Objectives: To compare tofacitinib safety and efficacy in RA pts who have previously failed tx (lack of efficacy and/or safety reasons) with csDMARDs, with pts who failed tx with either 1 or ≥2 prior bDMARDs.
Methods: Data from pts who received ≥1 dose of tofacitinib in 19 RA studies up to 96 months (2 Phase [P] 1; 9 P2; 6 P3; 2 LTE studies [1 LTE ongoing; data as of March 2015]) were used in this analysis. Data were pooled across all 19 studies for safety assessments in the All RA population: csDMARD-IR, n=4377; bDMARD-IR, n=838 (1 bDMARD-IR, n=533; ≥2 bDMARD-IR n=305). Safety was also assessed up to 24 months in pts randomised to tofacitinib 5 or 10 mg BID or placebo (PBO) in a pooled P2/P3 randomised controlled trial (RCT) population (8 P2, 6 P3 studies; csDMARD-IR, n=3328; bDMARD-IR, n=782). Incidence rates (pts with events/100 pt-years) were calculated for serious AEs (SAEs), serious infections (SIs) and herpes zoster (HZ). Efficacy was assessed by pts achieving ACR20 response and DAS28-4(ESR) ≤3.2 at Month 3 in a pooled P3 RCT population (csDMARD-IR, n=2375; bDMARD-IR, n=664).
Results: Prior to tofacitinib tx, bDMARD-IR pts had longer RA duration, greater disease burden and more corticosteroid use vs csDMARD-IR pts. SAEs were more common among bDMARD-IR vs csDMARD-IR pts in both the P2/P3 RCT and the All RA populations; SAE rates were not higher in pts failing ≥2 bDMARDs vs 1 bDMARD (Table). Incidence rates for SIs were generally greater in pts with IR to bDMARDs vs csDMARDs in the All RA population, but generally lower in pts with IR to 1 or ≥2 bDMARDs vs csDMARDs in the P2/P3 RCT population; incidence with 5 mg BID was lower for 1 vs ≥2 bDMARDs in the P2/P3 RCT population. Incidence rates for HZ were similar between pts with IR to csDMARDs or 1 bDMARD, but appeared numerically greater in pts with IR to ≥2 bDMARDs in both the P2/P3 RCT and the All RA populations. A similar pattern was observed across tofacitinib and PBO groups. Efficacy at Month 3 in the P3 RCT population was greater with both tofacitinib doses vs PBO. Although absolute response was smaller in pts with IR to bDMARDs vs csDMARDs, generally similar efficacy was observed in pts with IR to 1 or ≥2 bDMARDs (Table).

Table. Selected safety and efficacy outcomes by prior failed treatment.

