ABSTRACTS

Patient-reported well-being in value-based care using tildrakizumab in a real-world setting: Austrian subanalysis of 28-week interim data from the phase IV POSITIVE study

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Introduction: Psoriasis impairs patients' and families' social, emotional, functional and physical condition. Tildrakizumab is an anti-interleukin-23p19 indicated for moderate-to-severe plaque psoriasis. This analysis aimed to assess the effectiveness of tildrakizumab on the overall well-being and health-related quality of life (HRQoL) in Austrian patients with moderate-to-severe psoriasis from the POSITIVE study.

Methodology: This is a 24-month, phase IV observational multinational study in adults with moderate-to-severe plaque psoriasis receiving tildrakizumab in routine care. Well-being was assessed through the 5-item WHO Well-being Index (WHO-5; range 0-100, 100=maximal well-being). The HRQoL instrument was Dermatology Life Quality Index-Relevant (DLQI-R). Treatment satisfaction was assessed through the Treatment Satisfaction Questionnaire for Medication (TSQM-9). Here, we report the Austrian dataset of the 28-week (W) interim analysis based on observed cases.

Results: Forty-two patients were included (69.0% male, mean [SD] age: 45.6 [14.6]). Mean (SD) WHO-5 increased from 49.4 (19.6) at baseline to 69.1 (21.4) at W28 ($p<0.001$). Mean (SD) Psoriasis Area and Severity Index (PASI) decreased from 10.9 (5.6) at baseline to 0.6 (0.8) at W28 ($p<0.001$). At W28, 89.7%/68.4% of patients achieved PASI ≤3/≤1 responses. Mean (SD) DLQI-R decreased from 13.3 (8.1) at baseline to 2.4 (3.0) at W28 ($p<0.001$). At W28, mean (SD) scores on TSQM-9 domains were 84.1 (23.2)/90.0 (15.2)/89.8 (17.1) for effectiveness/convenience/global satisfaction. No adverse events were reported.

Conclusion: Results are consistent with those observed in the total POSITIVE population. Tildrakizumab significantly improved patients' well-being, skin symptoms and HRQoL, with high rates of treatment satisfaction and without safety concerns after 28 weeks in Austria.

Patient-reported well-being using tildrakizumab in a real-world setting: 28-week interim data in patients with nail psoriasis from the phase IV POSITIVE study

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Introduction: Nail psoriasis, a difficult-to-treat manifestation of psoriatic disease, affects 40-60% of patients with plaque psoriasis and often impairs health-related quality of life (HRQoL). Tildrakizumab is an anti-interleukin-23p19 indicated for moderate-to-severe plaque psoriasis. This subanalysis aimed to assess the effectiveness of tildrakizumab on the overall well-being and HRQoL in patients with nail psoriasis from the POSITIVE study.

Methodology: This is a 24-month, phase IV observational multinational study in adults with moderate-to-severe plaque psoriasis receiving tildrakizumab in routine care. Well-being was assessed through the 5-item WHO Well-being Index (WHO-5; range 0-100, 100=maximal well-being). The HRQoL instrument was Dermatology Life Quality Index-Relevant (DLQI-R). Nail assessments included Nail Psoriasis Severity

Index (NAPSI) and Nail Assessment in Psoriasis and Psoriatic Arthritis (NAPPA) scores. Here, we report 28-week (W) interim data of Austrian patients with nail psoriasis from the POSITIVE study based on observed cases.

Results: Twenty-five patients were included (72% male, mean [SD] age: 47.9 [14.4]). Mean (SD) WHO-5 score increased from 51.3 (18.6) at baseline to 70.9 (22.5) at W28. Mean (SD) Psoriasis Area and Severity Index (PASI) decreased from 11.1 (5.6) at baseline to 0.6 (0.6) at W28. At W28, 100%/75% of patients achieved PASI ≤3/≤1 responses. Mean (SD) DLQI-R score decreased from 14.2 (8.6) at baseline to 2.9 (3.5) at W28. Mean (SD) NAPSI/NAPPA decreased from 33.2 (32)/1.6 (1.1) at baseline to 15.3 (20.4)/0.5 (0.5) at W28. No adverse events were reported.

Conclusion: Tildrakizumab significantly improved patients' well-being, skin symptoms, nail outcomes, and HRQoL without safety concerns after 28 weeks.

Relapse and Maintenance of Clinical Response In the Randomized Withdrawal Arm of the TRuE-V Long-Term Extension Phase 3 Study of Ruxolitinib Cream in Vitiligo

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Introduction: Ruxolitinib (JAK1/JAK2 inhibitor) cream demonstrated statistically superior repigmentation to vehicle at Week 24 on primary and key secondary endpoints in two phase 3, randomized, controlled vitiligo studies.

Methodology: Patients (≥12 years) achieving near-complete facial repigmentation (≥90% improvement in facial Vitiligo Area Scoring Index [F-VASI90]), at Week 52 in TRuE-V1/TruE-V2 (NCT04052425/NCT04057573) entered a randomized withdrawal arm (1:1, twice-daily 1.5% ruxolitinib cream or vehicle) in the 52-week TruE-V long-term extension (LTE; NCT04530344) following 6-12 months of twice-daily treatment in parent studies. Time-to-relapse (less than F-VASI75) and F-VASI90 maintenance were assessed.

Results: A total of 111 patients were included (vehicle, n=56; ruxolitinib cream, n=55). F-VASI90 was maintained for 1 year in 21.4% and 61.8% of patients who applied vehicle and ruxolitinib cream, respectively. Median (95% CI) duration of F-VASI90 maintenance was 195.0 (113.0–372.0) days for vehicle and not estimable (NE) for ruxolitinib cream. In the withdrawal arm, 39.3% of patients randomized to vehicle had ≥F-VASI75 at 1 year. For the 28.6% of patients on vehicle who relapsed (less than F-VASI75), most events occurred within 3 months; median time-to-relapse, NE. Upon resumption of ruxolitinib cream, response was regained (median [95% CI], 85.0 [43.0–106.0] days). Treatment-emergent adverse events (TEAEs) occurred in 43.2% (ruxolitinib cream) and 36.2% (vehicle); treatment-related TEAEs (none serious) occurred in 5.2% in both arms.

Inference: Many patients who achieved near-complete facial repigmentation (F-VASI90) were able to maintain durable response after discontinuing ruxolitinib cream. Among those who lost response upon stopping active treatment, response was regained upon reinitiating ruxolitinib cream treatment.

Dupilumab Improves Itch, Skin Pain, and Sleep in Adult Patients With Prurigo Nodularis (LIBERTY PN-PRIME and PRIME2)

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Introduction: Prurigo nodularis (PN) is characterized by the presence of itchy nodules on the trunk/extremities, often accompanied by skin pain and sleep disruption. Psychometric validation and within-patient meaningful change thresholds for 3 patient-reported outcome instruments have been assessed in patients with PN: Worst Itch Numerical Rating Scale (WI-NRS), Skin Pain-NRS, and Sleep-NRS. The proportion of patients achieving clinically meaningful improvement in these scores was investigated in 2 pooled randomized, double-blind, placebo-controlled, phase 3 trials of dupilumab in adults with PN uncontrolled on topical therapies, LIBERTY-PN PRIME (NCT04183335) and PRIME2 (NCT04202679).

Methods: Adults with PN inadequately controlled on topical prescription therapies or when those therapies are not advisable were randomized 1:1 to dupilumab 300 mg every 2 weeks or matched placebo. Here we report the proportion of patients with a ≥4-, ≥4-, and ≥2-point improvement (within-patient meaningful improvement) in weekly average WI-NRS, Skin Pain-NRS, and Sleep-NRS (ranges 0–10), respectively, from baseline to Week 24.

Results: 311 patients were randomized (dupilumab/placebo, n=153/n=158). Baseline characteristics for WI-NRS, Skin Pain-NRS, and Sleep-NRS were balanced between treatment groups. Significantly more patients treated with dupilumab vs placebo achieved within-patient meaningful improvement in WI-NRS (58.8% vs 19.0%; P<0.0001), Skin Pain-NRS (49.7% vs 20.9%; P<0.0001), and Sleep-NRS (42.5% vs 23.4%, P<0.0001) from baseline to Week 24. The safety profile of dupilumab was consistent with the known safety profile in its approved indications.

Conclusion: Adults with PN uncontrolled on topical therapies treated with dupilumab achieved statistically significant and clinically meaningful improvement in itch, skin pain, and sleep quality.

Acral melanoma presenting as a chronic non-healing ulcer

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Die Veröffentlichung des Textes wurde zurückgezogen.

Oleogel-S10 reduziert die Belastung durch Verbandswechsel bei Patienten mit Epidermolysis bullosa

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Einleitung: Epidermolysis bullosa (EB) ist eine Genodermatose, charakterisiert durch Hautbrüchigkeit und Blasenbildung bei minimalen Traumata. Die Behandlung konzentriert sich auf eine anspruchsvolle Wundpflege, die in der Regel häufige und schmerzhafte Verbandswechsel erfordert. In der randomisierten, doppelblinden, Vehikel-kontrollierten klinischen Studie EASE wurde der klinische Nutzen von Oleogel S 10 (Birkenrinden-Triterpene) bei Epidermolysis bullosa (EB) nachgewiesen. Hier berichten wir die Ergebnisse einer Post-hoc-Analyse zur Reduktion der Häufigkeit der Verbandswechsel und der entsprechenden Zeitersparnis.

Methodik: In der EASE-Studie wurden Patienten mit dystropher EB oder junktionaler EB und ≥1 EB-Wunden von 10-50 cm² (Alter ≥21 Tagen und <9 Monaten) über 90 Tage (Doppelblindphase) mit Oleogel-S10 (n=109) oder Kontrollgel (n=114) behandelt. Diese Analyse schloss Patienten mit der höchsten Belastung ein, d.h. täglichem Verbandswechsel zu Studienbeginn (Oleogel-S10: n=47, Kontrollgel: n=53). Die für den Verbandswechsel benötigte Zeit wurde anhand publizierter Daten (Bruckner, Orphanet J Rare Dis 2020;15:1) kalkuliert (Patientenzeit und 66,7% des Pflegekraftzeitaufwands), um die Zeitersparnis zu berechnen.

Ergebnisse: In der Oleogel-S10 Gruppe konnten 35,6% der Patienten die Verbandswechsel-Frequenz reduzieren, gegenüber 10,6% der Kontrollgel-Gruppe. Die Reduktion wöchentlicher Verbandswechsel betrug 1,36±0,24 unter Oleogel-S10 gegenüber 0,41±0,23 unter Kontrollgel (Differenz -0,95±0,33; p=0,005), entsprechend einer Reduktion alle zwei Wochen um drei Verbandswechseln unter Oleogel-S10 gegenüber einem Verbandswechsel unter Kontrollgel. Die geschätzte Zeitersparnis beim Verbandswechsel betrug pro Woche 10,9 Stunden für Oleogel-S10 gegenüber 4,0 Stunden für Kontrollgel (6,6 vs. 2,4 Stunden pro Patient und 4,4 vs. 1,6 Stunden pro Pflegekraft)

Schlussfolgerung: Oleogel-S10 verringerte die Frequenz und damit den Zeitaufwand der mühsamen und schmerzhaften Verbandswechsel gegenüber Kontrollgel bei EB-Patienten mit anfänglich täglichem Verbandswechsel.

Langfristige Sicherheit und Wirksamkeit von Oleogel-S10 (Birkentriterpene) bei der Behandlung von Epidermolysis-bullosa-Wunden: Ergebnisse aus der 24-monatigen offenen Phase der EASE-Studie

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Einleitung: Die 90-tägige Doppelblindphase (DBP) der Phase-3-Studie EASE zeigte eine beschleunigte Wundheilung für Oleogel-S10 (Birkentriterpene) im Vergleich zu Kontrollgel bei Epidermolysis bullosa (EB).

Methodik: Hier berichten wir die Ergebnisse zur Sicherheit und gesamten Wundbelastung der 24-monatigen offenen Phase (OLP), in der alle Patienten mit Oleogel-S10 behandelt wurden. Die Daten zum EB Disease Activity and Scarring Index (EBDASI) und Body Surface Area Percentage (BSAP) werden ohne Besuchsfenster berichtet, um die reale Situation besser widerzuspiegeln, insbesondere unter Berücksichti-

gung der COVID-19-Pandemie. Die Population setzte sich aus Patienten mit dystropher EB (n=178; 86,8%) und junktionaler EB (n=25; 12,2%) zusammen. 141 Patienten (68,8 %) schlossen die OLP ab. Die mittlere (SD) Behandlungsdauer betrug 584,7 (246,1) Tage.

Ergebnisse: Unerwünschte Ereignisse wurden bei 77,1 % aller Patienten der OLP-Studie gegenüber 81,7 % der mit Oleogel-S10 behandelten Patienten der DBP-Studie gemeldet. Die mittlere BSAP der mit Oleogel-S10 behandelten Patienten ging von 12,1 % bei DBP-Studienbeginn auf 6,1 % nach 27 Monaten Behandlung zurück. Ähnlich verbesserte sich der mittlere EBDASI-Hautaktivitätswert in der Oleogel-S10-Gruppe von 19,6 auf 15,1 nach 27 Monaten. Ferner wurde bei den Patienten, die in der OLP von der Kontrollgruppe auf Oleogel-S10 umgestellt worden waren, eine Verringerung der BSAP- und der EBDASI-Werte gegenüber dem Ausgangswert der OLP beobachtet.

Schlussfolgerung: Diese Daten belegen ein beruhigendes Langzeit-Sicherheitsprofil von Oleogel-S10. Zudem bleibt die zuvor berichtete Verringerung der Wundlast nach 15 Monaten Behandlung mit Oleogel-S10 bis zum Ende der OLP erhalten. Dies ist ermutigend – angesichts der Art dieser chronischen genetischen Störung, bei der die fragilen Wunden der Patienten regelmäßig wiederkehren.

Maintenance of efficacy and safety with lebrikizumab up to one year of treatment in patients with moderate-to-severe atopic dermatitis with or without topical corticosteroids

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Introduction: ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) are phase 3 trials evaluating induction and maintenance treatment with lebrikizumab (LEB) monotherapy in patients with moderate-to-severe atopic dermatitis (AD). ADhere (NCT04250337) evaluated induction treatment with LEB+topical corticosteroids (TCS) in patients with moderate-to-severe AD. Patients completing ADhere could roll over into ADjoin (NCT04392154). Here, we describe maintenance of efficacy and safety in Week 16 responders of ADvocate1 and ADvocate2 (Weeks 16 to 52; pooled data) and ADjoin (Weeks 0 to 40) treated with LEB every 2 weeks (Q2W) or every 4 weeks (Q4W) for up to one year, with/without TCS.

Methodology: Non-responder imputation was used to handle missing data due to lack of efficacy (ADvocate1, ADvocate2, and ADjoin) or data after systemic rescue medication usage (ADvocate1 and ADvocate2 only; intermittent TCS use was allowed). Multiple imputation was used for other missing data.

