[1], T.D. de Gruijl[2], S. Gibbs[1,3]
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Background: The melanoma microenvironment promotes immune-escape and tumor progression, contributing to failure of melanoma therapies in a large group of treated patients. While 2D cultures lack tissue context, animal models poorly predict human immune responses, with the result that potential new drugs fail in the clinical setting. This highlights a pressing need for more physiological human melanoma models.
Objective: To establish an *in vitro* human melanoma model that mimics tumor progression and processes involved in immunosuppression.
Methods: Melanoma reconstructed human skin (Mel-RhS) was constructed by co-seeding melanoma cells and keratinocytes onto a fibroblast-populated dermal equivalent. (Immuno)histochemical staining was used to identify tumor cells. Culture supernatant was used to detect cytokine secretion (ELISA) and assess changes in monocyte-derived myeloid cells surface marker expression (FACS).
Results: Tumor nests developed overtime spreading towards the dermis. An increased IL-10 secretion in Mel-RhS compared to healthy controls was observed. In contrast, monolayer culture of melanoma cells did not produce detectable IL-10 levels. Mel-RhS-culture supernatant stimulated differentiation of monocytes into M2-like macrophages.
Conclusion: Features of the Mel-RhS resemble the initial stages of human invasive melanoma. The ability of Mel-RhS supernatants to promote a tolerogenic M2-like phenotype skewing in monocyte cultures is consistent with a switch towards a more immunosuppressive microenvironment. Collectively, this data demonstrates the potential of this model as a novel *in vitro* tool for preclinical testing of immune modulatory therapeutic agents.

6. MELANOMA PROGRESSION COINCIDES WITH INCREASED T CELL INFILTRATION AND PD-1 EXPRESSION ON SKIN-RESIDENT MEMORY T CELLS

M. Willemsen[1], D. Tio[1], G. Krebbers[1], F.R. Kasiem[1], W.J. Mooi[2], E.H. Jaspars[2], T.R. Matos[1], W.J. Bakker[1], M.W. Bekkenk[1], R.M. Luiten[1]
[1]Department of Dermatology and Netherlands Institute for Pigment Disorders, Amsterdam UMC, University of Amsterdam, Cancer Center Amsterdam, Amsterdam Infection & Immunity Institute, Amsterdam; [2]Department of Pathology, Amsterdam UMC, Amsterdam

Background: Tissue-resident memory T (Trm) have been correlated with improved survival of melanoma patients and vaccines can evoke potent Trm cell responses against established melanoma. Yet, their role in melanoma development remains unknown and might be relevant, since melanocytic skin lesions rarely progress into cancers.
Objective: This study aimed to identify the presence of Trm cells in relation to different melanoma stages.
Methods: FFPE sections from healthy skin (n=7), sun-exposed skin (n=7), lentigo maligna (LM, n=8), lentigo maligna melanoma (LMM, n=7), benign melanocytic nevi (n=8), primary melanoma (n=14), and (cutaneous) metastatic melanoma (n=14) were analyzed by immunohistochemistry and immunofluorescence for CD3, CD4, CD8, CD69, CD103 and PD-1 expression.
Results: More T cells (both CD4+ and CD8+) and CD69+ cells were found in melanoma, compared to non-malignant tissues. CD103+ cells were present at high levels in metastatic melanoma only. Data suggest that CD69+ are relatively more abundant in nevi, whereas Trm cells are only part of the T cell population found in primary melanoma. Although intralesional CD103+ T cells were found in metastatic melanoma, PD-1 expression suggest functional exhaustion and therefore inability to mediate effective anti-tumor immunity. TCGA analysis of PD-1 mRNA expression among 375 melanoma samples showed a strong correlation with CD69 and CD103 expression. Also, high expression of the Trm gene signature in tumors correlated with improved survival.
Conclusion: These data show that melanoma progression coincides with increased T cell infiltration, without specific enrichment of Trm cells, but rather with increased functional exhaustion.

7. PATIENT CHARACTERISTICS AND ONCOGENIC MUTATIONS OF METASTASIZED LENTIGO MALIGNA MELANOMA: RESULTS FROM THE DUTCH MELANOMA TREATMENT REGISTRY

D.C.K.S. Tio[1], M.W Bekkenk[1], R. Hoekzema[1], A.J.M van den Eertwegh[2], M. Louwmans[3], DMTR group[4], R.M. Luiten[1], W. Ouwerkerk[1,5]
[1]Department of Dermatology, Amsterdam UMC, University of Amsterdam, Netherlands Institute for Pigment Disorders, Amsterdam Infection & Immunity Institute, Amsterdam; [2]Department of Medical Oncology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam; [3]Integrated Cancer Center the Netherlands; [4]Dutch Melanoma Treatment Registry; [5]National Heart Centre Singapore, Singapore

Background: Lentigo Maligna Melanoma is a subtype of cutaneous melanoma. It is associated with chronic UV damage while superficial spreading (SSM) and nodular melanoma (NM) are associated with intermittent UV damage. We hypothesized that metastatic LMM (mLMM) is different in biological behavior compared to metastatic SSM (mSSM) or metastatic NM (nNM).
Objective: The goal of this study was to compare mLMM patients to mSSM and mNM on clinical and genetic characteristics.
Methods: In the Netherlands all metastatic melanoma patients are registered in the Dutch Melanoma Treatment Registry (DMTR). Data from the DMTR between 2013 and 2018 was analyzed, and the Dutch incidence of LMM, SSM and NM was collected between 2013-2018. Patient characteristics on clinical, histological, genetic aspects were compared. Efficacy of treatment and overall survival was investigated in both groups.
Results: A total of 59 mLMM patients and 2,313 mSSM/mNM patients were identified. mLMM patients were significantly older than mSSM/mNM patients. mLMM seems to have less metastatic potential (59 of 1,840; 3.21%) in comparison to SSM/NM (2,313 of 35,055; 6.60%). mLMM has less BRAFV600 mutations in general, but more specific BRAFV600K mutations and more KIT mutations. mLMM mortalities are less often melanoma related, while overall survival and treatment response did not differ. Treatment response and overall survival was not different. However, melanoma related mortality was lower.
Conclusion: mLMM appears to have a less aggressive presentation. Despite being older at diagnosis, mLMM patient have similar treatment response and overall survival, but mortality is less often caused by melanoma.

8. COMPOSITION OF CUTANEOUS BACTERIAL MICROBIOME IN SEBORRHEIC DERMATITIS PATIENTS

M. Sanders[1], T. Nijsten[1], J. Verlouw[2], R. Kraaij[2], L.M. Pardo[1]
[1]Department of Dermatology, Erasmus MC, Rotterdam; [2]Department of Internal Medicine, Erasmus MC, Rotterdam

Background: Seborrheic dermatitis (SD) is a chronic inflammatory skin disease with a multifactorial aetiology. Previous studies have shown that Malassezia yeasts are associated with the disease. The role of bacterial dysbiosis in SD has not been thoroughly investigated.
Objective: To profile the bacterial microbiome in SD patients and to compare its composition versus participants without the disease (controls).
Methods: We took skin swabs from naso-labial fold from patients with seborrheic dermatitis (lesional skin: n=22; non-lesional skin SD: n=75) and 200 controls. We characterized the bacterial microbiome using the 16S-rRNA V1-V3 regions. We estimated α-diversity between cases and controls and tested for associations between the microbiome composition between cases and controls using multivariate statistics (permANOVA). We extracted the top 20 genera with the largest effect sizes between cases and controls from the permANOVA analysis. Univariate statistics was also used to test per-genus associations.

Results: We found an increased α-diversity (Shannon- diversity) when comparing lesional skin versus controls (controls vs lesional cases; Wilcoxon rank sum test p-value=0.01). Multivariable statistical analysis also revealed significant associations between microbiome composition and SD for lesional skin against controls (p-value= 0.02;R2=1%). Rare genera (*Rothia, Parvimonas*) from oral microbiome and skin (*Finegoldia*) were amongst the top 20 genera with the largest differences between lesional cases and controls. This was mirrored in the univariate analysis although it was not significant after correcting multiple testing.
Conclusion: Our analysis suggests that rare genera from skin and oral microbiome are associated with seborrheic dermatitis.

9. GRAM-POSITIVE ANAEROBIC COCCI GUARD EPIDERMAL HOMEOSTASIS BY REGULATING HOST DEFENSE MECHANISMS

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Background: Low protein levels of filaggrin in the epidermis are characteristic for atopic dermatitis (AD) and correlate to a low abundance of proteolytic Gram-positive anaerobic cocci (GPAC) in the human skin microbiome. Individuals with AD are often colonized with the skin pathogen *Staphylococcus aureus*, which affects the severity of the disease.
Objective: We aimed to investigate the role of GPAC in relation to AD.
Methods: The direct influence of GPAC on the survival of *S. aureus* was assessed *in vitro*. Furthermore, to study host defense responses, the interaction of GPAC with peripheral blood mononuclear cells (PBMC) and human primary keratinocytes (monolayer cultures and 3D epidermal equivalents) was determined. Subsequently, we investigated if keratinocytes that were exposed to GPAC could limit the growth of clinical isolates of *S. aureus* that we have isolated from AD patients.
Results: GPAC did not directly affect the growth, virulence or biofilm formation of *S. aureus*. In contrast, keratinocyte antimicrobial peptide (AMP) expression was induced by GPAC. In addition, GPAC were able to elicit cytokine production in PBMCs, which could subsequently induce AMP expression in keratinocytes. GPAC exposed keratinocytes limited the growth of *S. aureus* strains.
Conclusion: In case of a skin barrier disruption, GPAC induce a rapid host-defense response in keratinocytes via AMP production. Cytokines produced by PBMC after GPAC exposure amplify this initial response in keratinocytes. This host defense response could protect against the colonization and infection of *S. aureus*, a mechanism that may be disturbed in AD patients.

10. SPA-TYPING OF THE *STAPHYLOCOCCUS AUREUS* POPULATIONS FROM NOSE AND SKIN IN ADULT PATIENTS WITH ATOPIC DERMATITIS

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Background: Staphylococcus aureus is frequently found in patients with atopic dermatitis (AD) and it's abundance is correlated to disease severity.
Objective: To assess similarities in genetic composition of *S. aureus* in patients with AD, found in nose and skin. Moreover, we want to gain insight into the temporal variation in genetic composition and the relation to disease severity.
Methods: Adult patients, with moderate-severe AD were included. Bacterial swabs were taken from the nose and lesional skin at baseline and after two weeks in which treatment was standardized with topical corticosteroid. Swabs positive for *S. aureus* were further characterized using spa-typing. Disease severity was assessed using Eczema Area and Severity Index (EASI).
Results: From the total of 100 patients included in this study, 91 were positive for *S. aureus*. We found 49 different spa-types, with the most common including t002, t091, t127, t571 and t189. At baseline, 58.2% of the patients had the same spa-type in nose and skin, compared to 50.5% at T1. Seventy-three patients were positive in nose at both time-points, including 56 (76.7%) with the same spa-type over time. For lesions skin, 42 (75.0%) of the 56 persistent carriers on skin, had equal spa-type over time. There was no difference in disease severity between patients with and without a change in spa-type.
Conclusions: We found a heterogeneous *S. aureus* population, with a high rate of persistent carriers. Our results implicate that the nose is an important reservoir for *S. aureus* transmission to the skin in patients with AD.

