SAT0150

EFFICACY OF TOCILIZUMAB FOR SUPPRESSING RADIOGRAPHIC PROGRESSION OF CERVICAL LESIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARISON WITH METHOTREXATE; THREE YEARS OF FOLLOW-UP ~A MULTICENTER REGISTRY STUDY ~

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Background: Cervical lesions are known to occur at high frequency as a complication of rheumatoid arthritis (RA). Treatment with biological agents are more clinically effective than the DMARDs that were in use previously, in particular, with their efficacy in suppressing joint destruction having been emphasized. We reported the efficacy of infliximab, anti-tumor necrosis factor antibodies for suppressing the radiographic progression of RA cervical lesions at ACR2009, EULAR2010, 11, 12, 13, 14, 16 and 18. However there is still few studies of efficacy of against RA cervical lesions of Tocilizumab (TCZ), anti-interleukin 6 receptor antibody.

Objectives: To evaluate the efficacy of TCZ for suppressing the radiographic progression of RA cervical lesions comparison with MTX for 3 years.

Methods: We used TCZ or MTX for treating Japanese patients with active RA who fulfilled the ACR criteria in 1987. The final study cohort of each 50 and 75 patients received continuous TCZ and MTX treatment for at least 3 years. For evaluation of cervical lesions, the atlanto-dental interval (ADI), the space available for the spinal cord (SAC), and the Ranawat value were measured by plain lateral radiographs in the flexion position, at initiation and Year 1,2 and 3.

Results: In the patients receiving TCZ (n=50) and MTX (n=75), the number of female were each 38(76%) and 52(69%) cases(p=0.416). The mean age was 58.7 ± 13.0 and 63.6 ± 11.0 years old (p=0.046); disease duration was 7.7 ± 7.8 and 8.0 ± 9.5 years (p=0.247) and the mean dose of MTX was 9.2 ± 3.6 and 8.2 ± 2.9 mg/w (p=0.146). Clinical findings related to RA were as follows; CRP 4.2± 3.4 and 1.7± 2.3 mg/dl(p<0.001); ESR 55.0± 24.0 and 31.9 ± 21.8mm/h(p<0.001); MMP3 401 ± 311 and 223 ± 350ng/ml(p<0.001); the number of RF-positive 40 (80%) and 60(80%) cases(p=0.999); DAS28-ESR 5.45 ± 0.98 and 4.30 ± 1.38 (p<0.001); ADI 2.9 ± 1.7 and 2.6 ± 1.6mm(p=0.335); SAC 18.9 ± 2.7 and 20.8 ± 2.5mm(p<0.001) and Ranawat value 15.2 ± 1.6 and 16.0 ± 1.5mm (p=0.008).

The respective changes in cervical lesion parameters after 3 years were as follows: ADI: 0.46 ± 0.79 and 0.71 ± 0.80 mm (p = 0.044); SAC: -0.34 ± 0.63 and -0.63 ± 0.82 mm (p = 0.027); and Ranawat value: -0.32 ± 0.59 and -0.44 ± 0.66 mm (p = 0.295) between TCZ and MTX patients (Fig.1).

The numbers of patients who did not showed progression in ADI, SAC and Ranawat value were each 34(68%) vs 37(49%) cases(p=0.039); 37 (74%) vs 40(53%) cases(p=0.020) and 37(74%) vs 49(65%) cases (p=0.306) after 3 years. Also the number who was able to suppress progression in all three parameters were each 34 cases (68%) receiving TCZ and 37 cases (49%) receiving MTX (p=0.039) after 3 years (Fig.2).

Conclusion: This study suggested that TCZ treatment can be used to suppress the progression of RA cervical lesions more than MTX treatment.

Figure 1 : Respective changes in ADI, SAC and Ranawat value from Year 0 to Year 3 between TCZ and MTX patients

Figure 2 : The rate of patients who did not showed progression in ADI, SAC, Ranawat value and all three parameters after 3 years

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SAT0151

TIME TO INITIATION OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN THE FRENCH COHORT ESPOIR

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Background: Access to biologic Disease-Modifying Anti-Rheumatic Drugs (DMARDs) of early rheumatoid arthritis (RA) patients is highly variable across countries and may depend on patient characteristics, disease expression, physicians behaviors as well as care organization in the patient region of living.

