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THU0207 FINDING THE OPTIMAL TREATMENT STRATEGY FOR DISEASE ACTIVITY-GUIDED DOSE REDUCTION OF ADALIMUMAB AND ETANERCEPT IN RHEUMATOID ARTHRITIS: A MODELLING STUDY

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Background: Several studies have shown that disease activity-guided dose reduction without deterioration of disease activity is possible, while saving costs in patients with stable and low disease activity.⁽¹⁾ Despite these positive results, questions remain on the optimal tapering strategy. Different strategies are conceivable, with varying results regarding the balance between number of flares, utilities and costs.

Objectives: The objective of this study was to investigate the most cost-effective TNFi dose reduction strategy for RA patients using a modelling design.

Methods: In a cost-utility analysis using Markov modelling based on data from the DRESS study, STRASS study, and the RA Nijmegen cohort, the following strategies were tested against continuation: 1. Four-step DRESS tapering (figure 1: 100%–67%–50%–0%); 2. Tapering with an extra dosage step of 33%; 3. Tapering without withdrawal; 4. Use of a stricter flare criterion (DAS >2.6); and 5. Use of a predictor (biomarker: 80% specific, 80% sensitive, € 100 per test) for successful tapering. Scenario analyses with 30% and 50% drug price discount and no discounting were executed. Also, it was examined how well a biomarker should be able to predict to become cost-effective compared to the other strategies.

Results: All examined tapering strategies were found to be cost saving but yielded more short-lived flares compared to continuation (table 1). The change in utilities was minimal and not clinically relevant. Strategy 1 was cost-effective compared to all other strategies (highest incremental Net Monetary Benefit (iNMB)). However, there was a large overlap in credible intervals, especially between strategy 1 and 2. Scenario analyses showed that 50% reduction of drug prices would result in the highest iNMB for strategy 2. A biomarker only becomes cost-effective when it has a sensitivity and specificity of at least 86%.

Data is mean values per patient over 1.5 years (95% credible intervals). *Stricter flare criterion (DAS28 >2.6). ** NMB=QALYs * WTP/WTa – costs; iNMBs are given at a WTP/WTa of € 80 000.

Conclusions: All dose reduction strategies dominated the continuation strategy regarding cost-effectiveness. Because our study showed a comparable iNMB for tapering in four or five steps, we recommend a choice between these strategies, based on shared decision making.

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THU0208 EFFECTIVENESS AND SAFETY OF CERTOLIZUMAB PEGOL IN RHEUMATOID ARTHRITIS PATIENTS AFTER FAILURE TO ANTITNF OR NAÏVE PATIENTS IN REAL WORLD SETTING. ONE YEAR FOLLOW-UP EXPERIENCE

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Background: Between 30%–40% of patients with rheumatoid arthritis (RA) discontinue at their first line biological therapy due to inadequate response or adverse events. There is currently a great controversy about using a second anti-TNF, after failure to the first one, or a therapeutic target change, due to the availability of a wide pharmacological arsenal for patients with RA.

Objectives: The objective of this study is to determine the effectiveness and safety during one year of Certolizumab pegol (CZP) in patients with RA in second line (after failed to a previous antiTNF) and compare it with those who received this therapy as first line (bio-naïve).

Methods: National, observational, prospective, longitudinal and multicenter study in patients with RA who received CZP as the first line of biological treatment or failure to a previous anti-TNF for lack of efficacy, during one year of follow-up. Demographic and clinical variables were collected (gender, age, disease duration, TJC, SJC, ESR, CRP, DAS28, HAQ), at baseline visit, 3 and 12 months of treatment. As response variables, DAS28 remission, low disease activity by DAS28 (LDA) and EULAR response, were used. The Student t test and the Mann-Whitney U test were used for the statistical analysis and a survival analysis (Kaplan-Meier) was performed

Results: A total of 360 patients were included, of which 272 (75.6%) were bio-naïve and 88 (24.4%) previous anti-TNF failure. Baseline characteristics of both groups are shown in table 1. Clinical variables of effectiveness at 3 and 12 months are summarised in table 2. Statistically significant differences in DAS28, HAQ and % patients with corticosteroids were observed in both groups at year of treatment comparing with baseline, even though bio-naïve group had a statistically lower DAS28 and a higher percentage response than the antiTNF failure group. According to Kaplan-Meier analysis, similar retention rates were observed independently if CZP were used as first (77.2%) or second line (73.9%). No differences were found in terms of safety at one year of treatment between both groups.

