(AOSD); all were exposed to a biologic agent: 16 Etanercept (ETA), 7 Adalimumab (ADA), 4 Infliximab (IFX), 1 Certolizumab (CTZ), 5 Rituximab (RTX), 1 Anakinra (ANK). Median age was 34 yrs (range 24–50). All patients treated with TNFi and ANK withdrew therapy in early pregnancy (<10 weeks gestational age). 2 RA patients had 2 pregnancies each, during ETA treatment. A RA woman became pregnant 4 times during RTX therapy. 10 patients were also on csDMARDs therapy at the time of conceptions: 7 Hydroxychloroquine (HCQ), 1 HCQ + Sulphasalazine (SSZ), 1 Cyclosporine A (CYA), which was continued, and 1 with Methotrexate which was immediately withdrawn. 1 RA patient started SSZ from the 24th week. 15 patients (7 RA, 2 PsA, 2 AS, 2 uSpA, 1 DM) started or increased oral and/or intra-articular steroids because of disease flare. A control group of 45 pregnancies observed in 42 patients not exposed to biologics was selected="selected" (19 RA, 12 uSpA, 3 Juvenile Idiopathic Arthritis (JIA), 5 PsA, 1 AS, 1 DM, 1 AOSD), median age 35 (range 22–42). 18 patients were treated with csDMARDs during pregnancy (8 HCQ; 4 SSZ; 2 CYA+HCQ; 4 SSZ+HCQ). No other drugs were taken at the time of conception, apart from low dose of steroids in 24 cases; in 1 case intra-articular steroids were given because of disease flare. Pregnancy outcomes are summarized in tab.1: therapeutic abortions were performed for an extrauterine pregnancy occurred twice in the patient with RA who became pregnant 4 times during RTX treatment, after the 5th and the 6th retreatment. After the 4th retreatment she had an early spontaneous abortion. Previously, she delivered 2 healthy children after exposure to ETA and 3 treatment cycles of RTX. No serious perinatal complication occurred, excluding very preterm baby delivery at 28th weeks, who needed neonatal intensive care. No congenital malformations were observed. Klinefelter syndrome was diagnosed in 1 case.

Tab. 1: Pregnancy outcomes of women with RD exposed to biological (BE) compared with pregnant women with RD non-exposed to biological agent (NE)

	BE group (34)	NE group (45)	p
Live births	29 (85.3%)	43 (95.5%)	ns
Spontaneous abortion	2 (5.9%)	2 (4.4%)	ns
Therapeutic abortion	2 (5.9%)	0	ns
Voluntary interruption of pregnancy	1 (2.9%)	0	ns
Pre-term delivery	5 (14.7%)	6 (13.3%)	ns
Preterm rupture of membrane	3 (8.8%)	4 (8.9%)	ns
Intra-uterine growth restriction	1 (2.9%)	1 (2.2%)	ns
Average birth weight	2875 g (720-4234)	3140 (1880-4200)	ns
Low birth weight (<2500 g)	6 (17.6%)	5 (11.1%)	ns

Conclusions: In our case series no significant differences did occur in pregnancy outcome between BE and NE group, according to the most recent data published in literature. Additional data from larger numbers of pregnancy exposed to biological agents are required.

Disclosure of Interest: None declared

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SAT0157 MYCOBACTERIUM TUBERCULOSIS SPECIFIC RESPONSES FROM CD8+ AND CD4+ T CELLS IN PATIENTS WITH LATENT AND ACTIVE FORM OF TUBERCULOSIS

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Background: Testing the presence of latent or active tuberculosis using IGRA tests is necessary part of the diagnostic screening at risk individuals. QuantIFERON-TB Gold Plus (QFT-Plus) is a test for cell-mediated immune (CMI) responses to peptide antigens that simulate mycobacterial proteins. Peptide antigens in TB1 tube elicit CMI responses from CD4+ T-helper lymphocytes, in TB2 tube from CD8+ T-cytotoxic lymphocytes. Test is based on the ability of effector T lymphocytes to produce the cytokine interferon gamma (IFN-γ).

Objectives: To compare and evaluate levels of IFN-γ produced by CD4+ and CD8+ cells in TB1 and TB2 tubes.

