long-term safety. To our knowledge, this is the first long-term comparative RWD analysis of tofacitinib.

Objectives: To compare 5-year adverse event (AE) incidence rates (IRs) in patients (pts) starting tofacitinib vs biological (b)DMARDs using cohorts from the US Corrona RA registry.

Methods: This prospective, observational 5-year study embedded in the ongoing US Corrona RA registry routinely collected 9 categories of predefined AEs from participating physicians. Real-world safety event rates of major adverse cardiovascular events (MACE), serious infectious events (SIEs) and herpes zoster (HZ; serious and non-serious) were compared in pts with RA who started tofacitinib or a bDMARD regardless of dose/schedule between 6 Nov 2012 (US FDA approval) and 30 Jun 2017 (follow-up through 31 Dec 2017). Endpoints were selected *a priori* as having sufficient power to detect a 2-fold difference between cohorts at this datacut; there was insufficient power to assess malignancy. Baseline variables with a standardised difference >|0.10| between tofacitinib and bDMARD initiators, and *a priori* selected covariates (gender, age, line of therapy, history of AE of interest) were used to construct propensity scores (PS) to derive a PS-trimmed (primary) population and a PS-matched population for sensitivity analysis (ratio: max. 4 bDMARD:1 tofacitinib; caliper=0.05). Pts were followed from initiation until an AE of interest, discontinuation and/or start of a new therapy +90 days, death or end of follow-up, whichever came first. Crude IRs (events/100 pt-years [PY]) were estimated; multivariable-adjusted Cox regression was used to estimate hazard ratios (HRs) comparing rates of first events between cohorts.

Results: In total, 1544 tofacitinib (2138.2 PY) and 7083 bDMARD (9904.9 PY) initiators were included. PS-trimming resulted in 1117 tofacitinib and 5542 bDMARD initiators. Rates of MACE and SIEs were similar in both cohorts (Fig 1A); adjusted HRs (95% confidence intervals [CIs]) were: MACE 0.60 (0.30, 1.18); SIEs 0.99 (0.72, 1.36; Fig 1B). HZ IR was higher for tofacitinib vs bDMARDs (Fig 1A); HRs for HZ were significantly increased with tofacitinib vs bDMARDs (adjusted HR 2.12 [1.22, 3.66]; Fig 1B); all HZ events were non-serious with tofacitinib. Similar results were observed in PS-matched populations.

FIG 1: A. Crude incidence rates* for MACE, SIEs and HZ; and B. Hazard ratios for MACE, SIEs and HZ

*Incidence rates are events per 100 PY. *MACE is defined as any myocardial infarction, stroke/transient ischaemic attack or cardiovascular death.

*bDMARD initiators were the reference population for calculation of HRs.

bDMARD, biological disease-modifying antirheumatic drug; CI, confidence interval; HR, hazard ratio; HZ, herpes zoster; MACE, major adverse cardiovascular event; PS, propensity score; PY, patient-years; SIEs, serious infectious events.

Conclusion: This is the first comparative analysis of RWD for tofacitinib and bDMARDs to use PS-trimmed and PS-matched analyses to adjust for channeling/prescribing patterns for newly approved therapies. Pts starting tofacitinib or bDMARDs for RA had similar rates of MACE and SIEs. Tofacitinib initiators had

higher HZ IRs vs bDMARD initiators. These results are consistent with long-term clinical trial findings.

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OP0029 SWITCHING BETWEEN THE JAK1-SELECTIVE INHIBITOR-UPADACITINIB AND ADALIMUMAB FOLLOWING INITIAL NON-RESPONSE: CLINICAL AND FUNCTIONAL OUTCOMES AMONG RHEUMATOID ARTHRITIS PATIENTS

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Background: Initiating advanced therapy for rheumatoid arthritis (RA) patients (pts) with a bDMARD or a Janus kinase (JAK) inhibitor is recommended if remission or low disease activity (LDA) is not achieved with csDMARDs.^{1,2} While data show that pts are switched alternately between bDMARD and JAK treatments, there is lack of evidence for pts with inadequate response (IR) to a JAK inhibitor switching to a bDMARD. Recently, the JAK1-selective inhibitor-upadacitinib (UPA) demonstrated superior clinical and functional outcomes through 26 wks to the standard of care-adalimumab (ADA) with continued background methotrexate (MTX).³

Objectives: To describe outcomes associated with treatment switch from UPA to ADA and vice-versa among RA pts who do not achieve initial response.

