Conclusions: This phase 3 randomised controlled trial demonstrated the comparability of CT-P10 with two rituximab in terms of efficacy, pharmacodynamics, immunogenicity and safety for 1 year.

References:
[1] Suh CH, et al. 2016 ACR Abstract No. 1634.
[2] Yoo DH, et al. 2016 ACR Abstract No. 1635.

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SAT0147 SERUM LEVELS OF THE ANTI-TNF BIOLOGICS CORRELATE WITH CLINICAL EFFICACY IN PATIENTS WITH INFLAMMATORY ARTHRITIS

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Objectives: To study the correlation between levels of the anti-TNF biologics and clinical efficacy in patients with inflammatory arthritis

Methods: Adult patients who fulfilled the criteria for rheumatoid arthritis (RA), spondyloarthritis (SpA) and psoriatic arthritis (PSA) and were commenced on standard doses of the anti-TNF biologics were recruited. Serum samples saved at baseline, month 6 and 12 were assayed for the trough levels of the biologics (± anti-drug antibodies) retrospectively. Patients were followed longitudinally and efficacy analyses were conducted at 3-month intervals without the knowledge of the drug levels. Biologics would be discontinued from 6 months onwards according to protocol-based improvement criteria for each disease. Clinical efficacy of the anti-TNF biologics was compared among patients with different levels of the drug by statistical methods.

Results: 112 patients were studied (58 RA, age 51.2±10.9 years, disease duration 72.9±67 months; 41 SpA, age 39.1±9.9 years, disease duration 74.3±81.6 months; 13 PSA, age 53.5±10.7 years, disease duration 44.3±35.4 years). The number of patients treated with infliximab (IFX), adalimumab (ADM), golimumab (GLM) and etanercept was 3, 31, 36 and 42, respectively. At month 12, neutralizing antibodies against IFX, ADM and GLM were present in 2 (67%), 14 (45%) and 1 (3%) of the patients, respectively. In ADM users, the drug level was significantly lower in those with antibodies than those without (1.81±2.63 vs 8.02±4.14 ug/ml; $p<0.001$). Antibody titer against ADM correlated negatively with the levels of ADM (Rho -0.72; $p<0.001$). Patients were stratified arbitrarily into 3 groups for each biologic according to the trough levels of the drugs. Low drug concentrations were defined as levels $\leq$1.30 ug/ml, 0.05 ug/ml and 0.60 ug/ml in ADM, ETN and GLM users, respectively. In patients with RA/PSA (N=71), patients with the lowest anti-TNF drug level group (N=30) had a non-significant trend of less improvement in DAS28, CDAI scores at month 12 when compared to others (N=41). However, significantly more patients withdrew treatment due to inefficacy at month 12 in this group compared to others (67% vs 7.3%, $p<0.001$). In patients with SpA (N=41), patients with lowest anti-TNF drug levels stratum (N=9) had significantly less improvement in ASDAS compared with others at month 12 (N=32) (-0.57±0.63 vs -1.93±1.28; p=0.003). The proportion of patients who achieved an ASAS20 response was also significantly lower in this group of patients (33% vs 75%; p=0.04). In all the 112 patients studied, the cumulative withdrawal rate of the anti-TNF biologics at month 12 (by Kaplan-Meier's analysis) was significantly higher in those with low drug levels when compared to others (26.1% vs 54.6%; $p<0.001$ by log rank test).

Conclusions: The presence of neutralizing antibodies to the anti-TNF monoclonals is associated with lower trough levels of the drugs. Trough level of the anti-TNF biologics is useful for optimizing the clinical efficacy of the drugs in patients with inflammatory arthritis.

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SAT0148 RABBIT RISK SCORE FOR SERIOUS INFECTIONS IN A ROMANIAN COHORT OF RHEUMATOID ATHRITIS TREATED WITH BIOLOGICS

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Background: The risk of infections, especially severe infections (SI), remains of particular interest in rheumatoid arthritis (RA), both defective immune response and therapeutic immunosuppression being responsible.

The RABBIT Risk Score (RRS), an instrument developed and validated for RA in the German Biologics Register RABBIT and replicated in other RA settings (British Register), allows the estimation of SI occurring during 12 months according to patient characteristics, based on data from similar risk profiles.

Objectives: To evaluate the RSS reliability in a Romanian RA cohort under different biologics, considering the agreement between observed and expected rates of SI at 12 months.

Methods: Longitudinal study on 272 consecutive RA with moderate-to-severe active disease, starting their biologic according to local guidelines, enrolled between 2008 and 2016 in a single academic center.

