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Low Interstitial Lung Disease Event Rate in Patients with Rheumatoid Arthritis: Pooled Post Hoc Analysis of Data from the Tofacitinib Clinical Development Program.

Objectives: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Interstitial lung disease (ILD) is a common extra-articular manifestation of RA [1]. We investigated incidence of ILD in patients with RA treated with tofacitinib in a post hoc analysis of data pooled from the tofacitinib clinical development program.
Methods: Incidence rates (IR; patients with events per 100 patient-years [PY]) of ILD events in patients with active RA, receiving tofacitinib 5 or 10 mg twice daily, were calculated using data pooled from 2 Phase (P)1, 10 P2, 6 P3, 1 P3b/4, and 2 long-term extension (LTE) trials (ORAL Sequel LTE main study database locked at time of analysis: March 2017). No patients with pre-existing ILD were included. Potential ILD events were adjudicated by 3 independent pulmonologists as 'probable' (compatible adverse event [AE] with supportive clinical evidence) or 'possible' (compatible AE with no supportive clinical evidence). ILD IRs are described by patient age and region, and over time. In P2/3/3b/4 studies, ILD IRs were compared for tofacitinib vs placebo. A descriptive case-matched control (1:5 ratio of patients with vs without ILD events, matched by age and gender) analysis identified potential ILD risk factors.
Results: Of 7061 patients (23,394 PY exposure), 42 (0.6%) had an ILD event (median time to event 1144 days). The ILD IR was 0.18 with both tofacitinib doses. IRs were numerically higher in patients aged ≥65 vs <65 years and Asian vs non-Asian countries; 95% confidence intervals were wide/overlapping. IRs generally remained stable over time. 17/42 ILD events (40.5%) were serious; 35/42 (83.3%) were mild to moderate in severity. ILD IRs were numerically lower with tofacitinib vs placebo. A numerically higher proportion of patients in the ILD group (n=42) vs control group (n=210) were: Asian (31.0% vs 17.6%); smokers/ex-smokers (50.0% vs 39.5%); RF-positive (89.2% vs 71.0%); anti-CCP antibody positive (54.8% vs 46.7%); had received prior MTX (90.5% vs 79.5%), non-MTX csDMARDs (61.9% vs 55.2%), TNF inhibitors (26.2% vs 18.6%), and concomitant glucocorticoids (71.4% vs 52.9%); and had higher baseline mean ESR (57.0 vs 46.9 mm/hr) and CRP (25.4 vs 15.4 mg/L).
Conclusions: In this post hoc analysis of data from P1/2/3/3b/4/LTE studies, ILD events following tofacitinib treatment were low, and were associated with known risk factors.

1.Curtis J et al. Arthritis Res Ther 2015; 17: 319