comparison of the data obtained, the adverse events reported for each drug were normalized using the number of treatments for the same period. The reporting odds ratio (ROR) and its 95% confidence intervals (CI) were calculated regarding the different categories of adverse events. The incidence of serious adverse events, serious infections, withdrawals due to adverse events and deaths were also calculated.

Results: The EudraVigilance database contains 851 882 adverse events reported for IFX, ETN, and ADA. During this period, the different TNF antagonists have shown almost the same safety profile. The reported adverse events were classified by systems organ class (SOC) and the most frequent were administration site conditions (28.8%) and infections and infestations (11.2%), Safety was not statistically different. The comparison between IFX originator and its biosimilar did not show statistically significant differences in safety (ROR 1.08 [0.80, 1.46]) during the initial 3-years after launch for both drugs. However, a small non-significant increase in immune reactions during administration was reported for IFX-biosimilar, which might reflect increasing attention for this class of drugs.

Conclusions: The comparison of reference IFX and IFX-biosimilar did not demonstrate statistically significant differences in safety. This pharmacovigilance study provides the first analysis of TNF antagonists from the EudraVigilance database and offers a framework for safety comparison between originators and biosimilar TNF antagonists.

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SAT0047 PREDICTING MAINTENANCE OF RESPONSE BASED ON DISEASE CHARACTERISTICS AND EARLY CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS UPON WITHDRAWAL OF ADALIMUMAB

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Background: Some patients (pts) with rheumatoid arthritis (RA) achieve low disease activity (LDA) after treatment with adalimumab (ADA) plus methotrexate (MTX) and can maintain LDA after ADA withdrawal[1]. However, others experience a flare in disease activity. The factors associated with loss or maintenance of response are not understood.

Objectives: To identify pt disease characteristics and early clinical responses, which predict maintenance of LDA upon ADA withdrawal in individual RA pts.

Methods: Data from the OPTIMA trial were used in this *post hoc* analysis. In period 1 (P1), pts were treated for 26 weeks (wks) with ADA+MTX or placebo (PBO) +MTX. Pts on ADA+MTX who achieved DAS28-CRP <3.2 at wks 22 and 26 (responders) were randomized to ADA withdrawal, or ADA+MTX continuation up to Wk 78. Responders to PBO+MTX in P1 continued on PBO+MTX up to Wk 78 (PBO continuation). Data from the ADA withdrawal arm were used to predict LDA at Wk 78 by DAS28-CRP (≤3.2) or SDAI (≤11). Potential factors including baseline (BL) disease characteristics and Wk 26 responses, including DAS28-CRP, SDAI, ACR score components, modified total sharp score (mTSS) and joint space narrowing score (JSN), were screened by the LASSO method[2], which performs variable selection by penalizing unduly complicated models, with/without incorporating the speed of DAS28-CRP or SDAI response as an individual predictor. Logistic regression on the LASSO-selected factors yielded coefficients used to derive individual scoring equations and prediction scores for Wk 78 outcomes (fig footnote). Prediction score cutoffs were established by the regression tree method[3]. The results were validated in data from the PBO continuation arm.

Results: For the prediction of DAS28-CRP LDA at Wk 78, BL physician global assessment (PhGA) and health-assessment questionnaire-disability index (HAQ-DI), and Wk 26 DAS28-CRP, HAQ-DI, JSN and CRP were selected by LASSO, and used to calculate the prediction score. Including speed of response did not affect the predictors chosen. Out of 9 pts predicted not to have DAS28-CRP LDA at Wk 78, 0 had LDA (NPV=100%) (fig 1). Out of 66 pts predicted to have DAS28-CRP LDA at Wk 78, 63 predictions were correct (PPV=96.5%). Results were comparable for most cutoff categories in the validation arm (PPV=82%); however, no pts were predicted to have a non-response at Wk 78. For the prediction of SDAI LDA at Wk 78, the NPV was 86% (1/7 predictions incorrect); PPV was 95% (39/41 predictions correct); in the validation arm, the PPV was 82%.

