Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.4269

THU0299

AN INTEGRATED ANALYSIS OF CHANGES IN LIPID LEVELS AND INCIDENCE OF CARDIOVASCULAR EVENTS FOLLOWING TOFACITINIB TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS ACROSS PHASE 3 AND LONG-TERM EXTENSION STUDIES

¹D.D. Gladman, C. Charles-Schoeman², I.B. McInnes³, D.J. Veale⁴, B. Thiers⁵, D. Graham⁶, C. Wang⁶, T.V. Jones⁷, R. Wolk⁶, R. DeMasi⁷. ¹University of Toronto, Toronto Western Hospital, Toronto, ON, Canada; ²University of California, Los Angeles, CA, USA; ³University of Glasgow, Glasgow, UK; ⁴St. Vincent's University Hospital and University College Dublin, Dublin, Ireland; ⁵Medical University of South Carolina, Charleston, SC; ⁶Pfizer Inc, Groton, CT; ⁷Pfizer Inc, Collegeville, PA, USA

Background: Cardiovascular (CV) disease and cardiometabolic syndrome are common comorbidities/causes of mortality in patients (pts) with psoriatic arthritis (PsA). Tofacitinib is an oral JAK inhibitor for the treatment of PsA.

Objectives: To investigate changes in lipid levels and incidence of CV events in pts with PsA treated with tofacitinib in Phase (P) 3 and long-term extension (LTE) studies.

Methods: Data were analysed for pts who received ≥ 1 dose of tofacitinib 5 or 10 mg BID or placebo (PBO), integrated across 2 P3 studies (OPAL Broaden [12 months (m); NCT01877668, including adalimumab control]; OPAL Beyond [6 m; NCT01882439]) and 1 LTE study (OPAL Balance [data cut-off May 2016; ongoing, database not locked; NCT01976364]). Lipid levels were assessed throughout P3 and LTE studies; this analysis included data from the PBO-controlled period (M0–3) of P3 studies. Blood pressure, hypertension events (standardised MedDRA query [narrow]) and adjudicated (independent/blinded to treatment) major adverse cardiovascular events (MACE) are reported for all pts who received ≥ 1 dose of tofacitinib (pooled across doses for hypertension and MACE). Incidence rates (IR; pts with events/100 pt-years [PY]) and 95% CI are reported.

Results: Overall, 783 pts (776 PY of tofacitinib exposure) were included in P3 and LTE studies; treatment duration was 1–927 days. After 3 m of tofacitinib treatment in P3 studies, dose-dependent increases in lipid levels were observed with tofacitinib; minimal changes were observed with PBO, except for triglycerides (figure 1). Concurrent increases in high-density and low-density lipoprotein (HDL/LDL) and no change in the total cholesterol/HDL ratio were shown. Across P3 and LTE studies, no clinically significant changes in mean systolic or diastolic blood pressure were seen to 24 m. Hypertension events were reported in 38 (4.9%) pts: IR 4.93 [95% CI 3.49, 6.77]. Of these events, 4 led to pt discontinuation and 2 were serious adverse events. MACE were reported for 3 (0.4%) pts receiving tofacitinib (IR 0.38 [95% CI 0.08, 1.11]) and included sudden cardiac death (57 days of exposure at time of event), myocardial infarction (197 days) and ischaemic stroke (80 days). This is within the range reported in tofacitinib studies in pts with psoriasis (IR 0.24 [0.15, 0.37]; 8,759 PY of exposure) and rheumatoid arthritis (RA) (IR 0.38 [0.30, 0.47]; 21,286 PY of exposure). No dose-dependent effects on blood pressure were apparent.

Figure. Mean % change from baseline in lipid levels to Month 3 integrated across Phase 3 studies

BID, twice daily; SE, standard error

Abstract THU0299 – Figure 1. Mean% change from baseline in lipid levels to Month 3 integrated across Phase 3 studies. BID, twice daily; SE, standard error

Conclusions: In pts with PsA, the magnitude and dose dependency of increases in lipid levels to M3 were consistent with findings in tofacitinib studies in pts with psoriasis and RA. In P3 and LTE studies, no clinically significant changes were seen in blood pressure or incidence of hypertension. Incidence of MACE was within the range reported in prior tofacitinib studies in psoriasis and RA; however, the long latency of MACE requires longer-term observation.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by A MacLachlan of CMC and funded by Pfizer Inc.