Results: In ADvocate1 and ADvocate2 pooled results, most patients treated with LEB Q2W and Q4W maintained an Investigator Global Assessment (IGA) 0/1 response (71.2% and 76.9%) and Eczema Area and Severity Index (EASI) 75 response (78.4% and 81.7%) at Week 52. Similarly, most patients treated with LEB+TCS Q2W and Q4W in ADjoin maintained an IGA 0/1 response (75.4% and 86.8%) and EASI75 response (85.6% and 81.2%) at Week 40. Across studies, most LEB-treated patients also maintained EASI90. Safety results were consistent with those previously published.

Conclusion: Patients maintained a similarly durable response in the signs and symptoms of moderate-to-severe AD when treated with LEB Q2W and Q4W with or without TCS.

Lebrikizumab provides long-term clinically meaningful responses in patients with moderate-to-severe atopic dermatitis

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Introduction: Clinically meaningful responses, assessed by signs, symptoms and quality of life (QoL) improvements in atopic dermatitis (AD), provided by LEB at Week 52 (W52) among W16 ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) adult responders (pooled data) are reported here.

Methodology: ADvocate1&2 were two identically designed, randomized, placebo-controlled, monotherapy Phase 3 trials assessing LEB efficacy and safety in patients with moderate-to-severe AD. Responders at W16 were patients achieving Eczema Area and Severity Index (EASI) 75 or Investigator Global Assessment (IGA) 0/1 with a ≥2-point improvement from baseline, without rescue medication. Responders to LEB 250 mg every two weeks (LEB Q2W) at W16 received LEB Q2W, every 4 weeks (LEB Q4W), or placebo (PBO) for 36 weeks. Signs were defined by EASI ≤7, symptoms by Pruritus Numeric Rating Scale (PNRS≤4), and QoL by Dermatology Life Quality Index (DLQI≤5). Post-hoc analysis reports proportion of patients achieving one or more clinically meaningful responses, and proportion of patients achieving all three clinically meaningful responses. Patients with baseline DLQI›5 and PNRS›4 were selected.

Results: At W52, 89.6% of patients in LEB Q4W, 84.3% in LEB Q2W and 72.9% in PBO achieved one or more of clinically meaningful AD responses. 57.6% of patients in LEB Q4W, 60.7% in LEB Q2W and 45.8% in PBO achieved all three endpoints.

Conclusion: At W52, LEB provided clinically meaningful responses for signs, symptoms, and QoL in adults with moderate-to-severe AD. In addition, more than half of patients achieved response in all three domains, which represents a status of minimal disease.

Lebrikizumab reduces the extent of AD signs across body regions at 52/56 Weeks

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Introduction: Lebrikizumab (LEB) efficacy was assessed in each body region measured by Eczema Area and Severity Index (EASI) in patients with moderate-to-severe AD. Pooled data from Phase 3 ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967A) (ADvocate1&2) and data from patients on Phase 3 ADhere (NCT04250337), assessing LEB+topical corticosteroids (TCS) up to 16-weeks, rolling over into the Phase 3 long-term extension ADjoin (NCT04392154), were analysed.

Methodology: In ADvocate1&2, responders to LEB 250 mg every two weeks (LEB Q2W) at Week 16 (W16) were re-randomised to receive LEB Q2W, every 4 weeks (LEB Q4W) or placebo (PBO) for 36 weeks. Patients were responders if they achieved EASI75 or Investigator Global Assessment (IGA) 0/1 with a ≥2-point improvement without rescue medication. In ADjoin, ADhere responders received LEB Q2W or LEB Q4W for 100 weeks. Mean percentage change from baseline (%CFB) at W52 (ADvocate1&2) and at W56 (ADjoin) was calculated for each body region.

Results: In ADvocate1&2, mean %CFB at W52 (PBO, LEB Q2W and LEB Q4W) in head&neck was -74.04, -79.28 and -81.60; lower extremities -68.34, -82.30 and -82.51; upper extremities -62.52, -78.47 and -79.43, and trunk -72.01, -84.82 and -86.30. In ADjoin, mean %CFB at W56 (LEB Q2W and LEB Q4W) in head&neck was -91.26 and -92.76; lower extremities -90.81 and -84.16; upper extremities -98.36 and -92.06; and trunk -92.22 and -89.73.

Conclusion: LEB as monotherapy and in combination with TCS reduced the extent of involvement and severity of AD across all body regions including head&neck region, a burdensome and difficult to treat area.

Efficacy of Dupilumab Up to 1 Year in Infants and Pre-schoolers With Atopic Dermatitis

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Introduction: Continuous use of several traditional systemic atopic dermatitis (AD) treatments in paediatric patients is not recommended due to safety concerns and lack of long-term efficacy data.

Methodology: Children aged 6 months to 5 years with moderate-to-severe AD who had participated in the 16-week, double-blind, phase 3 LIBERTY AD PRESCHOOL trial (NCT03346434, part B; parent study) were enrolled into an open-label extension (OLE) study (NCT02612454). Patients received subcutaneous dupilumab every 4 weeks (200 mg for children weighing 5 to <15 kg; 300 mg for 15 to <30 kg). Topical AD treatments were allowed.

Results: Relative to parent study baseline, mean percentage changes (± standard error) in Eczema Area and Severity Index score were −41.6 (±4.6) and −54.0 (±3.2) at OLE baseline, −74.5 (±3.7) and −81.7 (±1.8) at Week 16, and −85.6 (±3.5) and −86.4 (±2.2) at Week 52 in the 200 mg and 300 mg dupilumab groups, respectively. The number of patients (%) achieving an Investigator's Global Assessment score of 0/1 increased from OLE baseline (6/61 [9.8%] and 15/116 [12.9%]), to Week 16 (22/58 [37.9%] and 35/115 [30.4%]), and at Week 52 (16/34 [47.1%] and 18/54 [33.3%]) in the 200 mg and 300 mg dupilumab groups, respectively. Overall safety of dupilumab treatment administered for up to 1 year was consistent with the known dupilumab safety profile.

Inference: Dupilumab treatment for 1 year provides sustained improvement in signs of AD in patients aged 6 months to 5 years with moderate-to-severe AD.

Long Term Laboratory Safety of Dupilumab in Patients Aged 6 Months to 5 Years With Moderate-to-Severe Atopic Dermatitis

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Introduction: Systemic treatments often require laboratory monitoring. Here we report 52-week laboratory safety data for dupilumab-treated children aged 6 months to 5 years with moderate-to-severe atopic dermatitis (AD).

Methodology: LIBERTY AD PED-OLE (NCT02612454) is an open-label extension study of children aged 6 months to <18 years with moderate-to-severe AD. This analysis includes haematologic and chemistry laboratory parameters in children aged 6 months to 5 years treated with dupilumab every 4 weeks (q4w; 200 mg: ≥5kg to <15kg; 300 mg: ≥15kg to <30kg).

Results: Of the 180 patients enrolled, 122 (67.8%) completed up to 16 weeks and 30 (16.7%) completed up to 52 weeks.

Mean (SD) eosinophil counts increased slightly from baseline (1.15 × 109/L [1.18]) to Week 16 (1.5 × 109/L [1.91]), but then decreased below baseline by Week 52 (0.80 × 109/L [0.64]). Mean (SD) platelet counts were relatively stable with a modest decrease from baseline (388.7 × 109/L [102.51]) to Week 52 (356.1 × 109/L [107.48]). Chemistry parameters remained within the normal reference ranges. One patient (0.6%) reported a mild case of anemia, and one patient (0.6%) reported a mild case of thrombocytopenia, which were resolving and resolved at the time of this interim analysis, respectively. Overall safety was consistent with the known dupilumab safety profile.

Inference: No clinically meaningful changes in haematologic and chemistry parameters were observed during 52 weeks of dupilumab treatment. As with adults, adolescents and older children, routine laboratory monitoring is unnecessary in children aged 6 months to 5 years with moderate-to-severe AD.

Dupilumab Treatment in Patients With Hand and Foot Atopic Dermatitis: Results From a Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial

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Introduction: Atopic dermatitis (AD) of the hands and/or feet is often chronic, difficult to treat, and substantially impacts patient quality of life. We investigated the efficacy/safety of dupilumab in patients with hand and foot (H/F) AD using dedicated/validated clinical and patient-reported instruments.

Methodology: The phase 3, randomized, double-blind LIBERTY-AD-HAFT (NCT04417894) trial enrolled patients ≥12 years with moderate-to-severe (Investigator's Global Assessment [IGA] 3/4) H/F AD. Patients were randomized to dupilumab monotherapy 300mg q2w in adults; 200/300 mg every 2 weeks in adolescents, or placebo for 16 weeks. The primary endpoint was IGA (H/F) 0/1 score at Week 16. Safety/tolerability was assessed.

Results: The 133 patients enrolled were randomized to dupilumab (n=67) or placebo (n=66). At Week 16, the primary and all secondary endpoints were met. Significantly more patients in the dupilumab vs placebo group achieved IGA 0/1 (40.3% vs 16.7%; P=0.003; primary endpoint) and ≥4-point improvement in the H/F Peak Pruritus Numerical Rating Scale (52.2% vs 13.6%; P<0.0001; a key secondary endpoint). Dupilumab-treated patients experienced significant improvement in percent change from baseline in the modified Total Lesion Sign Score for H/F lesions vs placebo (LS mean [SE] −69.4 [5.8] vs −31.0 [5.9]; P<0.0001) and Hand Eczema Severity Index (LS mean [SE] −74.8 [6.3] vs −39.9 [6.2]; P<0.0001). The most common TEAEs (≥10%) of dupilumab vs placebo were nasopharyngitis (16% vs 11%) and dermatitis atopic (5% vs 18%).

Inference: Dupilumab significantly improved signs and symptoms in patients with H/F AD and had an acceptable safety profile.

Color-Matching Response Correlates With Repigmentation and Treatment Satisfaction: Pooled Subgroup Analysis of 2 Randomized Phase 3 Studies Evaluating Ruxolitinib Cream for the Treatment of Vitiligo

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Introduction: Vitiligo is a chronic autoimmune disease resulting in patches of skin depigmentation and reduced quality of life. In 2 randomized, double-blind, vehicle-controlled phase 3 studies in patients with nonsegmental vitiligo (TRuE-V1 [NCT04052425]; TRuE-V2 [NCT04057573]), application of ruxolitinib (Janus kinase [JAK]1/JAK2 inhibitor) cream was well tolerated and resulted in substantial repigmentation vs vehicle. Here, we present pooled analyses of color-matching data among adult and adolescent patients (aged ≥12 y) who were initially randomized to apply 1.5% ruxolitinib cream twice daily in TRuE-V1/TRuE-V2.

Methodology: Post hoc analyses of available data at Weeks 24 (primary analysis cutoff) and 52 (end of study) were performed to assess associations between color-matching response (scores of 1–3 ["excellent," "very good," or "good"] on a 5-point scale) and facial Vitiligo Area Scoring Index (F-VASI), treatment satisfaction (using the 9-item Treatment Satisfaction Questionnaire for Medication [TSQM-9]), and baseline patient characteristics. Polychoric (rpc) and tetrachoric (rtet) correlations were calculated for ordinal and binary responses, respectively.

Results: At Week 52, 273/350 patients (78.0%) achieved a color-matching response. Color-matching response correlated moderately with ≥75% improvement from baseline in F-VASI (F-VASI75; rtet, 0.45; P<0.0001), TSQM-9 overall satisfaction (rpc, 0.54; P<0.0001), and TSQM-9 effectiveness (rpc, 0.65; P<0.0001), but weakly with TSQM-9 convenience (rpc, 0.24; P=0.0047). Patients achieved a color-matching response regardless of disease duration, disease stability, previous therapy, and Fitzpatrick skin type.

Conclusion: Color-matching response after ruxolitinib cream application in patients with nonsegmental vitiligo correlated moderately but significantly with repigmentation response (assessed by F-VASI) and overall treatment satisfaction at Week 52.

Baseline Disease Duration and Disease Stability Correlations in Pooled Subgroup Analysis of 2 Randomized Phase 3 Studies Evaluating Ruxolitinib Cream for the Treatment of Vitiligo

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Methodology: Post hoc analyses of available data at Weeks 24 (primary analysis cutoff) and 52 (end of study) were performed to assess associations between disease duration and stability with facial Vitiligo Area Scoring Index (F-VASI), total VASI (T-VASI), treatment satisfaction, and prior therapy. Polychoric (rpc) and tetrachoric (rtet) correlations were calculated for ordinal and binary responses, respectively.

Results: The correlation between baseline disease duration and stability was weak but significant (rpc, −0.21; P=0.0020); no significant correlations were observed with previous therapy or treatment satisfaction. At Week 52, 176/350 patients (50.3%) achieved ≥75% improvement from baseline in F-VASI (F-VASI75) regardless of disease duration (rpc, 0.03; P=0.7108) or stability (rtet, −0.05; P=0.5886). Similarly, 179/350 patients (51.1%) achieved ≥50% improvement from baseline in T-VASI (T-VASI50) at Week 52 independent of disease duration (rpc, 0.12; P=0.1004) or stability (rtet, 0.08; P=0.3884).

Conclusion: Disease duration correlated weakly but significantly with disease stability in patients with nonsegmental vitiligo. At Week 52, F-VASI75 and T-VASI50 responses after ruxolitinib application were achieved regardless of disease duration or stability.

Comparison of mutation profiles of melanoma primary tumors and metastases

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Melanoma is the most malignant form of skin cancer. Due to its heterogeneity and aggressiveness, genetic characterization of melanoma primary tumors and/or metastases in advanced stages of the disease is crucial to find an appropriate therapy.

In this study, we investigated genetic profiles of melanoma primary and metastatic sites. Therefore, 261 FFPE tissue samples, corresponding to 208 patients, were analyzed using high throughput sequencing (customized AmpliSeq™ Cancer Hotspot v2 panel, Illumina®). Thereby, paired primary and metastatic site samples of 32 patients were available. The cohort included all AJCC stages and different melanoma subtypes.

Sequencing confirmed the four most frequently altered genes in melanoma BRAF, NRAS, TP53 and CDKN2A with 37.0%, 26.0%, 11.8% and 20.6%, respectively. When comparing pathogenic variants in primary lesions and metastatic sites, these genes showed higher mutation frequencies in metastases (mean=6.8%). The evaluation of paired tissue samples demonstrated divergences in one third of all paired tissue samples even including important driver genes like BRAF and NRAS. Additional mutations in the metastatic site, but also a decrease of pathogenic variants in the metastases were found. No associations were obvious regarding diverging mutation spectra and stage, metastatic localization or time until metastasis. Regarding melanoma subtypes, acral melanomas showed higher counts of identical mutation spectra compared to cutaneous melanomas (p-value=0.01).