Conclusions: DAS28-CRP LDA at 78 wks could be individually predicted for up to 63% pts in OPTIMA who withdrew ADA/continued PBO+MTX with 96.5% accuracy, based on demographics and clinical outcomes at 6 months. This instrument could help identify pts who may be able to maintain LDA upon ADA withdrawal.

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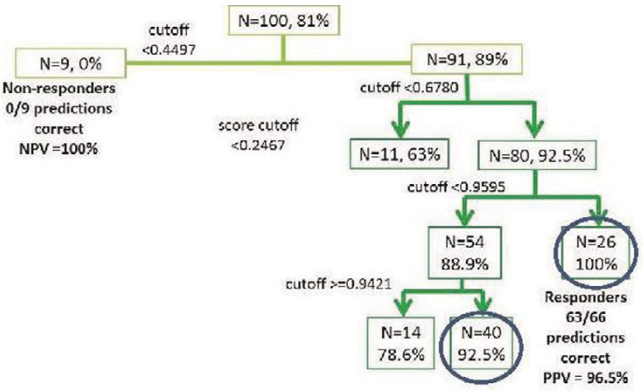

Figure 1: Regression tree to predict Week 78 DAS28-CRP LDA. The percentages of patients with an LDA response at Week 78 are indicated in the boxes. The encircled boxes indicate the patients predicted to have LDA at Week 78.

Individual scoring equation for reaching Week 78 DAS28_LDA: Logit = 6.717 – 0.212*HAQ – 0.039 * PhGA – 0.004 *DAS28_WK26 – 1.393*HAQ_WK26 - 0.027*JSN - 0.292*CRP_WK26

For reaching Week 78 SDAI LDA: Logit = 4.668 – 0.028 * PhGA – 0.161*CRP_WK26 – 1.411*RoW_indicator; RoW = rest of the world, including Argentina, Australia, New Zealand, South Africa

Individual prediction score: $\frac{\exp(logit)}{1+\exp(logit)}$.

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SAT0048 THE PATTERN OF ACPA REACTIVITIES IN ANTI-CCP POSITIVE INDIVIDUALS WITH NON-SPECIFIC MUSCULOSKELETAL SYMPTOMS AT RISK OF DEVELOPING RA

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Background: There is today a paucity of prospective studies to describe the natural longitudinal history of anti-ccp positive individuals developing RA or not developing RA. Further no study to investigate the detailed ACPA reactivities in such a setting is currently available.

Methods: Individuals at risk of developing RA were included in a cohort at Karolinska University Hospital, Stockholm. Examinations of peripheral joints was repeated at one year follow-up visit or at any time the patients experienced worsening of their symptoms. Peripheral blood samples were available at inclusion (n=70). Serum was run on a microarray based on the ImmuoCAP ISAC system testing for ACPA reactivities toward 13 different citrullinated peptides (fillagrin, fibrinogen, alpha-enolase, vimentin, histone) (1).

Results: Individuals referred from primary care with musculoskeletal complaints and positive anti-ccp test were systematically investigated as part of routine care at our rheumatology clinic. Individuals lacking self-reported history of suspect arthritis, clinical arthritis according to rheumatologist and signs of synovitis on ultrasound examination were included in a clinical Risk-RA program with life-style coaching and personalized information on the risk of developing RA. Seventy individuals, with a mean age of 48 years (SD 15) and 86% females, were included in the program. Twenty (29%) individuals developed arthritis during a medium follow up time of 7 months (range 1–25 months).

Number of ACPA reactivities at baseline was significant higher among those developing (in mean 6 reactivities) as compared to those not developing arthritis (in mean 4 reactivities). A increased proportion of individuals were showing reactivity towards citrullinated (cit) vimentin (vim) 60–75, fibrinogen (fib) 573 and enolase (eno) (CEP-1) among those developing arthritis (80% for anti-cit-vim 45% for anti-cit-fib and 60% for anti-cit eno) as compared to those not developing arthritis (41% for anti-cit-vim, 30% for anti-cit-fib and 52% for anti-cit-eno). Increased level of anti-cit-vim and anti-cit-eno antibodies was also observed at inclusion for those individuals developing arthritis as compared to those not developing arthritis.