Disclosure of Interest: D. Gladman Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, C. Charles-Schoeman Grant/research support from: AbbVie, Bristol-Myers Squibb, Pfizer Inc, Consultant for: Amgen, Gilead, Pfizer Inc, Regeneron-Sanofi, I. McInnes Grant/research support from: Celgene, Janssen, Novartis, Pfizer Inc, Roche, UCB, Consultant for: AbbVie, Celgene, Janssen, Novartis, Pfizer Inc, Roche, UCB, D. Veale Grant/research support from: AbbVie, Actelion, Bristol-Myers Squibb, Janssen, MSD, Novartis, Pfizer Inc, Roche, UCB, Speakers bureau: AbbVie, Actelion, Bristol-Myers Squibb, Janssen, MSD, Novartis, Pfizer Inc, Roche, UCB, B. Thiers Consultant for: Pfizer Inc, Valeant Pharmaceuticals, D. Graham Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Jones Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Wolk Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. DeMasi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2018-eular.1459

THU0300

NETWORK META-ANALYSIS OF TOFACITINIB VS bDMARDS OR APREMILAST FOR THE TREATMENT OF TNF INHIBITOR-NAÏVE PATIENTS WITH PSORIATIC ARTHRITIS

¹D.D. Gladman, A.-M. Orba², J. Gomez-Reino³, S. Chang-Douglass⁴, E. Leoncini⁴, H.E. Burton⁴, K.S. Kanik⁵, T. Hendriks⁶, J.C. Cappelleri⁵, M.-A. Hsu⁵. ¹University of Toronto, Toronto Western Hospital, Toronto, ON, Canada; ²Johns Hopkins University School of Medicine, Baltimore, MD, USA; ³Hospital Clínico Universitario, Santiago de Compostela, Spain; ⁴Decision Resources Group, London, UK; ⁵Pfizer Inc, Groton, CT; ⁶Pfizer Inc, Collegeville, PA, USA

Background: Tofacitinib is an oral JAK inhibitor for the treatment of psoriatic arthritis (PsA).

Objectives: To perform a systematic literature review (SLR) and network meta-analysis (NMA) to evaluate the efficacy of tofacitinib 5 and 10 mg BID relative to biologic disease-modifying antirheumatic drugs (bDMARDs) or a targeted synthetic DMARD (apremilast [APR]) in tumour necrosis factor inhibitor-naïve (TNFi-N) patients with active PsA.

Methods: The SLR identified randomised controlled clinical trials (RCTs) evaluating tofacitinib, bDMARDs or APR to treat patients with active PsA who were TNFi-N. Outcomes included American College of Rheumatology (ACR)20 response and change from baseline in Health Assessment Questionnaire-Disability Index (Δ HAQ-DI), Dactylitis Severity Score (Δ DSS) and Leeds Enthesitis Index (Δ LEI). Treatment effects were only evaluated during placebo (PBO)-controlled trial phases. The Bayesian NMA (with non-informative priors) was conducted using WinBUGS. The binomial logit model was used for ACR20, Δ HAQ-DI, Δ DSS and Δ LEI were analysed using the normal identity link model. A fixed-effect model was fitted to the data. Median treatment rankings represent data from each iteration of the model from which inferences are based, following model convergence.

Results: The SLR identified 25 RCTs and 21 were included in the NMA (see treatments in table 1). All trials allowed methotrexate use. PBO-controlled treatment durations ranged from 12–24 weeks. In general, patient characteristics were similar across trials. All treatments were associated with improvements in ACR20 and Δ HAQ-DI vs PBO. Tofacitinib 5 mg BID was associated with substantially decreased odds ratios (ORs) for ACR20 vs golimumab 50 and 100 mg Q4W, etanercept 25 mg BW, infliximab 5 mg/kg and secukinumab 150 mg QW-Q4W (table 1); ORs for all remaining comparators were not substantially different. Tofacitinib 10 mg BID was associated with a substantially increased OR for ACR20 vs APR 20 mg BID. Etanercept was associated with an improvement in Δ HAQ-DI vs tofacitinib 5 and 10 mg BID. There was no difference in Δ HAQ-DI for tofacitinib vs other bDMARDs. For ACR20, tofacitinib 5 and 10 mg BID were median ranked 14 (95% credible interval: 8, 17) and 9, ^{5, 14} respectively, among 18 comparators. For Δ HAQ-DI, tofacitinib 5 and 10 mg BID were median ranked 11^{4, 13} and 8, ^{2, 13} respectively, among 14 comparators. Two studies evaluated Δ DSS and Δ LEI; there were no substantial differences in Δ DSS and Δ LEI for tofacitinib 5 and 10 mg BID vs adalimumab 40 mg Q2W and ixekizumab 80 mg Q2W and Q4W.

