Late Breaking Abstracts

LB 1

Urinary squamous cell carcinoma antigen in psoriasis patients: the first pilot study

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Objectives: This is the first pilot study to investigate urinary squamous cell carcinoma antigen (SCCA) levels in psoriasis patients and its correlation with disease severity or treatment response.

Patients and Methods: SCCA was determined in 24-hours urine samples from 32 individuals (15 with psoriasis and 17 normal healthy volunteers) by Microparticle Enzyme Immuno Assay. We evaluated their urinary SCCA levels, serum SCCA levels, psoriasis area severity index (PASI), and quantitative body surface area (qBSA) at different visits (week 0, week 3, week 12) before and after adalimumab treatment.

Results: A significant increase was detected in urinary SCCA levels with psoriasis compared to control cases ($P < 0.05$, Mann-Whitney U test). After adalimumab treatment, PASI, qBSA and serum SCCA levels were significantly improved, but the urinary SCCA levels were not significantly decreased ($P > 0.05$). No relationship could be detected between disease severity and urinary SCCA levels.

Conclusion: Urinary SCCA might be a novel diagnostic biomarker for psoriasis, but its level is not correlated with disease severity or treatment response.

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LB 2

Epidermal neutrophil recruitment in response to staphylococcus aureus colonization of human skin

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Epi-cutaneous Staphylococcal colonization is increasingly recognized as important for priming the host dermal immune response towards this potential pathogen. The significant morphological and immunological differences between human and mouse skin encouraged us to develop a xenograft humanized model in which we study S. aureus skin colonization on living human skin.

We have identified an IL-8 mediated pro-inflammatory signaling that is upregulated in response to epi-cutaneous colonization of human skin by S. aureus USA300 in vivo and in vitro. The IL-8 response appears to be produced by the surface layers of keratinocytes and does not require invasive bacteria. This pro-inflammatory signal induces directed transmigration of neutrophils across the thick human epidermis. Blockage of this IL-8 signal in vitro is shown to reduce neutrophil transmigration. Neutrophil depletion in vivo leads to higher bacterial loads on the skin indicating that this epidermal neutrophil recruitment may function to control bacterial numbers on the skin surface.

Ongoing work aims to further elucidate the pro-inflammatory signaling pathways, the kinetics of this response and the specific cell types from which it originates. Furthermore, we are studying the bacterial mechanisms of adaptation to this microenvironment, polymicrobial interaction in colonization and how pathological skin conditions affect Staphylococcal colonization. This work has demonstrated a unique human response to epi-cutaneous Staphylococcus and we hypothesise that this sub-clinical response is a way for the tissue to control bacterial numbers.

LB 3

Efficacy and safety of BI 655130, an anti-interleukin-36 receptor antibody, in patients with a moderate-to-severe generalized pustular psoriasis flare

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Generalized pustular psoriasis (GPP) is a rare life-threatening, difficult-to-treat disease characterised by recurrent flares of pustular, erythematous rashes, and has a strong genetic linkage with the interleukin (IL)-36 pathway. The efficacy and safety of a single, open-label, intravenous (10 mg/kg) dose of BI 655130, an anti-IL-36 receptor monoclonal antibody, was assessed in a Phase I trial (NCT02978690) in seven patients presenting with moderate-to-severe GPP flare.

At baseline, all patients had a GPP Physician Global Assessment (GPPGA) score of 3 (moderate disease), with a pustule subscore of 2–4 (moderate to very high-density pustulation). Three patients carried a homozygous loss-of-function *IL36RN* mutation.

Overall, BI 655130 was well tolerated. Through 20 weeks, four patients (57.1%) had an investigator defined drug-related adverse event; all were graded as mild or moderate. In all patients, rapid improvements were seen in GPP Area and Severity Index (GPPASI), with a mean percentage change from baseline of 59.0%, 73.2%, and 79.8% at Weeks 1, 2, and 4, respectively. Pustules were completely cleared in three patients (42.9%) within 48 hours of treatment, in five patients (71.4%) by Week 1 and in six patients (85.7%) by Week 2. A GPPGA score of 0 or 1 was achieved in five patients (71.4%) at Week 1 and in all patients by Week 4. Efficacy endpoints were generally maintained up to Week 20. Treatment with BI 655130 led to improvements in patient-reported outcomes as early as Week 2. Marked reductions in C-reactive protein serum levels and blood neutrophil counts were rapid and sustained to the last measurement taken at Week 4. At baseline, global transcriptome analysis identified 3276 genes that were differentially expressed in lesional and non-lesional skin biopsies; by Week 1, the expression of 1444 genes in lesional skin reached near non-lesional skin levels.