Methods: This phase 3, double-blind, placebo (PBO)-controlled, head-to-head study of UPA 15 mg q.d. vs PBO or ADA 40 mg injection every other wk included MTX-IR patients; all pts continued stable background MTX through 26 wks. Pts without ≥20% improvements from bl in tender (68) and swollen (66) joint counts by wks 14, 18, or 22 were considered non-responders (NR) and switched without washout to either ADA (UPA group) or UPA (ADA group) in a bl fashion. Post-hoc analysis assessed clinical outcomes - DAS28 (CRP), CDAI, SDAI, and ACR responses (from baseline), and HAQ-DI at 3 and 6 mos (±2 wks) post-switch. Adverse events (infections) were summarized as n% (95% CI) through 6 mos post-switch (ps). Data were as observed.

n/N (%)	UPA 15 mg QD Non-responders Switched to ADA 40 mg eow (N=126)		ADA 40 mg eow Non-responders Switched to UPA 15 mg QD (N=77)	
	3 months post-switch	6 months post-switch	3 months post-switch	6 months post-switch
ACR20*	68/118 (58)	67/113 (59)	49/75 (65)	53/71 (75)
ACR50*	33/120 (28)	29/112 (26)	26/73 (36)	34/69 (49)
ACR70*	20/120 (17)	14/114 (12)	13/74 (18)	17/72 (24)
DAS28(CRP) <2.6	30/119 (25)	38/109 (35)	31/74 (42)	38/70 (54)
DAS28(CRP) <2.6	15/119 (13)	21/109 (19)	19/74 (26)	22/70 (31)
CDAI <10	33/120 (28)	42/114 (36)	24/73 (33)	39/70 (57)
SDAI <2.8	5/120 (4)	6/114 (5)	6/72 (8)	10/70 (14)
SDAI <11	32/119 (27)	41/109 (38)	26/71 (37)	33/69 (48)
SDAI <3.3	5/119 (4)	4/109 (4)	5/71 (7)	13/69 (17)
Mean change from baseline (95% CI)				
HAQ-DI	-0.49 (-0.60, -0.38)	-0.52 (-0.64, -0.41)	-0.63 (-0.76, -0.50)	-0.67 (-0.81, -0.53)
DAS28(CRP)	-1.79 (-2.03, -1.55)	-2.10 (-2.36, -1.84)	-2.36 (-2.66, -2.06)	-2.56 (-2.90, -2.22)
CDAI	-20.87 (-23.62, -18.11)	-23.61 (-26.48, -20.73)	-22.45 (-25.78, -19.12)	-24.59 (-28.35, -20.83)
SDAI	-18.11 (-21.70, -14.46)	-24.52 (-27.47, -21.56)	-19.12 (-22.69, -15.55)	-23.59 (-27.55, -19.63)

*Responses are based on percent improvement in American College of Rheumatology criteria from baseline at randomization.

UPA: upadacitinib; QD: once daily; ADA: adalimumab; eow: every other week; ACR: American College of Rheumatology.

DAS28(CRP): 28-joint disease activity score based on C-reactive protein; CDAI: clinical disease activity index; SDAI: simplified disease activity index; CI: confidence interval; TJC68: tender joint count based on 68 joints; SJC66: swollen joint count based on 66 joints; HAQ-DI: health assessment questionnaire disability index.

Results: Of the 651 and 327 pts randomized to receive UPA and ADA, 126 (19%) and 77 (24%), were considered NR and switched to ADA and UPA respectively. NR demographics were consistent with the overall randomized population. Of the switched pts, ~90% remained in the study through 6 mo ps. Patients switched to ADA (UPA-NR) achieved 59%/26%/12% improvements in ACR20/50/70 responses, and 35% achieved DAS28(CRP) ≤ 3.2 at 6 mos ps (**Table**). Patients switched to UPA (ADA-NR) achieved 75%/49%/24% improvements in ACR20/50/70, and 54% achieved DAS28(CRP) ≤ 3.2 at 6 mo- consistent with data observed in a phase 3 study of UPA in bDMARD-IR RA pts.⁴ The proportion (95% CI) of pts with infection and serious infection through 6 mos ps appeared consistent with those observed for ADA and UPA during comparable periods (ADA, switched from UPA: infection: 34.1 [26.43, 42.77], serious infection: 1.6 [0.44, 5.60]; UPA, switched from ADA: infection: 40.3 [30.02, 51.42], serious infection: 3.9 [1.33, 10.84]

Conclusion: Data from this blinded, controlled study indicate that pts with initial non-response to either UPA or ADA can benefit from switching to the other therapy. No additional safety concerns were observed. These are the first data to demonstrate effectiveness of a TNF inhibitor following failure of a JAK inhibitor.