Abstract THU0300 – Table 1. Fixed-effect NMA data for ACR20 and Δ HAQ-DI in TNFi-N patients with PsA – comparison of bDMARDs or apremilast vs tofacitinib 5 and 10 mg BID^{a,b}

Treatment	ACR20, OR (95% CrI) ^{a,c}		Difference in Δ HAQ-DI (95% CrI) ^{a,c}	
	vs tofacitinib 5 mg BID	vs tofacitinib 10 mg BID	vs tofacitinib 5 mg BID	vs tofacitinib 10 mg BID
Abatacept 125 mg	1.0 (0.4, 2.4)	0.7 (0.3, 1.6)	NA	NA
Adalimumab 40 mg Q2W	1.4 (0.8, 2.2)	0.9 (0.5, 1.5)	-0.1 (-0.2, 0.1)	0.0 (-0.1, 0.1)
Apremilast 30 mg BID	0.9 (0.5, 1.6)	0.6 (0.3, 1.0)	0.04 (-0.1, 0.2)	0.1 (-0.1, 0.3)
Apremilast 20 mg BID	0.7 (0.4, 1.3)	0.5 (0.3, 0.8)	NA	NA
Certolizumab 400 mg Q4W + 200 mg Q2W	1.6 (0.8, 3.2)	1.1 (0.5, 2.1)	NA	NA
Etanercept 25 mg BW	3.7 (1.7, 8.1)	2.4 (1.1, 5.3)	-0.9 (-1.3, -0.6)	-0.9 (-1.2, -0.5)
Golimumab 50 mg Q4W	4.9 (1.7, 19.4)	2.7 (1.1, 6.9)	-0.1 (-0.2, 0.1)	-0.03 (-0.2, 0.1)
Golimumab 100 mg Q4W	3.2 (1.4, 8.4)	2.1 (0.9, 5.5)	-0.2 (-0.3, 0.02)	-0.1 (-0.3, 0.1)
Infliximab 5 mg/kg	3.6 (1.7, 7.9)	2.4 (1.1, 5.0)	NA	NA
Ixekizumab 80 mg Q4W	1.4 (0.7, 2.7)	0.9 (0.5, 1.8)	-0.1 (-0.2, 0.1)	-0.01 (-0.2, 0.2)
Ixekizumab 80 mg Q2W	1.6 (0.8, 3.1)	1.0 (0.5, 2.1)	-0.2 (-0.3, 0.01)	-0.1 (-0.3, 0.1)
Secukinumab 150 mg QW three Q4W	2.5 (1.2, 4.9)	1.6 (0.8, 3.3)	-0.01 (-0.2, 0.2)	0.04 (-0.2, 0.3)
Secukinumab 300 mg QW then Q4W	2.2 (1.0, 5.3)	1.5 (0.6, 3.5)	-0.1 (-0.3, 0.2)	0.0 (-0.2, 0.2)
Ustekinumab 45 mg Q12W	1.0 (0.5, 1.8)	0.6 (0.3, 1.2)	-0.03 (-0.2, 0.1)	0.02 (-0.1, 0.2)
Ustekinumab 90 mg Q12W	1.2 (0.6, 2.3)	0.8 (0.4, 1.5)	-0.1 (-0.2, 0.1)	-0.02 (-0.2, 0.1)

^aResults which do not include the null value are bold and italicized

^bSLR-identified clinical manuscripts published between earliest available record from each database and 9 Oct 2017

^cA binary outcome, where an OR of 1 indicates that there was no difference in the odds of an ACR20 response between tofacitinib and comparator, an OR <1 favours tofacitinib and an OR >1 favours comparator

^dA continuous outcome (higher scores indicates worse disability), where a value of 0 indicates that there was no difference in the mean change in HAQ-DI from baseline between tofacitinib and comparator, a difference <0 favours comparator and a difference >0 favours tofacitinib

^eTo ensure robustness, each outcome was 50 000 burn-in and 150 000 samples (from three chains), and it was confirmed that all models converged