Conclusions: We describe here the pattern of ACPA reactivities in anti-CCP positive individuals with non-specific musculoskeletal symptoms at risk of developing RA and without clinical and ultrasonograph signs of synovitis and report that 30% of these patients will develop arthritis during a short follow-up. Number, frequency and titers of specific ACPA reactivities appear to be enriched already at inclusion among those patients that developed arthritis during follow-up.

References:

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SAT0049 21ST CENTURY STATE OF RHEUMATOID ARTHRITIS MANAGEMENT IN THE UK

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Background: The rheumatoid arthritis (RA) Treat to Target (T2T) recommendations[1] defined in 2010 aimed to support clinicians to achieve optimal therapeutic outcomes for their patients.
Objectives: 38 hospitals prospectively audited management of newly diagnosed RA patients to determine compliance with the T2T recommendations and therapeutic outcomes achieved.
Methods: From April 2012 to September 2016 and upon diagnosis of RA, data on disease history, management and clinical outcomes were collected prospectively in a web based tool. Follow up to date provides data for up to 24 months from diagnosis (baseline).
Results: 1571 patients were recruited in 38 centres, with 12 months' follow up for 713 patients and of these 269 also had 24 months' follow up. 1021 (65%) patients were female and 1360 (87%) had a treatment target documented at baseline (1235 [79%] disease activity score 28 (DAS28) remission and 125 [8%] low disease activity state (LDAS)). DAS28 remission is defined as DAS28 <2.6, LDAS is defined as DAS28 ≥2.6<3.2. Median baseline DAS28 scores were 4.9 and 5.3 for patients having a DAS28 remission and LDAS target, respectively. The table shows DAS28 scores at baseline, 12 and 24 months, and disease management received for the subset of patients with available DAS28 scores at the relevant time points, stratified by those who did/did not achieve their remission target and those with/without sustained remission at 24 months. Of the 108 patients eligible to receive biologic therapy, according to NICE guidance, 39 (36%) received a biologic within their first 24 months of treatment.

	Patients with 12 months follow up (n=713)		Patients with 24 months follow up (n=269)	
	In remission at 12 months [n=276]	Not in remission at 12 months [n=239]	Sustained remission at 24 months [n=32]	Remission not sustained at 24 months [n=96]
% patients compliant with TTT standards				
N (%) with baseline target set (remission or LDAS)	244 (88%)	183 (77%)	29 (91%)	76 (79%)
N (%) with >4 visits in the first year of management	207 (75%)	175 (73%)	31 (97%)	81 (84%)
N (%) with >4 DAS scores in the first year of management	180 (65%)	155 (65%)	24 (75%)	48 (50%)
N (%) with dual therapy within 6 months of diagnosis	148 (54%)	154 (64%)	17 (53%)	53 (55%)
Disease scores				
median baseline DAS28 (n with available score)	4.6 [n=226]	5.1 [n=193]	4.5 [n=26]	5.3 [n=67]
median 12 month DAS28 (n with available score)	1.9 [n=276]	3.9 [n=239]	1.9 [n=23]	2.9 [n=63]
median 24 month DAS28 (n with available score)	2.1 [n=43]	3.4 [n=43]	1.6 [n=32]	3.0 [n=96]

Conclusions: The results suggest that more patients with a target set at baseline are in remission at 12 months and at 24 months than those without a target set. Number of visits, number of DAS28 scores and starting dual therapy within 6 months do not appear to affect the proportion of patients in remission at 12 months, but active management in the first 12 months (>4 visits, >4 DAS28 scores) does appear to be associated with more patients in remission at 24 months. Thus we conclude that treating RA early and aggressively, in line with the T2T guidelines, leads to sustained clinical improvement.
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SAT0050 EARLY RESPONSE TO CERTOLIZUMAB PEGOL IN RHEUMATOID ARTHRITIS PREDICTS OUTCOME: DATA FROM A PROSPECTIVE OBSERVATIONAL STUDY