Objectives: 1) To assess the time to initiation of bDMARDs in the French cohort ESPOIR, and 2) To assess the factors associated with the timing of bDMARD initiation.

Methods: In this national multicenter cohort, 813 adult patients with suspected or confirmed early RA were included between December 2002 and March 2005, and followed up during 10 years. In the present analysis, we considered only patients who were fulfilling the ACR-EULAR 2010 criteria for RA at baseline. The primary outcome was the time to initiation of a biologic DMARD, in months, since diagnosis. It was assessed by Cox model based survival analysis with time dependent covariates; the threshold used for p-value was 0.05. Predictors collinearity was then assessed by adapted tests. All statistical analysis were done with R version 3.5.1.

Results: Among the 658 patients fulfilling the ACR-EULAR 2010 criteria for RA (77% women, 52% smokers at baseline, mean-aged 48 at diagnosis, with positive RF in 46.6%, positive ACPA in 43% and polyarticular presentation at baseline in 54.5%), 178 patients (31%, CI 95%=[27%;34.7%]) initiated a biologic DMARD during the 10-year follow-up (Figure 1). Variables associated with an earlier bDMARD initiation in the bivariate analysis were: 1) at baseline: younger age (p = 0.0016), younger age of first joint pain (0.0014), younger age of first joint swelling (0.0014), 2) during the follow up: joint pain (p < 0.0001), high HAQ (p <

0.0001) and DAS28 ($p < 0.0001$), radiologic progression ($p < 0.0001$), positive RF ($p < 0.0001$), positive ACPA ($p < 0.0001$), elevated ESR ($p < 0.0001$) and CRP ($p < 0.0001$). In multivariate analysis, DAS28 ($p < 0.0001$), radiologic progression ($p < 0.0001$) and positive ACPA ($p = 0.000176$) were significantly associated with an earlier initiation of a biologic DMARD, whereas an older age of first joint pain was a protective factor ($p < 0.0001$) (Table 1).

Conclusion: In this study, less than one third of the ESPOIR cohort patients initiated a bDMARD over the 10-year follow-up. RA poor prognostic factors were associated with earlier initiation as expected.

Figure 1: Biotherapy onset in the ESPOIR cohort

Table 1. Results of the multivariate analysis

Covariates	Hazard-ratios [95% CI]	p-value
Age of 1st joint pain	0.97 [0.96 ; 0.98]	< 0.0001
DAS28	2.04 [1.84 ; 2.26]	< 0.0001
Structural damage on X-rays	2.30 [1.64 ; 3.22]	< 0.0001
Positive ACPA	2.01 [1.40 ; 2.89]	0.000176

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PREVALENCE AND SUCCESS OF 'TRY AND SEE' SUBCUTANEOUS BIOLOGIC DMARD DOSE REDUCTION IN ROUTINE CARE AND COST SAVING IMPLICATIONS

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Background: Biologic disease modifying anti-rheumatic drugs (bDMARD) are widely used in rheumatologic practice. Subcutaneous bDMARDs are licenced in a fixed dose for all indications (RA, PsA, AS) yet therapeutic drug monitoring (TDM) of TNF inhibitors (TNFi) reveals a wide range of serum drug concentrations (1). EULAR recommendations (2) state that 'one can consider tapering bDMARDs' if a patient is in persistent remission (usually by lengthening the interval between subcutaneous injections), and in trials up to 80% sustain remission after tapering over 39 weeks (3). In routine care bDMARD dose reduction is usually initiated on a 'try and see' basis, in the absence of guidelines.

Objectives: To assess the prevalence and success of subcutaneous bDMARD dose reduction in routine care, per disease indication and bDMARD class, and the cost saving implications.

