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SAT0330 CHANGES IN LYMPHOCYTES AND LYMPHOCYTE SUBSETS IN TOFACITINIB-TREATED PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Tofacitinib is an oral Janus kinase (JAK) inhibitor for the treatment of psoriatic arthritis (PsA). Cytokines involved in lymphocyte development, function and homeostasis signal through JAKs, and reductions in mean lymphocyte count over time have been reported in tofacitinib-treated patients (pts) with rheumatoid arthritis.¹

Objectives: To characterise the effects of tofacitinib on absolute lymphocyte counts (ALCs) and lymphocyte subset counts (LSCs) in pts with PsA.

Methods: Data were pooled from 2 placebo (PBO)-controlled, double-blind, Phase 3 studies (OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439]). Pts had active PsA and inadequate response to ≥ 1 conventional synthetic DMARD (OPAL Broaden) or to ≥ 1 tumour necrosis factor inhibitor (OPAL Beyond). Pts were randomised to tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, adalimumab 40 mg subcutaneous injection once every 2 weeks (active control; OPAL Broaden only) or PBO. PBO pts advanced in a blinded manner to tofacitinib 5 or 10 mg BID at Month (M)3. ALCs and LSCs were collected every 3 months as part of safety monitoring procedures in the Phase 3 studies (any abnormalities were confirmed upon retesting). Median ALCs and LSCs are reported up to M6. Incidence rates (pts with event/100 pt-years) for serious infections (SIs) were assessed by confirmed (two sequential measurements) ALC categories (≥ 2.0 , <2.0 – 1.5 , <1.5 – 1.0 and <1.0 – $0.5 \times 10^3/\text{mm}^3$) up to M12.

Abstract SAT0330 – Table 1. Median (range) absolute lymphocyte counts and lymphocyte subset counts up to Month 6, pooled across OPAL Broaden and OPAL Beyond

	Tofacitinib 5 mg BID N=238	Tofacitinib 10 mg BID N=236	Adalimumab 40 mg SC Q2W ^a N=106	Placebo ^b N=236
ALC ($\times 10^3/\text{mm}^3$)				
Baseline	1.74 (0.78–5.24)	1.71 (0.72–4.20)	1.62 (0.79–3.20)	1.69 (0.60–3.78)
Month 3	1.71 (0.60–4.38)	1.75 (0.47–4.74)	1.96 (1.11–3.80)	1.69 (0.65–3.45)
Month 6	1.68 (0.22–4.42)	1.68 (0.55–4.51)	1.88 (0.87–4.69)	–
Total T cells: CD3+ ($\times 10^3/\text{mm}^3$)				
Baseline	1.32 (0.48–3.88)	1.35 (0.44–3.60)	1.27 (0.43–2.73)	1.28 (0.26–3.04)
Month 3	1.30 (0.41–4.45)	1.33 (0.49–3.18)	1.44 (0.62–3.04)	1.35 (0.34–2.69)
Month 6	1.25 (0.28–3.66)	1.33 (0.26–3.30)	1.47 (0.71–4.08)	–
T-helper cells: CD4+ ($\times 10^3/\text{mm}^3$)				
Baseline	0.88 (0.32–2.24)	0.87 (0.26–2.68)	0.78 (0.32–2.04)	0.84 (0.08–2.54)
Month 3	0.88 (0.29–3.77)	0.90 (0.32–2.30)	0.93 (0.28–2.15)	0.87 (0.22–2.15)
Month 6	0.84 (0.22–2.64)	0.91 (0.20–2.58)	0.91 (0.44–2.60)	–
Cytotoxic T cells: CD8+ ($\times 10^3/\text{mm}^3$)				
Baseline	0.41 (0.10–1.40)	0.40 (0.08–1.03)	0.39 (0.07–1.16)	0.41 (0.06–1.32)
Month 3	0.38 (0.08–1.43)	0.38 (0.09–1.08)	0.44 (0.09–1.17)	0.43 (0.07–1.18)
Month 6	0.37 (0.05–1.20)	0.36 (0.04–1.32)	0.50 (0.12–1.57)	–
B cells: CD19+ ($\times 10^3/\text{mm}^3$)				
Baseline	0.21 (0.00–1.48)	0.20 (0.00–1.30)	0.18 (0.01–0.62)	0.21 (0.00–1.15)
Month 3	0.27 (0.01–1.08)	0.30 (0.01–1.42)	0.27 (0.02–0.99)	0.22 (0.01–0.93)
Month 6	0.26 (0.01–1.32)	0.28 (0.00–1.22)	0.26 (0.02–0.95)	–
NK cells: CD16+56+ ($\times 10^3/\text{mm}^3$)				
Baseline	0.23 (0.06–1.39)	0.22 (0.06–0.94)	0.22 (0.03–0.60)	0.20 (0.04–0.75)
Month 3	0.20 (0.04–0.79)	0.18 (0.03–0.75)	0.22 (0.05–0.66)	0.22 (0.03–0.71)
Month 6	0.19 (0.04–0.83)	0.19 (0.04–1.09)	0.25 (0.05–0.75)	–