		csDMARD-IR-only	Overall bDMARD-IR	1 bDMARD-IR	≥2 bDMARD-IRs
P2/P3 RCT population (0–24 months);* incidence rate (pts with event/100 pt-years) (95% CI)					
SAEs	Tofacitinib 5 mg BID	12.4 (10.3, 14.8)	12.6 (7.8, 19.3)	12.7 (6.8, 21.7)	12.6 (5.4, 24.7)
	Tofacitinib 10 mg BID	9.7 (7.9, 11.8)	12.5 (7.6, 19.3)	12.1 (6.3, 21.1)	13.1 (5.6, 25.7)
	Placebo	11.5 (7.6, 16.8)	20.5 (9.8, 37.7)	19.8 (7.3, 43.1)	21.6 (5.9, 55.4)
SIs	Tofacitinib 5 mg BID	3.4 (2.4, 4.7)	1.7 (0.4, 5.0)	0.9 (0.0, 5.2)	2.9 (0.4, 10.6)
	Tofacitinib 10 mg BID	3.4 (2.4, 4.7)	3.0 (1.0, 7.1)	3.0 (0.6, 8.7)	3.2 (0.4, 11.4)
	Placebo	1.7 (0.5, 4.3)	4.1 (0.5, 14.7)	3.3 (0.1, 18.3)	5.4 (0.1, 30.1)
HZ	Tofacitinib 5 mg BID	3.9 (2.8, 5.3)	5.3 (2.4, 10.0)	2.8 (0.6, 8.3)	9.1 (3.4, 19.9)
	Tofacitinib 10 mg BID	4.8 (3.5, 6.3)	6.3 (3.0, 11.6)	6.2 (2.3, 13.4)	6.6 (1.8, 16.8)
	Placebo	2.6 (0.9, 5.5)	0.0 (0.0, 7.5)	0.0 (0.0, 12.1)	0.0 (0.0, 19.8)
All RA population (up to 96 months); incidence rate (pts with event/100 pt-years) (95% CI)					
SAEs	Tofacitinib 5 mg BID	9.7 (8.9, 10.6)	14.8 (11.4, 18.9)	15.9 (11.5, 21.3)	12.8 (7.7, 20.0)
	Tofacitinib 10 mg BID	9.7 (9.0, 10.4)	11.6 (10.0, 13.3)	11.8 (9.8, 14.0)	11.3 (8.8, 14.3)
	All tofacitinib doses	9.7 (9.2, 10.2)	12.2 (10.8, 13.8)	12.6 (10.8, 14.7)	11.6 (9.3, 14.3)
SIs	Tofacitinib 5 mg BID	2.9 (2.5, 3.4)	4.5 (2.8, 6.8)	4.7 (2.7, 7.8)	4.1 (1.6, 8.4)
	Tofacitinib 10 mg BID	2.7 (2.3, 3.1)	3.5 (2.7, 4.4)	4.0 (2.9, 5.3)	2.6 (1.5, 4.1)
	All tofacitinib doses	2.8 (2.5, 3.1)	3.7 (2.9, 4.5)	4.1 (3.2, 5.3)	2.9 (1.9, 4.2)
HZ	Tofacitinib 5 mg BID	3.7 (3.2, 4.3)	4.8 (3.0, 7.2)	3.6 (1.8, 6.4)	7.1 (3.5, 12.7)
	Tofacitinib 10 mg BID	4.2 (3.8, 4.7)	4.4 (3.5, 5.5)	4.1 (3.0, 5.5)	4.9 (3.3, 7.0)
	All tofacitinib doses	4.0 (3.7, 4.4)	4.5 (3.6, 5.5)	4.0 (3.0, 5.2)	5.4 (3.9, 7.2)
Efficacy endpoints in the P3 RCT population at Month 3; % of pts					
ACR20	Tofacitinib 5 mg BID	59.4***	43.5***	45.3*	40.6*
	Tofacitinib 10 mg BID	65.4***	50.6***	50.6***	50.6***
	Placebo	27.1	24.6	27.2	20.0
DAS28-4(ESR) ≤3.2	Tofacitinib 5 mg BID	15.9***	12.7*	11.9	14.0*
	Tofacitinib 10 mg BID	21.1***	15.8**	15.7*	16.5*
	Placebo	3.9	4.9	5.8	3.4

*p<0.05; **p<0.001; ***p<0.0001 vs placebo
[a]Placebo data up to 6 months only
Δ, change from baseline, BID, twice daily; bDMARD, biological disease-modifying antirheumatic drug; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28-4(ESR), Disease Activity Score in 28 joints with erythrocyte sedimentation rate, HZ, herpes zoster; IR, inadequate response, P, Phase, pts, patients, pt-years, patient-years; RA, rheumatoid arthritis; RCT, randomised controlled trial; SAE, serious adverse event; SI, serious infection

Conclusions: SAEs and SIEs were more common in tofacitinib- and PBO-treated pts with IR to bDMARDs vs csDMARDs; increased risk was generally not observed with increasing number of prior bDMARDs. HZ risk appeared greater with ≥2 bDMARDs vs 1 bDMARD. Efficacy was greater with tofacitinib vs PBO for csDMARD-IR and bDMARD-IR pts, with similar response observed in pts with IR to ≥2 or 1 bDMARD. These data support the use of tofacitinib in different lines of therapy, although the analysis is limited by smaller sample size in some groups.
Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by N Jones of CMC and was funded by Pfizer Inc.
Disclosure of Interest: C. Charles-Schoeman Grant/research support from: AbbVie, Bristol-Myers Squibb, Pfizer Inc, Consultant for: Amgen, Pfizer Inc, Regeneron-Sanofi, J. Kremer Shareholder of: Corrona, LLC, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Genentech, Eli Lilly, Pfizer Inc, Employee of: Corrona, LLC, S. Krishnaswami Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Soma Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Geier Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Zhang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Strengholt Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, G. Burmester Grant/research support from: UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Hexal, Janssen, Medimmune, MSD, Novartis, Pfizer Inc, Roche, Sanofi, Speakers bureau: AbbVie, Bristol-Myers Squibb, Hexal, MSD, Novartis, Pfizer Inc, Roche
DOI: 10.1136/annrheumdis-2017-eular.2346