Methods: It was studied 33 subjects with latent form of tuberculosis (LTBI) and 33 subjects with active TB. QFT-Plus was used to detect in vitro responses to peptide antigens associated with *Mycobacterium tuberculosis* infection (ELISA, QIAGEN). Results were obtained by calculation of INF-γ levels in Mitogen, TB antigen (TB1, TB2) and Negative control tubes using QFT analysis software.

Results: QFT-Plus positive results were observed in both groups of people. Increased levels of IFN-γ produced by CD4+ cells (TB1) has been detected in 21 subjects with LTBI (63.64%) and in all 33 subjects with active TB (100.0%). Increased levels of IFN-γ produced by CD8+ cells (TB2) has been detected in 27 people with LTBI (81.82%) and in all 33 people with active TB (100.0%). Joint increase levels of IFN-γ in the tubes TB1 and TB2 was observed in 16 individuals with LTBI (48.48%) and in all 33 individuals with active TB (100.0%). In the group of patients with a negative QFT-Plus it was not observed increased levels of IFN in tubes TB1 and TB2.

Conclusions: Our findings confirm specific CD4+ and CD8+ T cell response to mycobacterial protein antigens in individuals with LTBI and also in active TB subjects, in which INF-γ was frequently found. The immunological response represented by CD4+ and CD8+ T cells was not detected in subjects with QFT-Plus negative.

Disclosure of Interest: None declared

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SAT0158 EFFICACY OF SWITCHING FROM ETANERCEPT TO ADALIMUMAB IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS WHO EXPERIENCED A FIRST-LINE BIOLOGIC THERAPY FAILURE: THE FEARLESS STUDY

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Background: The strategy for the choice of the second biologic agent after the failure of the first TNF inhibitor (TNFi) is still an unclear aspect in the treatment of both rheumatoid arthritis (RA) and psoriatic arthritis (PsA). Switching between structurally different TNFis (from etanercept [ETN] to monoclonal antibody [mAb] or vice versa) has been proposed as a more effective procedure than switching among different mAbs, but to date no study has been specifically focused on exploring this topic.

Objectives: To evaluate the comparative 2-year retention rate and the 12-month efficacy of adalimumab (ADA) as second biologic agent in etanercept (ETN) non-responder RA and PsA patients in a multicentre retrospective study.

Methods: All RA and PsA patients from 11 Italian Rheumatology Units treated with ADA after a first-course ETN failure and with at least 12-month follow-up were retrospectively collected in a multicentre registry. Data analysis was limited to the period from January 2002 to May 2016. Two-year ADA retention rate was calculated by Kaplan-Meier method. 12-month ADA response was defined as achievement of disease activity score 28 calculated by using erythrocyte sedimentation (DAS28-ESR) <2.6 (remission) or >2.6 and <3.2 (low disease activity, LDA). Sub-analyses according to reason for ETN discontinuation and concomitant methotrexate in RA and PsA patients have been performed.

Results: The study population (219 patients) included 117 RA (female 85.5%, mean [± standard deviation, SD] age 53.2±13.5 years, mean [±SD] disease duration 10.1±7.7; positive rheumatoid factor 70.2%; positive anti-citrullinated peptide antibodies [ACPA] 59.6%; mean [±SD] baseline DAS28-ESR 4.97±1.3; MTX users 64.9%) and 102 PsA (female 63.7%; mean [±SD] age 51.7±10.6; mean [±SD] disease duration 7.1±5.1; mean [±SD] baseline DAS28-ESR 4.4±1.1; MTX users 50%). The 2-year retention rate was 48.2% in RA and 56.5% in PsA patients, irrespective of reason for ETN discontinuation. Similarly, concomitant MTX was not associated with an increased drug survival in both RA (p=0.09) and PsA (p=0.969) subgroup. 12-month clinical remission and LDA were achieved respectively in 27.3% and 23.9% RA patients, and 27.4% and 23.5% PsA patients.

Conclusions: In our large real-life cohort, the use of ADA in primary and secondary ETN failures was highly effective in both RA and PsA patients, with more than 50% of ADA treated patients achieving remission or LDA. Reasons for ETN discontinuation were not associated with different ADA clinical response, as well as concomitant MTX.

Disclosure of Interest: None declared

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SAT0159 IMPACT OF PARTICIPATION IN THE ADALIMUMAB PATIENT SUPPORT PROGRAM ON FUNCTIONAL AND CLINICAL OUTCOMES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: PASSION STUDY

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Background: Patients (pt) with Rheumatoid arthritis (RA) who are treated with adalimumab (ADA) are offered a Patient Support Program (PSP) with variety of services. To date, no prospective study has been conducted to analyze the acceptance and the impact of these PSPs on treatment effectiveness and pt satisfaction.