^aOPAL Broaden only; ^bPlacebo-controlled period was 3 months

ALC, absolute lymphocyte count; BID, twice daily; N, number of patients with observations at baseline; Q2W, once every 2 weeks; SC, subcutaneous

Results: The analysis included 816 pts: tofacitinib 5 mg BID, n=238; tofacitinib 10 mg BID, n=236; adalimumab, n=106; PBO, n=236. Up to M6, minimal decreases in median ALC were observed in pts who received tofacitinib 5 mg BID, tofacitinib 10 mg BID or PBO (up to M3 only) (Table). LSCs, including total T

cells (CD3+), cytotoxic T cells (CD8+) and NK cells (CD16 +56+), showed a similar trend to ALC for both tofacitinib doses and PBO (Table), with minimal decreases over 6 months. B cells (CD19+) showed numerical increases across treatments. Percentage changes from baseline in LSCs at M6 showed a generally similar pattern to absolute values. In adalimumab-treated pts, ALCs and all LSCs increased over 6 months. Up to M6, no pts receiving tofacitinib or adalimumab had confirmed $\text{ALC} < 0.5 \times 10^3/\text{mm}^3$; 1 pt receiving PBO had a confirmed $\text{ALC} < 0.5 \times 10^3/\text{mm}^3$ over 3 months, resulting in discontinuation from the study before advancing to active treatment. Up to M12, SIs were reported in 7 tofacitinib- (including 2 pts who advanced from PBO) and 1 adalimumab-treated pt; of these, 1 SI (PBO advanced to tofacitinib) occurred > 6 months after treatment initiation. There was no trend that suggested an increased risk of SIs in any ALC category (data not shown).

Conclusions: Up to M6 in tofacitinib-treated pts with active PsA, minimal changes in ALCs and LSCs were observed. Although incidence of SIs did not appear to be related to ALC, conclusions are limited by the small number of events.

REFERENCE:

[1] van Vollenhoven, et al. Ann Rheum Dis 2016;75(suppl 2):258.

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SAT0331 INFLAMMATORY MARKERS AND ADIPOKINES RELATED TO CARDIOVASCULAR RISK AND METABOLIC COMORBIDITIES IN PSORIATIC ARTHRITIS. IN VIVO EFFECTS OF APREMILAST

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Objectives: 1) To evaluate the role of inflammatory mediators and adipokines in the cardiovascular risk profile and the metabolic comorbidities associated with psoriatic arthritis (PsA). 2) To evaluate the effect of apremilast in the adipocytokine pattern, metabolic components and endothelial dysfunction in patients with PsA and metabolic syndrome (MetSyn).

Methods: 55 PsA patients and 30 age and gender-matched healthy donors (HD) were analysed. An extensive clinical analysis including body index mass, lipid profile, HOMA-IR and intra-arterial blood pressure was performed. Endothelial function was measured through post occlusive hyperemia using Laser-Doppler. Different proinflammatory cytokines (TNF α , IL1b and IL6), vascular adhesion molecules (VEGF and E-Selectin) and adipokines (adiponectin, leptin, resistin and visfatin) were analysed on serum by ELISA. Ten biological-naïve patients with PsA having metabolic syndrome were given apremilast 30 mg twice daily for 6 months. All the measures were carried out at basal, week 4 and week 24 after apremilast treatment.

Results: The prevalence of metabolic comorbidities such as MetSyn, obesity and insulin resistance (IR) was significant higher in PsA compared to HD. PsA patients had impaired endothelial function showed by a reduced peak flow and hyperaemia area and increased levels of VEGF and E-Selectin in serum. The levels of