^fSLR-identified study population arms (including placebo arms) ranged from n=30 to n=219 for ACR20

^gSLR-identified study population arms (including placebo arms) ranged from n=30 to n=206 for Δ HAQ-DI

ACR20, American College of Rheumatology 20 response; bDMARD, biologic disease-modifying antirheumatic drug; BID, twice daily; BW, bi-weekly; CrI, credible interval; HAQ-DI, Health Assessment Questionnaire-Disability Index; NA, not applicable; NMA, network meta-analysis; OR, odds ratio; PsA, psoriatic arthritis; Q2W, every 2 weeks; Q4W, every 4 weeks; SLR, systematic literature review; TNFi-N, tumour necrosis factor inhibitor-naïve

Conclusions: Based on the NMA of published RCTs in TNFi-N patients with PsA, tofacitinib 5 and 10 mg BID had similar efficacy vs many, but not all, bDMARDs and APR in improving ACR20 and Δ HAQ-DI.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by P Scutt of CMC and funded by Pfizer Inc.

Disclosure of Interest: D. Gladman Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, A.-M. Orbai Grant/research support from: Celgene, Eli Lilly, Horizon, Janssen, Novartis, Pfizer Inc, UCB, Consultant for: Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, J. Gomez-Reino Grant/research support from: AbbVie, MSD, Pfizer Inc, Roche, Consultant for: Pfizer Inc, Speakers bureau: AbbVie, Biogen, Bristol-Myers Squibb, Janssen, MSD, Pfizer Inc and Roche, S. Chang-Douglass Employee of: Decision Resources Group, E. Leoncini Employee of: Decision Resources Group, H. Burton Employee of: Decision Resources Group, K. Kanik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Hendrikx Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Cappelleri Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, M.-A. Hsu Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2018-eular.4823

THU0301 A NOVEL ROLE FOR THE PSORIATIC ARTHRITIS IMPACT OF DISEASE QUESTIONNAIRE (PSAID)

K. Johnson, J. Ye, V. Chandran, D. Gladman. *Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, Canada*

Background: Psoriatic arthritis (PsA) is an inflammatory arthritis that occurs in about 30% of patients with Psoriasis (Ps). Recently, a new Patient Reported Outcome Measure (PROM), Psoriatic Arthritis Impact of Disease (PsAID) was specifically developed for PsA Patients. The two versions of the PsAID, PsAID-9 and PsAID-12, are scored on a Numeric Rating Scale (NRS) of 0–10. The Minimal Disease Activity (MDA) is a composite outcome measure for PsA patients, which uses the Health Assessment Questionnaire (HAQ) as one criterion. However, the HAQ does not correlate well with measures of disease activity as PsA disease duration increases, and its use in the assessment of disease activity has been questioned.

Objectives: Our objectives were to 1) validate the PsAID within our patient cohort, 2) determine if the PsAID can replace any of the other PROMs administered in the clinic, and 3) determine if the PsAID can replace the HAQ in the MDA.

Methods: Patients were recruited from a large psoriatic arthritis clinic. All patients completed the PsAID and 10 other PROMs. Various measures of disease activity were recorded by a physician at each visit. Descriptive statistics (mean, median, SD, min, max) were calculated for all PROMs. PsAID cut-offs for use in the MDA were generated based on Remission (REM) and Low Disease Activity (LDA) disease states in the Clinical Disease Activity for Psoriatic Arthritis Index (cDAPSA).

Results: 115 patients completed the PsAID. There were 70 males, 45 females, with a mean PsA duration of 18.7 (± 11.6) years. Mean scores of PsAID-9 and PsAID-12 were 3.4 (± 2.4) and 3.2 (± 2.3) respectively. The PsAID correlated moderately well with 9 of the PROMs administered in the clinic ($R^2=0.51-0.78$). Four

PsAID cutoffs were generated for use in the MDA: REM PsAID-9, REM PsAID-12, LDA PsAID-9, and LDA PsAID-12. All four versions of the PsAID MDAs had a sensitivity greater than 85% with the HAQ MDA, and three versions of the PsAID MDA had a specificity greater than 85% with the HAQ MDA.

