score ranged from 6.2–6.5. Tofacitinib 5 and 10 mg BID achieved higher ACR responses and greater changes from baseline in DAS28-4(ESR) and HAQ-DI scores vs PBO at Month 3 in both populations (Table). Numerically higher proportions of non-MTX csDMARD-IR pts achieved efficacy outcomes vs 2nd-line population. CIRs for SAEs, DCs due to AEs and AEs of special interest were similar across groups; CIRs for TEAEs were higher with PBO vs tofacitinib. AE frequency was generally lower in the non-MTX csDMARD-IR population vs 2nd-line population.

Table. Efficacy outcomes at Month 3 and safety outcomes to Month 24

	Tofacitinib 5 mg BID		Tofacitinib 10 mg BID		PBO	
	Non-MTX csDMARD-IR	Second-line	Non-MTX csDMARD-IR	Second-line	Non-MTX csDMARD-IR	Second-line
% pts (95% CI) achieving efficacy outcome, FAS, NRI						
ACR20 response	69.3 (62.5–75.6)[a]	59.4 (56.1–62.5)[a]	74.0 (67.6–79.7)[a]	65.4 (62.3–68.4)[a]	25.0 (14.0–39.0)	27.1 (23.2–31.3)
ACR50 response	35.6 (29.1–42.7)[a]	30.7 (27.8–33.8)[a]	44.8 (38.1–51.6)[a]	35.0 (32.0–38.2)[a]	11.5 (4.4–23.4)	8.8 (6.5–11.7)
ACR70 response	16.3 (11.5–22.2)[b]	12.1 (10.1–14.4)[a]	23.3 (17.9–29.5)[a]	17.2 (14.8–19.8)[a]	5.8 (1.2–16.0)	2.7 (1.4–4.5)
DAS28-4(ESR)<2.6	9.2 (5.5–14.4)	6.5 (4.9–8.4)	16.9 (12.1–22.7)[a]	10.2 (8.2–12.5)	4.0 (0.5–13.7)	1.6 (0.7–3.3)
LSM (SE) change in score from baseline in efficacy outcome, FAS						
DAS28-4(ESR)	-2.1 (0.1)[a]	-1.9 (0.1)[a]	-2.5 (0.1)[a]	-2.1 (0.1)[a]	-1.0 (0.2)	-0.9 (0.1)
HAQ-DI	-0.5 (0.0)[a]	-0.5 (0.0)[a]	-0.6 (0)[a]	-0.5 (0.0)[a]	-0.2 (0.1)	-0.2 (0.0)
Safety outcomes, CIR (95% CI)						
TEAE	118.4 (99.9–139.2)	192.4 (179.8–205.8)	136.3 (116.8–158.1)	193.7 (181.3–206.9)	264.1 (183.9–367.3)	292.2 (265.8–320.5)
SAE	8.5 (5.2–12.9)	12.4 (10.3–14.8)	7.4 (4.6–11.3)	9.7 (7.9–11.8)	10.8 (1.3–39.1)	11.5 (7.6–16.8)
DC due to AE	7.1 (4.2–11.2)	9.7 (7.8–11.8)	7.2 (4.5–11.0)	10.4 (8.6–12.6)	10.8 (1.3–39.1)	11.9 (7.9–17.2)
SIE	2.8 (1.1–5.7)	3.4 (2.4–4.7)	1.4 (0.4–3.5)	3.4 (2.4–4.7)	5.4 (0.1–30.1)	1.7 (0.5–4.3)
OI, excluding TB	0.4 (0.0–2.2)	0.2 (0.0–0.7)	0.0 (0.0–1.3)	0.5 (0.2–1.1)	0.0 (0.0–19.9)	0.0 (0.0–1.6)
TB	0.0 (0.0–1.4)	0.0 (0.0–0.4)	0.3 (0.0–1.9)	0.7 (0.3–1.3)	0.0 (0.0–19.9)	0.0 (0.0–1.6)
Herpes zoster	1.2 (0.2–3.5)	3.9 (2.8–5.3)	3.5 (1.7–6.4)	4.8 (3.5–6.3)	0.0 (0.0–19.9)	2.6 (0.9–5.5)
MACE	0.8 (0.1–2.9)	0.4 (0.1–1.1)	0.7 (0.1–2.6)	0.6 (0.2–1.3)	0.0 (0.0–41.1)	0.6 (0.0–3.5)
Malignancies[#]	0.4 (0.0–2.2)	0.7 (0.3–1.4)	0.3 (0.0–1.9)	0.7 (0.3–1.5)	0.0 (0.0–19.9)	0.0 (0.0–1.6)

[a]p<0.001; [b]p<0.05 vs PBO; [#]excluding non-melanoma skin cancer; AE, adverse event; CI, confidence interval; CIR, crude incidence rate; csDMARD, conventional synthetic disease modifying antirheumatic drug; DAS28-4(ESR), disease activity score 28-4(ESR); DC, discontinuation; FAS, full analysis set; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, inadequate response; LSM, least squares mean; MACE, major adverse cardiovascular events; MTX, methotrexate; NRI, non-responder imputation; OI, opportunistic infection; PBO, placebo; SAE, serious AE; SE, standard error; SIE, serious infection event; TB, tuberculosis; TEAE, treatment emergent adverse event

Conclusions: This analysis indicates that tofacitinib is associated with similar efficacy and safety outcomes between csDMARD-IR (including MTX-IR) pts and those who are csDMARD-IR but not MTX-IR. This suggests a favourable tofacitinib benefit/risk profile for RA pts who have a contraindication to or refuse treatment with MTX and failed other csDMARDs.