REFERENCES:

- [1] Smolen, et al. *Ann Rheum Dis*, 2017;76:1113-36.
- [2] Singh, et al. *Arthritis Rheumatol*, 2016;68:1-26.
- [3] Fleischmann, et al. *Arthritis Rheumatol*, 2018;70(Suppl 10).
- [4] Genovese, et al. *Lancet*, 2018;391:2513-24.

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OP0030

RANDOMIZED CONTROLLED 24-WEEK TRIAL EVALUATING THE SAFETY AND EFFICACY OF BLINDED TAPERING VERSUS CONTINUATION OF LONG-TERM PREDNISONE (5 MG/D) IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ACHIEVED LOW DISEASE ACTIVITY OR REMISSION ON TOCILIZUMAB

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Background: Guidelines recommend low-dose, short-term glucocorticoid (GC) treatment for rheumatoid arthritis (RA).^{1,2} Long-term use, especially at prednisone-equivalent doses >5 mg/d, should be avoided,² but many patients (pts) with early established RA receive long-term GCs, often ≥ 5 mg/d.³

Objectives: Compare GC tapering vs continuation to maintain disease control in RA pts with chronic GC exposure receiving tocilizumab (TCZ) in a randomized controlled trial.

Methods: Before randomization pts had to receive TCZ $\pm$ conventional synthetic (cs)DMARDs and GC (prednisone-equivalent dose 5-15 mg/d) for ≥ 24 wks. At randomization pts had to be in at least low disease activity (LDA: DAS28-ESR ≤ 3.2) and receiving stable concomitant therapy (prednisone 5 mg/d [GC5mg]) and TCZ $\pm$ csDMARDs for ≥ 4 wks. Pts were randomized to continue blinded GC5mg for 24 wks or undergo blinded taper (GCTaper, from 4 mg/d with 1-mg reduction every 4 wks to 0 mg/d at wks 16-24) while receiving stable TCZ and csDMARD doses. Pts with RA flare (DAS28-ESR >3.2 and increase >0.6 vs baseline) received open-label rescue GC5mg for 2 wks and continued blinded treatment. Primary outcome was mean change in DAS28-ESR at wk 24. Key secondary outcome was treatment success—DAS28-ESR ≤ 3.2 at wk 24 and no RA flare during 24 wks and no adrenal insufficiency necessitating replacement therapy.

Results: 259 pts were randomized to GCTaper (n=131) or GC5mg (n=128); 114 and 112, respectively, completed 24 wks. Mean baseline DAS28-ESR was 1.9. Mean RA duration was 9.2 y. For the primary endpoint, the between-arm difference was 0.6 DAS28-ESR units (95% CI, 0.3, 0.9; $p<0.001$, ANCOVA) favoring GC5mg (Figure). Results were consistent for key subgroups (DAS28-ESR between-arm difference 0.5 [95% CI -0.1, 1.0] for TCZ monotherapy, 0.7 [0.4-1.0] for TCZ + csDMARDs, 0.6 [0.2-1.0] for baseline DAS28 <2 , and 0.6 [0.2-1.0] for baseline DAS28 ≥ 2). Most pts in both arms achieved treatment success (65% GCTaper vs 77% GC5mg; relative risk, 0.83 [0.71-0.97]; $p=0.021$, Cochran-Mantel-Haenszel test); 11% of GC5mg pts and 26% of GCTaper pts experienced RA flare. One GC5mg pt and no GCTaper pts discontinued blinded treatment due to insufficient flare control. Serious adverse events (no deaths) were reported for 5% of GC5mg vs 3% of GCTaper pts. No pts had symptomatic adrenal insufficiency.

Conclusion: Continued GC5mg provided better DAS28-ESR control than GC taper in RA pts in LDA or remission. The 0.6 DAS28-ESR unit between-arm difference should be interpreted in the context of approximately two-thirds of tapered pts experiencing treatment success and no tapered pts discontinuing due to lack of flare control. The taper schedule was safe regarding adrenal insufficiency. The results suggest that all pts achieving LDA or remission with TCZ and receiving long-term low-dose GC should be considered for GC tapering, ideally targeting discontinuation.

Figure. Primary Efficacy End Point: Change From Randomization to Week 24 in DAS28 ESR

REFERENCES:

- [1] Singh JA et al. *Arthritis Rheum*. 2016;68:1.
- [2] Smolen JS et al. *Ann Rheum Dis*. 2017;76:960.
- [3] Buttgerit F, Bijlsma JW. *Ann Rheum Dis*. 2017;76:1785.

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