THU0186 MAGNITUDE AND DURATION OF EARLY RESPONSE WITH TOFACITINIB: POST-HOC ANALYSIS OF TWO PHASE 3, PLACEBO-CONTROLLED STUDIES

D. Aletaha[1], A. Kivitz[2], G. Valenzuela[3], J. Tesser[4], S. Hays[5], H. Li[5], C.A. Connell[6], E. Bananis[5], A. Soonasra[5], J.S. Smolen[7]. *[1]Department of Internal Medicine 3, Medical University of Vienna, Vienna, Austria; [2]Altoona Center for Clinical Research, Duncansville, PA; [3]Integral Rheumatology & Immunology Specialists, Fort Lauderdale, FL; [4]Arizona Arthritis & Rheumatology Associates, Glendale, AZ; [5]Pfizer Inc, Collegeville, PA; [6]Pfizer Inc, Groton, CT, United States; [7]Division of Rheumatology, Medical University of Vienna and Hietzing Hospital, Vienna, Austria*

Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. ORAL Solo (NCT00814307) and ORAL Sync (NCT00856544) were two Phase 3 index studies that demonstrated the efficacy of tofacitinib in adult patients (pts) with RA who were DMARD inadequate responders (DMARD-IR). Early onset of effect is a clinically meaningful endpoint.
Objectives: This post hoc analysis examined the magnitude and durability of early response to tofacitinib in ORAL Solo and ORAL Sync.
Methods: ORAL Solo and ORAL Sync were double-blind, placebo (PBO)-controlled, parallel-group studies in pts with active RA and an inadequate response to ≥1 conventional synthetic (cs) or biologic (b) DMARDs. Pts were randomised to tofacitinib 5 mg BID, tofacitinib 10 mg BID, PBO advanced to tofacitinib 5 mg BID, or PBO advanced to tofacitinib 10 mg BID, either as monotherapy in ORAL Solo or with background csDMARDs in ORAL Sync. In ORAL Solo, pts randomised to PBO were advanced to tofacitinib at Month (M) 3; in ORAL Sync, pts randomised to PBO were advanced to tofacitinib at M3 (non-responders) or M6 (all other pts). In this post hoc analysis, the following clinical efficacy data for pts on tofacitinib or PBO (prior to advancement to tofacitinib) ± csDMARDs, were evaluated at Week 2, M3 and M6 (ORAL Sync only; no M6 PBO comparison in ORAL Solo): change from baseline (CFB) in Clinical Disease Activity Index (CDAI) >12,[1] HAQ-DI CFB ≥0.22, CDAI ≥50% improvement from baseline, CDAI ≥70% improvement from baseline, CDAI ≥85% improvement from baseline, Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) score improvement from baseline ≥4, Pain visual analogue scale (VAS) score CFB ≥10. This analysis was post hoc and multiplicity adjustment was done.
Results: Clinical efficacy endpoint data are summarised in the Table. At Week 2, more patients receiving tofacitinib 5 or 10 mg BID ± csDMARDs (compared with PBO ± csDMARDs) achieved a CDAI CFB >12, HAQ-DI CFB ≥0.22, CDAI ≥50% improvement from baseline and pain VAS CFB ≥10. By M3, more pts receiving tofacitinib 5 or 10 mg BID ± csDMARDs (compared with PBO ± csDMARDs) achieved the efficacy outcomes measured including improvements from baseline in FACIT-F scores ≥4, CDAI ≥50%, CDAI ≥70% and CDAI ≥85%. Responses attained at M3 were maintained or increased at M6.