11. DIFFERENTIAL INFLUENCE OF STREPTOCOCCUS MITIS ON HOST RESPONSE TO METALS IN RECONSTRUCTED HUMAN SKIN AND MUCOSA

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Background: Skin and oral mucosa are continuously exposed to potential sensitizers whilst hosting abundant commensal microbes. As commensal microbes influence various host events, it can be expected that they influence the host response to sensitizers. Additionally, the route of exposure, skin

versus oral mucosa, might influence the host response to sensitizers.
Objective: To determine how commensal bacteria, *S. mitis*, influences the host response to metals in reconstructed human skin (RHS) and gingiva (RHG).
Methods: RHS and RHG were topically exposed to *S. mitis*, in the presence or absence of nickel sulphate or titanium bis-ammonium-lactate-dihydroxide for 24 hours. Nickel is a well characterized contact sensitizer, whereas the sensitizing potential of titanium is still questionable. The host response was determined by histology, cytokine secretion (ELISA) and epidermal Toll-like receptor expression (Western blot, PCR).
Results: Neither *S. mitis* nor metals were cytotoxic and *S. mitis* remained viable. *S. mitis* increased the release of IL-6, CXCL8 and CCL20 in RHS but not in RHG; co-application with nickel further increased cytokine release. In contrast, titanium suppressed *S. mitis* induced cytokine secretion in RHS and had no influence on RHG. TLR1 and TLR4 expression were differently regulated in RHS and RHG after the exposure.
Conclusion: Co-exposure of *S. mitis* and nickel resulted in a more potent innate immune response in RHS than in RHG. In comparison, titanium was inert. These results indicate the important role of commensal microbes and route of exposure in the host response to metals.

12. DEVELOPMENT OF A 3D SKIN MICROBIOME MODEL TO STUDY HOST-MICROBE INTERACTIONS

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Background: Cutaneous microbial dysbiosis is linked to the pathogenesis of atopic dermatitis (AD). *In vitro* 3D skin models are a powerful tool to investigate AD pathophysiology. However, only sterile 3D models have predominantly been used to study epidermal expression alterations and barrier function, neglecting the interplay between keratinocytes and microbes.
Objective: To develop and validate a reproducible and standardized 3D skin microbiome model for studying host-microbe interactions.
Methods: Sterilized glass cloning cylinders were used for the application of bacteria onto human epidermal equivalents (HEEs). Inoculation density, co-culture duration and strain-specific keratinocyte responses were analyzed by morphology, immunohistochemistry and gene expression levels. Bacterial growth rate was determined to validate microbiome viability during co-culture.
Results: The application technique enabled localized topical inoculation of cutaneous microbes on HEEs resembling *in vivo*-like skin colonization. HEEs were successfully inoculated with specific single-strain bacteria, *in vitro* mixes of several bacteria or ex vivo microbiome samples. Co-cultures revealed normal epidermal morphology and viable microbes for an inoculation period of at least 7 days. HEEs were impermeable for microbes and no gross skin barrier defects were observed due to bacterial colonization. Therefore, only minor host-defense responses were elicited by the applied microbes.
Conclusion: We have developed a standardized and reproducible skin microbiome model which enables to study the interaction between keratinocytes and microbes. Next, the use of AD-associated microbial species (*S. aureus*) in combination with disease-specific cytokines (IL-4/IL-13) and the use of defined keratinocyte genotypes (FLG) can be used to elegantly mimic a more complete and complex AD model.

13. NOX2 EXPRESSION IS INCREASED IN KERATINOCYTES AFTER BURN INJURY

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Background: Reepithelialisation is crucial for effective wound repair in burns. Reactive oxygen species (ROS) have shown to be important in this. Recent studies suggest that NOX proteins produce ROS in keratinocytes. We have previously shown that C1-esterase inhibitor (C1inh) increased the rate of reepithelialisation in burns.
Objective: To investigate the putative role of NOX proteins in burns, including the effect of C1inh hereon.
Methods: Skin tissue from healthy control Wistar rats (n=6) were compared with burn-injured rats, with (n=7) or without C1inh treatment (n=7). After 14 days, rats were terminated. From the burn-injured rats, the entire wound and non-burned remote skin was excised. From the control rats dorsal skin was excised. In these skin samples NOX2 and NOX4 were analysed immunohistochemically.
Results: In non-burned rats NOX2 was found in keratinocytes; and the number of NOX2-positive keratinocytes was 367/mm2 (254 – 378). In burned rats the number of NOX2-positive keratinocytes was significantly increased in the newly forming epidermis to 1019/mm2 (649 – 1172), but significantly decreased in remote non-burned skin to 22/mm2 (6 – 89). C1inh treatment counteracted these changes in epidermal NOX2 expression in burned rats, both in the burned area as in remote non-burned skin. No NOX4 expression was found in the epidermis in none of the groups.
Conclusion: NOX2 expression was increased in keratinocytes in newly forming epidermis after burn injury and C1inh, a drug that increases the rate of reepithelialisation, counteracted this effect. These results suggest a role for NOX2 in the reepithelialisation of burns.

14. INNOVATION IN BURN WOUND TREATMENT – AN APPROACH AIMING AT DEVELOPMENT AND IMPLEMENTATION OF TISSUE-ENGINEERED, AUTOLOGOUS SKIN CONSTRUCTS

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Background: Scars have a major impact on the quality of life of burn patients. Standard treatment of large/deep burn wounds is the use of autologous (meshed) split-skin grafts. Major limitations of this technique are quality of scar formation, donor-site morbidity, and surface area that can be treated.
Objectives: 1) Development of an autologous full-thickness skin construct for acute (burn) wound treatment. The product should be able to cover a large wound area (± 300 cm2) in a short time (< 14 days) without the use of autologous skin grafts. 2) to investigate the regulatory feasibility of clinical implementation of the skin construct.
Methods: 1) Keratinocytes, melanocytes and fibroblasts are isolated from 3 cm2 of skin. Cells are amplified and seeded onto a dermal scaffold. Culture procedures are optimized conform European Medicinal Agency regulations. The construct is characterized using immunohistochemistry and cell counting. 2) A feasibility study is performed to indicate regulations and legalization of clinical implementation of the skin construct.
Results: 1) Defined culture media for keratinocyte and fibroblast expansion are identified. When seeded onto Matriderm, cells are viable and reside mainly in their native compartments. 2) Currently, no autologous full-skin constructs are commercially available within the European Union. Our product would fulfill a medical need in improving quality of healing. Production of our construct according to Advanced Tissue Medicinal Product regulations is feasible.
Conclusion: Our preliminary data indicate the tissue-engineered, autologous skin construct has the potential to overcome shortcomings in currently available treatments for acute burn wounds.

15. OBJECTIVE QUANTIFICATION OF MEAN GRAYSCALE VALUE USING OPTICAL COHERENCE TOMOGRAPHY IN CUTANEOUS WOUND HEALING

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Background: Close monitoring of wound healing is essential to assess the efficacy of novel compounds. Optical Coherence Tomography (OCT) is an emerging non-invasive imaging tool that generates real-time images of cutaneous morphology, however, current analysis modalities are limited. Measuring mean grayscale value (MGV) in OCT imaging can correspond with total collagen disposition (TCD) and can, subsequently, provide additional information in vivo throughout the maturation phase of wound healing.
Objectives: To evaluate the feasibility of using MGV as a biomarker for TCD using OCT.
Methods: An observational, single center, single-arm study was performed to characterize wound healing in 18 healthy volunteers. Wounds were induced by taking 3 mm skin punch biopsies from the lower back. Repeated 4 mm biopsies were randomly taken for TCD histological analysis. TCD was scored semi-quantitatively as absent (0), scant (1), moderate (2), and profound (3). Wound healing was assessed over time using MGV derived from ImageJ analysis of OCT-scans. MGV analyzed images were compared with histology.
Results: MGV decreased from baseline (mean 86.7 AU, SD 10.7 AU) up to day 10 (mean 74.3 AU, SD 9.1 AU) followed by an increase until day 56 (mean 91.5 AU, SD 9.2 AU). TCD also decreased from baseline (median 3, range 3) up to day 14 (median 1, range 1) after which an increase was observed up to day 56 (median 3, range 3).
Conclusion: MGV derived from OCT images can quantitatively assess the morphological collagen changes observed in histology and can be used as a biomarker for TCD.

16. ASSESSING THE THERAPEUTIC POTENTIAL OF HUMAN SALIVA USING IN VITRO WOUND HEALING MODELS

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Background: Injured oral mucosa heals faster and almost scar free compared to skin. Saliva is thought to be one of the main contributing factors to oral wound healing and may possibly also stimulate skin wound healing. If so, saliva will provide a novel therapy for treating skin wounds such as burns.
Objective: To investigate *in vitro* the therapeutic wound healing potential of human saliva and assess saliva donor variation.
Methods: Saliva of 16 healthy donors was collected (age 18-62) and filter sterilized before use. Two different *in vitro* wound models were investigated: open wounds represented by 2D cultures were used to assess fibroblast and keratinocyte migration and proliferation and freeze blister wounds were studied using 3D reconstructed human skin. Re-epithelialization and differentiation and inflammatory cytokine secretion was assessed.
Results: Saliva stimulated migration and proliferation of fibroblasts. No significant difference was observed in wound healing potency of saliva from different donors, based on age or sex.

Topical saliva application to the blister wound on reconstructed skin did not stimulate re-epithelization, but did stimulate keratinocyte migration on the open wound model. Saliva promoted CCL20, IL-6 and CXCL-8 secretion when applied to reconstructed human skin, without altering the specific epithelial differentiation.

Conclusion: Our results show that human saliva has the potential to stimulate skin wound closure independent of saliva donor age or sex. Topical application of saliva induces an inflammatory, which is required to drive wound healing. Saliva is therefore a potential cheap and always available therapeutic for treating open wounds.

