Methods: The inclusion criteria were diagnosis of RA, established at any time according to ACR (1987) or ACR/EULAR (2010) criteria; persons receiving or planning to receive targeted therapy for RA; signed informed consent to participate in the study. All episodes of treatment with TOFA in which there was at least 1 visit not earlier than 6 months since the start of the drug were included for efficacy analysis.

Results: Data of 48 patients treated with TOFA were extracted from the registry. Women were 41 (85.4%), mean age was 55.1 ± 12.4 years; age at the disease beginning was 44.3 ± 14.0 ; 6 (12.5%) of patients were smokers; mean time on TOFA was 552 ± 259 days. One of the independent predictors of achieved DAS28 was sex - 0.49 lower in men ($p < 0.001$). There was no correlation of achieved disease activity with number of previous failures with biologics. Patients seropositive for rheumatoid factor achieved significantly lower activity ($p = 0.015$). There was also a trend towards lower achieved activity in patients with rheumatoid nodules ($p = 0.059$).

On the first line of targeted treatment, survival of TOFA was significantly better than Infliximab, Adalimumab and Certolizumab pegol. On the second line - better than Infliximab. On the following lines TOFA was better than Adalimumab, but worse than Etanercept. Due to the fact that most of treatment episodes with TOFA are not completed, the average duration of treatment may be underestimated. There was no significant decrement of retention on therapy after multiple treatment failures (tab.).

Conclusion: The effectiveness and treatment survival of TOFA does not depend on the number of previous failures with biologics; the best results of TOFA can be expected in men and seropositive patients; the presence of rheumatoid nodules can be considered as a special indication for TOFA.

Table. Retention of targeted therapies in patients with rheumatoid arthritis

Drug	The 1-st line of therapy		The 2-nd line of therapy		The 3-d and subsequent lines of therapy	
	Number of cases / completed	Average duration estimate (95% confidence interval)	Number of cases / completed	Average duration estimate (95% confidence interval)	Number of cases / completed	Average duration estimate (95% confidence interval)
Tofacitinib	27/3	64.7 (55.8; 73.5)	27/7	28.5 (22.9; 34.2)	25/4	28.0 (23.5; 32.4)
Abatacept	81/24	109.1 (87.9; 130.3)	73/34	63.4 (43.7; 83.1)	36/18	73.7 (43.5; 103.8)
Adalimumab	166/82	57.1 (47.3; 66.9)*	36/23	44.6 (28.6; 60.6)	16/11	23.6 (12.1; 35.0)*
Certolizumab pegol	39/27	49.8 (31.7; 68.0)*	13/8	22.7 (10.5; 34.9)	5/3	25.8 (5.77; 45.9)
Etanercept	117/43	99.2 (77.5)	53/19	98.8 (73.2; 124.4)	24/13	43.7 (27.1; 60.2)*
Infliximab	129/115	28.1 (22.6; 33.5)*	14/12	11.3 (6.26; 16.2)*	3/2	14.8 (4.25; 25.4)
Rituximab	74/26	78.4 (64.2; 92.7)	41/18	66.1 (46.4; 85.7)	31/11	54.2 (37.8; 70.5)
Tocilizumab	74/27	101.3 (77.6; 125.0)	24/9	59.4 (43.3; 75.5)	20/6	41.2 (31.5; 50.9)
All	707/347	74.7 (66.5; 82.9)	281/130	67.2 (54.3; 81.1)	160/68	69.8 (46.5; 93.2)

* - statistically significant difference with Tofacitinib (log-rank test)

Figure 1

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3783

Rheumatoid arthritis – non biologic treatment

AB0417

EFFICACY AND SAFETY OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS ACCORDING TO DURATION OF PRIOR CSDMARD TREATMENT AND NUMBER OF PRIOR CSDMARDS: A POST HOC ANALYSIS OF PHASE 3 AND PHASE 3B/4 TRIALS

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). Previous analyses have reported greater improvements in efficacy outcomes with tofacitinib 5 mg twice daily (BID) ± conventional synthetic DMARDs (csDMARDs) in patients (pts) with early vs established RA.^{1,2}

Objectives: To evaluate the efficacy and safety of tofacitinib in pts with RA, stratified by prior csDMARD treatment duration and number of prior csDMARDs.