Table. Clinical efficacy endpoints from Week 2 to Month 6 in ORAL Sync and ORAL Solo (FAS[a]; NRI[b])

		ORAL Solo			ORAL Sync		
Improvement from baseline, % pts (95% CI)		Tofacitinib 5 mg BID (N=241)	Tofacitinib 10 mg BID (N=243)	PBO (N=122)	Tofacitinib 5 mg BID + csDMARDs (N=312)	Tofacitinib 10 mg BID + csDMARDs (N=315)	PBO + csDMARDs (N=158)
CDAI >12	Week 2	37.1 (31.0, 43.6)*	43.9 (37.5, 50.5)*	18.5 (12.0, 26.6)	30.4 (25.3, 35.9)*	36.8 (31.3, 42.5)*	17.4 (11.8, 24.3)
	Month 3	71.6 (65.4, 77.2)*	75.5 (69.6, 80.8)*	42.5 (33.5, 51.9)	56.0 (50.3,61.6)*	64.7 (59.1, 70.1)*	32.5 (25.2, 40.4)
	Month 6	79.5 (74.4, 84.6)	78.8 (73.7, 84.0)	NA	53.7 (48.0, 59.4)*	62.1 (56.4, 67.6)*	34.4 (27.0, 42.4)
HAQ-DI ≥0.22	Week 2	49.0 (42.5, 55.5)*	50.6 (44.1, 57.2)*	37.8 (29.1, 47.2)	45.6 (40.0, 51.4)*	53.1 (47.3, 58.8)*	34.2 (26.8, 42.2)
	Month 3	59.6 (53.1, 65.9)*	65.3 (58.9, 71.3)*	39.2 (30.4, 48.5)	49.0 (43.3, 54.7)*	57.1 (51.4, 62.7)*	23.7 (17.3, 31.2)
	Month 6	67.5 (61.6, 73.4)	66.1 (60.1, 72.1)	NA	49.7 (44.0, 55.4)*	55.5 (49.8, 61.2)*	23.7 (17.3, 31.2)
CDAI ≥ 50%	Week 2	19.8 (15.0, 25.5)*	25.1 (19.7, 31.1)*	8.4 (4.1, 14.9)	18.0 (13.8, 22.7)*	20.5 (16.1, 25.5)*	9.0 (5.0, 14.7)
	Month 3	57.3 (50.8, 63.7)*	58.1 (51.6, 64.4)*	25.8 (18.3, 34.6)	45.3 (39.7, 51.0)*	56.5 (50.8, 62.2)*	22.3 (16.1, 29.6)
	Month 6	68.6 (62.7, 74.5)	66.4 (60.4, 72.4)	NA	48.5 (42.9, 54.3)*	58.8 (53.1, 64.4)*	29.3 (22.3, 37.1)
CDAI ≥70%	Week 2	5.1 (2.6, 8.7)	11.3 (7.6, 16.0)*	2.5 (0.5, 7.2)	4.9 (2.8, 8.0)	8.6 (5.7, 12.4)*	3.2 (1.1, 7.4)
	Month 3	33.1 (27.1, 39.4)*	40.7 (34.4, 47.2)*	14.2 (8.5, 21.7)	24.3 (19.6, 29.5)*	31.4 (26.2, 36.9)*	7.6 (4.0, 13.0)
	Month 6	41.8 (35.6, 48.1)	49.0 (42.7, 55.3)	NA	31.4 (26.3, 36.9)*	37.9 (32.5, 43.6)*	16.6 (11.1, 23.3)
CDAI ≥ 85%	Week 2	2.1 (0.7, 4.9)	5.0 (2.6, 8.6)	2.5 (0.5, 7.2)	1.0 (0.2, 2.8)	3.3 (1.6, 6.0)*	0.7 (0.0, 3.5)
	Month 3	14.6 (10.4, 19.8)*	17.8 (13.2, 23.3)*	5.8 (2.4, 11.7)	9.4 (6.4, 13.2)*	11.4 (8.1, 15.6)*	1.3 (0.2, 4.5)
	Month 6	22.2 (16.9, 27.4)	27.0 (21.4, 32.6)	NA	10.7 (7.5, 14.7)	18.3 (14.1, 23.1)*	5.7 (2.7, 10.6)
FACIT-F ≥4	Month 1	NA	NA	NA	46.2 (40.4, 52.0)	58.1 (52.3, 63.7)*	39.0 (31.2, 47.1)
	Month 3	61.2 (54.7, 67.4)*	63.4 (56.8, 69.6)*	42.2 (33.1, 51.8)	38.6 (33.1, 44.3)*	51.2 (45.4, 56.9)*	21.8 (15.6, 29.1)
	Month 6	59.2 (53.0, 65.5)	62.4 (56.2, 68.6)	NA	40.9 (35.3, 46.6)*	47.2 (41.5, 53.0)*	21.2 (15.0, 28.4)
Pain VAS ≥10	Week 2	57.3 (50.8, 63.7)*	61.1 (54.6, 67.3)*	41.2 (32.2, 50.6)	46.3 (40.6, 52.0)*	52.9 (47.2, 58.6)*	36.5 (29.0, 44.6)
	Month 3	69.3 (63.1, 75.1)*	73.9 (67.8, 79.3)*	42.5 (33.5, 51.9)	50.0 (44.3, 55.7)*	57.5 (51.7, 63.1)*	28.7 (21.7, 36.4)
	Month 6	71.0 (65.2, 76.7)	71.0 (65.2, 76.7)	NA	48.4 (42.7, 54.1)*	56.2 (50.4, 61.8)*	30.6 (23.5, 38.4)

