confounding by indication will make the non-TNFi drugs appear less safe than the TNFi. A simple adjustment for age and sex will reduce this confounding dramatically, but residual confounding is still expected to give higher rates of AEs, and comparisons should be adjusted for medical history and comorbidities when possible.

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PsA: an integrated perspective

OP0201 A PHASE 3 STUDY OF THE EFFICACY AND SAFETY OF IXXEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITOR(S)

P. Nash¹, B. Kirkham², M. Okada³, P. Rahman⁴, B. Combe⁵, D.H. Adams⁶, L.N. Kerr⁶, C.H. Lee⁶, C.L. Shuler⁶, M.C. Genovese⁷. ¹Univ of Queensland, Brisbane, Australia; ²Guy's Hospital, London, United Kingdom; ³St Luke's International Univ, Tokyo, Japan; ⁴Memorial Univ of Newfoundland, St. John's, Canada; ⁵Lapeyrie Hospital, Montpellier Univ, Montpellier, France; ⁶Eli Lilly and Company, Indianapolis; ⁷Stanford Univ, Palo Alto, United States

Background: Tumour necrosis factor inhibitors (TNF-i) have revolutionised the management of psoriatic arthritis (PsA) yet some patients (pts) have an inadequate response (IR) or intolerance. Ixxekizumab (IXE), a monoclonal high affinity antibody that selectively targets IL-17, has shown efficacy in TNF-naïve PsA pts.¹

Objectives: To compare efficacy and safety of IXE with placebo in pts with active PsA who are TNFi-IR.

Methods: In the 24 week (wk), double-blind, placebo-controlled period of a Phase 3 PsA study (SPIRIT-P2; NCT02349295), pts with prior IR or intolerance to 1 or 2 TNF-i were randomised to SC placebo or IXE 80 mg every 2 (Q2W) or 4 wks (Q4W), following a 160 mg initial dose at Wk 0. Pts with IR to treatment (protocol defined) received rescue therapy at Wk 16. Primary endpoint was ACR20 at Wk 24. Continuous data were analyzed using mixed-effects model for repeated measures; categorical data, using a logistic regression model with missing values imputed by non-responder imputation, which treats IR as non-responders.

Results: 363 pts were randomized: ~52 yrs old on average, female (53%), white (~92%), and IR to 1 or 2 TNF-i (204 [56.2%], 128 [35.3%], respectively) or TNF-intolerant (31 [8.5%]). Most pts had current psoriasis (93.4%) and BSA_{≥3} (62.5%). The majority (87%) completed the 24-wk, double-blind period. A significantly higher proportion of IXE- vs placebo-treated pts at Wk 24 achieved ACR20 (65 [53.3%], 59 [48%] vs. 23 [19.5%]; Q4W, Q2W, placebo, respectively), ACR50 (43 [35.2%], 41 [33.3%] vs 6 [5.1%]; Q4W, Q2W, placebo, respectively), ACR70 (27 [22.1%], 15 [12.2%] vs 0; Q4W, Q2W, placebo, respectively), MDA (34 [27.9%], 29 [23.6%] vs 4 [3.4%]; Q4W, Q2W, placebo, respectively), DAS28-CRP, and reductions in functional disability (HAQ-DI) (Table). A significantly higher

Outcomes	Week 12			Week 24		
	Placebo (N=118)	IXEQ4W (N=122)	IXEQ2W (N=123)	Placebo (N=118)	IXEQ4W (N=122)	IXEQ2W (N=123)
ACR20 n (%)	26 (22.0)	61 (50.0)**	59 (48.0)**	23 (19.5)	65 (53.3)**	59 (48.0)**
ACR50 n (%)	4 (3.4)	38 (31.1)**	41 (33.3)**	6 (5.1)	43 (35.2)**	41 (33.3)**
ACR70 n (%)	2 (1.7)	18 (14.8)*	13 (10.6)*	0	27 (22.1)**	15 (12.2)**
HAQ-DI CFB LSM (SE)	-0.1 (0.06)	-0.4 (0.06)**	-0.4 (0.06)**	-0.2 (0.08)	-0.6 (0.07)**	-0.4 (0.07)**
DAS28-CRP CFB LSM (SE)	-0.6 (0.17)	-1.8 (0.17)**	-1.5 (0.16)**	-0.8 (0.20)	-2.1 (0.19)**	-1.8 (0.18)**
LEI (0) ^a n/N (%)	20/69 (29.0)	19/68 (27.9)	29/84 (34.5)	15/69 (21.7)	24/68 (35.3)	26/84 (31.0)
LDI-B (0) ^b n/N (%)	5/14 (35.7)	19/28 (67.9)	12/20 (60.0)	3/14 (21.4)	21/28 (75.0)*	10/20 (50.0)
PASI 75 ^c n/N (%)	7/67 (10.4)	39/68 (57.4)**	42/68 (61.8)**	10/67 (14.9)	38/68 (55.9)**	41/68 (60.3)**
Minimal disease activity (MDA) n (%)	6 (5.1)	31 (25.4)**	21 (17.1)*	4 (3.4)	34 (27.9)**	29 (23.6)**
Safety, n (%)						
TEAE	--	--	--	76 (64.4)	83 (68.0)	90 (73.2)
SAE	--	--	--	4 (3.4)	3 (2.5)	8 (6.5)
Discontinued from AE	--	--	--	6 (5.1)	5 (4.1)	8 (6.5)
Infections	--	--	--	35 (29.7)	47 (38.5)	47 (38.2)
Serious	--	--	--	0	0	3 (2.4)
Oral candida	--	--	--	0	0	4 (3.3)
Injection site reactions ^d	--	--	--	5 (4.2)	14 (11.5)**	29 (23.6)**

Abbreviations: CFB=change from baseline; SAE=serious adverse event.