Methods: This was a post hoc analysis of pooled data from 4 Phase (P) 3 trials (ORAL Scan [NCT00847613]; ORAL Solo [NCT00814307]; ORAL Sync [NCT00856544]; ORAL Standard [NCT00853385]) and 1 P3b/4 trial

(ORAL Strategy [NCT02187055]) of tofacitinib in pts with RA and an inadequate response to ≥ 1 DMARD. Pts treated with tofacitinib 5 mg BID as monotherapy or with csDMARDs were included. Outcomes were evaluated according to csDMARD treatment duration (≤ 1 , 1–2, > 2 years *y+) and number of csDMARDs (1, 2, 3, ≥ 4) prior to baseline (BL). Efficacy outcomes assessed at Months (M) 3, 6 and 12 were: change from BL (Δ) in CDAI and HAQ-DI, and rates of CDAI-defined low disease activity (LDA; ≤ 10) and remission (≤ 2.8). Safety outcomes, including treatment-emergent adverse events (AEs), serious AEs (SAEs) and AEs of special interest, were evaluated throughout the studies.

Results: In total, 1584 pts were included in the analysis; of these, 27.2% (n=431) had received csDMARDs for ≤ 1 y, 20.5% (n=325) for 1–2 y, and 52.1% (n=825) for > 2 y prior to BL (duration unknown for 3 pts). Roughly half (53.2%, n=842) had received 1 prior csDMARD; 26.4% (n=418), 13.8% (n=219) and 6.6% (n=105) had received 2, 3 and ≥ 4 prior csDMARDs, respectively. Most pts had previously received MTX (50.8%, n=805) or MTX + other csDMARDs (46.3%, n=733); 2.9% (n=46) received other csDMARDs only. Mean BL CDAI and HAQ-DI scores were similar, irrespective of prior csDMARD treatment duration or number of prior csDMARDs (Table). Generally, up to M12, no trends were observed for Δ CDAI, Δ HAQ-DI or CDAI LDA rates regardless of prior csDMARD treatment duration or number of prior csDMARDs (Table). When CDAI remission rates data were stratified by csDMARD treatment duration, no differences between pt groups were observed at M3 and M6; however, a numerically higher proportion of pts with prior csDMARD treatment duration ≤ 1 y achieved remission at M12 vs 1–2 y and > 2 y pts. Use of fewer prior csDMARDs appeared to be associated with higher remission rates up to M12. Although safety outcomes were similar when data were stratified by prior csDMARD treatment duration, there was generally a trend for increased rates of AEs, SAEs and AEs of special interest (serious infections, herpes zoster and opportunistic infections [excluding TB]) with increasing number of prior csDMARDs (Table).

Conclusion: In this post hoc analysis of pooled data from P3 and P3b/4 trials, no differences in the efficacy or safety of tofacitinib 5 mg BID were observed when pts were stratified by prior csDMARD treatment duration. Although pt numbers were small, use of fewer prior csDMARDs may be associated with improved remission rates and safety outcomes for pts treated with tofacitinib.

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Table: Baseline demographics and disease characteristics, and efficacy and safety outcomes for patients treated with tofacitinib 5 mg BID ± background csDMARDs, by prior csDMARD treatment duration and number of prior csDMARDs