Along with disease activity and therapeutic response, baseline RRS (http://www.biologika-register.de/en/home/risk-score/) was applied for each case, based on multiple risk factors for infections including age, functional status, chronic lung and renal comorbidities, previous SI, number of treatment failures, current biologic (TNF or non-TNF inhibitors), mean corticosteroid dose.

The predictive value of RRS was considered by comparing the number and rate of expected versus reported SI in the first year of biologics (ROC curve, $p<0.05$), assessing the number of adverse events per year and per 100 patient-years, cases with at least one infection.

Statistical analysis (univariate, multivariate) was stratified according to different predictors of infection, patients being classified in two groups based on their recruitment before (2008–2012) and after (2013 up to date) implementation of national biologic register RRBR.

Results: The performance of RSS was previously established in a pilot study on 181 RA. Currently, the RSS was considered in 144 RA recruited to the first group and 128 to the second. The prescription pattern significantly changed ($p<0.05$) for patients enrolled in last years: RA were more likely to receive earlier bDMARD, for lower activity and functional status; moreover, lower corticosteroids (dose, duration) and fewer synthetic DMARDs before starting biologics were reported ($p<0.05$).

24.63% RA developed SI (a total of 67 episodes, 1.47% fatal outcomes). Irrespective of RA settings and scenarios, history of biologics, specific drug administered (TNF or non-TNF), RRS indicated an outstanding agreement between the observed and expected SI rates ($p>0.05$).

In addition, the rate of SI was lower in RA recruited after 2013 ($p<0.05$), while RRS has better predictive significance in the second cohort ($p<0.05$).

Conclusions: The RABBIT Risk Score is a consistent tool, able to predict serious infections in Romanian RA receiving biological therapy (TNF and non-TNF drugs), optimizing the selection of appropriate medication based of individual infectious risk profile in routine practice.

Disclosure of Interest: None declared

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SAT0149 COMPARATIVE EFFECTIVENESS OF TOFACITINIB, BIOLOGIC DRUGS AND TRADITIONAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS

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Background: Most rheumatoid arthritis (RA) patients initiate therapy with methotrexate (MTX), but only 1/3 will have low disease activity with this agent alone. Several therapeutic options are available for patients with MTX-resistant RA, including new Janus kinase (JAK) inhibitors (eg.: tofacitinib).

Objectives: To compare the effectiveness of traditional disease-modifying antirheumatic drugs (DMARDs), biologic DMARDs and tofacitinib for RA patients with inadequate response to MTX.

Methods: We used MarketScan® databases (2011–2014) to study adult RA individuals previously treated with methotrexate (oral or SQ) and newly prescribed one of the medications under study. The date of first filled prescription or infusion drug was defined as the cohort entry and a 12-month pre-period was used to exclude prior users of biologics or tofacitinib. We required subjects to be continuously enrolled in the medical and pharmacy plan 12 months before and after the cohort entry. Effectiveness was access through an algorithm previously validated[1], based on the following criteria: 1) non-adherence; 2) switching/adding a new biologic or tofacitinib; 3) switching/adding a new DMARD; 4) increasing of the dose of the starting therapy; 5) use of glucocorticoid joint injections; and 6) increasing the dose of oral glucocorticoid. A patient's therapy was defined as not effective if at least one of the criterion occurred during the first year of follow-up.

Results: 16,305 RA patients were included; 2,879 began therapy with DMARD, 13,345 with biologics and 81 with tofacitinib. Among all patients, 77.5% were female and the mean age was 56.2 years (standard deviation 12.6). Table 1 shows the proportion of patients that meet the individual criterion and that achieved effectiveness at the end of one-year follow-up.

Conclusions: Similar rates of therapy effectiveness were observed among groups, although the rates for the individual criteria differed. Fewer patients initiating biologic agents were non-adherent compared to DMARD and tofacitinib therapy, but switch/adding and injections tended to be higher in this group.