17. EVALUATION OF THE HUMAN INTRADERMAL LPS CHALLENGE MODEL WITH TOPICAL AND SYSTEMIC CORTICOSTEROIDS

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Background: Intravenous lipopolysaccharide (LPS) administration to humans is a widely used, well-tolerated model to study TLR4-driven inflammation. A local LPS challenge, in the skin, would offer the advantage of repeated testing within one subject, in a peripheral tissue.
Objective: To evaluate whether corticosteroids suppress the inflammatory response following an intradermal LPS injection, quantified by imaging, cellular, and biochemical techniques.
Methods: 30 healthy volunteers participated in this trial. 24 subjects received clobetasol propionate on the volar forearm (2 days pretreatment, 0.05%, BID). 6 subjects received oral prednisolone (2 days pretreatment, 0.25mg/kg, BID). Subjects maximally received 4 intradermal LPS injections (10ng LPS/100ug saline) in the volar forearm. Non-invasive measurements included laser speckle contrast imaging (LSCI), thermography, and clinical erythema grading. Suction blisters were induced to analyze inflammatory cells and cytokines.
Results: Clobetasol propionate and prednisolone pretreatment caused a significant reduction in LPS-driven enhancement of LSCI-based skin perfusion. The maximal effect was -50% at 24h (38.8±13.7 AU for control, 20.9±12.7 AU for prednisolone, and 17.2±9.7 AU for clobetasol propionate). In contrast, the corticosteroids did not impair the acute cellular and cytokine response to LPS. However, at 24 and 48 hours after LPS injection, cell numbers in blister fluid were significantly reduced compared to the untreated areas, as observed for monocytes, dendritic cells, and T lymphocytes, but not for neutrophils.
Conclusions: We demonstrated that both local and systemic corticosteroids modulate LPS-driven skin responses in healthy volunteers. These data support the intradermal LPS challenge as clinical model for the evaluation of novel anti-inflammatory compounds.

18. CLINICAL AND HISTOPATHOLOGICAL CHARACTERIZATION OF PARADOXICAL HEAD AND NECK ERYTHEMA IN ATOPIC DERMATITIS PATIENTS TREATED WITH DUPILUMAB: A CASE SERIES

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Background: Dupilumab is the first biologic registered for the treatment of atopic dermatitis (AD). We report on an important new side effect that has not been reported in clinical trials.
Objective: To evaluate clinical and immunohistochemical characteristics of a paradoxical head-neck erythema which developed in AD patients during dupilumab treatment.
Methods: We recorded clinical features and obtained lesional skin biopsies for histological examination in 7 AD patients who developed a paradoxical head-neck erythema after 10-39 weeks of dupilumab treatment.
Results: Patients presented with a relatively sharp demarcated, patchy erythema in the head-neck area that showed no or less scaling compared to their usual eczema. Except for a notable "red face", eczema on other body parts had greatly improved in 6 out of 7 patients. Treatment of the erythema with topical and systemic drugs was unsuccessful. Despite the presence of this erythema, none of our patients discontinued dupilumab treatment. Lesional skin biopsies showed an increased number of ectatic capillaries, and a perivascular lymphohistiocytic infiltration in all patients. In addition, epidermal hyperplasia with elongation of the rete ridges was observed in 4 patients, resembling a psoriasiform dermatitis. Immunohistochemistry revealed normal numbers of mast cells and plasma cells. Interestingly, spongiosis and neutrophils were largely absent in all biopsies.
Conclusion: We report on AD patients treated with dupilumab developing a paradoxical erythema in a head-neck distribution. Both clinically and histopathologically we found a heterogeneous response, which was most suggestive of a drug-induced skin reaction.

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

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

Objective: Investigate whether aberrant expression of CER and FFA biosynthesis enzymes in AD skin can explain the changes in CER and FFA composition.
Methods: In 20 AD patients (SCORAD between 0 and 43.5, 8 with filaggrin mutations) and controls (no filaggrin mutations) the protein expression of enzymes involved in the biosynthesis of FFAs and CERs was analyzed in relation to the SC lipid composition. Additionally, their gene expression was examined in full thickness human skin equivalents (HSEs) generated with a cocktail of cytokines.
Results: Lesional skin showed an altered expression of SCD and ELOVL1, while expression in non-lesional skin remained similar to control skin. Concomitantly, increased unsaturated FFAs (SCD) and reduced FFA C22-C28 (ELOVL1) levels were observed in lesional skin. CER composition in lesional skin showed increased CER AS and NS (aSmase) and decreased esterified ω-hydroxy CERs (CerS3). These changes did not correlate to filaggrin expression. mRNA levels of almost all enzymes were reduced when HSEs were cultured in the presence of cytokines.
Conclusion: Alterations in gene and protein expression of key enzymes involved in SC lipid synthesis contribute to changes in the lipid composition in AD skin. The results indicate that inflammation influences the expression of these enzymes.

20. THE CLINICAL AND GENETIC OVERLAP OF X-LINKED ICHTHYOSIS WITH ICHTHYOSIS VULGARIS IN THE DUTCH POPULATION

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Background: X-linked ichthyosis (XLI) is after ichthyosis vulgaris (IV) the most frequent occurring genetic skin scaling disease (1 in 6,000). The disorder results from steroid sulfatase deficiency due to defects in the STS gene. Most patients (90%) have a genomic deletion encompassing the entire gene. Clinical distinction between XLI and IV may be difficult. Moreover, the incidence of FLG mutations causal to IV is high (5%) and therefore co-inheritance with STS mutations may occur, modifying the phenotype.
Objective: Genetic analysis of STS and FLG in patients clinically diagnosed with XLI to determine the spectrum of mutations and improve diagnoses.
Methods: Blood samples from 74 Dutch patients suspected having XLI were analyzed for the STS gene using MLPA and Sanger sequencing. Additionally, most samples were tested for FLG with smMIP analysis.
Results: In 53 of 74 patients (72%) the STS gene was affected, of which 42 involved a STS deletion (79%). The other 11 STS mutations are novel (n=9). In 8 of 21 patients, not having a STS variant, FLG mutations were detected. In 3 of the XLI patients also FLG mutations were identified.
Conclusion: In Dutch XLI patients a comparable percentage to literature carries the STS gene deletion. 9 novel mutations were added to the existing STS mutation database (12%). Part of the clinically diagnosed XLI are IV patients (11%), indicating the difficult distinction between the diseases. The phenotype of 3 XLI patients may be modified by FLG mutations, certifying DNA analysis of both genes to facilitate accurate diagnostic confirmation.

21. PREDICTING KERATINOCYTE CARCINOMA IN PATIENTS WITH ACTINIC KERATOSIS: DEVELOPMENT AND INTERNAL VALIDATION OF A MULTIVARIABLE RISK PREDICTION MODEL

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Background: Patients with actinic keratosis (AK) are at increased risk for developing keratinocyte carcinoma (KC) but predictive factors and their risk rates are unknown.
Objective: To develop and internally validate a prediction model to calculate the absolute risk of a first KC in AK patients.
Methods: The risk prediction model was based on the prospective population-based Rotterdam Study cohort. We hereto analyzed data of participants with at least 1 AK-lesion at cohort baseline using a multivariable Cox proportional hazards model and included 13 a priori defined candidate predictor variables considering phenotypic, genetic and lifestyle risk factors. KCs were identified by linkage of the data with the Dutch Pathology Registry.
Results: Of the 1,169 AK-participants at baseline, 176 (15.1%) developed a KC after a median follow-up of 1.8 years. The final model with significant predictors was obtained after backward stepwise selection and comprised the presence of 4-9 AKs (hazard ratio (HR): 1.68, 95% confidence interval (CI): 1.16-2.42), 10 or more AKs (HR: 2.43, 95% CI: 1.64-3.61), AK-localization on upper extremities (HR: 0.75, 95% CI: 0.52-1.08) or elsewhere except the head (HR: 1.40, 95% CI: 0.98-2.01), and coffee consumption (HR: 0.92, 95% CI: 0.84-1.01). Evaluation of the discriminative ability of the model showed a bootstrap validated c-index of 0.60.
Conclusion: We showed that the risk of KC in patients with AK can be calculated with the use of four easily assessable predictor variables. Given the c-index, extension of the model with additional, currently unknown predictor variables is desirable.

22. CUMULATIVE SUM ANALYSIS FOR THE LEARNING CURVE OF OPTICAL COHERENCE TOMOGRAPHY ASSISTED DIAGNOSIS OF BASAL CELL CARCINOMA

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Background: Optical coherence tomography (OCT) is a promising non-invasive technique for diagnosing basal cell carcinoma (BCC). Before implementation it is useful to have insight in the learning curve for OCT-assisted diagnosis of BCC.

Objective: The current study aimed to illustrate how cumulative sum (CUSUM) charts can be used to determine how many OCT scans should be evaluated by novice assessors to obtain adequate competence in distinguishing BCC from non-BCC lesions.
Methods: Patients were enrolled on the outpatient clinic of the department of Dermatology of the MUMC, Maastricht, the Netherlands. Four hundred lesions suspect for non-melanoma skin cancer were evaluated by OCT in combination with clinical pictures. The confidence in presence of BCC on OCT was assessed using a five-point Likert scale (0-4, '0': certainly no BCC, '1-4': higher scores representing increasing certainty). The diagnostic error rate was used to evaluate performance over time, with histopathologic diagnosis as reference standard. The acceptable and unacceptable error rates were set at 16% and 25%, respectively.
Results: Under the above conditions, the learning curve for diagnosing BCC indicated that acceptable performance was reached after assessing 183-311 scans, dependent on the cut-off value for a positive test result.
Conclusion: CUSUM analysis can be used to monitor progress in performance of OCT readers over time. Our results indicated that the caseload necessary for training purposes seems substantial.

23. EXTERNAL ANOGENITAL WARTS TREATMENT WITH TOPICAL DIGOXIN AND FUROSEMIDE GEL: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Background: Anogenital warts (AGW) are caused by low-risk human papillomavirus (HPV) types and represent the most common sexually transmitted viral disease. Current therapies for AGW have notable side effects and high recurrence rates. DNA viruses such as HPV rely on cellular K+ influx. Ionic contra-viral therapy (ICVT) comprised of digoxin and furosemide inhibits the K+ influx and is therefore a potential new treatment for AGW.
Objective: A randomized, controlled trial was performed to assess safety and tolerability and explore pharmacodynamics and clinical efficacy of ICVT in patients with AGW.
Methods: Twenty-four patients with at least 3 external AGW were randomized to either ICVT or placebo (ratio 3:1) and administered the gel once daily for 42 consecutive days. To assess safety and tolerability, laboratory safety testing was performed and adverse events, vital signs and ECGs were monitored. Clinical efficacy was assessed by lesion count and dimensions, measurement of viral load, HPV expression and histology. Patient-reported outcomes and quality of life (QoL) were assessed with use of an e-diary and paper questionnaires.
Results: ICVT was well tolerated as there were no clinically relevant safety findings and no serious adverse events. All adverse events (N=17) were of mild severity and self-limiting. No between-group differences in lesion count, dimensions, viral load, patient-reported outcomes and QoL were observed after treatment.
Conclusion: ICVT is safe to be administered in patients with AGW but shows no pharmacodynamic activity or clinical efficacy after 6 weeks of treatment.