Conclusions: Our cohort had lower mean PsAID scores than previously reported series suggesting that our patients are monitored carefully. The only moderate correlations with other PROMs suggest that the PsAID cannot replace any of these PROMs. The high sensitivity and specificity of the PsAID MDA with the HAQ MDA suggest that the PsAID is an effective replacement for the HAQ in the MDA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6751

THU0302 SURVIVAL OF DISEASE-MODIFYING DRUGS (DMARD) IN PATIENTS WITH RECENT DIAGNOSIS OF PSORIATIC ARTHRITIS IN DAILY CLINICAL PRACTICE

^{1,2,3}D. Freitas Nuñez, L. León², Z. Rosales^{1,2}, J. Font¹, C. Lajas¹, E. Pato¹, L. Rodríguez^{1,2}, B. Fernández¹, J.-A. Jover¹, L. Abasolo^{1,2}. ¹Rheumatology, Hospital Clínico San Carlos; ²Fundación para la Investigación Biomedica; ³Complutense University, Madrid, Spain

Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease that benefits from DMARDs, in this regard knowing more about these therapies is a great step forward in the management of these patients in daily clinical practice.

Objectives: To evaluate the survival of DMARDs used in recent diagnosis PsA patients as well as the causes of discontinuation and to analyse the possible associated factors.

Methods: Retrospective longitudinal observational study. **Subjects:** Inception cohort of patients from January 2010 to , December 2014 and followed up to December 2016, diagnosed with PsA according to ICD-10 code. **Main outcome:** discontinuation of conventional synthetic DMARDs (csDMARDs) and biological originator DMARDs (boDMARDs) due to: Adverse drug reactions (ADRs); Improvement or remission; Inefficacy; Patient's decision and Physician's decision. **Covariables:** sociodemographic and clinical. **Statistical analysis:** To estimate DMARDs discontinuation rates, survival techniques were used, expressing the incidence rate (IR) per 100 patients*year with their respective CI at 95%. Multivariate Cox regression models were performed to analyse the factors associated with DMARDs discontinuation and the results were expressed in Hazard ratio (HR) and 95% CI.

Results: 191 patients with recent diagnosis of PsA were included, with a 379.70 Patients*year follow-up. 50.3% were male, the mean age at diagnosis was 50 ± 14.6 years old. 46.6% of the patients had a history of cutaneous psoriasis. The HLA-B27 was positive in 20% of patients. 50% of the patients started a DMARDs at the first visit. Throughout the follow-up, all patients received csDMARDs and 23 used boDMARDs. The median DMARD per patient was 2¹⁻³. Methotrexate (MTX) was the most used drug 69.7%. According to the treatment regimen, 30% were on combination therapy, the most frequent was antiTNF + MTX (33%). 103 discontinuations were recorded with a IR 27.13 [22.36–32.90] within these, 44 were related with ADRs (IR 11.59 [8.62–15.57]), 24 (IR 6.32 [3.58–11.13]) were due to inefficiency, 9 (IR 2.37 [1.23–4.55]) were registered after remission, 12 (IR 3.16 [1.79–5.56]) by decision of the patient and 12 (IR 3.16 [1.79–5.56]) by doctor's decision. The DMARDs median survival was 1.8 years [1.4–2.7]. Table 1 shows the discontinuation rates for each type of DMARDs and the multivariate analysis for the factors associated with DMARDs discontinuation is in table 2.

Table 1:

Table 1	Patients*year	Events(n)	IR	95%CI
MTX orally	243.46	53	21.77	16.63–28.49
Sc MTX	49.90	18	36.07	22.73–57.25
Salazopyrine	84.80	30	35.37	24.73–50.59
Leflunomide	21.83	10	45.80	24.64–85.13
Antimalarials	25.34	8	31.56	15.78–63.12
boDMARDs	57.56	25	43.43	29.35–64.28

Table 2

	HR	95% CI	P
Women	1.51	0.61–3.09	0.436
Age at diagnosis	0.97	0.97–1.01	0.267
Distress level	1.87	1.00–3.48	0.049
C Reactive protein ≥ 1.05 gr/dL	1.85	0.99–3.48	0.055
Combination therapy	2.36	1.46–3.80	0.000
boDMARDs	1.05	0.52–2.11	0.886
MTX vs rest DMARDs	0.53	0.31–0.91	0.021

Conclusions: In our study, the DMARD discontinuation rate was 27.13, mainly related with ADRs. We have also found some psychological, clinical and therapy regimen factors that can modify the DMARDs survival on PsA. We observed that MTX, presented the longest survival independent of the rest of the factors.

Disclosure of Interest: None declared