In the STD group, 14 hospital admissions occurred, while in the TAP group there were 7 admissions ($p=0.128$). The corresponding figures for hospital admission due to infectious diseases were 6 in the STD group and 0 in the TAP group ($p=0.026$).

Conclusion: Tapering bDMARDs in RA patients in R/LDA is associated with fewer hospital admissions, with a possible protective effect especially toward infections.

Acknowledgments: The authors are indebted to Mrs Rosella Gramuglia and Mrs Cristina Olivieri for the management and analysis of the data on the flow of the drugs, and with Mrs Anna Consigliere, Mrs Anna Cosso, Mrs Romina Petralito and Mrs Laura Ravaschio for helping in retrieving clinical data.

Disclosure of Interests: Dario Camellino Consultant of: I have received consultancy fees from Celgene, Sanofi, Novartis, Janssen-Cilag, Accord, Paid instructor for: I have served as a paid instructor for Mylan, Andrea Giusti Consultant of: UCB, Amgen, Janssen, Eli Lilly, Abiogen, EffRx, Speakers bureau: UCB, Amgen, Janssen, Eli Lilly, Abiogen, EffRx, UCB, Speakers bureau: Abbvie, Abiogen, Alfa-Sigma, Amgen, BMS, Celgene, Chiesi, Eli Lilly, GSK, Janssen, Medac, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Sanofi Genzyme, Servier, UCB

DOI: 10.1136/annrheumdis-2020-eular.2483

AB0284 RHEUMATOID ARTHRITIS REFRACTORY TO BIOLOGICAL TREATMENT

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Background: In Rheumatoid arthritis (RA), between 20% and 40% of patients do not achieve a 20% improvement in American College of Rheumatology (ACR) criteria, another similar percentage loses response over time or experience adverse events that forces them to the suspension of treatment. Those patients who have failed one or more therapeutic strategies, are more refractory patients and the response to successive targets is usually lower than naive patients, with 50% ACR20 response percentages.

Objectives: To describe the clinical-analytical characteristics and response to the last treatment, in rheumatoid arthritis (RA) refractory to biological disease modifying anti-rheumatic drugs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs). To identify possible factors related to refractoriness to bDMARDs and tsDMARDs.

Methods: Retrospective multicentre, controlled study of patients with RA refractory to bDMARDs and tsDMARDs. Control group was formed by patients with non-refractory RA; matched by gender, age and diseaseduration. Refractoriness was defined as failure to more than 2 different targets of bDMARDs or tsDMARDs. Demographic, clinical-analytical data and rates of disease activity and physical function were collected. A descriptive analysis, a bivariate analysis and a binary logistic regression were performed to see the variables associated with refractoriness.

Results: A total of 94 patients were selected from HRUM and HCUVV: 47 with refractory RA and 47 with non-refractory RA. The clinical-epidemiological characteristics of both groups are classified in Table 1. The majority were women with a mean age of 57 years. There was a greater proportion of patients with multimorbidity and cardiovascular risk factors among the refractory to FAMEb. All patients affected a significant improvement with the new treatment in activity and physical function at 6 months compared to baseline. Refractoriness is associated with a higher body mass index [OR(IC95%), 7.73 (1.56-8.42); $p=0.012$], and depression [OR(IC95%), 1.11 (1.24-1.83); $p=0.035$].

Table 1. Clinical-epidemiological characteristics of patients.

Variable	Refractory RA (N=47)	Non-refractory RA (N=47)	p-value
Sex (female), n (%)	38 (80,9)	38 (80,9)	1,000
Age, means (SD)	57,1 (10,8)	57,4 (10,8)	0,896
Caucasian race, n (%)	45 (95,7)	44 (93,6)	0,646
Body mass index, means (SD)	30,4 (6,8)	26,5 (3,8)	0,002
Non-smoker, n (%)	26 (55,3)	28 (59,6)	
Former smoker>6 months, n (%)	16 (34,0)	7 (14,9)	
Smoker, n (%)	5 (10,6)	12 (25,5)	
Rheumatoid Factor, n (%)	40 (85,1)	42 (89,4)	0,536
Anti-cyclic citrullinated peptide, n (%)	37 (78,7)	38 (80,9)	0,797
Erosions, n (%)	33 (70,2)	28 (59,6)	0,280
Hypertension, n (%)	24 (51,1)	20 (42,6)	0,408
Obesity, n (%)	19 (40,4)	9 (19,1)	0,024
Diabetes Mellitus, n (%)	10 (21,3)	6 (12,8)	0,272
Dyslipidemia, n (%)	20 (42,6)	15 (31,9)	0,286
Neoplasia, n (%)	2 (4,3)	0 (0,0)	0,153
Fibromyalgia, n (%)	4 (8,5)	1 (2,1)	0,168
Depression, n (%)	18 (38,3)	4 (8,5)	0,001
Multimorbidity, n (%)	17 (36,2)	6 (12,8)	0,008
Comorbidities number, median (IQR)	2,0 (1,0-3,0)	1,0 (0,0-2,0)	0,002