Coherent mutation patterns in acral melanoma underline lower frequency of pathogenic variants in acral melanoma due to less UV exposure. Results underline the presence of subpopulations within the primary tumor and the occurrence of additional mutational events in disease progression.

Transitioning from insufficient acute therapy and prophylaxis to effective disease control in HAE using lanadelumab

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Introduction: Hereditary angioedema is a rare genetic disorder causing recurrent swelling of skin and mucous membranes. Besides C1-INH concentrates, androgens were used for prophylaxis, but usage declined due to side effects and superior alternatives. Recent pharmaceutical research has led to effective prophylactic treatments, such as lanadelumab, a monoclonal antibody blocking plasma kallikrein activity, resulting in less bradykinin generation, the primary driver of angioedema attacks.

Methods: Our HAE clinic offers annual swelling calendars to patients, used to record attack onset, treatment, symptom severity, and time to improvement. We analyzed the calendars and medical history of a mid-fifties male HAE patient over the past decade and graphically present the results this poster.

Results: The patient was diagnosed with C1-INH-HAE in 1995, with a history of 25 severe laryngeal attacks. Danazol was initiated for prophylaxis, but was discontinued in 2014 due to side effects. Attack frequency increased and peaked at 103 attacks in 2018. Treatment was then switched to on-demand C1-INH and icatibant, followed by long-term-prophylaxis with lanadelumab in July 2019. A total of 599 attacks were documented from 2012 to 2022. Fig.1 displays HAE attacks managed using C1-INH, icatibant, and lanadelumab, while Tab.1 presents attack traits from 2012 to 2022. No side effects have been reported after change of treatment to lanadelumab, and the patient reported improved quality of life and fewer sick leaves from work.

Conclusion: New treatments for hereditary angioedema show remarkable efficacy and safety, unlike our patient's use of attenuated androgens, linked to recurrent attacks and systemic side effects.

Disease Control in HAE with Lanadelumab: A Center's Real-World Experience

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Background: In Austria, the management of hereditary angioedema (HAE) has undergone substantial changes in recent years. Newer, more user-friendly treatment options with an excellent safety profile have become integral to patient care. Among these innovations is lanadelumab, a monoclonal antibody inhibiting kallikrein. Lanadelumab has been approved in Austria in early 2019 and has demonstrated in studies a remarkable mean attack reduction rate of 87.4% administered every two to four weeks subcoutaniously.

Methods: We examined the swelling calendars of five HAE patients, both before and after initiating lanadelumab treatment, with the goal of presenting real-life data on attack frequency and breakthrough attacks.

Results: Prior to lanadelumab, the patients recorded 844 attacks over an observation period of 7,092 days, with 46 of these attacks (5.45%) going untreated. Lanadelumab treatment resulted in a remarkable reduction of 97.39% in the total attack rate compared to their previous therapy, or -98.50% for treated attacks.

After these patients initiated lanadelumab prophylaxis, the total duration of prophylactic treatment spanned 4,181 days until December 31, 2022, with lanadelumab administered every 31.9 days on average. During this period, they experienced a total of 13 breakthrough attacks, with 4 requiring acute treatment, while 9 resolved spontaneously without intervention. The overall attack frequency was 0.09 attacks per month, and only 0.03 attacks per month necessitated treatment.

Conclusion: Real-world data from our small cohort – although with a significant number of attacks and attack history – showcased impressive outcomes exceeding published data.

A Debut Discovery: Concurrent PLG and HS3ST9 Gene Mutations in an HAE nC1-INH Patient

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Background: Hereditary Angioedema (HAE) is a rare genetic disorder causing recurrent swelling in different body parts, including the skin and mucous membranes. While most HAE cases result from SERPING1 gene mutations affecting C1-INH (C1 inhibitor) protein, some cases are even rarer, with normal C1-INH levels due to mutations in genes like PLG, F12, KNG1, ANGP1, MYOF, and HS3ST6.

Methods: Traditional diagnostic criteria for HAE involve low C1-INH and C4 levels. However, some patients with HAE-like symptoms lack these markers. In 2021, we began genetic testing for HAE subtypes with normal C1-INH levels, using whole exome sequencing in collaboration with our Human Genetics Institute at the Medical University of Graz, targeting genes linked to this condition.

Results: In late 2022, a 51-year-old woman visited our angioedema clinic with recurrent facial swelling, glossodynia, throat lump sensations, and gastrointestinal discomfort, occurring every two weeks without hives. Extensive diagnostics found no abnormalities. Antihistaminergic treatment and omalizumab did not yield significant improvement, leading to genetic testing for non-C1-INH-Hereditary Angioedema (nC1-INH-HAE).

Genetic testing revealed mutations in the HS3ST6 (c.70G>A, p.(Ala24Thr)) and PLG (c.2356C>T, p.(Arg786Cys)) genes. The detected variants are currently not sufficiently characterized and described in the literature or international databases to make a clear assessment of clinical relevance.

Conclusion: In summary, the discovery of two unique gene mutations in one nC1-HAE patient is a important discovery in uncovering the causes of the symptoms. Nevertheless, further investigations and treatment trials are essential to fully understand this complex case and provide the best care for the patient.

Subkutane Fettgewebsnekrosen im Neugeborenenalter

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Einleitung: Die subkutane Fettgewebsnekrose stellt eine seltene, selbstlimitierende Pannikulitis dar, welche sich meist innerhalb der ersten Lebenswochen bei Reif- und Spätgeborenen manifestiert. Es kommt zur Ausbildung plattenartiger rötlich-livider Verhärtungen, insbesondere an mechanisch traumatisierten Regionen. Mögliche Risikofaktoren umfassen Geburtstraumata, perinatale Asphyxie, Hypothermie, Mekoniumaspiration sowie maternale Erkankungen (wie Präeklampsie, Diabetes mellitus). Die Diagnose wird meist klinisch gestellt. In unklaren Fällen können eine Weichteilsonographie und eine Hautbiopsie zur Diagnosesicherung herangezogen werden. Mögliche extrakutane Komplikationen wie insbesondere Hyperkalzämie, seltener Thrombozytopenie, Hypoglykämie und/oder Hypertriglyceridämie müssen monitiert werden. Differentialdiagnostisch ist an ein Scleroedema neonatorum oder Battered-Child-Syndrom zu denken.

Methodik: Wir berichten über ein reifgeborenes Mädchen mit rötlich-lividen Hautveränderungen seit dem dritten Lebenstag, welches in unserer Ambulanz für pädiatrische Dermatologie vorgestellt wurde.

Ergebnisse: Die Patientin kam bei einer Spontangeburt komplikationslos zur Welt. Bei der Mutter waren keine Grunderkrankungen bekannt. In der dermatologischen Untersuchung zeigten sich mehrere schmerzlose subkutane rötlich- livide Plaques an beiden Oberarmen, am Rücken sowie sakral. Der weitere klinische Status war unauffällig. Regelmäßige Laborkontrollen ergaben keine Hinweise für extrakutane Manifestationen. Die subkutanen Fettgewebsnekrosen heilten innerhalb von zwei Monaten ohne Residuen spontan ab.

Schlussfolgerung: Obwohl die subkutane Fettgewebsnekrose als eine gutartige, selbstlimitierende Hauterkrankung gilt, kann sie mit schwerwiegenden extrakutanen Komplikationen einhergehen. In 50 Prozent der Fälle tritt eine Hyperkalzämie auf, welche unbehandelt lebensbedrohlich verlaufen kann. Regelmäßige laborchemische Kontrollen sollten für mindestens sechs Monate durchgeführt werden, wobei es meist innerhalb weniger Wochen/Monate zur spontanen Abheilung der Hautveränderungen kommt.

Mast cells as potential drivers of inflammation in psoriasis

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Little is known about IL-17A expression in psoriasis, particularly about its modulation after treatment. Recent studies have indicated that innate immune cells (such as mast cells (MC)), rather than T cells, are often IL-17A+ in IHC/IF staining of biopsies from psoriatic skin. However, the cellular sources of IL-17A still remain incompletely defined.

Using immunofluorescence staining, we show that high numbers of IL-17A+ MC persisted in resolved lesions after treatment (anti-IL-17A, anti-IL-23, UVB or topical dithranol). IL-17A+ MC were located in T cell clusters and often in close proximity to resident memory T cells (TRM). MC and TRM were IL-17A+ at baseline, whereas in resolved lesions TRM were mostly negative for IL-17A, while IL-17A+ MC persisted. CIBERSORTx analysis of RNA-Seq data showed that activated MC were increased in psoriatic skin, while resting MC were almost absent and both returned to normal levels after dithranol treatment. Activated memory CD_4 T cells were also increased at baseline and returned to normal levels after therapy. In situ mRNA detection in combination with antibody staining revealed positive mRNA signals for IL17A, IL17F, and RORC in tryptase+MC, showing that MC have the transcriptional machinery to actively produce IL-17. When MC isolated from human skin were stimulated with IL-23, they responded with increased IL-17A release (measured by ELISA). Taken together, MC expressed RORC, IL17F, and IL17A mRNA, were activated in psoriatic lesional skin, and produced IL-17A, which they store long-term. MC may be responsive to IL-23 and might play a crucial role in psoriasis recurrence.

Behandlung stagnierender Wunden mit Photobiomodulationstherapie: Fallserie von 12 Patient*innen.

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Einleitung: Die Behandlung akuter und chronischer Wunden stellt oftmals eine therapeutische Herausforderung dar. Trotz kausaler und symptomatischer Therapie kann die Wunde stagnieren. Eine effektive und nebenwirkungsfreie Option zur Unterstützung stellt neben dem feuchten Wundmanagement die zusätzliche Behandlung mit gepulstem kalten Rotlicht (Photobiomodulationstherapie – PBM) dar.

Methode: In einem Zeitraum von etwa 1 Jahr wurden in unserer Gefäßambulanz 12 Patient*innen (6 Männer und 6 Frauen) mit Ulcera unterschiedlicher Genese zusätzlich zur bisherigen phasengerechten lokalen Wundtherapie – welche beibehalten wurde – mit gepulstem kalten Rotlicht behandelt. Das dafür verwendete Gerät verfügt über 7 LED-Lampen mit einer Wellenlänge von 620-640 nm (gepulst und fokusiert), eine Eindringtiefe von bis zu 6 cm ins menschliche Gewebe, eine Intensität von 175 mW und eine Lichtenergie von 77 J/cm². Alle Patient*innen wurden 2x/Woche für 6 Minuten bestrahlt. Das Patient*innen Alter lag zwischen 24 und 89 Jahren; Bestandsdauer der Wunden war zwischen 3 Wochen und mehr als 3 Jahren.

Ergebnisse: Die Wunden von 10 Patient*innen zeigten bereits in der ersten Woche eine Heilungstendenz, Reduktion der Schmerzen und heilten innerhalb von 2 Wochen bzw. 9 Monaten ab. Es gab 2 Therapie Abbrüche aufgrund fehlender Compliance.

Schlussfolgerung: Gepulstes kaltes Rotlicht – sog. Photobiomodulation – stellt eine vielversprechende unterstützende Therapiemodalität in der Behandlung von akuten als auch chronischen Wunden dar. Die Ergebnisse unserer Fallserie konnten dies positiv unterstreichen. Die Anwendung ist schmerzfrei, ohne Nebenwirkungen, ohne Hitzeentwicklung und einfach in der Durchführung.

Inhibition of STAT3/5 pathway by multi-kinase inhibitor IQDMA reduces tumor growth and outperforms conventional phototherapeutic treatment regime in cutaneous T cell lymphoma murine model

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Introduction: Cutaneous T-cell lymphoma (CTCL), particularly its tumor stage mycosis fungoides (MF) subtype, poses a significant clinical dilemma due to the limited effectiveness of existing treatments. This study seeks to fill the void in targeted therapies by investigating the inhibition of the hyperactivated STAT3/5 pathway in CTCL.

Methodology: Utilizing a murine model with intradermally grafted malignant T-cell lymphoma cells, we compared the efficacy of IQDMA, a multi-kinase inhibitor, with the conventional, topical psoralen+UVA (PUVA) phototherapeutic regimen.

Results: Our data show that IQDMA substantially reduced tumor volume (p=0.0001) and was significantly more effective than PUVA (p=0.0074). Immunohistological analysis revealed that IQDMA treatment resulted in decreased tumor cell infiltration (p=0.03) and induced apoptosis, evidenced by elevated cleaved-caspase-3 levels. Furthermore, IQDMA treatment led to a significant decrease in KI67+ cells (p=0.03), indicating a reduced rate of tumor cell proliferation. A remarkable reduction was observed in both total-STAT5 (p=0.05) and STAT3 (p=0.01) levels of the infiltrated tumor cells. A positive correlation was identified between total-STAT5 levels and tumor cell infiltration area, confirming the role of the STAT3/5 pathway in the disease's pathogenesis. Unlike vehicle-treated controls, IQDMA disrupted the positive correlation between phospho-STAT5 and total STAT5 levels. As IQDMA targets PAK-kinase, a nuclear transporter for phospho-STAT5, we observed a compartmental shift of phospho-STAT5 from the nucleus to the cytoplasm (p=0.05), corroborating our initial hypothesis.

Conclusions: This study shows IQDMA significantly outperforms conventional photochemotherapy PUVA in treating CTCL, particularly tumor-stage MF, by reducing tumor volume, inducing apoptosis, and inhibiting the STAT3/5 pathway, warranting its clinical evaluation.

Topical Disinfection Rebalances Impaired Cytokines in Polymorphic Light Eruption: Implications to Microbiota-Dependent Immune Modulation

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Polymorphic light eruption (PLE) is a recurrent skin condition characterized by delayed-type hypersensitivity to UVR. To elucidate the role of skin microbiota in UV-induced cytokine responses in PLE, we conducted a randomized, placebo-controlled, double-blind pilot study involving PLE patients and healthy controls (CTRL). We assessed skin reactions, cytokine production from suction blister fluid, and apoptotic cell generation in epidermal blister tissue in both disinfected and non-disinfected skin areas following single and multiple solar-simulated UV exposures. Our baseline analysis utilizing OLINK® target 96 inflammation panel revealed a distinct impairment in the expression of 20 cytokines in PLE patients compared to healthy controls. These cytokines are pivotal for various immune mechanisms i.e., immune cell migration and recruitment (CCL11, CCL23, CX3CL1, CXCL6, MCP-2, and MCP-4), inflammatory responses (IL-7, IL-18, and IL-33) and induction of apoptosis (TWEAK and TRAIL). Remarkably, our intervention with topical disinfection restored this cytokine imbalance, especially evident after multiple solar-simulated UV exposures. Histological analysis of suction blister tissue countered previous findings, showing no enhanced apoptotic cell accumulation (mean number±standard deviation) per mm epidermal length in UV-exposed PLE skin at the single MED compared to CTRL upon disinfection (PLE, 9.2±5.1, CTRL,

12.5±5.9) and placebo vehicle (saline 0.9%; PLE, 9.6±4.1, CTRL, 9.6±7). While there were no significant changes in erythema and pigmentation upon topical disinfection and UV exposure, our findings strongly suggest the role of skin microbiota in UV-driven cytokine regulation in PLE. (This data have been presented in part at the ISID meeting, May10-13, Tokyo JP).

