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Lack of tuberculosis reactivation in 12,319 patients with psoriasis, psoriatic arthritis, or ankylosing spondylitis treated with secukinumab: An ad hoc analysis of pooled safety data from 28 clinical trials

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Introduction: TNFα inhibitors (TNFi) may increase the risk of tuberculosis (TB) and latent TB infection (LTBI) reactivation; however, data on the effects of newer biologic agents and TB is limited. This pooled safety analysis of patients treated with secukinumab, a human monoclonal antibody neutralizing IL-17A, reports long-term observed incidence rates of TB/LTBI in psoriasis (PsO), psoriatic arthritis (PsA) and ankylosing spondylitis (AS).

Methods: Before the study, patients underwent TB screening. Patients with active TB were excluded, and before randomization, LTBI was treated according to local guidelines. Data from PsO, PsA and AS patients who had received at least one approved dose of secukinumab were included. Safety analyses evaluated LTBI rates and active/reactive TB over a 5-year period using exposure-adjusted incidence rates (EAIR; patient incidence rates/100 patient-years) in 28 clinical trials.

Results: 12,319 patients were included, of which 631 (5.1%) had a positive LTBI screening at baseline. There were no new cases of active TB in the study population. Over 5 years, there were 7 reported cases of new LTBI; among 8819 PsO patients, there were 4 cases (EAIR 0.03 [95% CI 0.01-0.07]); in 2523 PsA patients, there was 1 case (EAIR 0.02 [95% CI 0.00-0.11]) and 2 cases in 977 AS patients (EAIR 0.08 [95% CI 0.01-0.28]).

Conclusions: In this pooled secukinumab safety analysis of PsO, PsA and AS patients, no active cases of TB or reactivation of baseline TB were reported. Newly reported LTBI following treatment was uncommon.

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Cardio-metabolic effects of long-term treatment with secukinumab in psoriatic arthritis and ankylosing spondylitis patients: Pooled 3 year analysis

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Introduction: Systemic inflammation may increase the risk of cardiovascular disorders in psoriasis (PsO), comorbid psoriatic arthritis (PsA), and ankylosing spondylitis (AS) patients. Secukinumab, a fully human monoclonal antibody that directly inhibits interleukin-17A, has demonstrated sustained efficacy and safety in patients with PsO, AS and PsA. Here, we report the long-term effects of secukinumab on key cardiometabolic parameters from pooled analysis of phase 3 clinical trials, through 156 weeks in AS/PsA patients.

Methods: Pooled data from AS (n = 892) and PsA (n = 2049) studies, with a fixed regimen of secukinumab 150 mg, secukinumab 300/150 mg, respectively, or placebo were included. Serum fasting glucose, body mass index (BMI), triglycerides (TG), total cholesterol (TC), TC/high-density lipoprotein cholesterol (TC/HDL-C), blood pressure (BP), and C-reactive protein (CRP) levels were assessed over 156 weeks in overall population and in subgroups by prior anti−tumor necrosis factor (TNF) therapy and concomitant methotrexate (MTX) usage.

Results: Baseline characteristics were comparable across secukinumab and placebo groups in both disease cohorts. Serum fasting glucose, BP, BMI, and lipid (TG, TC, TC/HDL) levels were minimally altered in secukinumab treated patients with AS and PsA through week 156; mean change from Baseline in AS/PsA were: TC (mmol/L) $\pm$0.1/$\pm$0.2, TG (mmol/L) 0.1-0.2/0.003-0.2, TC/HDL-C $\pm$0.2/$\pm$0.2, glucose (mmol/L) 0.08-0.2/$\pm$0.3, BMI (kg/m^2) 0.08-0.9/0.1-1.7, BP (mm Hg) $\pm$0.2 and $\pm$0.9/$\pm$4.0 and $\pm$1.0 (systolic and diastolic). The rapid decrease in CRP levels, observed as early as week 16, were maintained through week 156. A similar trend was seen in subgroups by prior anti-TNF therapy status and concomitant MTX use through week 156.

Conclusions: These results suggest that secukinumab was associated with minimal changes in cardiometabolic parameters over 3 years in patients with ankylosing spondylitis and psoriatic arthritis.

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Life cycle of a halo nevus: A noninvasive in vivo study using reflectance confocal microscopy

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Halo nevi consist of a central melanocytic nevus, outlined by a hypopigmented area believed to be caused by cytotoxic T-cells. They are clinically classified into stages I-IV. Stage I halo nevi contain a central pigmented nevus outlined by a circular or oval hypopigmented area; stage II halos contain a pink central nevus; stage III are described as depigmented macules lacking a central nevus; and stage IV show a partial or complete re-pigmentation of the skin. The current standard is to closely monitor or biopsy halo nevi because rarely, a similar hypopigmented pattern may arise from cutaneous melanoma. Reflectance confocal microscopy (RCM) is an innovative, noninvasive tool used to diagnose melanocytic lesions. We present a case series of ten clinically concerning halo nevi referred to our clinic. Using RCM, we determined the benign nature of the lesions and classified them according to clinical staging standards. Five were classified as Stage I, showing dermal and junctional nests, and numerous inflammatory cells lining the dermal-epidermal junction. Three were classified as stage II; confocal images showed areas of regression evidenced by dermal fibrosis, with few dermal and junctional nests. Two were classified as stage III; confocal images showed an atypical honeycomb pattern, small and large bright lymphocytes, and an absolute lack of epidermal pigmentation. None were classified as stage IV. No atypical round or dendritic melanocytes were observed in any confocal images. These findings support RCM as a viable technique for the diagnosis and monitoring of halo nevi, presenting an alternative to biopsy.

Commercial disclosure: None identified.

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Dupilumab improves patient-reported global assessments of disease severity and treatment effect: Data from a 16-week phase 3 placebo-controlled trial in adolescent patients with moderate to severe AD (LIBERTY AD ADOL)

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Background: Dupilumab is approved in the USA for adult and adolescent patients with inadequately controlled moderate to severe AD. We report the effect of dupilumab on adolescent patients' assessment of disease severity and treatment effect (LIBERTY AD ADOL: NCT03054428).

Methods: Patients (12-17 years) with moderate to severe AD inadequately controlled with topical therapies were randomized 1:1:1 to 16-week dupilumab 200 mg/300 mg every 2 weeks (q2w), dupilumab 300 mg every 4 weeks (q4w), or placebo. Two patient-reported global scales assessed disease severity and treatment effect on a 1-5 scale as follows: Patient Global Assessment of Disease Severity (PGADS): no symptoms (1), mild (2), moderate (3), severe (4), very severe (5); Patient Global Assessment of Treatment Effect (PGATE): much better (1), a little better (2), no difference (3), a little worse (4), much worse (5). These assessments provide a holistic patient perspective.

Results: 251 patients were randomized (q2w [82], q4w [84], placebo [85]). Baseline demographics and disease characteristics were similar among groups. The proportion of patients reporting "no or mild symptoms'' on PGADS at week 16 for q2w/q4w vs placebo was 51.2%/39.3% vs 12.9% ($P < .0001$ for both), compared with 9.8%/6.0% vs 11.8% at baseline. The proportion of patients reporting "much better'' on PGATE at week 16 was 57.3%/44.0% vs 7.1% ($P < .0001$ for both).

Conclusions: Patients' global assessment of their disease severity and treatment effect were significantly better in dupilumab- vs placebo-treated patients following 16-week treatment. The majority of patients receiving dupilumab q2w achieved no or mild symptoms and reported feeling much better after treatment.

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