Table 1. Proportion and 95% confidence interval (CI) of patients who achieved therapy effectiveness and the individual criteria

Effectiveness criteria	DMARD		Biologics		Tofacitinib	
	%	95% CI	%	95% CI	%	95% CI
Non-adherence	75.1	73.5; 76.7	54.5	53.6; 55.3	69.1	59.1; 79.2
Switch/add biologic or tofacitinib	16.1	14.8; 17.5	34.6	33.8; 35.4	18.5	10.1; 27.0
Switch/add DMARD	13.0	11.7; 14.2	16.6	16.0; 17.3	16.0	8.1; 24.0
Increase in dose or frequency	8.6	7.6;9.7	6.9	6.5; 7.3	0	0
Glucocorticoid joint injection	7.8	6.9; 8.9	14.0	13.4; 14.6	9.6	3.4; 16.4
Increase in dose of oral glucocorticoid	19.0	17.6;20.5	17.6	17.0;18.2	22.2	13.2;31.3
Effective therapy (none of the criteria)	15.5	14.2; 16.8	17.9	17.2; 18.5	14.8	7.1; 22.6

References:
[1] Curtis JR et al. Derivation and preliminary validation of an administrative claims-based algorithm for the effectiveness of medications for rheumatoid arthritis. Arthritis Res Ther. 2011;13(5).
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SAT0150 PROSPECTIVE, INTERVENTION, MULTICENTER STUDY OF UTILITY OF BIOLOGIC DRUG MONITORING WITH RESPECT TO THE EFFICACY AND COST OF ADALIMUMAB TAPERING IN PATIENTS WITH RHEUMATIC DISEASES: PRELIMINARY RESULTS OF INGEBIO STUDY

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Background: Adalimumab (ADL) tapering based on clinical assessment is a usual practice especially in patients who have achieved clinical remission.
Objectives: To analyze how personalized management guided by biological drug monitoring (BDM) in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) patients impacts the annual direct costs to the Health System and the quality-adjusted life year with respect to conventional practice in Spain. To evaluate the effectiveness of BDM in the reduction of the number of days with high disease activity compared with conventional practice.
Methods: In a pragmatic, non-randomized, non-inferiority clinical study, adult patients treated with ADL (40 mg sc) who remained clinically stable for at least 6 months were recruited in 3 sites. Patients were grouped in Control (CG) and Intervention groups (IG) according to the site. ADL frequency was adjusted based on physician criteria. Patients are assessed at 8 timepoints (8 visits) for up to 18 months. Trough ADL and anti-ADL antibodies levels are measured with Promonitor-ADL and Promonitor-ANTI-ADL (Progenika, SA). BDM data were released only to the IG, and blinded to the CG (managed according to clinical assessment only). Physicians in the IG were not obliged to follow any therapeutic algorithm based on BDM results but could use tests to alter doses based on their judgement. Endpoints include DAS28, BASDAI, BASFI and HAQ-DI scores at every timepoint. Cost-effectiveness will be evaluated according to associated costs and QALY.
Results: A total of 169 patients were recruited (disease, N IG, N CG, %) (RA, 30, 33, 37.3%; PsA, 33, 21, 32%; and AS, 46, 6, 30.8%). Median disease duration was 117, 98.5 and 101.5 months for RA, PsA and AS, respectively. At baseline, 10 (16.7%) and 29 (26.6%) patients had low disease activity, 50 (83.3%) and 80 (73.4%) patients were in remission, and median trough ADL levels were 5,5 and 5,3 mg/L in the CG and IG, respectively. Mean follow-up (FU) was 505 and 499 days in the CG and IG, respectively. ADL doses were tapered in 22/60 (36,7%) and 39/109 (35,8%) patients in the CG and IG, respectively. Patients were in remission an average of 329 vs 344 days in the CG and IG, respectively. The number of flares in the CG and IG was 53 and 69, respectively. The rate of flares per patient-year of FU is 0,639 vs 0,463 in the CG and IG, respectively (difference of -0,176; CI95%: -0,379 to 0,0289). The risk of flare is 27,5% lower in the IG (IRR=0,7252; CI95%: 0,4997 to 1,0578). Quality of life (EQ-5D-5L) was significantly better in the IG at visits 2 (p=0,001) and 3 (p=0,035); EQ-5D-5L was higher (although not statistically significant) in the IG in the remaining visits. Average cost of ADL per patient-year was 11.898,60€ vs 11.240,81€ (-657.78€) in the CG and IG, respectively.
Conclusions: Preliminary results show that rheumatic patients have better quality of life, lower risk of flares and incur in lower treatment costs if patient management is complemented with BDM data.
Disclosure of Interest: E. Ucar: None declared, Í. Gorostiza: None declared, C. Gómez: None declared, C. Pérez: None declared, J. De Dios: None declared, B. Alvárez: None declared, A. Ruibal: None declared, C. Stoye: None declared, M. Vasques: None declared, J. Belzunegui: None declared, A. Escobar: None declared, Z. Trancho: None declared, A. Ruiz del Agua Employee of: Employee of Progenika Grifols, A. Martínez Employee of: Employee of Progenika Grifols, C. Jorquera: None declared, D. Nagore Employee of: Employee of Progenika Grifols
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SAT0151 EFFICACY AND SAFETY OF BIOLOGIC THERAPY IN ELDERLY RHEUMATOID ARTHRITIS PATIENTS COMPARED TO YOUNG - A SYSTEMATIC REVIEW