Psoriasis and its impact on close relatives and partners of patients – a cross-sectional questionnaire study

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Background: Psoriasis is an immune-mediated disease with typical skin changes. Little is known about the impact of psoriasis on the disease burden of close relatives and partners of those affected by the disease. The aim of this study was to evaluate the quality of life in psoriasis patients and the impact of disease on partners and close relatives.

Methods: We conducted a single-centre, cross-sectional questionnaire study among psoriasis patients (recruited from the Psoriasis Registry Austria (PsoRA)) and close relatives/partners who attended the outpatient clinic at the Department of Dermatology (Medical University of Graz). Patient Family Impact Score (PFIS) was calculated from the FamilyPso questionnaire data to establish categories of disease burden.

Results: 250 plaque-type psoriasis patients (58.4 % male and 41.6% female) with mostly treatment-controlled disease (mean PASI of 1.7 (SD ± 3.6) and DLQI of 4.1 (SD ± 6.2)) were enrolled. Valid FamilyPso questionnaires were returned from 153 (61.2%) close relatives and partners. Correlation analysis revealed a significant association between PASI and DLQI ($r=0.512$, $p<0.001$), PASI and PFIS ($r=0.228$, $p=0.006$), and DLQI and PFIS ($r=0.210$, $p=0.014$). A small or larger disease burden was detected in nearly 78.7% of the male and 77.3% of the female relatives and partners quantified with categorized PFIS.

Conclusions: The study revealed a significant impact of patients' psoriasis on the disease burden of close relatives and partners, depending on the severity of PASI and extent of quality of life disruption in patients. (This data have been presented at the ISID meeting, May10-13, Tokyo JP).

Real life experience of JAK-inhibitors of patients treated at the university hospital in Graz

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Introduction: Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases. For some years JAK-inhibitors have been used for the treatment of AD. However, real life clinical data of these drugs is still limited.

Patients and methods: Data was analyzed retrospectively from a total of 28 patients (IGA ≥ 3) treated with Baricitinib (n=14) or Upadacitinib (n=13) at our clinic. Severity of AD, life quality and pruritus were assessed.

Results: In both groups an improvement of AD, DLQI and peak pruritus were observed. In Baricitinib group IGA decreased from 3,0 ± 0.9 (baseline; mean±sd) to 1.9 ±0.9 (week 4) and 1.9 ±1.3 (week 12). In Upadacitinib group 3.7 ±0.5 (baseline), 2.1 ±0.7 (week 4) and 2.0 ±1.2 (week 12) was observed.

In the Baricitinib group DLQI decreased from 17.7±6.2 (baseline) to 3.9 ±2.4(week 4) and was rising again to 8.6 ±7.6 (week 12). In Upadacitinib group DLQI at baseline was 11.6 (±8.2) and improved to 1.4 ±2.1 (week 4) and stayed constant until week 12.

4 of the patients (2 in each group) had to discontinue therapy due to side effects and 6 stopped due to worsening of AD (1 in Upadacitinib, 5 in Baricitinib).

Conclusion: Both drugs showed an improvement in different parameters of AD. In our data a trend towards lower values for interference with quality of life in patients treated with Upadacitinib could be observed. Further investigations should be made to gather a bigger sample size of real-world data.

Overview and Characterization of Syphilis Cases in Vienna between 2018 and 2023

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Introduction: Syphilis is a systemic sexually transmitted infection (STI) caused by the spirochaete Treponema pallidum and can progress into different clinical stages. The aim of this evaluation was to investigate and characterize the number of patients diagnosed with syphilitic infection from January 2018 to June 2023.

Methods: Patients with suspicious syphilitic infection or after risky sexual contact were referred to the Outpatients Centre and evaluated regarding gender, symptoms, and probable previous contact with syphilis. Serology (VDRL, TPPA, IgM) and laboratory diagnostics were performed by darkfield microscopy of smear material of suspected chancres to detect T. pallidum.

Results: In total, 382 (4.6%) out of 8430 screened patients had a syphilitic infection. The majority of patients was male (94%, n=359). 48.2% (n= 184) of patients tested positive for the latent stage of the infection, 26.7% (n=102) were in the primary stage of syphilis with positive serology, but without symptoms. 17.3% (n=66) suffered from primary syphilis with symptoms, mainly painless ulcers. Secondary syphilis was diagnosed in 7.9% (n=30) of patients. During the Covid-19 pandemic a decrease of syphilis cases was observed, notably during the first lockdown in March 2020 only 7 patients had a syphilitic infection. The initial phase of the pandemic was followed by a rise of 42.6% (2020 vs. 2022) in syphilis cases.

Conclusion: Despite the availability of diagnostic methods and treatment options, syphilis remains a public health issue. The increase of cases, especially in male patients, highlights the importance of safe sex and regular STD screenings including syphilis.

LIBERO VISIBLE: Disease Characteristics of Patients with Visible and/or Stigmatizing Psoriasis Lesions and Impact on Quality of Life

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Introduction: Stigmatization is one of the key challenges for patients with psoriasis, but only limited real world evidence is available.

Material and Methods: LIBERO VISIBLE is a German, prospective, multicenter, open-label, single-arm, observational, 60 weeks, non-interventional study (NIS) on brodalumab 210 mg in patients with stigmatizing and/or visible psoriasis lesions. In this interim analysis we describe baseline characteristics of patients with different stigmatizing and/or visible lesions.

Results: 490 patients (61.4% male, mean age 47.0 ± 15.3 years, mean weight 88.2 ± 20.9 kg, disease duration 15.6 ± 13.3 years) were included in the interim analyses. At baseline mean affected Body Surface Area (BSA) was 21.2 ± 15.3 % and mean Psoriasis Area Severity Index (PASI) 15.9 ± 10. The majority of patients suffered from scalp psoriasis (79.4%), 46.9% from facial psoriasis and 46.7% from genital psoriasis, followed by fingernails (40.2%), toenails (29.6%), palms (24.3%) and soles (17.4%). The main clinical symptom be-

sides plaques was itch (86.5%), in particular in patients with genital psoriasis (92.1%). Mean Dermatological Life Quality Index (DLQI) was 13.3 ± 7.7 with 18.7% of patients presenting a DLQI > 10, indicating a strong impact on patients´ quality of life. The strongest impact on quality of life was seen in face, genital and palmoplantar psoriasis.

Conclusion: LIBERO VISIBLE is the largest, prospective NIS in psoriasis patients with visible and/or stigmatizing manifestations. Baseline characteristics reveal that patients often suffer from psoriasis in different localizations and that visible and/or stigmatizing manifestations strongly impact quality of life.

LIBERO VISIBLE: 12 Week Effectiveness of Brodalumab in Patients with Visible and/or Stigmatizing Psoriasis Lesions

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Introduction: Patients with psoriasis often experience stigmatization based on the visibility or localization of their plaques. So far, only limited real world evidence has been available on effectiveness of treatments in those patients.

Material and Methods: LIBERO VISIBLE is a German, prospective, multicenter, open-label, single-arm, observational, 60 weeks, non-interventional study on brodalumab 210 mg in patients with stigmatizing and/or visible psoriasis lesions. In this interim analysis we describe the efficacy of brodalumab 210 mg after about 2, 4 and 12 W in patients with stigmatizing or visible lesions in different localizations.

Results: 490 patients (61.4% male, mean age 47.0 ± 15.3 years) were included in the interim analyses. At baseline mean Psoriasis Area Severity Index (PASI) was 15.9 ± 10.9. The majority of patients (70.2%) were treated with conventional systemic or UV therapy in the past and 22.5% with previous biologic therapy. Mean overall PASI was reduced from 15.9 to 8.6 at ~W2 and further improved to 3.1 at ~W12. Rapid and high response with mean improvement rates between 42.7 to 62.4% at ~W2 and 72.1 to 87.4% at ~W12 was shown with validated, area specific disease severity scores for scalp, face, genital and palmoplantar psoriasis. In nail psoriasis improvement between 42.0 to 54.3% at ~W12 was observed.

Conclusion: LIBERO VISIBLE confirms the fast onset and the high clearance rates in patients with visible and/or stigmatizing lesions treated with brodalumab 210 mg, which has been seen in phase 3 studies and in daily practice for the general psoriasis patient population.

First results of a non-interventional observational study to investigate the effectiveness of Brodalumab on difficult-to-treat body regions in everyday clinical practice – ODIN

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Introduction: Brodalumab is approved for the treatment of moderate to severe plaque psoriasis (PsO) in adults. The rapid onset of action and high PASI clearance have already been proven in multiple clinical studies. However, multi centric data on the effectiveness of difficult-to-treat areas, especially in a real world setting, are scarce.

Materials & Methods: In a non-interventional study (ODIN) a total of 9 centers included patients who were treated with Brodalumab in everyday clinical practice over a period of 60 weeks. The co-primary endpoints were PSSI75 at week 12 and/or NAPSI75 at week 24. Secondary endpoints included general skin improvement and patient satisfaction.

Results: A total of 87 patients were screened and enrolled. 90.3% of patients achieved NAPSI75 by week 24. PSSI75 was achieved by 93.5% of patients at week 12. Both PSSI75 and NAPSI75 were achieved by 87.1% of all 62 patients after 24 weeks of therapy. Mean BSA improved from 14% at baseline to 1.5% at week 12 and 1.0% at week 24. IGA improved from baseline 3.1 to 1.1 at week 12 and 1.0 at week 24. Mean DLQI

at baseline was 16 and decreased to 2 at week 12 and to 1 at week 24. PHQ9 improved markedly from 5 at baseline to 1.5 and 2 after week 12 and 24 – reflecting no indication of depression. Brodalumab was well tolerated.

Conclusion: In the ODIN study, the positive effect of Brodalumab on difficult-to-treat areas, especially scalp psoriasis and nail involvement, was clearly shown.

Baricitinib outcomes on atopic dermatitis lesion locations: Results from a cross-sectional patient survey in France, Germany and the United Kingdom

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Introduction: This survey aims to assess which body areas affected by atopic dermatitis (AD) are most bothersome for patients and to understand patients' perspectives on impact of baricitinib (BARI) treatment on lesion involvement in a real-world clinical setting.

Materials & Methods: Adults (≥18 years) with moderate-to-severe AD treated with BARI in routine clinical practice for ≥4 weeks in France, Germany, and the United Kingdom were invited to participate in the survey by their treating dermatologist.

Results: The survey was completed by 170 patients. At BARI initiation, all patients reported experiencing AD symptoms on ≥1 body location with 4%, 49% and 47% on 1, 2-3 and 4-6 body locations, respectively; most commonly on the arms/legs (85%; excludes hands/feet), trunk (74%), hands (71%) and head/neck (62%; includes scalp, face and neck). Of these body areas, head/ neck area was reported as the single most bothersome (36%). At survey completion, 11%, 26%, 52% and 10% of respondents reported AD on none, 1, 2-3 and 4-6 body locations, respectively. Patients reported AD symptoms on the arms/legs (59%), trunk (44%) and head/neck area (29%). Of those reporting AD on head/ neck at BARI initiation (n=106), 54% (n=57) experienced clearance while on BARI, most of whom (96%) were satisfied (n=39[68%]) or very satisfied (n=16[28%]) with their treatment.

Conclusion: Adult patients who participated in this survey reported the head and neck area as the single most bothersome body area for their AD. By survey completion, AD symptoms were reported on fewer body areas than at BARI initiation.

Patient Reported Outcomes for Scalp, Eyebrow and Eyelash hair loss in Patients with Severe Alopecia Areata Treated with Baricitinib: Week104 Results from Two Phase-3 Clinical-Trials

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Introduction: Here we report improvements in scalp hair, eyebrow (EB), and eyelash (EL) as reported by patients with severe alopecia areata (AA) treated with baricitinib for 104 weeks.

Methods: Data were pooled from Phase 3 BRAVE-AA1 and BRAVE-AA2 trials. Patients with baseline (BL) severe AA (Severity of Alopecia Tool (SALT) score= ≥50), were randomized (3:2:2) to receive once daily baricitinib 4mg, 2mg or placebo, respectively. The Scalp Hair Assessment PROTM and the PRO measure for EBTM and ELTM were used to assess treatment benefits.

Results: There were, respectively, 65 and 129 patients from baricitinib 2mg and 4mg groups who were responders (SALT score ≤20) at Week (W)52.

From W52-104, the proportion of patients with a reported scalp hair response was 72-81% for 2mg-and 86-90% for 4mg-treated patients.

During the same period, the proportion of patients with a reported EB response increased from 56% to 67% for 2mg-treated patients and from 64% to 75% for 4mg-treated patients. The proportion of patients with a EL response also increased from 52% to 70%, and 56% to 74% for 2mg and 4mg-treatment, respectively.

By Week 104, proportion of W52 responders having full EB (PRO EB=0) or full EL (PRO EL=0) was 57% and 60% with 2mg and 62% and 66% with 4mg.

Conclusion: PRO data provide further evidence of patients' benefit of treatment of severe AA with baricitinib. The cumulative improvements of EB and EL support previous observations that long treatment periods may be needed to achieve full benefit of these hair-bearing sites.

Injection Experience Satisfaction with a New, Citrate-Free Formulation of Ixekizumab in the United States Customer Support Program

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Objective: To evaluate satisfaction with the first injection experience of citrate-free ixekizumab in a real-world study.

Methods: Adults enrolled in the Lilly Ixekizumab US Customer Support Program, receiving either original ixekizumab for ≤1 year or initiating citrate-free ixekizumab for ≤1 month for psoriasis, psoriatic arthritis, or axial spondyloarthritis were included in the study.

Results: 451 patients were included in the analysis. Most patients were white (85.4%), had psoriasis and/or psoriatic arthritis (91.8%), (mean age: 45.3 years). Significantly more patients were "very" or "somewhat satisfied" with their first citrate-free ixekizumab injection experience than original ixekizumab (83.9% vs. 71.7% respectively; p=0.0001). Patients receiving original ixekizumab that were "very" or "somewhat satisfied" with their first injection did not differ by treatment duration: ≤1 month (N=40, 70.0%), 2-5 months (N=151, 70.2%), and 6-12 months (N=170, 73.5%) (p=0.7768). 93.9% and 93.4% of patients who switched from original ixekizumab were "definitely" or "mostly willing" to continue using citrate-free ixekizumab and recommend it to a friend or family member, respectively. 94.2% of patients who switched from original to citrate-free ixekizumab preferred citrate-free ixekizumab or had no preference. 74.5% of patients not previously exposed to ixekizumab were "very" or "somewhat satisfied" with their first citrate-free ixekizumab injection experience and 94.5% were "definitely" or "mostly willing" to continue using citrate-free ixekizumab.