24. MOLECULAR TESTING IN METASTATIC BASAL CELL CARCINOMA: A CASE SERIES

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Background: Metastatic basal cell carcinoma (mBCC) is a very rare entity and the diagnosis remains challenging. Therapeutic options are limited and only one third of the patients respond to targeted therapy with vismodegib.
Objective: We aimed to demonstrate a clonal relationship between BCCs and their metastases and additionally, to explore which hedgehog pathway related mutations are involved in mBCC.
Methods: From April 2016 to May 2019 genetic analysis was conducted of eleven primary BCCs and their metastases. Genes relevant for BCC development were analyzed in tumor and metastasis material, either with small molecule molecular inversion probes (smMIPs) for PTCH1, PTCH2, SMO, SUFU, GLI2 and TP53, or with targeted next generation sequencing (tNGS) of the same genes and CDKN2A, CDKN2B, CIC, DAXX, DDX3X, FUBP1, NF1, NF2, PTEN, SETD2, TRAF7, and the TERT promoter.
Results: In eight of eleven patients identical gene mutations could be demonstrated in the primary tumors and their metastases. In one patient only analysis of the primary tumor was successful and in the remaining two patients analysis of both primary tumor and metastasis samples were unsuccessful. Seven patients harbored PTCH1 mutations (78%), four SMO mutations (44%), and one a SUFU mutation (11%). All SMO mutations found are known to cause resistance to targeted therapy with vismodegib.
Conclusion: Molecular testing can help to confirm the diagnosis mBCC and may be of prognostic and therapeutic value.

25. POSTOPERATIVE RADIOTHERAPY FOR HEAD AND NECK CUTANEOUS SQUAMOUS CELL CARCINOMA WITH MICROSCOPIC RESIDUAL DISEASE

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Background: Studies on the efficacy of postoperative radiotherapy (PORT) after incomplete excision of cutaneous squamous cell carcinoma (cSCC) are limited. A recent study by Ruiz et al. (JAMA Dermatology 2019) describes 11 patients who received salvage limited-field radiotherapy after incomplete excision. They reported poor outcomes (local recurrence (LR), metastasis, or disease-specific death (DSD)) in 9 patients (82%). In our experience PORT for this indication provides better outcomes.
Objective: To compare our outcomes of PORT after excision with microscopic residual disease to previously published data.
Methods: Patients diagnosed with cSCC in the head and neck region between 1 January 2000 and 1 January 2014 and treated with PORT after incomplete excision were retrospectively included. Poor outcome was defined as disease progression, containing LR, metastasis and DSD. Disease-free survival was calculated using Kaplan-Meier survival analysis.
Results: Our preliminary results show that 48 patients received PORT for the treatment of primary, incompletely excised cSCC. Nine of them (18,8%) showed disease progression. Seven patients (14,6%) had LR, 3 patients (6,3%) nodal metastasis (NM), and 3 patients (6,3%) died due to disease progression. Mean disease-free survival of all patients was 124 months (95% CI 102 – 146).
Conclusion: PORT for patients with positive surgical margins is a viable option to prevent disease progression if re-excision of the tumor is not possible or not preferred. More research with a larger sample size is necessary to confirm these results.

26. THE AUTOIMMUNE IGG SUBCLASS RESPONSE DEFINES THE IGG DEPOSITION PATTERN IN PEMPHIGUS PATIENT SKIN

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Background: In pemphigus, circulating autoimmune IgG binds to desmoglein 1 and/or 3 in the epidermis, and/or the mucosa. This IgG deposition pattern can vary; most patients have depositions containing IgG clusters. The clusters are thought to be caused by desmoglein crosslinking with IgG. In a minority of patients clustering is absent and the IgG is evenly deposited. The autoimmune IgG response is mainly IgG4 and can be accompanied by the other subclasses. Only IgG4 is capable of Fab arm exchange i.e. half-molecules of IgG4 recombine with other IgG4 half-molecules; changing from monospecific bivalent molecules to bispecific monovalent. It is estimated that ~99% of IgG4 in the body are hybrid molecules.
Objective: In this study we investigated the role of IgG subclass in the deposition pattern in patient skin. We hypothesized that due to monovalency a pure IgG4 response cannot crosslink desmogleins, leading to a smooth deposition.
Methods: To test this hypothesis we stained 20 biopsies for all subclasses. Corresponding sera were analyzed by ELISA for circulating anti-desmoglein subclass IgG.
Results: We found 5 biopsies that had a smooth deposition pattern and the autoimmune response in all 5 cases was purely IgG4. In contrast, the other 15 biopsies had varying degrees of clustering, which corresponded with an additional response of anti-desmoglein IgG1 and/or IgG2.
Conclusion: We conclude that the deposition pattern of IgG in skin is defined by the subclass response and that the data observed here underlines that the clustering of IgG in patient skin is caused by desmoglein crosslinking.

27. EXPRESSION OF HSPCA1 AND ULTRASTRUCTURAL ANALYSIS OF THE SKIN BEFORE AND AFTER LASER THERAPY IN HAILEY-HAILEY DISEASE

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Background: Hailey-Hailey disease (HHD) is an autosomal dominant hereditary acantholytic dermatosis caused by mutation in the ATP2C1 gene encoding calcium pump hSPCA1. This calcium pump is crucial for the formation of desmosomes. HHD is characterized by painful erosions restricting patients in daily life. Ablative laser therapy results in long-term remission.
Objectives: Primary aim is to understand the fundamental mechanisms of remission after laser therapy. Secondary outcomes are quality of life (QoL) and evaluation of optical coherence tomography (OCT) as a diagnostic tool.
Methods: We recruited eight patients with HHD. Biopsies were taken from affected and clinically unaffected skin before and six weeks upon treatment. Immunofluorescence was performed to study the localization of several desmosomal proteins and adherence junction protein beta-catenin. Ultrastructure of the epidermis and desmosomes was studied by electron microscopy. OCT characteristics of HHD before and after laser therapy were defined. QoL was measured with validated questionnaires DLQI and Skindex-29.
Results: Immunofluorescence studies demonstrated perinuclear distribution of desmosomal proteins but not beta-catenin, in affected skin. Normal cell membrane distribution was seen after treatment. Electron microscopy of affected skin showed acantholysis, defective desmosomes and perinuclear aggregation of tonofilaments, but normal epidermal structure after treatment. Different OCT characteristics have been

defined in unaffected and affected skin. QoL analysis showed significant improvement.
Conclusion: Immunofluorescence, electron microscopy and OCT demonstrated resolution of disease upon laser therapy. OCT can be used as complementary diagnostic tool. QoL increased significantly. Preliminary data suggest that desmosomes and not adherence junctions are important in the pathogenesis of HHD.

28. IGE IN SKIN AND SERUM OF NONBULLOUS AND BULLOUS PEMPHIGOID PATIENTS

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Background: Nonbullous pemphigoid (NBP) is a pemphigoid variant, in which for unknown reason patients do not develop blisters. In bullous pemphigoid (BP) accumulating evidence suggests a role for IgE in disease pathogenesis, and possibly in blister formation.
Objective: To study IgE autoantibodies in serum and skin of BP and NBP patients.
Methods: IgE in serum was measured by enzyme linked immunosorbent assay (ELISA), and in skin stained by immunofluorescence techniques.
Results: We included 67 NBP and 50 BP serum samples, and control sera of 25 pemphigus patients, and 25 elderly patients with pruritus. Total IgE was elevated in 60% and 63% of BP and NBP, and in 20% and 60% of pemphigus and elderly controls. IgE ELISAs were more frequently positive in BP than in NBP (NC16A 18% vs. 9%, p=0.139; BP230 34% vs. 22%, p=0.149). Surprisingly, elderly controls had IgE antibodies to NC16A and BP230 in 8% and 20%, while all pemphigus controls were negative. Skin biopsies of 14 BP and 14 NBP patients with highest anti-NC16A IgE ELISA titers were additionally stained for IgE. Two biopsies (7%; 1 NBP, 1 BP) showed linear IgE along the basement membrane zone, while IgE was most often bound to the surface of dermal cells in both pemphigoid phenotypes (71% NBP, 86% BP).
Conclusion: IgE was present in serum and skin of both NBP and BP patients, suggesting a supportive role of IgE instead of being a key mediator of blister formation in pemphigoid.

P1. TOPICAL APPLICATION OF GLYCEROL FOR INCREASING PENETRATION DEPTH IN DIAGNOSIS OF BASAL CELL CARCINOMA WITH OPTICAL COHERENCE TOMOGRAPHY

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Background: Optical coherence tomography (OCT) is a non-invasive imaging technique, allowing high-resolution *in vivo* imaging of the skin with a penetration depth around 1.5 mm. OCT is promising for diagnosis of basal cell carcinoma (BCC), but might be limited by the penetration depth in subtyping of BCC. With optical clearing agents, such as glycerol, it is possible to reduce light scattering in skin to increase optical penetration depth.
Objective: To investigate whether topical application of glycerol can increase the penetration depth for improved detection of BCCs.
Methods: Patients with a histopathologically confirmed BCC were included. For each patient, OCT scans were obtained before and after application of an 85% glycerol solution. A commercially available Vivosight OCT device was used to scan the marked biopsy area with a 6mm field of view. The average penetration depth for each OCT scan was acquired by automatically tracing both the skin surface and the point of signal loss at all locations using a custom-made MATLAB program. The average penetration depth before and after application of glycerol were compared using a paired student's t-test.
Results: In all 72 included patients both OCT scans were successfully obtained. The average penetration depth significantly increased with 2.3% after application of glycerol (902 µm vs 882 µmm, p = 0.008).
Conclusion: Application of an 85% glycerol solution increases optical penetration depth during OCT measurements of the skin. Further research will follow to investigate if this statistically significant increase is clinically relevant.