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THU0196 SYSTEMATIC REVIEW AND META-ANALYSIS OF MALIGNANCIES, EXCLUDING NON-MELANOMA SKIN CANCER, IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB OR BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

J.J. Gomez-Reino[1], T. Checchio[2], J. Geier[3], M. Boy[2], S. Ahadieh[2], S. Menon[2], S. Krishnaswami[2]. *[1]Fundacion Ramon Dominguez, Hospital Clinico Universitario, Santiago de Compostela, Spain; [2]Pfizer Inc, Groton, CT; [3]Pfizer Inc, New York, NY, United States*

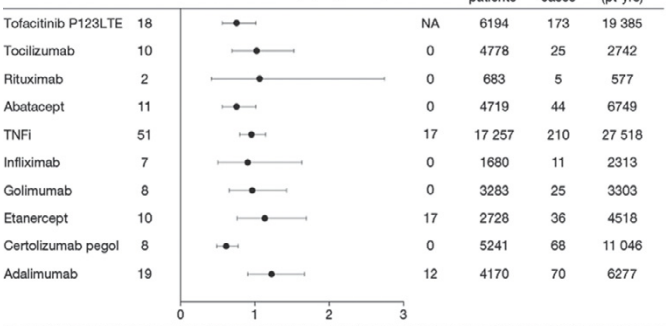
Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). The limited size of the control groups (placebo and active comparator) and limited duration of treatment within the tofacitinib RA clinical trial programme do not permit precise direct comparative assessments for adverse events of long latency, including malignancies, therefore a meta-analytic approach was taken.

Objectives: To compare the rate of malignancies in patients (pts) with moderately to severely active RA within the tofacitinib RA clinical trial programme with estimates from published trial data of approved biologic (b)DMARDS using meta-analytic methods.

Methods: Incidence rates (IR; pts with events per 100 pt-years [yrs] exposure) for tofacitinib were calculated using pooled data from randomised controlled trials (RCT) and long-term extension (LTE) studies. Two Phase (P) 1 studies, 9 P2 studies, 6 P3 studies and 2 LTE studies (one study ongoing; database unlocked at March 2015 data cut off) constituted the P123LTE dataset; pts received 1, 3, 5, 10, 15, 30 mg BID or 20 mg QD of tofacitinib. A systematic literature review of published RCT and LTE studies (through August 2014) of approved bDMARDs (abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab) was conducted. IRs for the endpoint of interest (all malignancies [excluding non-melanoma skin cancers (NMSC)]) were calculated for each bDMARD utilising a random-effects meta-analytic model with a restricted Maximum Likelihood Estimator for between-study variances. Estimates of Q statistic and I^2 were generated to determine the existence and degree of heterogeneity related to the study pool.

Results: The tofacitinib P123LTE dataset included 6194 pts with a total exposure of 19 385 pt-yrs. A total of 64 bDMARD articles were extracted for analysis, representing 58 unique studies and approximately 27 000 pts. Study populations were generally consistent across studies and treatments: mean pt age ranged from 51–54 yrs; mean percentage of pts who were female was 74–84%; and mean baseline C-reactive protein level was 20–31 mg/L. The IR (95% confidence interval [CI]) of malignancy for tofacitinib in the P123LTE dataset was 0.89 (0.76, 1.04) (Figure). Estimated IRs (95% CI) of malignancy were 0.75 (0.56, 1.01) for abatacept, 1.06 (0.41, 2.74) for rituximab, 1.02 (0.69, 1.52) for tocilizumab and 0.95 (0.79, 1.14) for tumour necrosis factor inhibitors (adalimumab, certolizumab, etanercept, golimumab and infliximab) (Figure).

Figure. Incidence rates for all malignancies (excluding NMSC) with biologic DMARDs and tofacitinib across RCTs and LTE studies



The results displayed include a continuity factor (r=0.05) to account for zero incidence rates. Tofacitinib data included through March 2015. Clinical trials for non-tofacitinib studies were conducted between 1997 and 2014.
CI, confidence interval; DMARD, disease-modifying antirheumatic drug; I^2, percent of total variability due to heterogeneity; LTE, long-term extension; NA, not applicable; NMSC, non-melanoma skin cancer; pt-yr, patient-year; RCT, randomised controlled trial; TNFi, tumour necrosis factor inhibitor

Conclusions: The results of this meta-analysis indicate that the tofacitinib IR for all malignancies (excluding NMSC) in pts with moderately to severely active RA is within a similar range to those reported in published interventional studies of similar RA populations treated with approved bDMARDs.

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THU0197 TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF RHEUMATOID ARTHRITIS: SAFETY AND EFFICACY IN OPEN-LABEL, LONG-TERM EXTENSION STUDIES OVER 8 YEARS

J. Wollenhaupt[1], J. Silverfield[2], E.B. Lee[3], K. Terry[4], K. Kwok[5], S. Abramsky[5], M. Wang[5], C. Nduaka[6], R. DeMasi[6], L. Wang[4]. *[1]Schön-Klinik Hamburg-Eilbek Teaching Hospital of the University of Hamburg, Hamburg, Germany; [2]Healthpoint Medical Group, Tampa, FL, United States; [3]Seoul National University, Seoul, Korea, Republic Of; [4]Pfizer Inc, Groton, CT; [5]Pfizer Inc, New York, NY; [6]Pfizer Inc, Collegeville, PA, United States*

Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).

Objectives: The objective of this analysis was to report tofacitinib safety, tolerability and clinical efficacy in long-term extension (LTE) studies with up to 105 months of observation.

Methods: Data were pooled from two open-label studies (NCT00413699 [ongoing; database not locked at January 2016 data-cut] and NCT00661661) of patients with RA who had participated in Phase 1/2/3 tofacitinib studies. Patients received tofacitinib 5 or 10 mg twice daily (BID) as monotherapy or with background disease-