*p<0.05 vs PBO; the normal approximation for the difference in binomial proportions was used to test the superiority of each dose of tofacitinib to PBO. [a]Included all randomised patients who took ≥1 dose of study medication. [b]Patients who withdrew for any reason before Month 6, or patients who were advanced to tofacitinib after Month 3 (only for ORAL Sync) had their values on or after withdrawing or advancing set to Non-Response in this analysis. N = total number in each treatment group, number of patients available for the analysis may vary for individual endpoints. PBO group included only those patients who had not yet advanced to tofacitinib.
Comparisons for tofacitinib vs PBO at Month 6 not available for ORAL Solo as all PBO patients advanced to tofacitinib at this time point.
BID, twice daily; CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic DMARD; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; FAS, full analysis set; NA, not available; NRI, non-responder imputation; PBO, placebo; Pts, patients; VAS, visual analogue scale.

Conclusions: DMARD-IR pts with active RA receiving tofacitinib ± csDMARDs appeared to show greater improvements compared with PBO in clinical disease

activity, HAQ-DI, and pain as early as Week 2 (first post-baseline assessment), and improvements in fatigue by M3. Responses were maintained or improved through M3 (monotherapy) or M6 (with background csDMARDs).

References:
[1] Curtis JR et al. Arthritis Care Res (Hoboken) 2015; 67:1345–1353.

Acknowledgements: Previously presented at ACR 2016 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by AG McCluskey of CMC and was funded by Pfizer Inc.

Disclosure of Interest: D. Aletaha Consultant for: AbbVie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, and UCB, A. Kivitz Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Genentech, Pfizer Inc, Consultant for: AbbVie, Amgen, Bristol Myers Squibb, Genentech, Pfizer Inc, Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Genentech, Pfizer Inc, G. Valenzuela Speakers bureau: AbbVie, Janssen, Eli-Lilly, Merck, Novartis and Pfizer Inc, J. Tesser Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, S. Hays Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, H. Li Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. A. Connell Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, E. Bananis Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, A. Soonasra Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. S. Smolen Grant/research support from: AbbVie, Janssen, Lilly, MSD, Pfizer Inc, and Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Glaxo, ILTOO, Janssen, Lilly, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, and UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Glaxo, ILTOO, Janssen, Lilly, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, and UCB

DOI: 10.1136/annrheumdis-2017-eular.1556

THU0187 DO WE TODAY ALTERNATIVE THERAPIES RHEUMATOID ARTHRITIS TWO OR MORE DISEASE-MODIFYING DRUGS? THE STORY OF HOW A SIMPLE DRUG PENTOXIFYLLINE MAY ENHANCE THE ACTION OF METHOTREXATE IN RHEUMATOID ARTHRITIS

D.S. Bublikov, D.A. Anchugina, I.E. Babushkin. *Altay State Medical University, Barnaul, Russian Federation*

Background: The treatment of patients with RA (rheumatoid arthritis) is a complicated task, because the achievement of remission and low level of activity often requires administration of 2–3 disease-modifying drugs. In such conditions we often face with the rise of treatment costs and with the increase of therapy side effects. That is why relevant is the search of the drugs increasing the effect of the "gold standard" of RA – therapy - methotrexate, and also frequently used sulphasalazine and leflunomid. Treatment of prior to "Treat to target" is difficult enough, forcing researchers around the world to look for the ways to improve the effectiveness of RA treatment.