Overall, blockade of the IL-36 pathway with a single dose of BI 655130 was highly effective and well tolerated in patients with a moderate-to-severe GPP flare.

LB 4

Guselkumab demonstrates superior long-term responses to secukinumab at Week48 in the treatment of moderate to severe psoriasis: Results from the ECLIPSE trial

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Objective: To compare efficacy and safety of guselkumab (GUS) and secukinumab (SEC) over one year of treatment for moderate to severe plaque psoriasis.

Materials/Methods: Patients were randomized to receive GUS 100mg at Weeks 0/4/12, then every 8 weeks (n=534), or SEC 300mg at Weeks 0/1/2/3/4, then every 4 weeks (n=514), both through Week44. Because psoriasis is a chronic disease requiring long-term treatment, the primary endpoint was the proportion of patients achieving a PASI90 response at Week48. The primary and major secondary analyses were pre-specified and tested in a fixed sequence to control Type1 error rate. Missing data were imputed as non-response.

Results: The primary endpoint was met, with GUS demonstrating a superior PASI90 response at Week48 vs SEC (GUS-84.5% vs SEC-70.0% of patients [p<0.001]). The first major secondary endpoint was the proportion of patients with a PASI75 response at *both* Week12 and Week48. Non-inferiority of GUS vs SEC was demonstrated (GUS-84.6% vs SEC-80.2% of patients [p<0.001]); however, superiority was not established (p=0.062). Consequently, p-values for all subsequent comparisons tested in the fixed sequence were considered nominal. Additional major secondary endpoints testing for non-inferiority or superiority of GUS vs SEC, respectively, included: PASI90 response at Week12-GUS-69.1% vs SEC-76.1% of patients (p=0.127, not demonstrating non-inferiority); PASI75 response at Week12-GUS-89.3% vs SEC-91.6% of patients (p<0.001, demonstrating non-inferiority); PASI100 response at Week48-GUS-58.2% vs SEC-48.4% of patients (p=0.001, demonstrating superiority); Investigator's Global Assessment (IGA) score=0 (clear) at Week48-GUS-62.2% vs SEC-50.4% of patients (p<0.001, demonstrating superiority); and IGA score=0/1 (clear/minimal) at Week48-GUS-85.0% vs SEC-74.9% of patients (p<0.001, demonstrating superiority). After reaching maximum responses, PASI90 data showed stable efficacy responses for GUS over time compared to declines in responses for SEC. Adverse events observed were generally consistent with the established safety profiles for GUS and SEC. Three SEC patients reported events of Crohn's disease vs none among GUS patients.

Conclusions: GUS demonstrated superior long-term efficacy compared to SEC in the treatment of moderate to severe psoriasis.

LB 5

Exit of human cutaneous resident memory CD4 T cells that enter the circulation and seed distant skin sites

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As a barrier organ the skin harbors immune cells, a majority of which are tissue-resident memory T cells (TRM) that are thought to persist locally without recirculation, providing front-line defense against recurring insults. TRM at barrier surfaces are defined in part by expression of the markers CD103 and/or CD69 which function to retain TRM in epithelial tissues. However, strict tissue compartmentalization of resident memory in tissues versus lymphoid organs may pose certain disadvantages for a large barrier organ like the skin. We have therefore studied the long-term migratory behaviour of human TRM and their contribution to the memory pool.