P2. PATIENT-REPORTED QUALITY OF LIFE IN SOLID ORGAN TRANSPLANT RECIPIENTS WITH KERATINOCYTE CARCINOMA

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Background: Although keratinocyte carcinoma (KC) is common in solid organ transplant recipients (SOTRs), no studies describe effects of these on health-related quality of life (HRQoL) in this patients.
Objective: To examine generic HRQoL of SOTRs with and without KC and to identify factors associated with KC-specific HRQoL-scores.
Methods: Cross-sectional, single center study among 1033 SOTRs. 106 SOTRs with histologically-confirmed KC were identified by medical record review. Nine SOTRs were excluded because of prior melanoma or being deceased. All SOTRs who indicated they were never diagnosed with skin cancer (n=939) served as the control group.

Results: All participants filled out the SF-36 questionnaire. Of the eligible 97 SOTRs with KC, 94 (96.9%) filled out the BaSQoL. Generic HRQoL did not differ significantly between SOTRs with and without KC. With respect to disease-specific HRQoL, the 'Worries' and 'Behavior' subscales of the BaSQoL showed low to moderately elevated scores. In multivariate analyses, female gender (β 0.13, 95% CI 0.02-0.23, P-value =.019) and number of KC lesions (β 0.23, 95% CI 0.10-0.37, P-value = .001) were independently associated with higher scores on the 'Appearance' subscale. The number of KC was independently associated with higher 'Behavior' subscale scores (β 0.28, 95% CI 0.11-0.45, P-value = .001).
Conclusions: These findings serve to highlight the importance for transplant physicians and dermatologists to be aware of the effect KC can have on HRQoL and to optimize patient care accordingly.

P3. TREATMENT BURDEN IN OLDER ADULTS WITH HIGH-RISK BASAL CELL CARCINOMA

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Background: It is sometimes presumed that treating older adults with basal cell carcinoma (BCC) with conventional excision (CE) is less burdensome than Mohs micrographic surgery (MMS), although data on treatment burden in this patient group is currently lacking.
Objective: To study the surgical treatment burden as experienced by older BCC patients.
Methods: A prospective multicenter cohort study was performed studying treatment burden (visual analogue scale measured 3 months after treatment; lower scores indicate a higher treatment burden) as experienced by patients aged 70 years and over with BCC in the head-and-neck area. Quantile regression was used to study differences in treatment burden between MMS and CE patients after correction for various patient-, tumor- and treatment characteristics, including frailty-related aspects: age, Charlson comorbidity index, polypharmacy and dependency in (instrumental) activities of daily living.
Results: A total of 539 patients were included with a median age of 78 years (range 70-95 years), 296 were treated with MMS and 243 with CE. No significant difference in treatment burden was seen between the MMS and CE groups (medians were 8.6 and 8.7 respectively, p=0.093), even after correction for patient-, tumor- and treatment characteristics; median difference in treatment burden was 0.20 (p=0.301; 95% CI [-0.15;0.49]).
Conclusion: This prospective multicenter cohort study shows a low overall surgical treatment burden as experienced by older patients with high-risk BCC. No significant difference in experienced treatment burden between MMS or CE was seen. Further research is needed to assess what variables might predict experienced treatment burden, for instance frailty.

P4. HIGH TREATMENT ADHERENCE IN CLINICAL TRIALS WITH THE USE OF A MOBILE E-DIARY APPLICATION

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Background: Assessment of treatment effects in clinical trials requires valid information on treatment adherence, adverse events and symptoms. Paper-based diaries are often inconvenient and have limited reliability, particularly for outpatient trials.
Objectives: To investigate the utility of an electronic diary (e-diary) application for patients with skin diseases in outpatient clinical trials.
Methods: An e-diary application was developed and technically validated. Treatment adherence as defined as topical administration by the patient and patient-reported outcomes, i.e. pain and itch, were evaluated by the e-diary in six clinical trials on newly tested topical drugs. Additionally, the proportion of patients capturing the applied topical drug by camera and filling in the pain and itch scores as defined as e-diary adherence, patients' perception of usefulness and acceptability of the e-diary were evaluated.
Results: Treatment adherence rates of the included 256 patients were high (median 98%, range 97-99%). E-diary adherence was also high with a median of 93% (range 87-97%) for capturing the applied drug by camera, 89% (range 87-96%) and 94% (range 87-96%) for entering respectively the itch and pain score. Daily symptom scores provided good insights in the disease burden and patients rated the e-diary as good to excellent with respect to user acceptability.
Conclusions: The results suggest that the e-diary is an excellent way to ensure proper treatment administration, indicated by both the high user acceptability scores and high treatment adherence. Moreover, the e-diary may also be valuable for frequent and reliable monitoring of patient-reported outcomes in daily clinical practice.

P5. INCIDENCE RATES OF PEMPHIGOID DISEASES, PEMPHIGUS DISEASES, AND DERMATITIS HERPETIFORMIS IN THE NETHERLANDS DURING THE 1991-2018 PERIOD

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Background: The incidence of autoimmune bullous diseases (AIBDs) in the Netherlands is unknown.
Objective: To determine the yearly nationwide incidence of AIBDs, specifically pemphigoid diseases, pemphigus diseases, and dermatitis herpetiformis (DH), in the Netherlands in the 2009-2018 period. To enable analysis of the incidence over a longer period of time, data from 1991 and 2000 were additionally included.
Methods: Reports concerning cases of pemphigoid diseases, pemphigus diseases and DH were derived from the computerised database of the Dutch pathology registry, which contains data on all histopathology and cytopathology reports in the Netherlands. Incidences were estimated using the annual total number of inhabitants, registered by the Dutch population registry.
Results: In the 2009-2018 period, the incidence of pemphigoid diseases ranged from 2.80 to 3.40 per 100,000 per year, that of pemphigus diseases from 0.31 to 0.51 and that of DH from 0.27 to 0.31. Compared with 1991 and 2000, the incidence of pemphigoid diseases appeared to have increased and that of DH to have decreased, whereas the incidence of pemphigus diseases was stable. The mean annual incidence in the 2009-2018 period was highest in men above 80 years for pemphigoid diseases, in both men and women above 80 years for pemphigus diseases and in men aged between 70-79 for DH.
Conclusion: This is the first report of the Dutch nationwide incidence of pemphigoid diseases, pemphigus diseases and DH. We found no increase in the total number of AIBD cases nor the incidence during the 2009-2018 period.

P6. PATIENTS' PERSPECTIVE ON CURRENT TREATMENTS AND DEMAND FOR NOVEL TREATMENTS FOR VITILIGO

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Background: To date, there is no curative treatment for non-segmental vitiligo (NSV). Current treatments often achieve suboptimal clinical results in a majority of patients. It is, however, unknown whether there is a demand for novel therapies and if patients are willing to participate in clinical trials.
Objective: The aim of this prospective questionnaire study was to assess the patients' perspective on current and novel therapies for vitiligo.
Methods: A prospective questionnaire study was conducted in a cohort of NSV patients that visited the Amsterdam UMC outpatient clinic between April 2017 and December 2018. This questionnaire was used to assess patient and vitiligo characteristics, treatment history, efficacy and satisfaction, demand for new treatments, willingness to pay and willingness to participate in clinical trials.
Results: Of the respondents (N= 324) 94% believed that new and improved treatment modalities are needed for vitiligo. 86% would be willing to participate in clinical trials and 69% would agree on using a new effective medication if it consisted of weekly injections. For an effective treatment, 39% was prepared to pay over €2,000. Of the patients that had received therapy, 52% felt that the current treatment was not effective and 53% was not satisfied with the current treatment.
Conclusion: There is a substantial demand for new vitiligo therapies. A considerable amount of patients in our study is dissatisfied with the current treatments and the majority is willing to participate in clinical trials.

P7. THE EFFECT OF FOUR TREATMENT APPROACHES FOR ACTINIC KERATOSIS ON THE QUALITY OF LIFE, ASSESSED BY SKINDEX-29 AND AKQOL

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Background: Large areas of actinic keratosis (AK) are best treated with field-directed therapy. One of the reasons to treat AK is improvement of the health-related quality of life (HRQoL) of patients.
Objective: To analyze the effect of four AK treatments on HRQoL.
Methods: From 2014 to 2018 a total of 624 patients with a minimum of five AK lesions on the face or scalp were randomized to 5-fluorouracil (5-FU), imiquimod (IMQ), ingenol mebutate (IM) and methylaminolevulinate photodynamic therapy (MAL-PDT) Patients completed the Skindex-29 and the AKQoL as measures of HRQoL at baseline, 3 and 12 months after treatment. Independent samples t-tests were conducted to compare the mean change between treatment groups at 12 months post-treatment.
Results: At 12 months post treatment, improvement in HRQoL, reflected by decrease in Skindex-29 and AKQoL score, was found in all treatment groups. The mean change in Skindex-29 score was -4.89 (SD=6.88) for 5-FU, -4.80 (SD=9.54) for IMQ, -4.30 (SD=8.29) for IM, and -2.93 (SD=7.55) for MAL-PDT. P-values comparing MAL-PDT with 5-FU, IMQ and IM were p=0.021, p=0.067, and p=0.319, respectively. The mean change in AKQoL score was -0.90 (SD=3.08) for 5 FU, -0.99 (SD=2.66) for IMQ, -1.14 (SD=3.47) for IM, and -0.19 (SD=2.86) for MAL-PDT. P-values comparing MAL-PDT with 5-FU, IIMQ and IM were p=0.040, p=0.014, and p=0.011, respectively.
Conclusion: Treatment and especially topical treatment, led to an improvement in HRQoL in patients with AK, no matter the effectiveness.

P8. EFFECT OF CYTOKINES ON PD-L1 EXPRESSION ON MELANOMA CELLS AND T CELL EFFECTOR FUNCTION

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Background: The immune inhibitory molecule PD-L1 is commonly involved in immune evasion by tumors. Therefore, it is important to understand the regulation of PD-L1 expression on tumor cells and their normal counterparts. IFN-γ upregulates PD-L1 expression, but the effect of other cytokines is less known.
Objective: We investigated the effect of type I interferons and immunosuppressive cytokines on PD-L1 expression by melanoma cell lines and normal skin cell types.
Methods: PD-L1 expression on melanoma cells and cytokine production by autologous T cells after co-culture experiments was analyzed by flow cytometry.
Results: PD-L1 expression was not only induced by IFN-γ, but also by IFN-α, IFN-β, IL-4 and IL-10. Analysis of 375 cutaneous melanoma samples (TCGA) showed significant correlations of *PD-L1* and *IFN-γ*, *IFN-β1* or *IL-10* mRNA expression in the tumor tissue. Activation of T cells by autologous IFN-γ or IFN-β1a-stimulated melanoma cells, was increased by blocking either PD-1 or PD-L1 signaling. Interestingly, cytokine exposure also increased the constitutive PD-L1 expression by healthy human melanocytes, fibroblasts and the human keratinocyte cell line HaCat. The finding that these cytokines induce PD-L1 upregulation to the same extent both in cancer cells and normal tissue cells suggests that tumor immune escape by PD-L1 upregulation is not a tumor characteristic acquired by malignant transformation, but results from high cytokine levels in the tumor micro-environment.
Conclusion: These data demonstrate that type I interferons and anti-inflammatory cytokines can increase PD-L1 expression on melanoma cells and normal skin cells, with negative consequences for T cell effector function against melanoma.