	Prior csDMARD treatment duration			Number of prior csDMARDs			
	≤ 1 year (N=431)	1–2 years (N=325)	> 2 years (N=825)	1 (N=842)	2 (N=418)	3 (N=219)	≥ 4 (N=105)
Baseline demographics and disease characteristics							
CDAI score, mean (SD)	38.8 (12.8)	37.8 (12.3)	37.7 (12.3)	38.5 (12.4)	37.3 (12.3)	38.6 (12.4)	36.0 (12.7)
HAQ-DI score, mean (SD)	1.5 (0.7)	1.4 (0.6)	1.5 (0.6)	1.5 (0.6)	1.5 (0.7)	1.5 (0.6)	1.5 (0.7)
Efficacy							
Δ CDAI, mean (SD)							
Month 3	-21.4 (13.7)	-21.0 (14.2)	-20.7 (13.2)	-22.3 (13.8)	-19.5 (13.4)	-20.1 (12.6)	-16.9 (12.7)
Month 6	-24.3 (14.1)	-23.7 (14.5)	-23.7 (13.6)	-25.1 (14.2)	-22.4 (13.2)	-23.4 (13.3)	-20.2 (14.3)
Month 12	-27.1 (13.1)	-24.9 (14.6)	-26.3 (13.5)	-27.3 (13.9)	-24.6 (13.2)	-25.9 (12.5)	-23.1 (12.9)
Δ HAQ-DI, mean (SD)							
Month 3	-0.6 (0.7)	-0.5 (0.6)	-0.5 (0.6)	-0.5 (0.6)	-0.5 (0.6)	-0.5 (0.6)	-0.5 (0.5)
Month 6	-0.6 (0.7)	-0.6 (0.6)	-0.5 (0.6)	-0.6 (0.6)	-0.6 (0.6)	-0.6 (0.6)	-0.5 (0.6)
Month 12	-0.7 (0.7)	-0.6 (0.7)	-0.6 (0.6)	-0.7 (0.6)	-0.6 (0.6)	-0.6 (0.6)	-0.6 (0.6)
CDAI-defined LDA (≤ 10), n (%)							
Month 3	138 (34.6)	91 (31.4)	265 (31.7)	278 (34.8)	129 (33.0)	67 (32.4)	24 (24.5)
Month 6	178 (45.6)	121 (41.4)	346 (45.7)	369 (47.7)	157 (42.0)	81 (40.3)	40 (43.5)
Month 12	168 (58.7)	129 (52.7)	330 (55.8)	352 (56.8)	151 (54.3)	86 (57.0)	38 (52.1)
CDAI-defined remission (≤ 2.8), n (%)							
Month 3	24 (5.9)	20 (6.6)	45 (5.7)	54 (6.7)	24 (6.1)	10 (4.8)	2 (2.0)
Month 6	46 (11.8)	32 (11.0)	79 (10.4)	92 (11.9)	42 (11.2)	18 (9.0)	6 (6.5)
Month 12	58 (20.3)	37 (15.1)	102 (17.3)	112 (18.1)	51 (18.4)	25 (16.6)	9 (12.3)
Safety							
AEs, n (%)	300 (69.6)	219 (67.4)	532 (64.3)	532 (68.0)	280 (67.0)	163 (74.4)	79 (75.2)
SAEs, n (%)	41 (10.4)	33 (10.2)	85 (10.3)	76 (9.0)	42 (10.0)	27 (12.3)	18 (17.1)
AEs of special interest, IR* (95% CI)							
Serious infections							
	1.14	1.15	1.04	1.17	1.07	0.77	2.26
	(0.39; 1.99)	(0.35; 2.30)	(0.73; 1.70)	(0.62; 1.62)	(0.64; 1.56)	(0.25; 1.80)	(0.97; 4.43)
	[n=12]	[n=10]	[n=24]	[n=19]	[n=14]	[n=3]	[n=8]
	0.77	1.17	1.07	0.94	1.02	0.63	2.83
	(0.31; 1.52)	(0.36; 2.16)	(0.75; 1.74)	(0.55; 1.50)	(0.33; 1.78)	(0.17; 1.60)	(1.29; 5.37)
	[n=8]	[n=10]	[n=24]	[n=17]	[n=12]	[n=3]	[n=9]
	0.19	0.34	0.05	0.11	0.08	0.31	0.28
	(0.02; 0.68)	(0.07; 0.99)	(0.00; 0.28)	(0.01; 0.39)	(0.00; 0.46)	(0.04; 1.11)	(0.01; 1.57)
	[n=2]	[n=3]	[n=1]	[n=2]	[n=1]	[n=2]	[n=1]
Opportunistic infections (excluding TB)*							
	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	[n=0]	[n=0]	[n=0]	[n=0]	[n=0]	[n=0]	[n=0]

*IR in patients with events per 100 patient-years
*Opportunistic infections included the following adjudicated events: herpes zoster (≥ 2), herpes zoster disseminated (≥ 1), cytomegalovirus characteristic (≥ 1), cryptococcal pneumonia (≥ 1), and pneumocystis jirovecii pneumonia (≥ 1)
†Change from baseline. AE, adverse event; CDAI, Clinical Disease Activity Index; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, incidence rate; LDA, low disease activity; SAE, serious adverse event; SD, standard deviation; TB, tuberculosis

Acknowledgement: Study sponsored by Pfizer Inc. Medical writing support was provided by Kirsten Woolcott of CMC Connect and funded by Pfizer Inc.