Conclusion: Patients with refractory RA have an adequate response to subsequent treatment lines. These patients have a remarkable percentage of associated comorbidities.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.2954

AB0285 RANDOMIZED, OPEN-LABEL, SINGLE-DOSE, PARALLEL-GROUP PHARMACOKINETIC STUDY OF PF-06410293, AN ADALIMUMAB BIOSIMILAR, BY SUBCUTANEOUS DOSING USING A PREFILLED SYRINGE OR A PREFILLED PEN IN HEALTHY SUBJECTS

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Background: Similarity in efficacy, safety, and immunogenicity (IMG) of PF-06410293 (ADL-PF), an adalimumab (ADL) biosimilar, and reference ADL sourced from the European Union (ADL-EU), by subcutaneous (SC) injection using a prefilled syringe (PFS), have been demonstrated in a randomised controlled trial in patients with rheumatoid arthritis (RA) (NCT02480153).

Objectives: To determine if the pharmacokinetics (PK), safety and tolerability of ADL-PF were similar following a single SC dose by prefilled pen (PFP) or PFS in healthy subjects (NCT02572245).

Methods: In this phase 1, 2-arm study, healthy subjects, aged 18–55 years, were randomised (1:1) to receive ADL-PF (40 mg, SC) in the lower abdomen or upper anterior thigh by PFS or PFP. Primary endpoints were maximum observed serum concentration (C_{max}) and area under the serum concentration–time profile from time 0–2 weeks after dosing (AUC_{0-2wk}). Safety, including injection-site reactions (ISRs), and secondary PK endpoints, were also assessed. Bioequivalence between ADL-PF administered by PFS or PFP device was demonstrated if the 90% confidence intervals (CIs) for the test/reference ratios of AUC_{0-2wk} and C_{max} fell within the 80.00–125.00% pre-specified margin.

Results: A total of 164 subjects, stratified by body weight were randomised and assigned to treatment; ADL-PF PFS (n=81) and PFP (n=83). Baseline characteristics were comparable between treatment arms. 163 subjects were included in the primary PK analysis. The concentration–time profiles were comparable between the ADL-PF PFS and PFP treatment arms, and were characterized by an increase in serum drug concentrations, with the C_{max} achieved at approximately 6–7 days, followed by a multi-phasic decline in drug concentrations. The 90% CIs for test/reference ratios of the geometric means for the primary PK parameters fell within the pre-specified margin (Table). In total, 50 and 51 treatment-emergent adverse events (AEs) were reported in 31 (38.3%) and 29 subjects (34.9%), respectively, in the ADL-PF PFS and PFP groups. One subject experienced an unrelated serious AE in the ADL-PF PFP group. Injection-site pain was similar between treatment arms at all time points, and for the 2 injection-site locations. IMG testing was limited to subjects experiencing an ISR and/or rash AE, and a matched control group, with 11 (11/15; 73.3%) and 7 (7/15; 46.7%) subjects, respectively, testing anti-drug

antibody (ADA)-positive. Amongst ADA-positive subjects, a majority (12/18) also tested positive for neutralising ADAs (7/11 [63.6%] and 5/7 [71.4%] subjects, respectively).

Conclusion: This study demonstrated that the PK of ADL-PF was comparable following SC administration using either a PFS or PFP device. ADL-PF by PFS or PFP injection was well tolerated by healthy subjects, with the distribution of AEs, including ISRs, being similar between treatment arms.

Table. Summary of Statistical Comparisons of PK Exposure Parameters between Test and Reference Treatments (PK Analysis Set)

PK parameter (units)	Adjusted geometric means		Ratio ^{a,b}	90% CI for ratio ^b
	ADL-PF PFP (test)	ADL-PF PFS (reference)		
C _{max} (µg/mL)	4.45	4.13	107.74	99.16–117.06
AUC _{0–24h} (µg·hr/mL)	1150	1100	104.89	95.76–114.89
AUC _T (µg·hr/mL)	2040	2100	97.23	86.75 – 108.98
AUC _{0–inf} (µg·hr/mL)	2200	2150	102.27	91.12 – 114.78
T _{max} (hr) ^c	142 (45.4, 336)	166 (47.7, 674)		

^a (test/reference) of adjusted means.

^b Ratios and 90% CIs are expressed as percentages.

^c Median (range).

ADL-PF, PF-06410293; AUC, area under the serum concentration–time profile; AUC_{0–24h}, AUC from time 0–24 hours after dosing; AUC_{0–inf}, AUC from time 0 extrapolated to infinity; AUC_T, AUC from time 0 to the time point of the last quantifiable concentration; C_{max}, maximum observed serum concentration; CI, confidence interval; h, hour(s); PK, pharmacokinetic(s); PFP, prefilled pen; PFS, prefilled syringe; T_{max}, time of maximum serum concentration.

Acknowledgments: Medical writing support was provided by Iain McDonald of Engage Scientific Solutions. The study was funded by Pfizer.