P9. CHARACTERIZATION OF SKIN INFLAMMATORY MODELS IN HEALTHY VOLUNTEERS

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Background: Early phase clinical research for drug development requires investigation of safety, tolerability and efficacy. The latter is hampered by absence of the disorder in healthy volunteers. Therefore challenge models are often applied in order to demonstrate 'proof of pharmacology' of novel compounds. These challenge models are often translated from animal work and can inform drug developer which dose, dosing regimen or application frequency should be selected prior to phase 2 studies in target population.
Objective: To evaluate current literature on local inflammatory models and to provide an oversight on caused immune responses and pharmacodynamic effects of these models.
Methods: A non- comprehensive literature search resulted in approximately 100 articles deliberating ten skin challenge models in the categories: inflammation, itch and UV-exposure. Imiquimod induced skin inflammation, histamine and cowhage provocation, UV-B skin irradiation and KLH induced skin inflammation were selected to be evaluated.
Results: The challenges caused the desirable expected effect, i.e. inflammation, itch, skin irradiation and hypersensitivity, respectively. However, only imiquimod and KLH skin challenge model were well described and assessed with a toolbox of imaging, biophysical, clinical, cellular and molecular measurements. Topical application of imiquimod resulted in a quick innate immune response followed by an adaptive response while histamine and UV-B irradiation only generated innate immune responses. KLH induced only an adaptive immune response.
Conclusion: All four evaluated models seem appropriate for future *proof-of-pharmacology* of novel compounds. Depending on the expected mode of action of novel compounds, the right challenge model can be chosen.

P10. IGM-MEDIATED BULLOUS PEMPHIGOID: AN ENIGMA

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Background: Bullous pemphigoid (BP) is an autoimmune blistering disease (AIBD), characterized by the presence of pruritus, tense blisters and erosions of the skin and/or mucosa, subepidermal splitting and linear IgG and/or complement deposition along the epidermal basal membrane zone (EBMZ), directed against the hemidesmosomal proteins BP180 and BP230. Deposition of IgA in conjunction with IgG is regularly found in BP, while the presence of only IgM deposition in pemphigoid has rarely been described and the relevance of IgM in the pathomechanism of AIBD is still debated.
Objective & Methods: We describe an unique case involving a patient with BP clinically, in which exclusively tissue bound- and circulating IgM class antibodies where present and no evidence of immunoglobulin class-switching could be found.
Results: A healthy 49-year-old woman presented with a six-year history of spontaneous blisters with involvement of the buccal mucosa, without scarring. Exceptionally, pruritus was not present. Direct immunofluorescence (DIF) showed a strong linear n-serrated deposition of IgM and complement along the EBMZ, without the presence of IgG or IgA. Indirect immunofluorescence of salt-split skin (IIF-SSS) showed a strong epidermal staining for IgM, whereas IgG and IgA were negative. Investigations were frequently repeated in the following years, but only deposition of IgM antibodies could be demonstrated. The patient was therapy resistant, and only with HIVIG-infusions she could be kept in remission for years.
Conclusion: This case proves that IgM-mediated (bullous) pemphigoid exists and is one of those rare autoimmune cases in which immunoglobulin class-switching does not seem to appear.

P11. MEDICAL HISTORY OF PATIENTS WITH PSORIASIS TREATED WITH APREMILAST IN THE NETHERLANDS: INTERIM RESULTS FROM 145 PATIENTS IN THE PROSPECTIVE, MULTICENTER, REAL-WORLD APRIL STUDY

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Background: Psoriasis is associated with high disease burden and increased risk of comorbid diseases.
Objective: To compare disease burden and comorbidities in patients with mild to moderate vs. severe psoriasis.
Methods: The prospective, multicenter, observational APRIL study (NCT02652494) assessed quality of life (QOL) using the Dermatology Life Quality Index (DLQI), specific manifestations of psoriasis (nail, scalp, palmoplantar), and common comorbidities of psoriasis in patients with plaque psoriasis treated with apremilast in The Netherlands. An interim analysis compared results in patients with mild to moderate (BSA≤10%) vs. severe (BSA>10%) psoriasis.
Results: There were 145 patients included in the analysis (BSA≤10%, n=100; BSA>10%, n=45). Mean baseline DLQI scores were 11.0 vs. 11.2 for the BSA≤10% vs. BSA>10% groups , indicating a very large impact on QOL. Specific manifestations of psoriasis for patients with BSA≤10% vs. BSA>10%, respectively, were: nail (53.0% vs. 54.3%), scalp (72.0% vs. 80.4%), and palmoplantar (22.0% vs. 43.5 %). Comorbidities ≥5% in either group (BSA≤10% vs. BSA>10%) included psoriatic arthritis (17.0% vs. 20.0%), cardiovascular disease (16.0% vs. 24.4%), hypercholesterolemia (12.0% vs. 15.6%), pulmonary disease (10.0% vs. 20.0%), depression (12.0% vs. 11.1%), malignancy (11.0% vs. 11.1%), hypertension (9.0% vs. 11.1%), type 2 diabetes (4.0% vs. 6.7%), gastrointestinal disease (4.0% vs. 6.7%), history of infection (2.0% vs. 6.7%), latent tuberculosis (0% vs. 6.7%), and kidney disease (1.0% vs. 6.7%).
Conclusions: In patients with mild to moderate vs. severe psoriasis, QOL was generally similar whereas differences in comorbidities were present.

P12. GENE EXPRESSION PROFILE OF LESIONAL SKIN IN BULLOUS AND NONBULLOUS PEMPHIGOID: AN EXPLORATIVE PILOT STUDY

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Background: Bullous pemphigoid (BP) is an autoimmune bullous disease. Studies suggested complement dependent and independent blister mechanisms, and important roles for eosinophils and mast cells. Nonbullous pemphigoid (NBP) is a clinical variant of pemphigoid in which blisters are absent. The pathogenesis of NBP was not studied before.
Objective: To assess gene expression profiles of lesional skin in NBP and BP.
Methods: Histopathology biopsies of 12 NBP and 12 BP patients were retrospectively selected. Immunosuppressive drugs were not allowed at time of biopsy. Gene expression was quantified by the digital color-coded barcode technology of the Nanostring nCounter. Data analysis was performed with nSolver Analysis Software.
Results: Gene expression was successfully measured in 10 BP, and 12 NBP biopsies. Complement activation related genes were highly expressed in 6 BP biopsies, while 4 BP and 12 NBP biopsies showed lower expression. Expression of T helper 1 (Th1) and 2 (Th2) related genes was high in all BP biopsies. In NBP, genes involved in Th1 responses were highly expressed in 33%, and genes involved in Th2 responses in 17%. Differential expression analysis identified several genes that differed most in expression between NBP and BP biopsies, including SERPINB2, FOSB, CXCL8, and ATF3. None of the p-values were close to significance after correcting for false discovery rates. Limitations: Multiple testing combined with a small sample size led to a multiple testing problem.
Conclusion: Our findings support the hypothesis that complement activation, and both Th1 and Th2 helper responses might be important for blister formation in BP.

P13. EXTERNAL VALIDATION: A CLINICAL PREDICTION MODEL FOR SURGICAL SITE INFECTION IN DERMATOLOGIC SURGERY

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Background: Surgical site infection (SSI) is the most common complication in dermatologic surgery and probably a determinant for worse cosmetic outcome. A model predicting the individual probability of developing an SSI after dermatologic surgery based on clinical parameters (defect size, tumor location and type of closure) was developed and internally validated by Liu et al. (2018) in the MUMC+.
Objective: To externally validate the clinical prediction model to implement the model in medical practice.
Methods: The study included 6359 Mohs' Micrographic Surgery (MMS) procedures in 5638 patients. Data was retrospectively collected in three private hospital locations in the Netherlands between January 2017 and July 2019. Patients with a history of perioperative use of oral antibiotics and patients with lacking information on drug-use in the country-wide database were excluded. Finally, 2645 MMS procedures were eligible for analysis. Performance of the model was measured using the discriminative ability and was quantified as the area under the receiver operating characteristic curve (AUC). Accuracy of the prediction was displayed by a calibration slope measured in the calibration plot.
Results: A total of 89 patients developed an SSI after MMS. The AUC was 0.67 (95% confidence interval 0,62–0,73). The estimated slope of the calibration plot was 0.49.
Conclusion: The previously published prediction model showed a less predictive performance in the external validation

cohort. Although data validity is limited due to the high number of excluded patients, development of a better fitting prediction model may be necessary to predict SSI after dermatologic surgery in this cohort.

P14. INTERPRETABILITY OF THE QUALITY OF LIFE IN HAND ECZEMA QUESTIONNAIRE (QOLHEQ)

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Background: The Quality Of Life in Hand Eczema Questionnaire (QOLHEQ) is used to measure impairment of health-related quality of life (HRQoL) in hand eczema. Its interpretability is unknown.
Objective: Here, we prospectively studied the interpretability of international QOLHEQ scores.
Methods: The questionnaire was completed at three time points: baseline, after 1-3 days (T1) and after 4-12 weeks (T2). Adult patients with hand eczema completed the QOLHEQ and anchor questions for overall assessment of HRQoL impairment. Interpretability of single scores was assessed at baseline by defining severity bands based on agreement with the anchor questions. Smallest detectable change (SDC) was calculated at T1. Minimally important change (MIC) of improvement was calculated at T2 using three methods: mean cut-off, receiver operating curve (ROC) and 95% limit.
Results: N=294 adult patients were included (N=160 males, mean age 44.9). The final proposed severity band of overall QOLHEQ single scores (κ-coefficient of agreement, 0.431) was: not at all, 0-10; slightly, 11-39; moderately, 40-61; strongly, 62-86; very strongly, ≥87. Separate overall severity bands were proposed for males and females, and the four subscales of the QOLHEQ. The SDC in N=166 unchanged patients was 18.6 points. The preferred MIC, obtained with the ROC method was 21.5 points.
Conclusion: An overall QOLHEQ score of ≥ 22 is recommended as cut-off for a minimally important, real change. The reported values for interpretability of QOLHEQ single scores and change scores aid clinical decision making and research in hand eczema patients.