Objectives: The purpose of this study was to examine the effectiveness of ADA on rheumatoid arthritis (RA) treatment course in the context of PSP participation.

Methods: PASSION (NCT01383421) was a 78-week (wk) post-marketing observational study of pts with RA receiving ADA in routine clinical care. Pts from the EU, Israel, Mexico, Puerto Rico, and Australia with an insufficient response to ≥1 disease-modifying antirheumatic drug (DMARD) newly initiating ADA (1 prior

biologic DMARD was allowed) were enrolled. The primary endpoint was the % of pts achieving the minimal clinically important difference (MCID; improvement of ≥ 0.22 compared to baseline [BL]) in the Health Assessment Questionnaire Disability Index (HAQ-DI) at wk 78. Non-responder imputation (NRI) was used to account for the missing values. Secondary clinical parameters included % of pts achieving MCID in HAQ-DI at wks 24 and 52 and changes in the 28-joint DAS based on CRP (DAS28(CRP)), Simplified Disease Activity Index (SDAI), and Clinical Disease Activity Index (CDAI) at wks 24, 52, and 78 vs BL. Pts were categorized based on their participation in the PSP: ever (PSP users) vs never (PSP non-users) and outcomes were compared after adjusting for corresponding BL values.

Results: Overall, the primary endpoint, percentage of pts achieving the MCID for HAQ-DI, was achieved by 72.1% (as observed) and 42.8% (NRI) of pts at week 78 with the percentage of pts achieving the MCID for HAQ-DI significantly higher in PSP users vs PSP non-users (48.1% vs 37.8% [NRI]; $P < 0.001$). From 1,025 pts, 48.7% pts were PSP users (BL: mean age, 54.3 years (y); % female, 77.1%; mean RA duration, 7.8 y; mean HAQ-DI, 1.5; mean DAS28(CRP), 5.3; mean SDAI, 35.6; mean CDAI, 33.3; 17.8% pts had received prior biologic DMARD. Significant changes ($P \leq 0.05$) from BL to wk 78 were observed for pts using the PSP vs PSP non-users in HAQ-DI (0.53 vs 0.39), DAS28(CRP) (-2.33 vs -1.97), SDAI (-24.5 vs -19.8), and CDAI (-22.66 vs -18.55) scores (Figure). Study discontinuation rates were significantly ($P < 0.001$) lower among PSP-users vs PSP non-users (25.5% vs 41.6%). Reasons for discontinuations are listed in the Table.

Figure: Changes from baseline in DAS28 (CRP) (A), SDAI (B), CDAI (C), and HAQ-DI (D) over time between PSP users and PSP non-users.

*Significantly different between PSP users and PSP non-users ($P < 0.05$). Data represented by LOCF imputation for intent-to-treat population. Results are adjusted for BL DAS28(CRP), SDAI, CDAI, and HAQ-DI. LOCF=Last Observation Carried Forward

Table: All reasons for study discontinuation by PSP utilization category

Subject Disposition	All Patients N=1025	PSP user N=499	PSP non-user N=526
Discontinued (%)***	346 (33.8)	127 (25.5)	219 (41.9)
Adverse event	52 (5.1)	22 (4.4)	30 (5.7)
Withdrew consent	37 (3.6)	13 (2.6)	24 (4.6)
Lost to follow-up	46 (4.5)	17 (3.4)	29 (5.5)
Serious adverse events	24 (2.3)	10 (2.0)	14 (2.7)
Lack of efficacy	168 (16.4)	66 (13.2)	102 (19.4)
Other	51 (5.0)	16 (3.2)	35 (6.7)

***Statistically significant at $P < 0.001$

Conclusions: The final study results showed that, in pts with moderate to severe RA who initiated ADA, significantly better improvement in functional and clinical outcomes was achieved in the PSP users vs the PSP non-users. Improvements were achieved at early timepoints and continued to increase throughout the study.

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SAT0160 IMMUNOGENICITY OF BIOSIMILARS FOR THE TREATMENT OF INFLAMMATORY RHEUMATIC DISEASES: A REVIEW FROM CONFIRMATORY CLINICAL TRIALS

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Background: The assessment of immunogenicity is mandatory during the comparability exercise of biosimilar candidate drugs, as even small structural differences can potentially elicit antidrug antibodies (ADA) and affect efficacy and safety.