Conclusions: This study, derived from the experience of national clinical practice with CZP, demonstrates the effectiveness and safety of this drug in patients with RA regardless of its use in the first line or after failure to a previous antiTNF, with better response scores in bio-naïve patients. No differences were observed in the retention rate in both groups.

Abstract THU0207 – Table 1. Main outcomes of each strategy

Outcome measure	0. Continuation (comparator)	1. DRESS strategy (four-step tapering)	2. Five-step tapering	3. No withdrawal	4. Stricter flare criterion	5. Predictor
Costs (€)	21 071 (20,563–21,383)	13 198 (12,469–13,988)	13 794 (13,150–14,496)	14 266 (13,685–14,856)	15 943 (15,115–16,793)	14 327 (13,281–15,359)
QALYs	1.182 (1.165–1.199)	1.177 (1.160–1.193)	1.181 (1.165–1.197)	1.182 (1.166–1.198)	1.189 (1.173–1.205)	1.185 (1.168–1.200)
Mean number of short-lived flares	0.53 (0.35–0.73)	0.97 (0.83–1.12)	0.74 (0.58–0.93)	0.69 (0.52–0.87)	2.08* (1.80–2.41)	0.55 (0.53–0.56)
iNMB**	-	7434 (6,514–8,302)	7176 (6,307–8,000)	6798 (5,977–7,539)	5650 (3,598–7,625)	6938 (5,863–8,040)

Abstract THU0208 – Table 1. Baseline characteristics

	Bionave	Bioexperience (after antiTNF failure)	P
Gender, female %	78.3	73.9	NS
Age, years, mean (Q1-Q3)	52.8 (18-82)	54.8 (19-82)	NS
Disease duration, years, mean (Q1-Q3)	5.8 (0-37)	8.0 (1-33)	<0.001
> 2 yr	58.2	89.0	<0.001
Never smoker %	68.4	69.2	NS
Seropositivity, %	73.9	73.6	NS
Erosions, %	47.6	61.9	0.023
Comorbidities (yes), %	32.7	40.9	NS
Corticosteroids (yes), %	72.8	63.6	NS
Prior Biologic Treatment %	-	Etanercept 46.6 Adalimumab 39.8 Infliximab 11.4 Golimumab 2.3	
CZP monotherapy, %	14.3	19.3	NS
>1 concomitant csDMARD, %	8.5	2.3	0.047
TJC, mean (SD)	9.3 (±6.2)	9.6 (±6.4)	NS
SJC, mean (SD)	6.7 (±4.7)	7.2 (±5.8)	NS
CRP, mg/L, mean (SD)	6.6 (±15.8)	9.2 (±14.7)	NS
ESR, mean (SD)	29.6 (±22.8)	30.1 (±24.5)	NS
HAQ, mean (SD)	1.2 (±0.7)	1.2 (±0.7)	NS
DAS28, mean (SD)	4.7 (±1.1)	4.7 (±1.1)	NS

Disclosure of Interest: None declared

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THU0209 4 YEARS FOLLOW-UP OF A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS IN SUSTAINED CLINICAL REMISSION AND OPTIMISATION OF BIOLOGICAL THERAPY

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Background: The objectives of Rheumatoid Arthritis (RA) treatment comprise achieving persistent Clinical Remission (CR) or sustained low clinical activity. Nowadays management follows a “treat to target” strategy based on adjustment of treatment in accordance with protocols. In patients with persistent disease activity after treatment with at least two of the classic disease-modifying antirheumatic drugs the use of biological therapy is recommended. Once sustained CR is achieved, the most efficient strategy is optimisation, by tapering the dose of the biological therapy or by increasing administration intervals. Searching for the lowest effective dose for each patient could minimise the risk of adverse effects and improve the cost-effectiveness of RA treatment.