^aOnly pts with enthesitis at baseline (LEI>0) were included in the analysis.

^bOnly pts with dactylitis (LDI-B>0) at baseline were included.

^cOnly pts with psoriatic lesions $\geq 3\%$ of BSA at baseline were included.

^dInjection site reactions is a high-level term consisting of multiple lower-level terms.

*P<0.05; **P<0.001.

proportion of IXE-Q4W- vs placebo-treated pts reached complete resolution of dactylitis (LDI-B=0). Although enthesitis improved from baseline with both IXE doses, rates of complete resolution (LEI=0) were not significantly different compared to placebo. At Wk 24, significantly greater proportions of IXE-treated pts with $\geq 3\%$ BSA achieved PASI 75 than placebo-treated patients. The incidence of treatment-emergent adverse events (TEAE) was similar across groups (83 [68%], 90 [73.2%] vs 76 [64.4%]; Q4W, Q2W, placebo, respectively). A numerically higher proportion of IXE-treated pts reported infection and a significantly higher proportion reported injection site reactions (the majority were mild) (Table). Serious infection (0, 3 [2.4%], 0; Q4W, Q2W, placebo respectively), serious AE, and oral candidiasis were numerically higher with Q2W vs placebo. No deaths or cases of inflammatory bowel disease, uveitis, TB reactivation, or grade ≥ 3 neutropenia were reported.

Conclusions: IXE improved arthritis¹, physical function, and psoriasis^{2,3} vs placebo with no unexpected safety findings in patients with active PsA and prior IR or intolerance to TNF-inhibitor(s).

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OP0202 EFFICACY AND SAFETY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND AN INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS: OPAL BEYOND, A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 3 TRIAL

D.D. Gladman¹, W.F.C. Rigby², V.F. Azevedo³, F. Behrens⁴, R. Blanco⁵, A. Kaszuba⁶, E. Kudlacz⁷, C. Wang⁷, S. Menon⁷, T. Hendriks⁸, K.S. Kanik⁷.

¹Department of Medicine, University of Toronto, Toronto Western Hospital,

Toronto, Canada; ²Geisel School of Medicine at Dartmouth, School of Medicine,

Lebanon, United States; ³Universidade Federal do Paraná, Curitiba, Brazil;

⁴Johann Wolfgang Goethe University & Fraunhofer IME-TMP, Frankfurt,

Germany; ⁵Hospital Universitario Marques de Valdecilla, Santander, Spain;

⁶Specjalistyczne Gabinety Lekarskie "DERMED", Lodz, Poland; ⁷Pfizer Inc,

Groton, CT; ⁸Pfizer Inc, Collegeville, PA, United States

Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for treatment of PsA.

Objectives: Evaluation of efficacy and safety of tofacitinib vs placebo (PBO) in adult patients (pts) with active PsA and an inadequate response (IR) to TNF inhibitors (TNFi).

Methods: Eligible pts in this 6-month, randomised, PBO-controlled, double-blind, multicentre, Phase 3 study had ≥ 6 months' PsA diagnosis, met CASPAR criteria, had active arthritis (≥ 3 tender/painful and ≥ 3 swollen joints) at screening and baseline, active plaque psoriasis at screening and IR to ≥ 1 TNFi (discontinued due to inadequate efficacy or adverse event [AE]). Pts were randomised 2:2:1:1 to tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID or PBO (advancing to tofacitinib 5 or 10 mg BID in a blinded manner at Month [M]3). Ongoing treatment with 1 conventional synthetic DMARD was required. Pts were followed through M6. Primary endpoints were ACR20 response rate and change (Δ) from baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) at M3.

Results: Pts were 92.1% white, 55.3% female and mean age was 50.0 years. At baseline, mean swollen and tender/painful joint counts were 22.0 and 11.8 respectively; mean HAQ-DI score was 1.3; 69.8% of pts had LEI >0 ; 49.2% had Dactylitis Severity Score (DSS) >0 . Most patients (62.7%) had $\geq 3\%$ BSA affected by psoriasis, for whom median PASI score was 7.9. Discontinuation rate at M3 was 7.6%, and 87.6% completed M6. ACR20 response and Δ HAQ-DI significantly improved with both tofacitinib doses vs PBO at M3 (Fig 1A,B) and were maintained to M6 (Fig 1C,D). Tofacitinib 5 mg and 10 mg BID demonstrated superior ACR20 response vs PBO as early as Week 2 (26.7% [$p \leq 0.05$] and