Pain is a common and debilitating feature of rheumatoid arthritis (RA) and a level >40 mm on a Visual Analogue Scale (VAS) of pain (scale 0–100 mm) has been suggested as a measure of unacceptable pain. While many studies have focused on the effect on inflammation of different pharmacological options, few earlier reports have directly compared pain outcomes between common treatment strategies.

Objectives: The aim of this study was to investigate pain development and unacceptable pain over 2 years after start of biological as compared to conventional combination therapy in early RA patients.

Methods: The multicentre SWEFOT (Swedish FaMCaTherapy) trial was designed as a randomised, active-controlled, open-label study, enrolling new-onset (<1 year) patients fulfilling 1987 American College of Rheumatology criteria for RA Oct 2002 to Dec 2005. After a 3 month run-in period on methotrexate (MTX), patients who did not reach low disease activity (Disease Activity Score using 28-joint count; DAS28-CRP <3.2) were randomised to addition of infliximab (IFX) or sulfasalazine + hydroxychloroquine (SSZ + HCQ). Results for disease activity, radiographic data and health-related quality-of-life have been published earlier. Here, unacceptable pain (VAS pain >40 mm) at 2 years follow-up and area under the curve (AUC) for VAS pain were used as outcome measures. We used intention-to-treat with last observation carried forward in case of protocol breach as study approach. Statistical analyses were performed by logistic regression for patients with unacceptable pain and analysis of covariance for AUC for VAS pain, adjusting for age, sex, and VAS pain at randomisation.

Results: 487 RA patients were enrolled of whom 258 (who did not respond sufficiently to MTX) were randomly allocated to either addition of IFX (n=128) or SSZ + HCQ (n=130). Baseline characteristics were similar between the two groups. Out of patients assigned to IFX, 32% had unacceptable pain at 2 years follow-up (21 months after randomisation), while the same figure for SSZ + HCQ (n=130) was 45% (adjusted odds ratio 0.41 [95%CI 0.23–0.73]; p=0.003). Serial VAS pain measurements are displayed in figure 1. An AUC analysis for mean VAS pain levels from randomisation to 2 years follow-up confirmed significantly lower levels for patients randomised to IFX compared to SSZ + HCQ (p=0.01).

Conclusions: Despite early active treatment, a large share of new-onset RA patients showed unacceptable pain after 2 years. Interestingly, both the fraction of patients with unacceptable pain and assessment of pain over time were substantially lower for patients randomised to addition of IFX compared to SSZ + HCQ, contrasting to earlier SWEFOT reports where significant between-group differences at 2 years follow-up for disease activity and health-related quality-of-life were not seen. This suggests a better effect on long term pain for the biological therapy, which could be taken into account when choosing treatment strategy in patients responding insufficiently to MTX.

References:

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Abstract THU0164 – Figure 1. Effect of Anti-drug Antibody on ACR20 Response Rates

Conclusions: In a pooled analysis, the development of ADAbs to TNFi is associated with reduced clinical efficacy and increased incidence of IR/IRIR in patients with RA.

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THU0185
THE VALUE OF ADALUMAB TROUGH LEVELS AND CLINICAL ASSESSMENTS IN PREDICTING CLINICAL RESPONSE IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO METHOTREXATE

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Background: Low trough levels of the tumour necrosis factor inhibitor, adalimumab (ADL), and anti-ADL antibodies (AAA) were reported to be correlated with lack of response at later time points in patients (pts) with rheumatoid arthritis (RA).1

Objectives: To assess the ability of ADL trough levels and clinical assessments at Week 12 to predict clinical remission (REM) after 24 weeks (wks) of treatment with ADL+MTX (MTX) in established RA pts.

Methods: Data from MTX inadequate responders (MTX-IR) pts with established RA with available measurement of ADL trough levels and clinical assessments at Wks 12 and 24 from several clinical trials were pooled: for pts who received ADL+MTX combination therapy from DE009, DE019, M10–261 and M13–390; for pts who received ADL monotherapy from DE011, M10–261 and M13–390. Efficacy endpoints at Wk 24 were DAS28-CRP<2.6 and DAS28-CRP low disease activity (LDA,<3.2), remission (REM) and LDA by simplified disease activity index (SDAI,<3.3 and<11 respectively); REM and LDA by clinical disease activity index (CDAI,<2.8 and<10 respectively). Each of the pooled datasets was randomly and equally split into training and testing sets. Predictive modelling was performed on the training set, and the best-performing model was selected and validated in the testing set. The performance of the final model was reported based on the testing set.

Results: Based on the cutoffs selected by the predictive model, ADL concentrations at Wk 12 were only slightly predictive for Wk 24 clinical assessment in the ADL monotherapy group, but not in the ADL+MTX group (table 1). However, based on achievement of the specified CDAI, SDAI or DAS28-CRP score at Wk 12 (selected by the model), pts were correctly predicted to reach Wk 24 REM or LDA with an accuracy of 80%–90% and area under the receiver operating characteristic curve (AUC) of 75%–90% (table 2). As an example, pts on ADL monotherapy with DAS28<3.3 at Wk 12 had 60% and 70% chance of reaching Wk 24 DAS28-CRP<2.6 and LDA respectively, whereas pts with DAS28>3.3 had 0% and 7% chance of achieving Wk 24 DAS28-CRP<2.6 and LDA, respectively (table 1). Pts on ADL+MTX with Wk 12 SDAI<12.5 had a 25% and 77% chance of achieving SDAI REM and LDA at Wk 24, respectively.

Abstract THU0185 – Table 1

Conclusions: The ADL concentrations at Week 12 selected by the prediction model were weak predictors of disease control at 6 months, especially for pts on ADL+MTX combination therapy. However, using the model-selected cutoffs of composite clinical endpoints at Wk 12, disease control after 6 months of ADL ±MTX treatment could be correctly predicted in 70%–80% of pts.

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