P15. HIDRADENITIS SUPPURATIVA HAS A CLEAR IMPACT ON WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT

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Background: Hidradenitis suppurativa (HS) is a chronic, autoinflammatory skin disease characterised by painful inflammatory nodules and abscesses. It has a profound impact on the quality of life and predominantly affects individuals in their work-productive years. The impact of HS on work productivity remains unknown.
Objective: To examine the extent of both work productivity impairment and activity impairment outside work due to HS.
Methods: A cross-sectional study was performed collecting data through registries from the UMCG and Erasmus MC between April 2015 and July 2019. Main outcomes were derived from the Work Productivity and Activity Impairment (WPAI) questionnaire and included activity impairment outside work, absenteeism (sick leave), presenteeism (reduced work performance), and at-work productivity loss (overall work productivity loss) in the last week. All outcomes were scaled 0-100%, with higher percentages indicating higher impairments.
Results: In total 843 patients were included (71.6% female; mean age 38.0 ± 12.2 years) and 33.7% had severe HS based on the refined Hurley classification. Among both workers and non-workers median activity impairment outside work was 40.0% [IQR: 10.0-70.0]. Among workers (n=529; 62.8%) median absenteeism was 0.0% [IQR: 0.0-5.3] and 26.4% of workers reported taking sick leave. Median presenteeism was 20.0% [IQR: 0.0-52.5] and at-work productivity loss was 20.0% [IQR: 0.0-69.0].
Conclusion: This study demonstrated that sick leave due to HS was reported in a quarter of patients. While working, HS patients experience reasonable at-work productivity loss. In addition, HS has major impact on people's activities outside of work.

P16. QUALITY OF LIFE, TREATMENT SATISFACTION AND ADHERENCE TO TREATMENT, IN PATIENTS WITH RECURRENT VESICULAR HAND ECZEMA – A CROSS SECTIONAL STUDY

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Background: Recurrent vesicular hand eczema frequently results in chronic hand eczema and need for long-term treatment.
Objectives: To evaluate health related quality of life (HRQOL), treatment satisfaction and adherence in patients with vesicular hand eczema.
Methods: Patients using one main treatment for at least three months were included. Data on HRQOL (Quality of Life in Hand Eczema Questionnaire, QOLHEQ), treatment satisfaction (Treatment Satisfaction Questionnaire for Medication II, TSQM) and treatment adherence (Morisky Medication Adherence Scale, MMAS-4) were collected. Uni- and multivariable regression analysis were used to predict variables associated with HRQOL.
Results: HRQOL was moderately impaired, with highest impact in the QOLHEQ subdomain symptoms. Female sex, more severe hand eczema and lower treatment satisfaction were associated with more impairment in HRQOL. Patients with

severe/very severe hand eczema had significant lower global treatment satisfaction scores compared to the other severity groups. The global treatment satisfaction and treatment adherence in patients using systemic treatment was significantly higher compared to those with only topical treatment.
Conclusions: In patients with vesicular hand eczema disease severity affects both HRQOL and treatment satisfaction. Systemic treatment of severe hand eczema could improve the severity and as a result also HRQOL, treatment satisfaction and medication adherence.

P17. GENOTYPE-PHENOTYPE CORRELATION AND EFFECTIVENESS OF USTEKINUMAB IN CARD14-ASSOCIATED PAPULOSQUAMOUS ERUPTION

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Background: CARD14-associated papulosquamous eruption (CAPE) is a rare autosomal-dominant inherited dermatosis characterized by palmoplantar keratoderma and follicular keratotic papules coalescing into erythematosquamous plaques. It bears similarities with psoriasis and pityriasis rubra pilaris (PRP) and is resistant to classical systemic therapies. The causal activating mutation in the CARD14 gene results in NFκB activation.
Objective: Identifying a possible genotype-phenotype correlation and study the ustekinumab effect in Dutch CAPE patients.
Methods: Data of Dutch patients with activating CARD14 mutation was retrospectively analyzed using a modified genodermatosis deep phenotyping list of the European Reference Network-Skin. The effect of ustekinumab was evaluated using the investigator global assessment (IGA) and PASI-scores from photographic documentation.
Results: Currently 7 patients have been included. CAPE shows onset within the first year of life, starting with facial erythema and scaling, followed by erythematosquamous plaques on the trunk and extremities. Diagnostic delay ranged from 2-56 years. Identifying a genotype-phenotype correlation was not possible yet. Four patients received ustekinumab with pretreatment IGA median of 4, decreasing to 2 after 6-12 months. PASI could be collected in 3 patients with a mean of 23,3 (19,1-31,2) ameliorating to 3.8 (3,5-4,1) after 6-12 months in case of patient 1 and 3. Patient 6 scored 15.6 after 5,5 years of therapy, with earlier data unavailable.
Conclusion: CAPE is a rare disease with a long diagnostic delay. Ustekinumab is an effective treatment modality. Currently no genotype-phenotype correlation could be identified. Therefore, we are gathering data from other European countries to build a larger cohort.

P18. INTRADERMAL MICRONEEDLE DELIVERY COMPARED TO SUBCUTANEOUS ADMINISTRATION OF ADALIMUMAB: PHARMACOKINETICS AND PAIN

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Background: Adalimumab is an effective treatment for a variety of auto-immune diseases administered via subcutaneous injection. The drawback of this approach is that subcutaneous injections are being perceived as unpleasant and painful. Therefore, there is an unmet need for less invasive administration of drugs.
Objective: To compare the pain perception and pharmacokinetics of adalimumab administered subcutaneously versus intradermally via microneedles in healthy volunteers.
Methods: A randomized, double blind, placebo controlled, double dummy clinical trial was performed. Twenty-four healthy volunteers received two injections, i.e. a single dose of 40 mg adalimumab and placebo. One injection was administered subcutaneous, the other was administered intradermally with a MicronJet600® hollow microneedle (NanoPass, Israel) in the right or left thigh in a counterbalanced manner. Furthermore, pain perception on the needle insertion and fluid injection was quantified using a visual analogue scale (VAS).
Results: The bioavailability of adalimumab was higher (29%) after an intradermal injection compared to a subcutaneous injection ($p<0.05$). A population pharmacokinetic model showed that intradermal injection had an initial fast absorption phase (3.5 mg/day), whereas the subcutaneous injection had a slower initial absorption phase (0.5 mg/day). No significant difference was observed between needle insertion pain but contrary to expected, the healthy volunteers preferred subcutaneous injection over intradermal injection based on VAS scores ($p<0.0001$) that is likely related to the injected volume.
Conclusion: In conclusion, this study showed that intradermal delivery of adalimumab using microneedles is safe, and reaches clinically relevant concentration, but warrants further investigation into volumes that are suitable for microneedle administration.

P19. EUROPEAN EVIDENCE AND CONSENSUS-BASED (S3) GUIDELINE FOR THE DIAGNOSIS AND TREATMENT OF MUCOUS MEMBRANE PEMPHIGOID

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Background: Mucous membrane pemphigoid (MMP) describes a group of subepidermal bullous disease primarily affecting mucous membranes. In 2002, a consensus based guideline for the diagnosis and management of MMP was developed.

However, new insights have led to the need for an update of the guideline.
Objective: To develop a multidisciplinary S3 European guideline based on both evidence and expert opinion.
Methods: A literature search in MEDLINE and EMBASE databases was performed based on formulated questions regarding clinical presentation, diagnostics, outcome measurements and management. Relevant articles that answer the research questions were selected. The level of evidence of the studies are separately graded by using the Oxford Centre for Evidence-Based Medicine (OCEBM) 2011 Levels of Evidence. Recommendations were formulated and were based on both evidence and expert opinion.
Main results: Direct immunofluorescence (DIF) microscopy has the highest sensitivity and is recommended in all patients with suspicion of MMP. A second DIF biopsy from a different site is recommended in case of an initially negative DIF. To detect circulating autoantibodies, an indirect immunofluorescence (IIF) microscopy on human salt-split skin should be performed. In contrast to the previous guideline, rituximab is added as second line therapy in severe MMP. Both ODSS and the oral part of MMPDAI and ABSIS are validated disease severity scoring tools for oral MMP.
Conclusion: This updated guideline presents new evidence and consensus based conclusions and recommendations regarding the diagnostic strategy, management including a flowchart for systemic treatment and validated disease severity scoring tools for oral MMP.

P20. ASSESSMENT OF DIAGNOSTIC STRATEGY IN MUCOUS MEMBRANE PEMPHIGOID

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Background: Mucous membrane pemphigoid (MMP) describes a group of autoimmune bullous diseases with predominantly mucosal involvement and a tendency to scar. A significant diagnostic delay is often seen due to the highly variable symptoms in various subtypes, low-autoantibody titers and different biopsy sites in multi-site involvement.
Objective: To assess the optimal diagnostic strategy for diagnosis of MMP.
Methods: Retrospective study of patients with mucosal lesions suspected of MMP. Eligible patients had a mucosal biopsy for direct immunofluorescence (DIF) microscopy; indirect immunofluorescence microscopy (IIF) on a human salt-split skin (SSS), and one or more immunoassays pairwise performed between 2002 and 2019.
Results: 792 patients were included, of which MMP was diagnosed in 122 patients. The oral mucosa was the most affected site in MMP (106/122, 87%), with multisite mucosal involvement seen in 45/122 (37%) MMP patients. Skin lesions were present in 24/122 (20%) MMP patients.
The sensitivity of DIF on oral, ocular and anogenital mucosa was 91%, 83% and 91%. A perilesional oral biopsy showed higher sensitivity than taken from healthy mucosa (93% vs 81%). DIF was positive in 51/66 (77%) available skin biopsies of MMP patients, including 34 patients without any skin symptoms. Serological test were highly specific, but lacked sensitivity. Highest sensitivities were seen for immunoblot (62.8%) and IIF SSS (47.5%).
Conclusion: A perilesional biopsy for DIF of the affected mucosa is the reference standard for diagnosis of MMP. Performing IIF SSS, immunoblot or a skin biopsy for DIF may increase the diagnostic yield to identify this heterogeneous disease.