Disclosure of Interests: Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Juan Jose Gomez-Reino Grant/research support from: Biogen, Gilead, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, Consultant for: Biogen, Gilead, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, Gerd Rüdiger Burmester Consultant for: Roche, Sanofi-Genzyme, Speakers bureau: Roche, Sanofi-Genzyme, Ronald van Vollenhoven Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, GSK, Pfizer Inc, Roche and UCB, Consultant for: AbbVie, AstraZeneca, Biotest,

Bristol-Myers Squibb, Celgene, Crescendo, Eli Lilly, GSK, Janssen, Merck, Novartis, Pfizer Inc, Roche, UCB and Vertex, Jose Luis Rivas Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Salim Benkhalifa Shareholder of: Pfizer SAS, Employee of: Pfizer SAS, Palle Dahl Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Harry Shi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Lisy Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc
DOI: 10.1136/annrheumdis-2019-eular.417

AB0418 INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB

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Background: The presence of interstitial lung disease (ILD) is a common extra-articular manifestation in patients diagnosed with Rheumatoid Arthritis (RA), dyspnea being its cardinal symptom. Several of the drugs commonly used to treat this condition, such as TNF inhibitors (anti-TNF) and Disease Modifying Antirheumatic Drugs (DMARDs), have been implicated in the development or exacerbation of ILD. In regard to Tofacitinib, results of post hoc analysis of its pivotal and extension studies report a numerically lower ILD incidence rate in the group that received this drug compared with placebo.

Objectives: To describe the evolution of dyspnea, spirometric parameters, DLCO and high resolution computed tomography (HRCT) findings in patients with RA diagnosis with associated PID who received Tofacitinib for a period of 12 months.

Methods: Patients with a diagnosis of RA who fulfilled criteria ACR 1987/ACR-EULAR 2010, with interstitial lung disease previously diagnosed from clinical findings, spirometry and/or HRCT were included. Tofacitinib was used in dose of 10 mg/day orally. Design: Descriptive, retrospective, multicentric study. The following variables were analyzed: change at 12 months from baseline in the degree of dyspnea (according to the modified scale of dyspnea MMRC), forced vital capacity (FVC), DLCO and findings in HRCT. Continuous variables were reported as mean and standard deviation or median and interquartile range as appropriate. The categorical variables were reported as percentages.

Results: Fifteen patients were included. 60% (n: 9) were women. The mean age was 64.4 years ($\pm$ 10.92). The median time of evolution of RA was 9 years (IQR: 4-40). The median time of evolution of interstitial lung disease was 4 years (IQR: 1-24). 13% (n: 2) of the patients were receiving methotrexate (MTX) at the time of evaluation, 60% (n: 9) of the patients had previously received it. 80% (n: 12) had previously received DMARD different from MTX. 33% of the patients (n: 5) had received previous biological treatment. All patients received tofacitinib at a dose of 10mg/day. 47% of patients (n = 7) received tofacitinib monotherapy and 53% (n = 8) received it combined with DMARDs. 27% (n: 4) of the patients had grade 3-4 dyspnea at baseline. Improvement in the dyspnea scale was observed in 8 patients, while in the rest, it remained stable. The forced vital capacity (FVC) at baseline was <80% in 5 patients and > 80% in 2 patients. At 12 months, 4 patients achieved a FVC > 80%. The average of DLCO at baseline was 45.6 ($\pm$ 18.84), with an improvement of 30% at 12 months in 4 patients. No progression of the disease was observed in the HRCT at 12 months in any of the patients evaluated.

Conclusion: The present preliminary study was performed with patients of daily practice, not being available in all cases, the corresponding respiratory functional examinations. However, despite these limitations, none of the patients showed worsening of dyspnea, with improvement in some patients. Regarding respiratory functional examinations and DLCO, not only they remained stable after treatment in the majority of patients evaluated, but 4 patients presented improvement with respect to baseline parameters. It is necessary to perform more studies, with systematized controls of the pulmonary function and images, to corroborate this hypothesis.