Here, we found that CD4+CD69+CD103+ TRM in human skin can downregulate CD69, exit the tissue and be identified as a novel, phenotypically unique population in the circulation of healthy individuals. These circulating TRM produce the cytokines IL-22 and IL-13, and express genes consistent with a role in host-defense and tissue-repair responses. RNA- and TCR-sequencing demonstrated that CD103+ TRM in the blood are transcriptionally and clonally closely related to CD69+CD103+ TRM in the skin. Furthermore, using a skin xenograft model, we confirmed that human cutaneous CD103+ TRM can exit the skin, enter the circulation, and recirculate to secondary human skin sites where they re-assume a TRM phenotype.

Our data demonstrate that, although as a population CD4+ TRM in the skin are largely sessile, recirculation of cutaneous CD4+CD103+ TRM does occur in the steady state in humans, and these recirculating (rc)TRM cells can promote the spread of this functionally specialized T cell population throughout the skin.

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LB 6

Secukinumab Shows Sustained Efficacy in Difficult-to-Treat Palmoplantar, Nail, and Scalp Psoriasis: Long-term Results from 3 Phase III Placebo-Controlled Randomized Trials

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Introduction: Psoriasis localized to scalp, nails, palms and soles remains difficult-to-treat, and can result in significant physical and psychosocial disability. Secukinumab, a fully human monoclonal antibody that selectively neutralizes IL-17A, has demonstrated significant efficacy in the treatment of moderate-to-severe plaque psoriasis and psoriatic arthritis, exhibiting sustained responses up to 5 years with a favorable safety profile. We report the results from 3 phase III studies evaluating the effect of secukinumab treatment on palmoplantar (GESTURE; NCT01806597), nail (TRANSFIGURE; NCT01807520) and scalp (SCALP; NCT02267135) psoriasis.

Methods: GESTURE, TRANSFIGURE, and SCALP study included subjects with moderate-to-severe palmoplantar (N=205, Palmoplantar Investigator's Global Assessment [ppIGA] ≥3), nail (N=198, Nail Psoriasis Severity Index [NAPSI] ≥16 and ≥4 fingernails involved), and scalp (N=102, Psoriasis Scalp Severity Index [PSSI] ≥12) psoriasis, respectively.

Results: In GESTURE, significantly higher proportion of subjects achieved ppIGA 0/1 response (clear/almost clear disease) with secukinumab 300 mg (33.3%) and secukinumab 150 mg (22.1%) vs placebo at Week 16 (1.5%; both $p<0.001$). The efficacy continued to improve with more than half of all subjects on secukinumab 300 mg (57.2%) achieving ppIGA 0/1 response at 1.5 years. In TRANSFIGURE, the mean change in NAPSI score from baseline to Week 16 with secukinumab 300 mg and secukinumab 150 mg was −45.3% and −37.9% respectively. Nail psoriasis continuously improved up to almost 70% at 1.5 years (−68.7% with secukinumab 300 mg). In SCALP, PSSI 90 response rates were achieved by a significantly higher proportion of subjects receiving secukinumab 300 mg vs placebo at Week 12 (52.9% vs 2.0%; $p<0.001$), which further improved up to Week 24 with secukinumab 300 mg (58.8%). In all the studies, quality of life (QoL) improved, and no new or unexpected safety signals were identified. Similar trends were observed at 2.5 years for GESTURE and TRANSFIGURE.

Conclusion: Secukinumab demonstrated clinically meaningful sustained efficacy, improved QoL and a favorable safety profile in all the 3 studies. Secukinumab treatment can provide complete relief beyond skin psoriasis in palmoplantar, nail, and scalp manifestations.

LB 7

Secukinumab Provides Sustained Improvements in the Signs and Symptoms of Active Psoriatic Arthritis: Long-term (4-Year) Data from a Phase 3 Study

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Background/Purpose: Secukinumab, a fully human monoclonal antibody that selectively neutralizes IL-17A, provides sustained improvement in the signs and symptoms of active psoriatic arthritis (PsA).1 Here we report long-term (4-yr) efficacy and safety results in patients from FUTURE 2 study.