Objectives: To prove that the performance of an optimisation strategy in patients with RA and sustained CR under biological treatment maintains the proportion of patients with DAS28 ≤2.6 after 4 years, to assess the maintenance of the effectiveness of the optimisation at 4 years in terms of clinical manifestations, and to analyse the time until relapse.

Methods: An open observational prospective study that included 70 patients with RA (CREATE registry) in CR at least for 6 months, under treatment with tapered dose of biological therapy (TNFi, abatacept or tocilizumab). Treatment effectiveness was assessed with the main variable DAS28 ≤2.6. Statistical analysis included a descriptive study of variables and a confidence interval of 95% (95% CI) was estimated. For bivariate analysis, we used Student t-test for independent samples, repeated measures analysis of variance and mixed analysis of variance, and as a post-hoc contrast, Sidak adjustment. The log-rank test was used to compare the time until relapse according to the biological therapy.

Results: The mean age of the patients was 56.9 (13.7) years, 78.6% were women, 68.8% were rheumatoid factor (RF) positive and 66.7% ACPA positive; the mean DAS28 at the beginning of the optimisation was 2.24 (0.73). After 4 years, 27.7% (95%CI:16.82%–38.58%) of patients maintained CR with the optimised dose, with a DAS28 2.15 (0.81). Through the first year, the percentage of relapses was 15.71%, in the second year, 7.35% and 4.61% relapsed during the third year. The median time of optimisation until relapse was 13.83^{3,18} months (95% CI:7.6–20.06). No significative differences were found at comparing the survival curves of the optimised patients until relapse for 4 years according to the biological therapy (TNFi vs no TNFi) (log-rank test:0.865, p:0.352) (graphic).

Conclusions: After 4 years, all of the patients maintained DAS28 levels of low disease activity, including those who had suffered a previous relapse and had turned back to the previous dose of biological treatment. In view of this outcomes, optimisation strategy in clinical practice is possible and effective in patients with persistently controlled RA.

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THU0210 SAFETY, TOLERABILITY AND EFFICACY OF SUBCUTANEOUS TOCILIZUMAB ADMINISTERED AS MONOTHERAPY OR IN COMBINATION WITH CSDMARDS IN RHEUMATOID ARTHRITIS: RESULTS FROM THE OSCAR STUDY

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Background: Efficacy and safety of intravenously (IV) administered tocilizumab (TCZ) in rheumatoid arthritis (RA) has been shown. Recently, efficacy and safety was confirmed for subcutaneous (SC) administration of TCZ.¹ The possible effects of SC TCZ upon tapering of GCs/NSAIDs has not been investigated.

Objectives: First, to establish the safety and efficacy of SC TCZ monotherapy or in combination with csDMARDs in DMARD-IR RA. Second, to assess GC/NSAID dose reduction and/or discontinuation under SC TCZ treatment.

Methods: The OSCAR study was a Dutch multicenter, open-label, single arm phase IV study within the phase 4 TOZURA program.¹ RA patients with an inadequate response (IR) to csDMARDs and 1 bDMARD were treated with weekly SC

Abstract THU0208 – Table 2. Effectiveness of CZP. Comparing at 12 months bionave and bioexperience groups

	Bionave	Baseline Bioexperience (after antiTNF failure)	Bionave	3 months Bioexperience (after antiTNF failure)	Bionave	12 months Bioexperience (after antiTNF failure)	P
HAQ, mean (SD)	1.2 (±0.7)	1.2 (±0.7)	1.1 (±0.7)	1.1 (±0.7)	0.9 (±0.6)	0.9 (±0.7)	0.925
DAS28, mean (SD)	4.7 (±1.1)	4.7 (±1.1)	3.5 (±1.3)	3.7 (±1.2)	3.0 (±1.3)	3.4 (±1.3)	0.011
Corticosteroids (yes), %	72.8	63.6	61.8	56.8	43.8	45.5	0.780
DAS28 remission,%	-	-	25.2	17.9	45.5	32.1	0.031
DAS28 LDA,%	-	-	43.6	31.0	61.7	45.2	0.008
EULAR Response,%	-	-	60.2	54.8	77.1	64.3	0.020