P21. DISCOVERY OF ARTHRITIS IN PSORIASIS FOR EARLY RHEUMATOLOGIC REFERRAL (DAPPER): A CROSS-SECTIONAL STUDY

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Background: One in three patients with psoriasis (Pso) will develop psoriatic arthritis (PsA). When untreated, this can lead to disability and irreversible joint damage. Current screening methods are mostly based on questionnaires. These lack specificity and sensitivity. Thus, a significant portion of PsA patients remains undetected.
Objective: Our main objective is to ascertain the prevalence of PsA in a cohort of Pso patient, treated at a dermatology outpatient clinic. Secondary, we wish to discover clinical and biochemical characteristics which may help the dermatologist to discover the presence of PsA.
Methods: A sample of 300 patients, stratified for current skin therapy (topical, systemic non-biologic, biologic), will be screened by a rheumatology resident for PsA signs and symptoms. When PsA is suspected, patients are referred to a rheumatologist for confirmation. Clinical characteristics and biomaterials are gathered at the screening visit.
Results: 72 patients with Pso were screened at the moment of writing. 62% were male. Average age was 56 years old. 27 patients used biological therapy, 23 used systemic non-biologic therapy and 20 used only topical medications. Twelve patients (17%) were known to have PsA. Seven patients (10%) were referred for to the rheumatology department. One of these showed active PsA requiring a treatment change, two had alternative diagnosis (osteo-arthritis) and four are still under evaluation.
Conclusion: Preliminary data of the DAPPER study reveal that the prevalence of confirmed PsA in Pso patients is 18%. If all suspected PsA are confirmed, this rises to 24%.

P22. TOPICAL PATHOGENESIS-BASED THERAPY IN CONRADI-HUNERMANN-HAPPLE SYNDROME

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Background: Conradi-Hunermann-Happle syndrome (CHH) is a rare, X-linked dominant inherited genodermatosis with characteristic features in mosaic pattern due to X-inactivation. The disorder is associated with mutations in the emopamil-binding protein (EBP) gene, essential for cholesterol biosynthesis. Sufficient treatment is lacking.
Objective: In order to decrease the effect of toxic cholesterol precursors and restore cholesterol in the skin, a topical statin/cholesterol lotion was administered as pathogenesis-based therapy.
Methods: A 9-year old girl with genetically proven CHH was enrolled. The simvastatin (5 grams) / cholesterol (5 grams) suspended in 240 ml paraben-preserved water was applied twice daily for 9 months. The effect was monitored at a 6-8 week interval with a diversity of indices.
Results: After 9 months of treatment, disease severity indices (PASI and EASI) showed a reduction of respectively 47 and 49% from baseline. The Numeric Itch Rating Scale did not show improvement. Interestingly the Patient Orientated Eczema Measure increased over time. The only reported side-effect was dryness of the skin after application. Routinely blood testing after 12 and 36 weeks did not show significant changes compared to baseline.
Conclusion: Topical statin/cholesterol is a safe and effective treatment in CHH. The increased POEM-values during treatment might be explained by increased dryness caused by the suspension as the questionnaire assesses the flaking and the feeling of dryness or roughness of the skin. With increased understanding of genodermatoses in dermatological practice, awareness of comparable pathogenesis-based treatment strategies is essential for optimizing treatment.

P23. OBSERVATIONAL STUDY ON THE EFFECT OF DUPILUMAB ON HAND ECZEMA IN PATIENTS WITH ATOPIC DERMATITIS: AN UPDATE

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Background: Systemic treatment options for chronic hand eczema are limited. Dupilumab is used in atopic dermatitis (AD)but is not licensed for (isolated) hand eczema (HE).
Objective: The aim of this study was to determine the response of HE to dupilumab in patients with AD.
Methods: Observational prospective study. Adult patients with HE and AD were treated with dupilumab subcutaneously in a 600mg loading dose, followed by 300mg every two weeks. Primary outcome was a minimum improvement of 75% on the Hand Eczema Severity Index after 52 weeks (HECSI-75). Secondary outcomes were hand eczema severity measured using the Photographic guide for severity; quality of life improvement measured using the Dermatology Life Quality Index (DLQI) and The Quality Of Life in Hand Eczema Questionnaire (QOLHEQ) score as patient reported outcomes; and the Eczema Area and Severity Index (EASI).
Results: Thirty-eight patients were included (28 males, 10 females; mean age 47 years). HECSI-75 was achieved by N=33 (86.8%). Mean reduction in HECSI score was 56.0 (88.7%). 27 patients (71.1%) were classified as responder on the Photographic guide. There was no difference in response between chronic fissured and recurrent vesicular clinical subtypes. Similar percentages of EASI-75 and HECSI-75 were seen after 52 weeks. The results of the difference in DLQI and QOLHEQ scores will be available at the NVED 2020 meeting.
Conclusion: This study shows a positive response of AHE to dupilumab. This poses the question whether a response will also be seen in isolated hand eczema.

P24. 3D HUMAN EPIDERMAL EQUIVALENTS FOR DRUG POSITIONING: AN UNBIASED APPROACH ILLUSTRATED BY AHR AGONISTS FOR ATOPIC DERMATITIS TREATMENT

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Background: Modelling diseases is a vital part in the development of therapeutics. Three dimensional (3D) human epidermal equivalents (HEEs) offer a compelling technology for modeling skin diseases and positioning therapeutics. However, an unbiased overview comparing these HEEs to *in vivo* healthy and diseased skin is still lacking.
Objective: To provide an unbiased comparison between HEEs, monolayer keratinocyte cultures and *in vivo* human epidermis to assess their ability to model atopic dermatitis (AD) and drug effects.
Methods: HEEs from three donors were cultured with IL-4 to induce AD hallmarks and treated with AHR ligands (SGA derivatives) to determine their therapeutic potential. RNA was collected and sequenced using Illumina sequencing. Data will be compared to previously collected data from submerged cultures and publicly available datasets on *in vivo* skin.
Results: RNAseq data of normal and AD-like HEEs compared to data from submerged cultures and *in vivo* normal and AD skin provide an unbiased overview by comparing the entire RNA expression profile by means of at least heat map analysis and PCA plot analysis. RNAseq of the HEEs resulted in high quality reads and will be mapped and analyzed using established STAR scripts and R software.
Conclusion: Results of this study will reveal whether HEEs can faithfully mimic the epidermal transcriptome of normal and inflamed skin and highlight their potential for drug screening and the positioning of small molecules like the SGA compounds targeting the aryl hydrocarbon receptor as novel therapeutics.

P25. THE EXPRESSION PATTERN OF N-ACETYLTRANSFERASE 1 IN HEALTHY HUMAN SKIN

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Background: N-acetyltransferases 1 (NAT1) is an enzyme expressed among other in keratinocytes in the human skin. NAT1 is important in the biotransformation of aromatic amines, an important example being P-phenylenediamine (PPD). Unoxidized PPD, that penetrates the stratum corneum of the skin is N-acetylated by NAT1 into mono-acetyl PPD (MAPPD) and diacetyl PPD (DAPPD).
Objectives: To investigate into detail the expression pattern of NAT1 in human skin.
Methods: Cryosections obtained from normal human skin were stained with a monoclonal antihuman NAT1 antibody and a fluorescein isothiocyanate-labeled secondary antibody. Staining patterns were observed using immunofluorescent microscopy. Immunofluorescence double stainings with antibodies against lysosomes, endosomes, Golgi apparatus, mitochondria and corneodesmosomes were performed to obtain information on the location of NAT1 in keratinocytes.
Results: Immunofluorescence microscopy showed a speckled, granular staining of NAT1 in the stratum granulosum and in the lower epidermis as well. Local differences in NAT1 expression pattern were observed. The speckled staining pattern suggested NAT1 to be present in organelles. Therefore double stainings with selected organelles were performed. No co-localization with either lysosomes, endosomes, Golgi apparatus, mitochondria or corneodesmosomes was found.
Conclusions: NAT1 is expressed in the stratum granulosum and in the lower epidermis as well with local differences in expression pattern. The speckled or granular pattern suggest that NAT1 can be found in organelles. However, no co-localization was observed in the selected organelles and further studies should be performed to investigate the function and expression of NAT1 in human epidermis.

P26. PERSONAL TREATMENT GOALS IN PSORIATIC PATIENTS WITH A STABLE LOW DISEASE ACTIVITY

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Background: Contrary to patients with severe psoriatic disease, little data is available on the needs of patients with a low, stable disease activity.
Objective: To get insight in unmet patient needs of psoriatic patients on biologic therapy with a stable, low disease activity.
Method: Treatment goals were explored by using the Patient Needs Questionnaire (PNQ) in patients treated with adalimumab, etanercept or ustekinumab. All patients had a Psoriasis Area and Severity Index (PASI) score ≤5 and stable psoriasis for at least 6 months at inclusion. Data was analysed per PNQ subscale, type of biologic, gender, and age group (<50 years vs > 50 years old) using descriptive statistics, independent sample T-tests or Mann-Whiney U-tests.
Results: Most patients rated 'be free of itching', 'be healed of all skin defects' and 'have confidence in the therapy' as quite/very important (78.5%). Of the 5 PNQ subscales, most importance was assigned to building confidence into therapy (mean PNQ score 2.85 ± 1.26). Reducing social impairments were of least importance (mean PNQ score 1.97 ± 1.36). Compared to male patients, female patients reported higher importance scores in most treatment goals, with significant differences for 'feel less depressed' (Mean PNQ score 2.43 vs 1.57) and 'be comfortable showing yourself more in public' (Mean PNQ score 3.10 vs 2.11). Younger patients reported higher mean importance scores in 23 out of 25 treatment goals compared to patients > 50 years old.
Conclusion: Patients with stable disease and low psoriatic disease activity still have substantial personal unmet treatment goals.

P27. THE SCOPE-ITSCC METASTASES STUDY

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Background: Organ transplant recipients (OTR) have a highly increased risk of cutaneous squamous cell carcinoma (cSCC) compared to the general population and many OTR develop multiple cSCC. Metastases of cSCC can lead to the death of the patient. So far no good prospective cohort studies are available to estimate the cumulative incidence of cSCC metastases in OTR. The SCOPE-ITSCC Metastases study is a multicenter prospective observational study which was initiated in 2013.
Objective: The first objective is to estimate the cumulative incidence of metastases of a single cSCC in OTR during a 2-year follow-up period. The second objective is to assess possible clinical and histological risk factors for metastases.
Methods: Data from all patients were collected in an Access database and analyzed using SPSS 25. Cumulative incidence of metastases was calculated by Kaplan Meier analyses. Multivariable Cox proportional hazard analyses were used for determining risk factors for metastases.
Results: In total, 505 OTR with a histologically proven cSCC were included in 19 centers. 34 OTR developed metastases (7.9%), 18 (4.2%) from the included cSCC. Older age at transplantation stands out as an important risk factor for metastasis. Differentiation grade, Breslow thickness, perineural invasion and invasion in deep structures were important histological risk factors.
Conclusion: Despite the fact that OTR develop more cSCC than immunocompetent patients, our results showed an incidence rate of metastases that is in line with the immunocompetent population. This study provides better insight in risk factors for metastases in OTR.