Methods: Dose interval information was collected prospectively in patients on subcutaneous bDMARDs with RA, PsA and AS attending for routine

review at St George's University Hospitals NHS Foundation Trust from October – November 2018. Department practice is that bDMARD dose reduction is discussed (but not mandated) with patients in sustained remission on a 'try and see' basis, without TDM.

Results: Data on 88 patients (female 46) were collected, RA 39, PsA 36, AS 13, mean age 50 years (range 24-78), TNFi n=75, other bDMARDs n=13. The dose interval was per licence in 79.5%, less frequent in 18% and more frequent in 2.5%. In those taking a bDMARD less frequently than per licence, the dose interval was increased by a mean 2.15 x licenced interval (range 1.14 – 6 x); in RA 1.88x, PsA 2.12x and AS 2.64x. Dose reduction had been attempted in 32%, but failed due to loss of efficacy in 43% of these (13.6% of entire cohort), including 50% with RA, 46% PsA and 20% AS. In those attempting a dose reduction, there was no difference in the % sustaining this for Etanercept 57% (8/14) and Adalimumab 50% (5/10) but lower for all TNFi (54%, 13/24) treated patients compared to other bDMARDs (75%, 3/4). Dose reduction had not been attempted at any stage in 66% (RA 72%, PsA 61%, AS 62%). Cost savings from 16 patients with sustained dose reduction over 3 years in this cohort were £97,653, extrapolated to 18% of the entire population (n~1500) on subcutaneous bDMARDs at our Trust makes £1.65 million saving over 3 years.

Conclusion: 'Try and see' dose reduction of subcutaneous bDMARDs has been attempted in one third of patients in routine care, with more success in AS where 80% sustained a lower dose at a mean 2.64 x licenced interval, compared to 50% of RA and 54% PsA patients at 1.88 and 2.12 x licenced interval respectively. Guidelines, possibly based on TDM, are needed to optimise current practice which falls short of the success of dose reduction in clinical trials (3). Even with a 'try and see' approach failing in 43% of attempts, the cost savings are very substantial to the healthcare economy.

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SAT0153

1,25(OH)₂D AND IL-6 BLOCKADE SYNERGISTICALLY REGULATES RHEUMATOID ARTHRITIS VIA SUPPRESSION OF TH17 AND OSTEOCLASTOGENESIS

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Background: Immune cells express vitamin (vit) D receptor and vit D is known as a potent immune-modulator.

Objectives: Based on negative association of serum vit D level with rheumatoid arthritis (RA) disease activity on previous studies, we aimed to evaluate the role of the vit D in treatment response in RA patients on anti-IL-6 receptor antibody – tocilizumab.

Methods: RA patients on tocilizumab were enrolled, and data were collected retrospectively. Disease activity (disease activity score (DAS) 28), serum 25(OH)D level, modified Sharp's score of hand x-ray at the time of tocilizumab initiation and follow up were analyzed. Peripheral blood mononuclear cells (PBMCs) were differentiated into Th17 or osteoclast in the presence or absence of various concentrations of tocilizumab and/or 1,25(OH)₂D. Proportion of Th17 was analyzed by FACS.

Results: Among 98 RA patients on tocilizumab, 34 (34.7%) patients had sufficient serum 25(OH)D level (≥ 30 ng/mL) when tocilizumab was initiated. On 24 weeks, DAS 28 reduction was greater ($64.6 \pm 15.5\%$ vs. $52.7 \pm 20.7\%$, $P=0.004$) and more patients achieved low disease activity (91.2% vs. 70.3% , $P=0.018$) or remission (82.4% vs. 57.8% , $P=0.014$) in vit D sufficient group. On 48 weeks, DAS28 reduction and proportion of patients with remission was greater in vit D sufficient group as well. However, there was no significant difference in hand & wrist erosion progression. In vitro, tocilizumab and active vit D 1,25(OH)₂D treatment synergistically suppressed Th17 differentiation and osteoclastogenesis from PBMC.

Conclusion: RA patients being treated with IL-6 blocker show better response when they have sufficient serum vit D level. Active vit D