Objectives: To explore the possibilities of reducing RA activity on the disease activity score DAS28 CRP by adding pentoxifylline to the methotrexate, sulfasalazine and leflunomide treatment.

Methods: This study included women (n=131) with RA longer than 1 year in duration, having a seropositive rheumatoid factor, and DAS28 CRP activity score of 3.2–5.1. Middle aged – 46.44±3.24 years old. All patients received a 15.50±2.50 mg oral dose of methotrexate per week, 2000±500 mg oral dose of sulfasalazine per day, 20±5 mg oral dose of leflunomide per day. Patients were divided into two groups - those who only had disease-modifying drugs (DMARDs) (n=80) and those who were treated with an oral dose of methotrexate and 1200 mg of pentoxifylline per day (n=51).

Results: The baseline for both groups of RA patients did not differ significantly in terms of the level on the DAS28 CRP (p=0.812). On 14th day of the group who were taking pentoxifylline, the DAS28 CRP disease activity score was significantly lower by 12.5% ($p<0.001$). After 28 days, the users had a DAS28 CRP disease activity score index difference. The difference between two groups is statistically significant. In the group that were treated with pentoxifylline in addition to DMARDs (p=0.001) the index was found to be 8.3% lower. For 28 days, the methotrexate group's disease activity according to the DAS28 CRP activity score significantly decreased by 14.3% from the baseline ($p<0.001$). For 28 days, the pentoxifylline + DMARDs group also achieved a statistically significant reduction in the index according to the DAS28 CRP activity score by 20.5% ($p<0.001$)

The disease activity index for the two groups for 14 and 28 days is shown in the table.

The DAS28 CRP Index in the two groups of RA patients

Groups of patients Observation time	Group DMARDs (n=80)	Group DMARDs +) Pentoxifylline (n=51)	Statistical significant differences between the two groups
Baseline	3.11±0.05	3.13±0.05	p=0.812
For 14 days	3.06±0.05	2.69±0.06	p<0.001
For 28 days	2.71±0.04	2.48±0.06	p=0.001

Conclusions: Thus, converting the monotherapy DMARDs to pentoxifylline will significantly reduce the activity of RA, while avoiding many of the adverse effects of the other combination therapies. This data requires further long-term research.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7019

THU0188 EFFICACY AND SAFETY OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO DID NOT RESPOND TO SYNTHETIC AND BIOLOGICAL DMARDS IN CLINICAL PRACTICE

E.L. Luchikhina[1], D. Karateev[2], A. Misiyuk[1], N. Demidova[1], G. Loukina[1], D. Abdulganieva[3], A. Baranov[4], A. Babaeva[5], L. Evstigneeva[6], O. Ivanova[7], V. Mazurov[8], O. Semagina[9], A. Sizikov[10], V. Sorotskaya[11], E. Nasonov[2]. *[1]Early arthritis department; [2]Nasonova Research Institute of rheumatology, Moscow; [3]Kazan State Medical University, Kazan; [4]Yaroslavl State Medical University, Yaroslavl; [5]Volgograd State Medical University, Volgograd; [6]Ekaterinburg 1st Regional Clinic Hospital, Ekaterinburg; [7]4 Voronezh Regional Clinical Hospital, Voronezh; [8]North-western State Medical University named after I.I.Mechnikov, Saint-Petersburg; [9]Samara Regional Clinical Hospital, Samara; [10]Scientific Research Institute of Clinical immunology, Novosibirsk; [11]2nd Sity Hospital, Tula, Russian Federation*

Background: Tofacitinib (TOFA) is so far the only representative of a new class of Jak-kinase inhibitors in rheumatology. Despite extensive data on TOFA obtained from 3rd phase studies, for use in clinical practice, the information is limited.

Objectives: To study the efficacy and safety of TOFA in RA in clinical practice.