Conclusion: Citrate-free ixekizumab was preferred and well accepted by most patients who switched from original ixekizumab, they were satisfied with their first injection experience, were willing to continue using and recommend to others, and preferred the new formulation.

New therapeutic strategy to control Psoriasis by inhibiting Eukaryotic translation initiation factor 4E (eIF4E)

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Introduction: Psoriasis is a chronic, immune-mediated inflammatory skin disease characterized by overexpression of eIF4E. In the initiation of translation, eIF4E plays a central role by binding to the 5'-m7G cap and is therefore critical for cell progression through the cell cycle. The eIF4E polypeptide is considered to be the rate-limiting component of the eukaryotic translational apparatus and is involved in the mRNA-ribosome binding step of eukaryotic protein synthesis. We hypothesized that targeting eIF4E would result in lower expression in psoriasis lesions, which should be reflected at protein and mRNA levels.

Methodology: In our study, a keratinocyte cell line was treated with a new eIF4E inhibitor. The mRNA and protein expression levels of eIF4E, eIF4A, eIF4G, and proinflammatory cytokines (e.g. IL -17, IL -22, IL-1b, TNF-α) were analyzed by quantitative real-time polymerase chain reaction (qRT-PCR) and Western blotting.

Results: Inhibition of eIF4E in HaCaT cells resulted in a significant decrease in mRNA and protein levels of eIF4E and its associated partners eIF4G and eIF4A. In particular, there was a remarkable decrease in proinflammatory cytokines IL -17, IL -22, IL -1b and keratinocyte markers such as S100A8 and FLG, which play an important role in the pathogenesis of psoriasis.

Conclusion: Direct targeting of eIF4E opens a variety of new possibilities for effective treatment of severe psoriatic lesions.

'Tinea Genitalis' in Men who have Sex with Men: An Emerging Sexually Acquired Dermatophyte Infections

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Introduction: Men who have sex with men (MSM) are over-proportionally affected by sexually transmitted infections (STI). The recent outbreak of Mpox among MSM highlights this population's vulnerability to an extended spectrum of infections. Tinea is commonly passed on between individuals as smear infection, yet data on tinea among MSM is scarce.

Methods: To investigate dermatophyte infections and the linkage to sexual activity, all positive mycological tests between 01/2014-03/2022 at the HIV/STI-clinic, Medical University of Vienna were analyzed. Details on course of disease and patient characteristics were collected.

Results: We identified 973 positive mycological tests: 3%(26/973) were dermatophyte infections, 93%(909/973) yeast and 4%(45/973) undetermined. Sixty-five percent (17/26) of dermatophyte infections (N=16 Trichophyton sp., N=1 Microsporum canis) affected MSM in the genital (58%,10/17), inguinal (12%,2/17), pubic (18%,3/17) or perioral (12%,2/17) region and were considered 'tinea genitalis'. All MSM reported recent sexual encounters. Notably, 59%(10/17) of tinea genitalis cases occurred between 01/2020-03/2022. The remaining nine dermatophyte infections affected the trunk or capillitium and could not be linked to sexual activities.

Individuals with tinea genitalis were either HIV+ (65%,11/17) or HIV pre-exposure prophylaxis-users (35%,6/17). All received topical treatment, however, six cases required systemic treatment (range 4-134 days). Concomitant infections with syphilis, gonorrhea, and chlamydia were found in 12%(2/17), 18%(3/17), and 12%(2/17), respectively.

Conclusion: We observed several cases of tinea genitalis among sexually active MSM, suggesting transmission via sexual intercourse. Thus, tinea genitalis should be considered in MSM presenting with typical skin lesions to enable treatment and prevent further transmission of this potentially severe infection.

Optical coherence tomography angiography enables visualization of microvascular patterns in chronic venous insufficiency

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Introduction: Valvular dysfunction in chronic venous insufficiency (CVI) can affect veins with diameters as small as 100µm, which has shed light on the etiology of skin alterations in individuals with minor insufficiency of truncal veins. While Doppler sonography provides hemodynamic information on larger vessels, it lacks the ability to visualize structural changes on a capillary level. Optical coherence tomography angiography (OCTA) may close this diagnostic gap providing a non-invasive, high resolution, and volumetric imaging approach to investigate the cutaneous vasculature.

Methods: Participants with CVI encompassing all CEAP C stages and healthy controls were recruited. Specially designed OCTA technology was employed for high-resolution imaging up to 1 mm below the skin surface. Following microvasculature extraction, artifact removal, and feature analysis, parameters including vessel radius, vascular density, fragment count, and tortuosity were evaluated.

Results: Incorporating 53 CVI patients and 13 healthy controls, this study revealed significant qualitative and quantitative variations in microangiographic patterns. Telangiectasias and corona phlebectatica displayed notably larger vessel radii compared to controls. Vascular fragmentation increased from C0 to C5, potentially indicating a decline in capillary density with CVI progression. Conversely, venous leg ulcers demonstrated augmented vascular density. Additionally, computed tortuosity measures progressively increased from C4 to C6.

Conclusion: This study provides crucial insights into cutaneous microvasculature changes in CVI patients applying OCTA, elucidating distinct vascular patterns across different stages. These findings offer a visual foundation for understanding disease progression. Micro-imaging techniques hold promise in identifying patients at risk for CVI-associated skin changes, ulcer formations, and enabling targeted early interventions.

Retrospektive Einzelfallberichte über die Behandlung von Patienten mit fortgeschrittenem BRAFV600-mutiertem malignen Melanom mit Encorafenib plus Binimetinib (REMI-NISCENCE): Fokus auf Patienten mit Hirnmetastasen

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Hintergrund: Eine Herausforderung in der Therapie des fortgeschrittenen, BRAF V600-mutierten Melanoms besteht in der Definition einer individualisierten Therapiesequenz hinsichtlich zielgerichteter und Immuntherapien. Im retrospektiven Fallberichtsprojekt REMINISCENCE wurden beispielhafte Einzelfallberichte mit Therapieverläufen während/nach Kombinationstherapie mit Encorafenib und Binimetinib (EB) als Grundlage für wissenschaftliche Diskussionen und Schulungen gesammelt.

Methoden: Fälle Erwachsener mit lokal fortgeschrittenem oder metastasiertem, BRAF V600-mutiertem Melanom und laufender/abgeschlossener EB-Therapie in unterschiedlicher Therapieline wurden retrospektiv in standardisierten Fallberichtsbögen dokumentiert.

Ergebnisse: Insgesamt wurden 17 PatientInnen aus 5 Zentren (D, AT) dokumentiert (07/2020-02/2022). Die fünf dokumentierten Fälle mit Hirnmetastasen werden vorgestellt inkl. Patienten-/Behandlungsprofilen, Ansprechen und Sicherheit: 1) männlich, 60 Jahre (J), Progress nach langer Remission, EB

in Erstlinie (bestes Ansprechen [BA]: anhaltende partielle Remission [PR] nach toxizitätsbedingtem EB-Therapieabbruch nach 0,6 J); 2) männlich, 53 J, multiple Metastasen und komplexe Vortherapien, EB in später Therapielinie und begleitende ZNS-Bestrahlung/Operation (Therapiedauer zum Cutoff [TC]: 1,4 J; BA: PR); 3) männlich, 75 J, hohe Tumorlast (S100 und LDH erhöht), multiple Metastasen, EB in Erstlinie nach vorangegangener Stereotaxie (TC: 0,3 J; BA: PR); 4) weiblich, 82 J, schlechte Prognose (LDH erhöht, Autoimmunerkrankung), EB in Erstlinie nach Resektion und Stereotaxie mit adäquater Verträglichkeit (TC: 1 J; BA: PR); 5) männlich, 59 J, kardiovaskuläre Begleiterkrankungen, multiple Metastasen, Zweitlinientherapie mit EB nach vorangegangenem Progress unter Checkpoint-Inhibitoren (TC: 1,3 J).

Schlussfolgerung: Die Darstellung der klinisch relevanten Therapieeffekte einer EB-Therapie bei Hirnmetastasen trägt zur Diskussion eines optimalen Managements dieser Patientenpopulation bei, die häufig aus Studien ausgeschlossen wird. Sponsor: Pierre Fabre, Erstpublikation: EADO 2023

eIF4E: A New Potential Diagnostic Tool for Mycosis Fungoides

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Background: Parapsoriasis is a rare inflammatory skin disease that can develop into overt cutaneous lymphoma, most commonly Mycosis fungoides (MF), and it is very difficult to distinguish between these two conditions. MF inflammation is also associated with overexpression of eukaryotic translation initiation factors (eIFs), which critically regulate gene expression in many important cellular processes, including proliferation, apoptosis, and differentiation. However, the relationship between overexpression of eIF4E and MF is unknown. Here, we investigated the role of eIFs, especially eIF4E, as a diagnostic target of parapsoriasis and MF.

Methods: In this translational observational study, 15 paraffin-embedded human MF and parapsoriasis samples and frozen MF samples were analyzed. Levels of proinflammatory cytokines IL -4, IL -5, IL -13, IL -22, IL -23, IL -31, and transcription factors STAT3, STAT5, and eIF4E were analyzed by immunohistochemistry and qRT-PCR.

Results: Overexpression of eIF4E was observed in MF patients, whereas no change in expression was detected in samples from parapsoriasis patients. eIF4E overexpression in MF patients was associated with higher cell proliferation (Ki-67) and higher levels of proinflammatory cytokines (e.g., IL -4, IL -5, IL -13, IL -22, IL -23, IL -31) and transcription factors (e.g., STAT3 and STAT5).

Conclusion: These results indicate an imbalance in translation and highlight the crucial role of eIF4E in the pathophysiology of MF. This work potentially opens new avenues in the diagnosis of inflammatory skin diseases by using eIF4E as a new diagnostic or prognostic tool to distinguish between parapsoriasis and MF.

Therapie-Update Skabies

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Einleitung: Seit 2015 sehen wir einen deutlichen Anstieg von Skabies-Fällen. Zeitgleich mehren sich europaweit Berichte von Therapieversagen nach Anwendung der bis 2019 einzigen in Österreich zugelassenen Lokaltherapie mit Permethrin.

Methodik: In 3 klinischen Studien wurde in der Universitäts-Hautklinik Salzburg die Wirksamkeit der verfügbaren Antiskabiosa untersucht.

Ergebnisse: In der ersten klinischen Studie (2019) fanden wir eine Wirksamkeit nach zweimaliger Anwendung (Tag 0 und 7; Gruppe A) der 5%-Permethrin-Creme von lediglich 30%. Diese konnte nicht weiter verbessert werden, wenn zu-

dem täglich über 7 Tage die betroffenen Hauptlokalisationen (Hände und/oder Füße, genital) behandelt wurden (Gruppe B) bzw. eine Therapiewiederholung in Woche 3 erfolgte.

In der zweiten Studie (2021) verglichen wir die head-to-head Wirksamkeit von Benzylbenzoat gegen Ivermectin bei 224 Probanden was in einer Heilungsrate von 87% bzw. 86% resultierte. Eine Therapiewiederholung (nach Therapieversagen) mit dem gleichen Therapeutikum führt in nahezu allen Fällen zum Therapieerfolg.

In der letzten randomisiert doppelblinden Studie (2023) bei 110 Probanden konnte beim direkten Vergleich von Permethrin vs. Benzylbenzoat eine Wirksamkeit von 27% zu 87% demonstiert werden. Damit waren die Ergebnisse im Einklang mit den Wirksamkeitsdaten der vorhergehenden Studien, was die Validität der Daten insgesamt untermauert.

Schlussfolgerung: Topisches Permethrin zeigt einen anhaltenden Wirkverlust, während topisches Benzylbenzoat bzw. Ivermectin ein sehr gutes Ansprechen aufweisen. Letztere Mittel bieten sich daher als first-line Therapeutika. Die Ergebnisse sollten Berücksichtigung beim Leitlinien-Update finden.

Retrospektive Auswertung der Risikofaktoren von Patientinnen und Patienten der Ambulanz für melanozytäre Nävi am LKH Graz in den Jahren 2006-2019

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Einleitung: Eine der Hauptursachen für die Entstehung von Melanomen ist die langanhaltende, wiederholte Exposition gegenüber UV-Strahlung. Personen mit über 100 Nävi, einer Melanom-Vorgeschichte oder familiärer Vorbelastung haben ein erhöhtes Risiko.

Methodik: Untersucht wurde die Verbindung zwischen bestimmten Risikofaktoren und der Entstehung von Melanomen bei Patienten der Ambulanz für melanozytäre Nävi an der Universitätsklinik für Dermatologie am LKH Graz. Die Daten wurden aus Fragebögen, welche von Patienten und in dieser Ambulanz tätigen Ärzten ausgefüllt wurden, gewonnen und retrospektiv ausgewertet. Die Studienteilnehmer waren Patienten, die zwischen 2006 und 2019 in der dermatologischen Ambulanz für melanozytäre Nävi behandelt wurden. Die Studienpopulation wurde in zwei Gruppen unterteilt: Patienten mit und ohne Vorgeschichte von zumindest einem Melanom.

Ergebnisse: Die Studienteilnehmer setzten sich aus 2164 Personen mit einem Durchschnittsalter von 39,4Jahren zusammen. Von ihnen hatten 1935 bisher kein Melanom entwickelt, während 229 eine Melanom-Vorgeschichte aufwiesen.

Die Anzahl der Nävi zeigte, mit einem Korrelationskoeffizienten von 0,93, einen signifikanten Zusammenhang mit der Entwicklung von Melanomen.

Überraschenderweise stieg die Anzahl der Patienten ohne Melanom mit zunehmender Sonnenexposition. In der Gruppe mit gelegentlicher Sonnenexposition hatten 38% der Patienten kein Melanom, während es in der Gruppe mit häufiger Sonnenexposition 55% waren. Die Anzahl der Sonnenbrände im Leben war ebenfalls relevant: Die Rate der Patienten ohne Melanom sank von 30% bei 1-5 Sonnenbränden auf 16% bei mehr als 20 Sonnenbränden.

Diskussion: Diese Studie bestätigte einige bekannte Risikofaktoren für Melanome, darunter die Anzahl der Nävi bei Verwandten ersten Grades als erhöhtes Risiko. Solariumbesuche konnten jedoch in unserer Patientengruppe nicht als Risikofaktor bestätigt werden.

COVID-19 vaccines: anaphylaxis and anxiety – an experience report from an allergy unit

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Introduction: Vaccination against SARS-Cov-2 was one crucial element to overcome the corona-pandemic. Even though anaphylaxis to vaccines is rare, 47 patients came to the Allergy Unit at the University Hospital Graz, Austria, reporting symptoms of anaphylactic reactions immediately after administration of COVID-19 vaccines. In addition, 29 patients, who had previously experienced anaphylaxis against drugs, wanted to be tested for a possible sensitization against COVID-19 vaccines or ingredients, such as polyethylene glycol (PEG) or polysorbate 80 (PS80) before their first COVID-19 vaccination. Intradermal tests were performed in all 76 patients, mostly using PEG and/or PS80, but sometimes also COVID-19 vaccines dependent on availability.