Methods: Overall, 397 patients with active PsA were randomized to either secukinumab (300, 150, or 75mg) or placebo weekly, followed by every 4 weeks (wks) starting at Wk8.1 Approximately 1/3 of patients had inadequate response [IR] to prior anti-TNF use. Pts were escalated from 150 to 300mg and from 75 to 150/300mg starting at Wk128, if active signs of inadequate control of disease were observed. Assessments at Wk208 included ACR20/50/70, PASI 75/90, HAQ-DI, SF-36 PCS, and resolution of dactylitis/enthesitis. Analyses by prior anti-TNF use (naïve/IR) and with/without concomitant methotrexate (MTX) were assessed. Safety analysis included all patients who received ≥1 dose of secukinumab.

Results: Overall, 69/100 (69%), 70/100 (70%), and 62/99 (63%) patients originally randomized to secukinumab 300, 150, and 75mg, respectively, completed 208wks of treatment; 46/100 (46%) patients in the150mg group were escalated to 300mg and 56/99 (57%) patients in the 75mg group escalated to 150/300mg. Clinical responses were sustained through Wk208. In the overall population response rates at Wk 208 in the 300, 150, and 75mg groups were 71.2%, 75.0% and 69.4% for ACR 20, and 80.6%, 81.4% and 66.7% for PASI 75, respectively; the proportion of patients with complete resolution of enthesitis/dactylitis were 70.7%/85.3%, 71.7%/88.0% and 64.4%/92.3%, respectively. In patients who had dose-escalation, the proportion of

patients with non/low level ACR responses improved, with corresponding increases in the proportion of patients achieving moderate/high ACR responses. The type, incidence, and severity of adverse events with secukinumab were consistent with previous reports.1

Conclusion: Secukinumab 300 and 150mg provided sustained improvement in the signs and symptoms of PsA over 4 yrs. Secukinumab was well-tolerated, with no new/unexpected safety signals.

1. McInnes IB, et al. Rheumatology (Oxford) 2017;56:1993–2003.

LB 8

Secukinumab Provides Sustained Improvements in the Signs and Symptoms of Active Psoriatic Arthritis: Long-term (4-Year) Data from a Phase 3 Study

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Background: Secukinumab, a fully human monoclonal antibody that neutralizes IL-17A, has shown significant efficacy in the treatment of moderate to severe psoriasis and psoriatic arthritis, demonstrating sustained high levels of efficacy with a favorable safety profile. Here we report secukinumab's long-term sustainability and safety through 5 years of continuous treatment at the approved dose.

Methods: In the core SCULPTURE study, Psoriasis Area and Severity Index (PASI) 75 responders at Week (Wk) 12 continued receiving subcutaneous secukinumab 300 mg every 4 weeks until Year 1 (n=168 at Wk 52). Patients subsequently entered the extension phase and continued double-blinded treatment to Year 3, and thereafter un-blinded treatment to Year 5 (n=126 at Wk 260). Here we report final PASI 75/90/100 and absolute PASI ≤1/≤2/≤3 responses, Dermatology Life Quality Index (DLQI) 0/1 response, and safety/tolerability to Year 5. Efficacy data are reported as observed; multiple imputation (MI) data are reported for PASI responses as additional supportive analysis.

Results: Mean baseline PASI and body surface area (BSA) involvement were 23.5 ± 8.8 and 33.1% ± 18.9, respectively. PASI 75/90/100 responses at Year 1 (88.9%, 68.5%

and 43.8%, respectively; MI: 88.6%, 68.6% and 43.9%) were well sustained to Year 5 (88.5%, 66.4% and 41%; MI: 80.1%, 58.6% and 35.6%). The average improvement in mean PASI was approximately 90% compared to baseline through 5 years. Absolute PASI ≤1/≤2/≤3 responses at Year 1 (58.6%, 67.9% and 74.1%, respectively; MI: 58.9%, 68.1%, and 73.6%) sustained to Year 5 (53.3%, 66.4% and 75.4%; MI: 47%, 58.4% and 66.9%). Two thirds of patients reported no impact of skin disease on their lives over 5 years (DLQI 0/1: 72.7% at Year 1 and 65.5% at Year 5). The most common adverse events included nasopharyngitis, upper respiratory tract infection and headache.

Conclusions: Secukinumab 300 mg treatment sustained high levels of skin clearance, improved quality of life, and a favorable safety profile through 5 years in patients with moderate to severe psoriasis.