Methods: We represent the combined data from two parallel IV Phase open-label observational clinical trials, modelling clinical practice, conducted by very similar protocols in 11 rheumatology centers in Russia. Inclusion criteria were active RA, methotrexate (MTX) failure, and/or other synthetic or biologic DMARDs failure. In total, 142 pts (26 males, 116 females, age 51,5±12,2 years, disease duration 88,6±78,1 months, 86,6% RF(+), 76,6% ACPA(+), 81,7% with erosive disease, DAS28-ESR 5,89±1,03, SDAI 35,7±13,4, HAQ 1,59±0,64) were included. 32 (22,5%) pts had biologics in history. TOFA used in the dose of 5 mg BID for 6 months, with possibility to increase to 10 mg BID (carried out in 27 pts after 11,3±2,7 weeks). 115 (81%) pts received TOFA in combination with MTX (18±4,5 mg per week), 18 with leflunomide or sulfasalazine, 9 pts used TOFA in monotherapy.

Results: 129 (90,8%) pts successfully completed the six-month period of treatment. TOFA was withdrawn due to lack of response in 6 cases, adverse events (AEs) in 4 (pneumonia, arterial hypertension, skin vasculitis, mouth ulcers), withdrawal of informed consent – 2, protocol violation – 1. At month 3 SDAI score decreased to 14,6±10,9 ($p<0,01$), 55 (42,6%) pts achieved SDAI LDA and 22 (17,1%) SDAI remission; HAQ decreased to 0,95±0,61, HAQ≤0,5 observed in 36 (27,9%) pts. After 6 months, SDAI and HAQ scores decreased to 10,5±8,6 and 0,83±0,64 resp. ($p<0,01$); 81 (62,8%) pts achieved SDAI LDA and 29 (22,5%) SDAI remission; HAQ≤0,5 observed in 48 (37,2%) pts. Results of treatment in patients with and without biological DMARDs in history were similar. Pts who needed dose escalation of TOFA had worse results at month 3 compared to others (SDAI 21±10,2 and to 13,2±10,7 resp., p=0,02), but after increase of the dose to 10 mg BID at month 6 they showed a slightly better result (SDAI 9,5±7,1 and to 10,7±8,9 resp., p=0,54). Only 2 serious AEs (pneumonia and skin vasculitis) observed. We didn't see any case of Herpes zoster in our group.

Conclusions: TOFA was effective in patients with severe RA who did not respond to both synthetic and biological DMARDs (achievement of SDAI LDA in 42,6% of pts at month 3 and in 62,8% at month 6). Dose escalation to 10 mg BID can be useful in ¼ of patients who do not respond to standard dose of TOFA. TOFA has shown a good safety profile.

Acknowledgements: This scientific study was supported by grant by Pfizer.

Disclosure of Interest: E. Luchikhina Grant/research support from: Pfizer, Biocad, Speakers bureau: Abbvie, Pfizer, Tirupharm, D. Karateev Grant/research support from: Pfizer, Consultant for: Pfizer, Tirupharm, Biocad, Egis, R-Pharm, Novartis, Speakers bureau: Abbvie, Bristol Myers Squibb, Pfizer, Roche, Tirupharm, Biocad, R-Pharm, Novartis, Egis, MSD, UCB, A. Misiyuk: None declared, N. Demidova: None declared, G. Loukina: None declared, D. Abdulganieva: None declared, A. Baranov: None declared, A. Babaeva: None declared, L. Evstigneeva: None declared, O. Ivanova: None declared, V. Mazurov: None declared, O. Semagina: None declared, A. Sizikov: None declared, V. Sorotskaya: None declared, E. Nasonov: None declared

DOI: 10.1136/annrheumdis-2017-eular.5475

THU0189 SAFETY OF FOUR TREATMENT REGIMENS IN EARLY RHEUMATOID ARTHRITIS

E. Fedorenko[1], G. Lukina[2], Y. Sigidin[3], D. Karateev[3]. *[1]Moscow Clinical Scientific Center; [2]Moscow Clinical Scientific Center, V.A.Nasonova Research Institute of Rheumatology; [3]V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Objectives: To compare safety data in patients (pts) with early (<2 years duration) RA who were randomised to receive 4 different regimens of treatment.

Methods: One hundred forty-one pts with RA of less than 2 years duration (122 women, mean age 51 years, mean disease duration 24 weeks, mean DAS 28 5,9; 64% RF-positive,59% ACCP-positive) were randomly allocated to receive one of the following treatment regimens: methotrexate (MTX, up to 20 mg/week,