Methods: We aimed at getting an overview of this patient cohort and therefore developed a questionnaire to collect more information about the patients' anaphylactic responses, their willingness to vaccinate against SARS-Cov-2 in the future and reasons for their decision. 34 filled-in questionnaires were analyzed.

Results: Of the 47 anaphylactic patients, most were female (40 female/7 male). The intradermal test – even when performed with COVID-19 vaccines – was negative in all but one patients. Most patients, who experienced anaphylaxis after a COVID-19 vaccination, did not want another COVID-19 vaccination at the time of filling in the questionnaire. Most were concerned about another anaphylactic response at the next shot. Premedication with antihistamines significantly lowered (n=74 vaccinations) anaphylaxis severity after COVID-19 vaccinations.

Conclusion: The intradermal test does not seem suitable to predict anaphylaxis to COVID-19 vaccines. Premedication with antihistamines can ameliorate anaphylactic responses to COVID-19 vaccines.

Circulating tumor cells in melanoma: a potential biomarker in early stages?

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Melanoma represents one of the most malignant forms of skin cancer. Early diagnosis has proven critical to reduce risk of metastasis. Nonetheless, there is a need to stratify patients at higher risk also in early stages, as progression occurs in 10% of patients with local disease. As an additional biomarker, liquid biopsy emerged as minimally invasive approach to depict metastatic potential as well as tumor heterogeneity. Thereby, the role of circulating tumor cells (CTCs) still remains to be enlightened, especially regarding early stage melanoma.

For CTC enrichment from blood samples, a novel approach using recombinant malaria protein (rVAR2) was applied. In order to account for melanoma heterogeneity, a staining cocktail including tumor initiating cell markers in addition to established melanoma markers enabled fluorescent CTC detection. Relapse-free survival was compared between patients with ≥1 CTCs at initial diagnosis versus those without detected CTCs.

In 21% of AJCC I-IV patients (n=112) CTCs were detected at time of initial diagnosis. Regarding the cohort with AJCC stage I-II, CTCs were observed in 21 out of 93 (23%) patients (mean follow-up 13 months, IQR 6-18). CTC detection was significantly associated with unfavorable clinical outcome (likelihood ratio test $p<0.05$).

Detection of CTCs in blood at initial diagnosis of melanoma patients with localized disease seems to be associated with unfavorable clinical outcome. This could underline the role of early tumor cell dissemination for metastatic manifestation. CTC assessment may represent a valuable additional biomarker to facilitate risk stratification of early stage melanoma patients to improve personalized treatment approaches.

Diverse virus-specific tissue-resident T cells are detected in the oral mucosa of healthy volunteers

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Introduction: In healthy individuals, SARS-COV-2 infection and current COVID-19 vaccines elicit a broad immune response. A reliable, long-lasting protection is particularly based on the generation of memory T cell populations within the affected tissues. Consequently, the assessment of specific T cell subpopulations is of utmost importance for the evaluation of adaptive cellular immune responses.

Methods: We performed flow cytometry analysis and single cell RNA sequencing via the 10X-Genomics protocol on blood and oral mucosa samples from healthy, SARS-CoV2 recovered individuals 1 month after infection. Cell types were annotated based on widely accepted marker genes and Python package CellTypist. Differential gene expression and TCR receptor analysis were performed using the Python toolkits SCANPY and SCIRPY.

Results: We found that the majority of SARS-CoV2-specific T cells in blood samples were central memory T helper cells (TCM) and, in oral mucosa samples, cytotoxic tissue-resident memory T cells (TRM). While SARS-CoV2-specific mucosa T cells had a balanced ratio of Type-1 helper cells and cytotoxic TRM cells, Epstein-Barr virus- and Yellow-Fever-virus-specific cells consisted predominantly of cytotoxic TRM cells. The most diverse phenotypic repertoire including regulatory T cells was found among Influenza- and Cytomegalovirus-specific cells. The differential gene expression enabled the distinction between gene programs involved in early/late tissue residency and circulating T cells.

Conclusion: Our data provide valuable insights into the distribution of T cell subpopulations and their respective TCR-specificity in healthy oral mucosa. This ongoing project may contribute to further understanding of T cell responses at effector sites following viral infection and vaccination.

Detection of Trichophyton indotineae in Austria: a case report

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Objectives and aim: Trichophyton (T.) indotineae is a newly described species of dermatophyte. This fungal pathogen is widespread in India and is responsible for chronic or recurrent widespread superficial infections. It is often associated with resistance to terbinafine, caused by a point mutation in the gene encoding squalene epoxidase.

Patients and Methods: A female patient (32 years old) with extensive tinea corporis was referred to the Outpatient´s centre. Skin scrapings were collected and analysed by cultivation in fungal culture media (Sabourand agar at 28° for 21 days) and KOH direct test. The species of the growing culture was determined by colony morphology and microscopic observation. The identification was additionally carried out by sequencing the entire ITS region of the rDNA and subsequent database comparison of the sequencing result (courtesy of Labor Mölbis, Leipzig, Germany). Antifungal susceptibility was tested using the Ezy MICTM (Himedia).

Results: Based on colony appearance and microscopic characteristics, the fungus was identified as a member of the T. mentagropyhtes/interdigitale complex. However, as the patient was from India, T. indotineae was suspected. Sequencing demonstrated a clear and 100% match with the above species (Trichophyton indotineae = T. mentagrophytes ITS genotype VIII India). Nevertheless, antifungal susceptibility testing revealed an undiminished susceptibility to terbinafine.

Conclusion: Our results proved the identity of the dermatophyte and confirmed the spread of the fungus across Europe. It was one of the first T. indotineae isolates in Austria.

Diagnosis of Dermatophytes using Molecular Technology – a one year experience

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Objectives and aim: DNA amplification is a sensitive method for identifying infections. Although fungal culture is a well-established method for diagnosing fungi, the PCR is a highly sensitive molecular technology and provides results in short time. The study's objective was to compare multiplex qPCR and culture using patient samples from various cutaneous regions and nail scrapings.

Patients and Methods: A total of 971 samples (402 from men, 569 from women) from the skin (255; 26.3%) and nails (716; 73.7%) were examined. Samples from patients referred to the Outpatients Centre (849; 87.4%) or mailed (122; 12.6%) were simultaneously analysed by cultivation in fungal culture media (Sabouraud agar at 28°C for 21 days), KOH direct tests and by multiplex qPCR (DermaGenius, Pathonostic).

Results: qPCR demonstrated the presence of dermatophyte DNA in 359 (37%) of 971 samples from nails (72.7%) and skin (27.3%). Of the qPCR-positive samples, growth of the dermatophyte was observed in 30.9% for nails and 18.1% for skin scrapings. Both technologies yielded positive results in 176 (18.1%) of all samples tested, leaving 183 infections (51%) missed by culture. The most common species was T. rubrum, detected in 11.3% by culture and 25.7% by qPCR.

Conclusion: Our results demonstrate the high sensitivity of qPCR. It overcomes cumbersome culture methods. Importantly, one half of dermatophyte infections were detected only by qPCR. The rapid and accurate performance of qPCR allows timely and appropriate treatment allocation. Cultivation methods remain important for antifungal resistance testing and non-dermatophyte diagnosis.

Phosphomevalonatkinase-Defizienz als Ursache eines neuen hereditären Autoinflammationssyndroms

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Hintergrund: Hereditäre Autoinflammationssyndrome bezeichnen genetisch bedingte Erkrankungen, die durch periodische oder chronische Entzündungsreaktionen charakterisiert sind und oft von kutanen Manifestationen begleitet werden. Einige dieser Syndrome, wie die Mevalonatkinase-Defizienz (MVKD), entstehen durch enzymatische Defekte innerhalb des Isoprenoid-Biosynthesewegs, in welchem Mevalonatkinase und Phosphomevalonatkinase eine Schlüsselrolle in der Synthese von Sterol- und Nichtsterol-Isoprenoiden zukommt. Bislang wurden jedoch keine Fälle eines Autoinflammationssyndroms durch Mutationen im Phosphomevalonatkinase-Gen beschrieben. Diese Studie beschreibt die erste Patientin mit nachgewiesenem Phosphomevalonatkinase-Mangel und beleuchtet die klinischen, biochemischen und immunologischen Konsequenzen einer homozygoten Missense-Variante in PMVK.

Methoden: Mittels Whole-Exome-Sequenzierung wurde die DNA der Patientin analysiert. Zusätzlich wurden funktionelle Zellstudien durchgeführt, um die Pathogenität der Variante zu bestätigen.

Ergebnisse: Die identifizierte homozygote Missense-Variante in Phosphomevalonatkinase korrelierte mit einer stark reduzierten Enzymaktivität. Die Patientenzellen zeigten einen Defekt in der Prenylierung der Proteine, was als Ursache einer erhöhten Inflammasomaktivität angenommen wird. Klinisch wies die Patientin sowohl Ähnlichkeiten als auch Unterschiede zu Patienten mit Mevalonatkinasedefizienz auf und sprach gut auf eine Behandlung mit IL-1-Inhibitoren an.

Schlussfolgerungen: PMVK-Defizienz erweitert das genetische Spektrum von hereditären Autoinflammationssyndromen. Die Studie unterstreicht die Bedeutung von genetischen Untersuchungen bei unklaren Fällen und betont die Notwendigkeit einer interdisziplinären Kooperation von Dermatolog*innen, Kinderärzt*innen, Rheumatolog*innen und Genetiker*innen für umfassende Diagnostik und Therapie.

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A Rare Case of Congenital Self-Healing Reticulohistiocytosis

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Background: CSHR is a variant of LCH with only skin involvement. CSHR first described by Hashimoto and Pritzker in 1973, more than 100 cases have been reported. No treatment is required for CSHR.

Case description: A 3-days-old term newborn boy presented to the pediatric department of the ''Muratsan''Hospital Complex of Yerevan State Medical University with multiple red-purple lesions appeared at birth. At presentation the patient had several nodular, erythematous lesions on the face, limbs, trunk and abdomen, some recovered to crusts.

The serology of TORCH group was negative. Chest and bone radiographs, abdominal ultrasound were unremarkable. Retinopathy of the newborn with punctated subretinal lesions was presented on the entire periphery of both eyes which resolved spontaneously.

Skin biopsy showed dense clusters of histiocytic cells over the entire height of the dermis, which were CD1a and Langerine positive. Immunostaining showed that these cells were BRAF V600E positive. These results confirm the diagnosis of LCH.

2 months later, the patient no longer had skin lesions. Conclusion was made that it was a CSHR. The patient is undergoing regular outpatient follow-up.

Discussion: This is a case report of a newborn with “blueberry muffin syndrome”, who finally was diagnosed with CSHR.

The objective of this clinical observation was to emphasize the importance of clinical and laboratory monitoring /or follow up/ of CSHR owing to the possibility of recurrence and progression.

Conclusion: Our case clearly shows that spontaneous regression of the lesions and lack of systemic manifestations are the only tools to differentiate this disorder.

Autophagy degrades non-cytoskeletal proteins in hair keratinocytes

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Introduction: Hair shafts are formed by terminal differentiation of hair keratinocytes which synthesize and cross-link keratins and keratin-associated proteins. Here we tested the hypothesis that maturation of hair shafts also involves the coordinated degradation of non-cytoskeletal proteins by autophagy.

Methods: The essential autophagy regulator Atg7 was deleted in keratinocytes of the epidermis and skin appendages, including hair, of mice. The protein composition of hair shafts from fully autophagy-competent and epithelial autophagy-deficient mice was determined by mass-spectrometry-based proteomic analysis.

Results: The abrogation of keratinocyte autophagy led to the increased abundance of hundreds of functionally diverse proteins whereas the abundance of keratins was significant-

ly decreased in hair shafts. The elevation of translation initiation factors, tRNA-ligases, ribosomal proteins and subunits of proteasomes in the absence of autophagy indicated a central role of autophagy in regulating protein turnover within hair keratinocytes. The eight subunits of chaperonin, also known as T-complex protein Ring Complex (TRiC), were most significantly increased in hair of epithelial autophagy-deficient mice.

Conclusions: These results demonstrate that hair keratinocytes depend on autophagy for establishing the mature protein composition of hair and suggest that the proteomic analysis of hair shafts may be used for the diagnosis of impaired autophagy.

Modification of transglutaminase-1 during cornification of epidermal keratinocytes

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Introduction: Transglutaminase 1 (TGM1) cross-links proteins in the epidermis. Mutations in the TGM1 gene cause autosomal recessive congenital ichthyosis (ARCI1) of the lamellar form.

Methods: To determine the dynamics of TGM1 expression and activity in the epidermal cell layers and in cultured keratinocytes, we established a protocol for the antibody-dependent detection of TGM1 protein and the parallel detection of TGM activity.

Results: TGM1 immunoreactivity initially increased and co-localized with membrane-associated transglutaminase activity during keratinocyte differentiation. Unexpectedly, further differentiation of keratinocytes was associated with the loss of TGM1 immunoreactivity while transglutaminase activity persisted. Similarly, when HEK293T cells were transfected with TGM1, the recombinant protein was detected by the anti-TGM1 antibody only transiently whereas transglutaminase activity remained present after the loss of TGM1 immunoreactivity, suggesting that binding of the antibody was prevented by a modification of active TGM1. To screen for candidate proteins controlling this TGM1 modification, we performed a virotrap assay in which proteins binding to TGM1 are trapped in viral particles. Mass spectrometry identified the CAPNS1 subunit of calpain as interaction partner of TGM1. Consequently, we treated keratinocytes and TGM1-transfected HEK293T cells with chemical inhibitors of calpain. Both N-acetyl-Leu-Leu-norleucinal (ALLN) and calpeptin suppressed transglutaminase activity and allowed the maintenance of immunodetection of TGM1.

Conclusions: TGM1 undergoes a modification that is controlled by calpain and possibly affects epidermal cornification.

Cefiderocol penetration in subkutanes und muskuläres Gewebe

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Hintergrund: Cefiderocol ist ein neuartiges siderophores Cephalosporin-Antibiotikum, das möglicherweise zur Behandlung von Haut- und Weichteilinfektionen eingesetzt werden kann. Die Pharmakokinetik (PK) von Cefiderocol in menschlichem Weichteilgewebe wurde jedoch noch nicht bestimmt. Ziel der vorliegenden PK-Studie war es, die Cefiderocol-Gewebekonzentrationen zu untersuchen.