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Background: Treat-to-target strategies for rheumatoid arthritis (RA) require reliable clinical markers of treatment response in order to adapt therapy. Markers of early treatment failure can be used to ensure that patients (pts) are not unnecessarily exposed to ineffective therapy. Data from interventional clinical trials suggest that early clinical measures of disease activity (such as CDAI, DAS28 or HAQ-DI) after 12 weeks (wks) of treatment can reliably predict treatment failure at 1 year (yr).[1–3] However, it is unknown how such indicators perform in real-world settings.
Objectives: To evaluate the performance of clinical markers of early treatment failure (Wk12) as predictors of treatment failure at 1yr in everyday clinical practice.
Methods: Data from a 1yr interim analysis of the ECLAIR study were used: a longitudinal, prospective, observational, multicentre study of pts with RA starting treatment with certolizumab pegol (CZP) in France. Pts were evaluated at study entry and thereafter at 3-monthly routine consultations. Disease activity was assessed at each visit using CDAI, DAS28 and HAQ-DI. At Wk12, pts with missing data or no longer taking CZP were excluded from the analyses. Linear interpolation, LOCF or NRI were used to impute missing data at 1yr, including data from pts who left the study early. Different definitions for treatment non-response were applied based on CDAI or ΔDAS28 and ΔHAQ-DI relative to pre-treatment values. Non-response at Wk12 was defined as CDAI>10, ΔDAS28<1.2 or ΔHAQ-DI<0.22. Then, failure at 1yr was defined as CDAI>22, DAS28>3.2 and HAQ-DI>0.5. Positive predictive values (PPV; proportion of treatment failures at 1yr in Wk12 non-responders) were used to evaluate the predictive performance of each tool.
Results: Overall, 792 pts were enrolled and data from 730 pts analysed. Performance of CDAI at predicting treatment failure at 1yr was assessed in 532 pts (198 data values missing at Wk12). Response and failure rates at Wk12 and 1yr are presented (see Table). The PPV for CDAI was 88.8%, indicating that almost 9/10 pts identified as non-responders at Wk12 fail to respond at 1yr. Specificity was also high (96.0%), indicating that <5% of pts who achieved CDAI response at 1yr were non-responders at Wk12. Similar analyses performed for DAS28 and HAQ-DI produced PPVs of 69.0% and 75.4%, respectively.

Table: Response and failure rates of CZP-treated patients at Week 12 and 1 year

	CDAI at 1 year		
CDAI at Week 12	**>22 (Failure)**	**≤22 (Response)**	**Total**
>10 (Non-response)	79	10	89
≤10 (Response)	205	238	443
Total	284	248	532
	Sensitivity=27.8%, Specificity=96.0%, PPV=88.8%, NPV=53.7%		
	DAS28 at 1 year		
ΔDAS28 at Week 12	**>3.2 (Failure)**	**≤3.2 (Response)**	**Total**
<1.2 (Non-response)	136	61	197
≥1.2 (Response)	102	135	237
Total	238	196	434
	Sensitivity=57.1%, Specificity=68.9%, PPV=69.0%, NPV=57.0%		
	HAQ-DI at 1 year		
ΔHAQ-DI at Week 12	**>0.5 (Failure)**	**≤0.5 (Response)**	**Total**
<0.22 (Non-response)	175	57	232
≥0.22 (Response)	154	110	264
Total	329	167	496
	Sensitivity=53.2%, Specificity=65.9%, PPV=75.4%, NPV=41.7%		

CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score; HAQ-DI: Health Assessment Questionnaire-Disability Index; NPV: Negative predictive value; PPV: Positive predictive value.

Conclusions: The PPV describing the performance of early CDAI measure as a