Objectives: To review the incidence of ADA and neutralizing ADA (nADA) in confirmatory clinical trials of biosimilar drugs approved for the treatment of inflammatory rheumatic conditions in the European and North-American markets; to review the type of assays used for this purpose; to compare the incidence of ADA with historical data from reference biotechnological drugs.

Methods: We performed a literature search in the Medline database and hand searched EULAR and ACR meeting abstracts to identify phase I and III confirmatory clinical trials of biosimilar drugs for the treatment of rheumatic conditions approved in the European and North-American markets. Open-label extensions involving biological switch were not included. All outcomes regarding immunogenicity were extracted (ADA, nADA and type of immunogenicity assays).

Results: We screened 255 articles by title and abstract and 7 publications fulfilled our inclusion criteria. Three meeting abstracts were also included. Six studies assessed infliximab biosimilars (CT-P13 and SB2), three studies assessed etanercept biosimilars (SB4 and GP2015) and one study assessed an adalimumab biosimilar (ABP 501). All but two concerned phase III trials and seven were performed on rheumatoid arthritis patients. All biosimilars had comparable immunogenicity profiles in respect to their reference drugs, except for the etanercept biosimilar SB4, which presented significantly less ADA when compared to reference etanercept (0.7% vs 13.1% at 24 weeks and 1.0% vs 13.2% at 52 weeks, $p < 0.001$ for both). As expected, infliximab had the highest incidence of ADA; the proportion of ADA in studies of infliximab and adalimumab was higher when compared to historical data. Only 4 studies reported nADA, which were highest in the infliximab biosimilar CT-P13 54-week study in ankylosing spondylitis patients. Electrochemiluminescence immunoassay was the preferred method to measure ADA. Table 1 summarizes the main findings in the included studies.

Table 1. Immunogenicity of biosimilars approved for the treatment of inflammatory rheumatic diseases. ADA: antidrug antibody, NA: not available, nADA: neutralizing antidrug antibody. *The EGALITY study presented a four-arm design in which two arms were continuously treated with either reference etanercept or GP2015 and the other two arms were systematically switched. The results presented in this table concern the groups continuously treated with reference etanercept or GP2015

Study population	Reference drug ADA (%)	Reference drug nADA (%)	Biosimilar ADA	Biosimilar nADA (%)	ADA/nADA assay
Rheumatoid arthritis					
CT-P13 (infliximab)					
Yoo 2013 (PLANETRA, 30 w)	48.2	NA	48.4	NA	Electrochemiluminescence immunoassay/NA
Yoo 2016 (PLANETRA, 54 w)	36.0	NA	41.1	NA	Electrochemiluminescence immunoassay/flow-through immunoassay
SB2 (infliximab)					
Choe 2015 (30 w)	49.7	NA	55.1	NA	Electrochemiluminescence immunoassay/ competitive ligand-binding assay
Choe 2015 (54 w)	57.5	NA	62.4	NA	NA
SB4 (etanercept)					
Emery 2015 (24 w)	13.1	3	0.7	0	Electrochemiluminescence immunoassay/ competitive ligand-binding assay
Vencovsky 2015 (52 w)	13.2	NA	1.0	NA	NA
ABP 501 (adalimumab)					
Cohen 2015 (24 w)	38.2	11.1	38.3	9.1	NA
Ankylosing spondylitis					
CT-P13 (infliximab)					
Park 2013 (PLANETAS, 30 w)	22.5	NA	27.4	NA	Electrochemiluminescence immunoassay/NA
Park 2016 (PLANETAS, 54 w)	23.0	100	19.5	100	Electrochemiluminescence immunoassay/ flow-through immunoassay
Psoriasis					
GP2015 (etanercept)					
Griffiths 2016 (EGALITY, 52 w)*	1.9	0	0	0	Electrochemiluminescence immunoassay/ competitive ligand-binding assay

Conclusions: Currently approved biosimilars for the treatment of rheumatic diseases have comparable immunogenicity profiles in respect to their reference drugs. The discrepancy in ADA between SB4 and reference etanercept did not correlate with efficacy or safety and did not preclude biosimilarity, according to the regulatory agencies. The higher proportion of ADA compared to historical data may be explained by the greater sensitivity of current immunogenicity assays, such as electrochemiluminescence.

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