Methoden: Es wurde eine offene, an einem Zentrum durchgeführte PK-Studie mit 8 gesunden männlichen Freiwilligen durchgeführt. Eine einzelne intravenöse Dosis von 2 g Cefiderocol wurde über 3 Stunden verabreicht. Die Wirkstoffkonzentrationen wurden im Plasma, im Muskel und im subkutanen Fettgewebe bestimmt. Die freien Plasmakonzentrationen wurden anhand der durch Ultrafiltration bestimmten Plasmaproteinbindung (PPB) berechnet. Die Konzentrationen im freien Gewebe wurden durch Mikrodialyse (MD) ermittelt. Die PK-Parameter wurden mittels nicht-kompartimenteller Ana-

lyse und pharmakokinetischer Modellierung berechnet. Die Penetrationsverhältnisse wurden als AUCo-8 Gewebe /AUCo-8 freies Plasma berechnet.

Ergebnisse: Die mittleren Penetrationsverhältnisse betrugen 0,81 ± 0,26 für die subkutane und 0,76 ± 0,26 für die Muskelgewebe. Die mittlere PPB betrug 44 %. Cefiderocol hat eine zeitabhängige Abtötungsaktivität gezeigt. 75 % *f*T>MIC wurden als PK/PD-Zielwert für die Erzielung einer bakteriziden Wirkung festgelegt. Der mittlere %*f*T>MIC-Wert für freies Plasma betrug 99 %, 96 % und 83 % für MHKs von 2, 4 bzw. 8 mg/L. 75% *f*T>MIC wurde auch für alle MHKs in Muskel- und subkutanem Gewebe erreicht.

Schlussfolgerung: Diese Studie zeigt, dass mit einer intravenösen Infusion von 2 g Cefiderocol ausreichende bakterizide Konzentrationen für die wichtigsten Bakterienstämme im Plasma erreicht werden. Geht man von einem ähnlichen PK/PD-Zielwert für Weichgewebe aus, kann auch im subkutanen Gewebe und im Muskel eine gute Wirksamkeit erwartet werden.

Lerneffekt und Patientenzufriedenheit durch die regionale teledermatologische Triage-Vernetzung zwischen niedergelassenen Allgemeinmediziner*innen und Dermatolog*innen in der Steiermark

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Einleitung: Zur Verbesserung der dermatologischen Patientenversorgung in ländlichen Gebieten wurde das wegweisende Projekt „Teledermatologie in der Steiermark“ am 1.1.2020 gestartet. Gefördert durch steirische Ärztekammer, Gesundheitsfonds, die ÖGK und die Universitätsklinik für Dermatologie wurden 15 Allgemeinmediziner*innen mit 2 erfahrenen Dermatolog*innen digital verbunden.

Methodik: Im Rahmen des Projektes wurden Patient*innen mit Hauterkrankungen direkt bei Allgemeinmediziner*innen betreut, die digital von Dermatolog*innen eine Behandlungsempfehlung erhielten. Nach dreijähriger Laufzeit wurden Akzeptanz und potentieller Lerneffekt der Allgemeinmediziner*innen untersucht.

Ergebnisse: Bis Ende 2022 wurden 2552 Fälle abgeschlossen. Eine herausragend hohe Patientenzufriedenheit von über 96% wurde durch eine Umfrage mit 600 Teilnehmer*innen ermittelt, wobei insbesondere der schnelle Erhalt einer Diagnose und gegebenenfalls einer Therapie äußerst positiv bewertet wurde. Nur in 32% aller Fälle stimmten initiale Verdachtsdiagnose und finale dermatologische Diagnose überein. Die fachärztliche Korrektur der Diagnose war häufiger, wenn die Behandlung von Dermatolog*nnen empfohlen und von Allgemeinmediziner*innen durchgeführt wurde und war seltener wenn keine Therapie indiziert war. Auch bei den neun Allgemeinmediziner*innen mit intensiver Nutzung des Systems (>60 Fälle) zeigte sich keine Steigerung der diagnostischen Treffsicherheit.

Schlussfolgerung: Überraschend sind hohe Patientenzufriedenheit und Zeitersparnis, die deutlich den Wert einer solchen, digital unterstützten Triage zeigen, unabhängig von Extremsituation, wie der Covid-19-Pandemie. Auch bei häufigen Fallzahlen zeigte sich keine Steigerung der diagnostischen Treffsicherheit durch die Allgemeinmediziner*innen. Unsere Ergebnisse unterstreichen erneut die Wichtigkeit konsistenter und konsequenter Kommunikation sowohl zwischen Ärzt*innen und Patient*innen, als auch zwischen Ärzt*innen unterschiedlicher Fachrichtungen. Diese Erkenntnisse können dazu beitragen, zukünftige telemedizinische Projekte zu optimieren und die Qualität der Patientenversorgung weiter zu verbessern.

FceRI receptor density on basophil granulocyes as potential marker for severity of hymentoptera venom allergy

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Insect venoms are the most common cause for anaphylactic reactions in adult persons. Until today no biomarker has been established to reliably predict the severity of anaphylaxis upon sting reaction. We therefore examined if the high affinity IgE-receptor (FceRI) expression on basophils could serve as marker for hymenoptera venom allergy.

Total and free IgE-receptor density on basophil granulocytes were assessed via FACS analysis of 31 hymenoptera venom allergic patients. Functional basophil activation test (BAT), clinical parameters including anaphylaxis grading (Ring & Messmer) and routine blood tests were assessed and used for correlation analysis. Ten healthy blood samples served as controls.

In the mean higher levels of total-FceRI and lower levels of IgE-free FceRI expression on basophils were seen compared to healthy controls. High expression of total FceRI was highly correlated with low expression of IgE-free FceRI in the same patient. Total FceRI expression was significantly correlated with total IgE and in bee venom allergic patients also with sIgE to bee venom. Total FceRI expression was significantly but inversely correlated with anaphylaxis grading.

To our knowledge this is the first report that a low total IgE-receptor density on basophils was associated with increased severity of anaphylaxis in insect venom allergic patients. This marker should be further assessed in larger cohorts for its relevance and to explore if it can be used for risk assessment for sensitized patients. Furthermore, the change of the FceRI expression should be studied throughout the course of specific immunotherapies.

The keratin-associated protein epiplakin is down-regulated in psoriasis.

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Epiplakin (EPPK1) is a protein that specifically interacts with keratin filaments in the epidermis. It helps to stabilize this filament network when the cells are under stress. In the present study we investigated how EPPK1 is regulated during the process of keratinocyte differentiation and in psoriasis, an inflammatory skin disease in which this process is disturbed.

We analyzed sc-RNA-seq data of 33 patients and found that EPPK1 was downregulated both in lesional and non-lesional psoriasis. By using transcriptomics analysis and real-time PCR to measure the levels of EPPK1 mRNA in keratinocytes that were either undifferentiated or differentiated, we found that EPPK1 was preferentially expressed in the differentiated cells. By immunostaining we could show that EPPK1 was specifically expressed in the granular layer of healthy human skin. In psoriatic skin the mRNA and protein levels of EPPK1 were strongly down-regulated. To investigate the mechanism behind the EPPK1-regulation in psoriasis, we treated in vitro 3D skin models and ex vivo skin samples with different cytokines, including IL1β, IL17 and IFNγ and found that EPPK1 expression was consistently downregulated in skin treated with IFNγ.

In summary, our findings indicate that EPKK1 is part of the group of proteins that are preferentially expressed in differentiated keratinocytes. Moreover, the observed deregulation of EPPK1 in psoriasis, which is likely due to the effects of the inflammatory environment, may be a contributing factor to the aberrant epidermal abnormalities observed in this skin disease.

Spektrum der Photodermatosen in einer photodermatologischen Ambulanz: Monozentrische Registerstudie

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Einleitung: Photodermatosen sind eine Gruppe von Hauterkrankungen, die durch Exposition gegenüber ultravioletter und/oder sichtbarer Strahlung ausgelöst, aufrechterhalten und/oder verschlechtert werden. Es gibt nur wenige Studien, die die Prävalenz dieser Erkrankungen darstellen. Ziel der Studie war es, die Verteilung von Photodermatosen an unserer Spezialambulanz für Photodermatologie zu erheben.

Methodik: Es wurden retrospektiv die Daten von Patienten erhoben, welche in den letzten 25 Jahren an der photodermatologischen Ambulanz der Universitätsklinik für Dermatologie und Venerologie am LKH-Klinikum Graz aufgrund von Photodermatosen betreut wurden. Die demographischen und krankheitsspezifischen Daten dieser Patienten wurden aus den Ambulanzkarten und dem elektronischen Patientendokumentationssystem der Ambulanz für Phototherapie extrahiert und in das Kooperative Photodermatosen-Register der Medizinischen Universität Graz übertragen. Es erfolgte eine Auswertung mit deskriptiver Statistik.

Ergebnisse & Schlussfolgerung: Die Daten von insgesamt 493 Patienten mit Photodermatosen konnten erfasst werden. Darunter die Daten von 25,8% Männern (127) und 74,2% Frauen (366). Am häufigsten, mit 70,0%, wurde die Polymorphe Lichtdermatose (Frauen/Männer: 4,7:1), gefolgt von der erythropoetischen Protoporphyrie (6,9%; 1:1) und der Urticaria solaris (5,9%; 1,4:1) diagnostiziert. Seltener wurden Patienten mit einer Porphyria cutanea tarda (3,4%; 1:4,7), Hidroa vacciniformia (2,4%; 1:1,4), Prurigo actinica (1,2%; 5:1) und chronisch aktinischer Dermatitis (0,4%, 1:1), sowie bestimmten genetischen Erkrankungen mit DNA-Reparaturdefekten (Xeroderma pigmentosum und Rothmund-Thomson Syndrom) 3,0% (2:1) an der Spezialambulanz vorstellig. Die Verteilung der Patienten mit den unterschiedlichen Photodermatosen wird mit jener in anderen Ländern und Regionen verglichen, um mögliche regionsspezifische Faktoren zu ermitteln.

Differential Distribution of Dendritic Cells and T Cells in the Skin Tumor Microenvironment.

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Introduction: Immunophenotyping of tumor infiltrating immune cells has become increasingly pivotal for skin cancer diagnosis and treatment. However, the establishment of immunofluorescence (IF) staining procedures of formalin-fixed paraffin-embedded (FFPE) tissue samples can be challenging due to tissue condition and antibody availability and affinity.

Method: To elucidate the tumor immune microenvironment, we aimed to determine the abundance and spatial distribution of dendritic cells (CD1a+) and T cells (CD3+) within different skin cancer types, actinic keratosis, squamous cell carcinoma, basal cell carcinoma, and melanoma, using immunofluorescence. In each FFPE tumor sample, we investigated four distinct areas: intratumoral, tumor margin, intraepidermal, and intradermal. From each area, 5-8 images were selected, and CD1a+ cells and CD3+ cells were counted using the ImageJ software.

Results: Our findings confirmed the presence of both CD1a+ and CD3+ cells in all examined skin cancer types and areas. Intriguingly, the spatial distribution of CD1a+ dendritic cells and CD3+ T cells varied. A predominance of CD1a+ dendritic cells was observed within the tumor and the epidermis, while CD3+ T cells were predominantly localized near the tumor margin.

Conclusion: Our study highlights distinct infiltration patterns of dendritic and T cell within skin cancers. As a subsequent step, we aim to establish a multiplex staining procedure for simultaneous detection of various immune cell types. Additionally, we intend to compare this data with results from flow cytometry analysis, enriching our understanding of the immune landscape in skin cancers.

The role of tissue-resident memory T cells in anticancer skin defenses of organ transplant receivers

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Background: Life-long immunosuppressive therapy is required for Organ transplant receivers (OTR) to prevent graft rejection. This puts them at an increased risk for keratinocyte cancers (KC), namely squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). Despite immunosuppressive therapy, not all OTR develop KC in the post-transplant period (PTP). Additionally, the common trend of having more BCC than SCC in the general population is reversed in OTR. This indicates that the immune defenses against human papillomavirus (HPV) may be weakened in some patients, pointing to skin specific immune players in the protection against KC in OTR. Tissue resident memory T cells (TRM), especially CXCR3+ TRMs, contribute to anti-viral and anti-cancer defenses at skin level. This project aims at understanding their possible role in KC cancer prevention in OTR.

Methods: We selected a matched cohort of OTR patients, matched for age, gender, post-transplant period and immunosuppressive therapy. The first OTR cohort (OTR_A) was defined by having had more than 5 histologically confirmed KC in the PTP. The matched cohort (OTR_B) had no KC in the PTP. We obtained skin biopsies from the two OTR groups, OTR_A (n=10), OTR_B (n=10) and Healthy controls (n=10). After embedding in OCT, we performed cryosectioning, and immunofluorescence, with a staining for CD3, CD8, CD4, CD69 and CXCR3 to identify TRMs.

Results and Conclusion: We successfully established the staining for CXCR3+ TRMs in our samples. We plan to proceed with the analysis of CD4+CXCR3+ TRMs and CD8+ CXCR3+ TRMs. Preliminary results will be presented at the conference.

Hereditäres oder erworbenes Angioödem?

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Einleitung: Ursachen von Angioödemen (AE) sind vielfältig. Wenn es nicht auf hochdosierte Kortikosteroide anspricht, sollte an ein Bradykinin-vermitteltes AE gedacht werden.

Wir berichten über einen 68-jährigen Mann, der nach einem Schlaganfall vor 5 Jahren sporadische Schwellungen an Händen und Füßen entwickelte, die innerhalb von 48 Stunden abklangen, sowie gelegentlich abdominelle Beschwerden. Ein Jahr nach dem Schlaganfall entwickelte er Prostatakrebs, der auf die Chemotherapie ansprach und seitdem in Remission ist. Weitere 2 Jahre später entwickelte er ein massives Gesichtsödem, nachdem einer zahnärztlichen Behandlung unter Lidocain. Im Folgenden traten zunächst einmal im Monat später wöchentlich leichte Gesichtsschwellungen auf. Die Gattin war überzeugt, dass er an einer Lidocain-Allergie leidet.

Methoden: Für die diagnostische Abklärung wurden Blutbild, Chemie, Elektrophorese, ANA, Subsets, dsDNA-Antikörper, C4, C1-INH-Protein und -Aktivität, C1q, ß2-Microglobulin abgenommen und eine Lidocain-Exposition mit stationärer Observanz über Nacht durchgeführt. Die beiden Töchter des Paares wurden ebenso auf HAE getestet und er auf SERPING-1 Mutation.

Ergebnisse: C4, C1-INH-Protein und -Aktivität waren massiv erniedrigt. Alle anderen Bluttest-Ergebnisse waren im Normbereich. Eine Lidocain-Allergie konnte ausgeschlossen werden. Die beiden Töchter hatten normale C1-INH-Werte. Der C1q-Wert, kontrolliert alle 6 Monate, ist stets im Normbereich.