Disclosure of Interests: Marisel Bejarano: None declared, Maria Natalia Tamborenea: None declared, Mario Alberto Goñi: None declared, Lina Saldarriaga: None declared, Cecilia Pisoni: None declared, Rodrigo Garcia Salinas: None declared, Mariana Salcedo: None declared, Claudia Helling Employee of: I am an employee of Pfizer, Adrian Salas Consultant for: Pfizer, Employee of: I am an employee of Pfizer
DOI: 10.1136/annrheumdis-2019-eular.4896

AB0419 FRACTURE RISK IN PATIENTS ON LONG TERM GLUCOCORTICOIDS WITH INFLAMMATORY ARTHRITIS

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Background: A main stay treatment of inflammatory arthritis is glucocorticoids (GCs)^[1]. However, long term use of GCs has been associated with an increased risk of fracture, with studies estimating up to 12% of patients having sustained a fracture whilst on GC treatment^{[1][2]}.

Objectives: The aim of this study was to determine the prevalence of fractures in a cohort of patients on long term GCs with a diagnosis of inflammatory arthritis.

Methods: A database of patients with inflammatory arthritis attending the rheumatology department at the Midlands Regional Hospital Tullamore, since 2009, was reviewed. Patients on long term GCs were identified and outpatient summaries were analysed. Data collection included age, sex, diagnosis, vertebral fracture, other fracture sites and osteoporosis treatment.

Results: As of September 2018, out of the 2118 patients with a diagnosis of inflammatory arthritis 364 were on long term GCs. 10% of patients had reported vertebral fractures on imaging. 36.4% of patients had other types of fractures reported on imaging; 20%, and the most common site of fracture, were wrist fractures. 83.7% of those who suffered from a vertebral fracture were female. 18.2% of those who sustained fractures were not on any osteoporosis treatment.

Conclusion: The incidence of fracture in our cohort of patients was higher than suggested in previous studies. Furthermore, it highlights the need for patients on long term GCs to be given osteoporosis prevention therapy.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8014

AB0420 A PROSPECTIVE, OBSERVATIONAL STUDY ON THE CLINICAL EFFICACY AND SAFETY OF LEFLUNOMIDE IN EGYPTIAN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: CLEAR STUDY

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Background: Due to its anti-inflammatory and immunomodulatory properties, leflunomide can be used as a monotherapy or in combination with other conventional synthetic DMARDs (csDMARDs) in treating active RA.¹

Objectives: The aim of this observational study was to assess efficacy and safety of leflunomide in Egyptian patients with active RA, whether used as first-line and/or add-on therapy to other csDMARDs, with or without steroids.

Methods: Adult Egyptian patients with active RA, fulfilling the ACR/EULAR 2010 classification criteria, for whom leflunomide was prescribed, were included and followed up for 9 months. Leflunomide was prescribed at the physicians' sole discretion for patients who have previously experienced resistance, inadequate response or intolerance to other csDMARDs. Data about CDAL score and HAQ-DI score were acquired from patients who fulfilled the eligibility criteria, along with patients' demographics, medical history, physical examination, concomitant medications, and RA history including disease duration, previous RA medications and treatment response. This study was registered on clinicaltrials.gov (NCT03599986) and the preliminary results were previously published in 2018.²

Results: A total of 398 patients were enrolled in this study. Three hundred sixty-six patients with a mean age of 43.7 (SD 10.2) years and median disease duration of 2 (IQR 5.5) years were eligible for efficacy evaluation; 309 (84.4%) were female. We found that 86.1% of patients were leflunomide naïve. Patients who previously received leflunomide (13.9%) had a wash out period of at least 6 months prior to study enrolment. Patients were either prescribed leflunomide 20 mg/day (37.7%) or were prescribed a loading dose of 100 mg/day for the first 3 days of treatment then maintained with 20 mg/day (62.3%). Leflunomide was prescribed as first-line therapy in 21.1% of patients, as add-on therapy to other csDMARDs without steroids in 34%, and as add-on therapy to other csDMARDs with steroids in 44.9%. The mean total CDAL score