Disclosure of Interests: Donna Cox Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Daniel Alvarez Shareholder of: Pfizer, Employee of: Pfizer, Amy Bock Shareholder of: Pfizer, Employee of: Pfizer, Carol Cronenberger Shareholder of: Pfizer, Employee of: Pfizer

DOI: 10.1136/annrheumdis-2020-eular.454

AB0286 EFFICACY AND SAFETY OF INTRA-ARTICULAR INJECTION OF ETANERCEPT IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Refractory mono-oligo-arthritis is still a challenging clinical situation in rheumatoid arthritis. Intra-articular corticosteroids are the first-line therapy; however, their efficacy is rather varying and many patients experience relapses within 6 months after injection. ⁽¹⁾ Intra-articular anti-TNF has the potential of being less toxic and cost effective compared to its systemic usage. ⁽²⁾ Recent evidences have shown a reduction in the synthesis of either the T helper 1 cytokines or in the interleukin-6/17 axis cytokines at joint level following intra-articular injection of etanercept. ⁽³⁾

Objectives: Our aim was to evaluate the safety and efficacy of intra-articular injection of etanercept in patients with rheumatoid arthritis.

Methods: This study included 23 rheumatoid arthritis patients diagnosed according to the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) 2010 diagnostic criteria for RA ⁽⁴⁾, who suffered from flare of activity in one joint. Patients were selected from the outpatient clinic and the in-patient section of Physical Medicine, Rheumatology and Rehabilitation Department, Faculty of Medicine, Tanta University Hospitals, Egypt. The degree of swelling and tenderness of the affected joint was evaluated on a score (0–3) and the degree of pain was assessed by using visual analog scale (VAS). Musculoskeletal ultrasound (MSUS) examination was done to assess synovitis which was evaluated on two axes, longitudinal and transverse and was semiquantitatively scored on a (0–3) scale, synovial vascularity was assessed using power Doppler and it was semi-quantitatively scored on a (0–3) scale. **Follow-up:** Patients were examined both clinically (degree of swelling, degree of tenderness and VAS), and by MSUS on weeks: 1, 4 and 12 after injection.

Results: No serious or life-threatening adverse effects were noticed in any patient during the follow-up periods and up till the end of the study except for temporary local soreness during the injection, there was a significant improvement of VAS, tenderness and swelling scores after 1-week $p < 0.002$ and 1-month $p < 0.003$ follow-up periods, but there was insignificant change after 3 months $p = 0.116$, by MSUS, there was an insignificant change in synovitis $p = 0.112$, but a significant change was found in power Doppler after 1-week $p = 0.046$ and no significant changes were detected further.

Conclusion: Intra-articular injection of etanercept is a safe and an encouraging treatment modality in managing refractory mono-arthritis in rheumatoid arthritis patients. Further researches are needed to study the use of repeated injection of etanercept to get more sustained effects.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1441

AB0287 HEMATOLOGICAL SIDE EFFECTS OF BIOLOGICAL THERAPY IN RHEUMATOLOGY: DATA FROM THE TUNISIAN REGISTER

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Background: During the last decade, the treatment of chronic inflammatory rheumatism (CIR) has been greatly improved with the advent of biotreatment. However, the use of biological treatment can lead to a number of side effects including abnormalities in the blood count.

Objectives: The aim of this study was to assess the different hematological side effects of biological treatment in patients with rheumatoid arthritis (RA) and spondyloarthritis (SA).

Methods: This study included patients with RA (ACR/EULAR 2010) and SA (ASAS 2009) registered with the Tunisian Biologic National Registry (BINAR). Patients were followed and treated with biologics for 2 years or less. Clinical data relative to biological treatment, including haematological side effects, have been collected.

Results: Two hundred and ninety-eight patients (178 women and 111 men) were included in the study.

The mean age was 49.2 ± 14.1 years. The male/female ratio was 0.6. The mean diseases durations for RA and SA were respectively 6.7 ± 3.5 years and 6.5 ± 3.6 years.

Anti-TNFα agents were prescribed in 87.9% of patients (n = 263) with respectively: Infliximab (20.4%) Etanercept (23.1%), Adalimumab (24.6%) and Certolizumab (26.5%).

Tocilizumab and Rituximab were prescribed in 10.4% and 5% of the patients, respectively.

Blood count abnormalities were noted in 15.4 % of patients (n=46).

Neutropenia was the most frequently anomaly met on the hemogram (9.1%) followed by anemia (3.4%) and thrombocytopenia (3%). Pancytopenia was found in 11.4% of patients (n=34).

The median time between biological therapy initiation and the onset of hematologic manifestations was 4.8 months [1–12]. Biological treatment was interrupted in two patients.

In the other cases, the biological treatment was maintained with close monitoring of blood cell count. No case of death related to these hematological disturbances has been reported.

Conclusion: In our registry, hematological side effects of biological treatment were found in 15.4% of cases and were noted with a median delay of 4.8 [1–12] months after the treatment initiation. Further studies are needed to confirm our preliminary results.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.6251