Schlussfolgerung: Eine positive Familienanamnese konnte ausgeschlossen werden. Bei erworbenem Angioödem liegen bekannterweise hämatologische Malignome vor jedoch keine soliden Tumore. Aufgrund seiner Testergebnisse und der Remission seiner Krebserkrankung, gehen wir derzeit davon aus, dass es sich hier um ein sehr spät einsetzendes hereditäres Angioödem handelt. Wir verschrieben Icatibant und unterrichteten die Gattin in der Applikation von subkutanen Injektionen.

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High prevalence of Chlamydia trachomatis and Neisseria gonorrhoeae at pharyngeal and anorectal sites in patients presenting to an STI outpatient ward

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Introduction: Extragenital STIs commonly run an asymptomatic course, resulting in delayed diagnosis and treatment, increasing the risk of further transmission.

Methods: We conducted a single-center retrospective analysis of patients, who presented between 10/2019 and 02/2021 at our STI outpatient clinic, and had a pharyngeal and/or rectal swab taken. Analysis included demographics, clinical symptoms, serology, and multiplex PCR results.

Results: We analyzed data from 440 patients (345 male [78%], mean age 34.6 years, and 95 female [22%], mean age 31.5 years). 174 patients were heterosexual (61.9%), 97 males reported having sex with men (34.5%), 31 were bisexual (11.0%), 159 (36.1%) did not report their sexual orientation. Of the 440 patients, 303 (68.9%) presented due to symptoms (68.9%), remaining patients presented due to concern on the presence of an STI.

An STI was confirmed in 195 patients (44.3%), 109 patients (24.8%) tested positive at extragenital sites (pharyngeal: 71 [65.1%], anal: 61 [56.0%], both: 23 [21.1%]). The most frequently detected extragenital pathogen was N. gonorrhoeae (pharyngeal: 71.8% [51/71], anorectal: 55.7% [34/61]), followed by C. trachomatis (pharyngeal: 5.6% [4/71], anorectal: 41.0% [25/61]). Of those suffering from an extragenital STI, 64.2% (70/109) tested negative for relevant pathogens at genital sites. Pharyngeal and anorectal infections were asymptomatic in 88.7% [63/71] and 65.6% [40/61], respectively.

Conclusion: Two-thirds of patients with an anal STI and the vast majority of patients with a pharyngeal STI show an asymptomatic course, irrespective of symptoms at genital sites. Our results highlight the relevance of extragenital testing regardless of the presence of symptoms.

Treatment of hidradenitis suppurativa with secukinumab: real-life and long-term experience from a specialty clinic

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Background: Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition characterized by increased interleukin(IL)-17A/C/F. Since June 2023 the IL-17A inhibitor Secukinumab is approved for the treatment of HS. Phase III trials suggest favorable outcomes with up to 46% of patients achieving HiSCR by week 16 and only minor side effects.

Objectives: This retrospective cohort study aimed to assess the clinical response and safety of Secukinumab in a real-life setting.

Methods: Patients were treated with Secukinumab 300mg either every 2 or 4 between 2020 and 2022. Patient records were screened to determine treatment response (HiSCR, IHS4, VAS, DLQI) and tolerability after 12 weeks.

Results: 12 patients (f:m 1:1, average 48.5 years) were treated. 67% of them had Hurley III disease. 50% of all patients achieved HiSCR at week 14. In 3 cases patients received add-on treatment with doxycycline before week 14. Mean IHS4 decreased from 18.2 (min 3, max 55) to 6.3 (min 0, max 17) at week 14. The mean Dermatology Life Quality Index decreased from 16.9 to 10.2 at week 14. Mean VAS was 3.9 at therapy initiation and 2.3 at week 14. Four patients stopped Secukinumab due to lack of efficacy. Mean duration on Secukinumab was 55.5 weeks. At this point 9 of 12 patients reported at least 50% improvement (patient global assessment). No treatment related adverse events occurred.

Conclusion: Secukinumab was well tolerated and lead to clinical improvement in one half of the patients. Add-on treatment and dose escalations might be required in select patients.

Therapieresistentes Ulcus der Wange

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Einleitung: Eine 52-jährige Patientin wurde mit einem schmerzhaften, 3x1cm haltenden Ulcus an der rechten Wange zugewiesen. Dieser bestand seit drei Wochen und trat gemeinsam mit einer vorbekannten rezidivierend nekrotisierenden Skleritis am rechten Auge auf. Anamnestisch kam es bereits vor 8 Jahren zum Auftreten einer ähnlichen, schmerzhaften, ulzerierenden Läsion am linken Oberarm, wo sich klinisch eine atrophe Narbe zeigte. An Vorerkrankungen waren ein Diabetes mellitus und eine chronisch entzündliche Darmerkrankung bekannt.

Methodik: Aufgrund der rezidivierenden Abszesse mit Augenbeteiligung kam differentialdiagnostisch ein M. Behcet, ein Schleimhautpemphigoid, sowie Ulcera infektiöser Genese, Wundheilungsstörung bei vorbekannten Diabetes mellitus oder ein granulomatöses Pyoderma Gangränosum in Frage. Umfassende Untersuchungen hinsichtlich einer infektiösen Genese inklusive Leishmanien und Mykobakterien wurden eingeleitet.

Ergebnisse: Die Mykobakterien- und Leishmanien-PCR, sowie bakterielle und fungale Breitspektrum-PCR waren negativ, ebenso ein Quantiferon-Test. Die durchgeführten histologischen Aufarbeitungen zeigten wiederholt ein unspezifisches, gemischtzelliges granulomatöses Infiltrat. Im Rahmen der Durchuntersuchung wurde als Zufallsbefund ein multifokales papilläres Schilddrüsenkarzinom diagnostiziert, welches chirurgisch saniert und mit Radiojodtherapie behandelt wurde.

Weder eine tuberkulostatische Therapie, noch eine Steroid-Stoßtherapie, noch eine anti-TNF alpha Therapie führten zu einem therapeutischen Ansprechen, sodass die Diagnose eines granulomatösen fazialen Pyoderma Gangraenosum gestellt wurde. Erst durch den Einsatz von Immunglobulinen nach Absetzten aller anderen Therapien kam es zu einer Abheilung der Läsion.

Schlussfolgerung: Ein granulomatöses faziales Pyoderma Gangraenosum ist eine seltene Sonderform des Pyoderma gangraenosum und stellt eine extrem herausfordernde und therapierefraktäre Autoimmunerkrankung dar.

Phototherapeutic treatment survival in patients with psoriasis

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Introduction: The aim of this study was to determine survival of phototherapy in psoriasis patients.

Methods: Preliminary data from the Phototherapy Registry Graz and the Austrian Psoriasis Registry (PsoRA) were scrutinized to determine phototherapeutic survival rates regarding patient and disease characteristics, irrespective of the treatment type or number of administered UVB and/or PUVA phototherapy cycles. Survival rates were analysed for the period between start of the first phototherapy cycle until the end of the last phototherapy or follow-up/treatment discontinuation. The documented discontinuation of phototherapy or the prescription of systemic treatments were considered as treatment discontinuation.

Results: Data of 829 patients (47.9% women) were eligible for this analysis. The total treatment survival after 5 years was 48.0%. Palmar and/or plantar involvement (hazard ratio [HR] 1.44, $p<0.01$) and palmoplantar pustulosis (HR 2.01, $p<0.001$) significantly decreased phototherapy survival, while female gender (HR 1.18, $p=0.16$), involvement of nails (HR 0.97, $p=0.85$) and scalp (HR 0.82, $p=0.09$) did not. Psoriatic arthritis, involvement of inverse body sites and other pustular psoriasis types could not be analysed due to low patient numbers.

Conclusion: Phototherapy survival compares well to that of biologics. However, disease characteristics should be considered when treating psoriasis patients with phototherapy. Phototherapy survival is significantly reduced in patients with palmar and/or plantar plaque psoriasis and in patients with (psoriatic) palmoplantar pustulosis.

mTOR inhibition is efficient in cutaneous sarcoidosis and results in a long-lasting decrease of disease-associated fibroblasts

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Background: Sarcoidosis is an inflammatory disease of unknown etiology that belongs to the group of multisystem granulomatous disorders. Recent evidence indicate an important role of mTOR for granuloma formation. We conducted a clinical study of patients with persistent cutaneous sarcoidosis treated with the mTOR inhibitor sirolimus.

Methods: We included patients of full age with persistent, histologically-proven, cutaneous sarcoidosis. All patients received sirolimus 1mg/ml, once daily for 4 months. Treatment efficacy was assessed before and after each treatment phase using clinical scores. Skin biopsies were taken before and after therapy and after a two months follow-up period without treatment. Skin was processed for single-cell RNA sequencing, and immunofluorescence protein staining was performed on cryosections from the same biopsies.

Results: Systemic treatment resulted in clinical and histologic remission of skin lesions in 70% of patients with a long-lasting improvement of cutaneous lesions for up to 1.5 years. Clinical improvement correlated with a lasting decrease of macrophages, T cells and fibroblasts in treatment responders, which are known to represent the building blocks of sarcoidosis granulomas. Importantly, we identified a significant higher baseline mTOR activation in tissue immune and non-immune cells from treatment responders, which was especially prominent in granuloma associated tissue fibroblasts.

Conclusion: mTOR inhibition with sirolimus presents an efficient new treatment option for persistent cutaneous sarcoidosis by directly affecting disease-associated macrophages, T cells and fibroblasts in the skin. Therefore, we propose that targeting high mTOR activation in tissue fibroblasts represents the key for successful sirolimus treatment in sarcoidosis with prolonged clinical resolution.

Ecthyma gangrenosum due to Pseudomonas aeruginosa septicemia

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Objectives: A 20-month-old girl was referred to our dermatology outpatient emergency clinic with acute onset of perianal skin lesions and fever of 40°C of three days' duration. Physical examination revealed multiple punched-out fibrin-coated ulcers bilaterally with an erythematous-violaceus rim, approximately 1-2cm in diameter. Our main differential diagnoses included Lipschütz ulcer, neutropenic ulcers and other infectious causes.

Methods: Routine blood test, virus serology, microbiological swabs, blood cultures, multiplex PCR and skin biopsy specimen were taken.

Results: Lab-tests revealed markedly elevated CRP (31.28 mg/dl [reference range <0.5]) and IL-6 levels ([1929.00 pg/ml [<7]), while WBC count was 5.06 G/l (5.0-15.0 G/l). Viral serology was negative. Histopathological examination showed subtotal dermal necrosis but was lacking distinctive features. Blood cultures and multiplex PCR yielded growth of pseudomonas aeruginosa.

Despite aggressive IV antibiotic treatment (vancomycin, meropenem, clindamycin) rapid clinical deterioration warranted extensive surgical debridement. After diagnosing pseudomonas sepsis, treatment with meropenem was continued for 14 days. In a subsequent comprehensive immunologic work-up no immunodeficiency could be detected. Silver-coated foam dressing was used for post-operative wound care. She is currently undergoing routine follow-ups and silicone dressings are applied to flatten hypertrophic scars.

Discussion: Ecthyma gangrenosum (EG) is a rare ulcerating skin infection, most commonly associated with Pseudomonas aeruginosa bacteremia. It is usually seen in immunocompromised patients and can be indicative of an underlying subclinical immunodeficiency (primary/acquired) in previously healthy individuals. As in our case, EG can also occur in non-immunocompromised children. In any case, rapid diagnosis and adequate treatment is crucial to reduce mortality.

CXCR3+ CD56+ skin T cells play an anti-cancer protective role in the skin of organ transplant

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Background: Organ transplant receivers (OTRs) are at 60-100-fold higher risk of developing keratinocyte cancers (KC), probably due to the long-term systemic immunosuppressive therapy (SIT) to prevent graft rejection. However, not all patients develop KC in the post-transplant period (PTP) and OTRs show increased risk for HPV-related squamous cell carcinoma (SCC) compared to basal cell carcinoma (BCC), inverting the SCC:BCC ratio of the general ageing population. Such clinical observations point to the pre-existence of patients- and skin-specific immune players in the protection against KC in OTRs.

Methods: 20 OTRs with and without a diagnosis of KC in the PTP were matched for age, gender, length of PTP and immunosuppressive drugs. We performed flow cytometry, tissue FAXS and RNA- and single-cell RNA-Seq matched with T-cell receptor (TCR) analysis of skin and PBMCs.

Results: Skin CD4+ T cells are reduced in OTRs compared to HC independent of the KC prevalence, which might reflect the general effects of SIT. In OTR that are protected from KC, we identified increased numbers of skin CD8+ T cells with higher levels of CXCR3 and CD56. Single-cell RNA sequencing revealed increased activation state of T cells in the skin of patients protected from KC.

Conclusion: Our results indicate an infiltration and local activation of protective Th1-like and CD8 cytotoxic T cells in normal skin of OTR protected from KC. Further analysis will help identifying the origin and function of cancer-protective T cells and mechanisms to enhance tissue-specific anti-cancer defenses.

Mogamulizumab in patients with mycosis fungoides or Sézary syndrome: interim analysis of the German non-interventional MINT study

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Introduction: Mogamulizumab is a humanized monoclonal antibody against CCR4, approved for the treatment of adult patients (pts) with mycosis fungoides (MF) or Sézary syndrome (SS), who have received at least one prior systemic therapy.

Materials and methods: MINT is a combined retrospective and prospective, multicenter non-interventional study in Germany, sponsored by Kyowa Kirin GmbH (2020-25-DE-POT). We present interim analyses, conducted after at least 3-month data were available for 40 pts. Results are descriptive; missing data were not substituted (observed cases analysis).

Results: Mean age was 68.2±11.0 years; 18/40 pts (45.0%) were male. 23/40 pts (57.5%) were diagnosed with SS and 17/40 pts (42.5%) with MF– further specified as classical (12/17 pts, 70.6%), folliculotropic (2/17 pts, 11.8%), other (2/17

pts, 11.8%) and pagetoid reticulosis (1/17 pts, 5.9%). Disease stage was ≥IIB for 35/40 pts (87.5%) and ≥IVA for 26/40 pts (65.0%). Median follow-up was 10.3 months. At this stage – with only 12/40 (30%) TTNT/PFS events – median TTNT and median PFS were both 28.9 months using KM estimates for all 40 pts (with and without events), and both 6.2 months for the 12 pts who showed progression and started a new therapy (with events). The ORR was 55.0% (22/40); 56.5% (13/23) in SS and 52.9% (9/17) in MF. Interestingly, 70.0% (7/10) pts who developed mogamulizumab-associated rash (MAR) responded vs. 50.0% (15/30) pts without MAR. Any-grade treatment-emergent adverse events (TEAE) considered treatment-related were reported in 40.0% (16/40) pts; the most common being drug eruption (15.0%; 6/40) and lymphopenia (10.0%; 4/40). 27.5% (11/40) pts experienced a TEAE ≥Grade 3, the most common being cellulitis affecting 5.0% (2/40) pts.

Conclusion: This interim analysis of the MINT study suggests that the effectiveness of mogamulizumab in real-world German clinical practice is in line with efficacy and safety demonstrated in global clinical trials.

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