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Background: Rheumatoid arthritis (RA) patients are disproportionately older (33% >60 years). With improved biologic therapy for RA, there is a need to understand the efficacy and safety of biologic therapies in older RA (oRA) patients.
Objectives: To systematically review published literature to summarize the available evidence of efficacy and safety of biologic agents in oRA compared to young RA (yRA) patients.
Methods: A search in EMBASE, MedLine, Toxline, clinicaltrials.gov and Cochrane database was performed to identify clinical trials (RCT) and observational (OBS) studies of >6 months comparing the efficacy and safety of biologic agents in oRA relative to yRA. The biologics of interest were all anti-TNF agents, abatacept (ABA), tocilizumab (TCZ), rituximab (RTX) and tofacitinib (TOF). English language studies conducted in adult RA that reported age-associated outcomes were included. Studies assessing juveniles, inflammatory arthritis or not reporting older age outcomes were excluded. Safety outcomes included infections, adverse drug reactions (ADR), and malignancy. 2 independent rheumatologists reviewed abstracts, full text articles, and abstracted data from included articles. Conflicts were resolved by a 3rd reviewer. Abstracted data was summarized and evaluated for use within a meta-analysis
Results: Of 5353 abstracts, 187 were identified for full text review and 32 articles were included in this review. Articles were focused on efficacy (n=9), safety (n=15), or both (n=8). Most articles (n=22; 69%) focused on anti-TNF agents, then TCZ (n=4), ABA (n=2), TOF (n=2), RTX (n=1) and all biologics (n=1). Most studies were OBS studies (n=28, 88%) and fewer (n=4) were post-hoc analyses of RCT. In total, 99947 unique patients were identified, of which ~24% were older. Most studies used valid definitions of RA and outcomes; only 25% of the studies have <20% loss to follow up. There was heterogeneity in reporting outcomes and time of follow up.
Out of the 12 efficacy studies focusing on anti-TNF agents, 9 (75%) showed a reduced efficacy in oRA on DAS28, HAQ, CDAI, SDAI, EULAR or ACR response scales relative to yRA. Studies focusing on TCZ (n=2) and RTX (n=1) also showed a reduced efficacy in oRA. OBS studies in ABA (n=2) showed comparable efficacy in oRA and yRA. Meta-analysis was limited by heterogeneity.
Safety was the focus of anti-TNF (n=15), TCZ (n=3), 2 on TOF (n=2), 1 on ABA (n=1), RTX and all biologics (n=1) studies. Among these 23 safety studies, 74% (n=17) demonstrated worse safety outcomes in oRA. like in oRA. Of studies focusing on infection in anti-TNF agents, 82% (9 of 11) reported increased risk in oRA. Among the anti-TNF studies, 2 out of the 4 (50%) measured more ADR in oRA. A meta analysis of 4 studies reporting infectious outcomes in anti-TNF agents at >1 year found a pooled risk estimate was 1.59 (95% CI 1.45–1.76).

Figure 1: Forest plot of studies of anti-TNF agents measuring risk ratio of efficacy on EULAR or DAS28 response scale

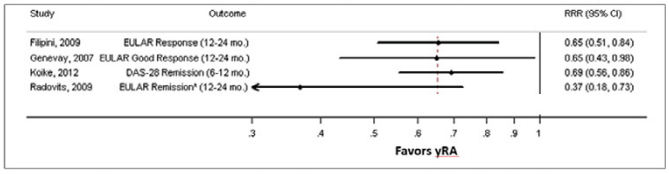
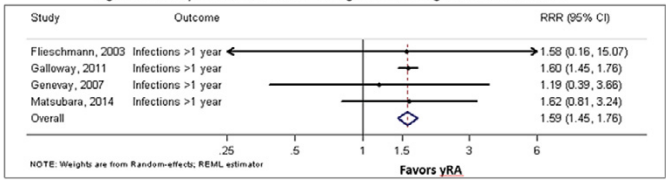


Figure 2: Forest plot of studies of anti-TNF agents measuring risk ratio of infections



Conclusions: There is heterogeneity within the literature of biological agents in RA, particularly when age is considered. Given the anticipated population increase in the oRA, there is an urgent need for analysis of these medications in oRA patients for both safety and efficacy.
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