APCDD1, DNASE1LS1, and PIM3 correlated with both duration of treatment and FIL dose (FDR<10%). CISH and SOCS confirm JAK pathway modulation.

Figure 1 Heatmap of 453 DAS28-correlated genes and the corresponding change in gene expression with 12 wk FIL in Phase2b RA studies

Conclusions: RA patients treated with FIL show reproducible changes in gene expression consistent with modulation of JAK/STAT signaling and innate and adaptive immunity. FIL was shown to partially reverse the dysregulated gene expression profile associated with baseline DAS28 score, consistent with the efficacy observed in RA patients.

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METHOTREXATE TREATMENT IN RHEUMATOID ARTHRITIS AND ELEVATED LIVER ENZYMES: A LONG-TERM FOLLOW-UP OF OCCURRENCE, PREDICTORS, SURVEILLANCE, AND OUTCOME IN CLINICAL PRACTICE

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Background: Hepatotoxicity is an important safety issue in long-term methotrexate (MTX) treatment. Guidelines, including the widely used American College of Rheumatology guidelines, therefore recommend testing of liver enzymes at intervals of 6–12 weeks in all MTX-treated patients with rheumatoid arthritis (RA), making this one of the most frequent screening tests in rheumatology care. Although a number of potential risk factors for liver toxicity have been identified, individual risk stratification is still not part of guidelines. Besides, it is unclear what proportion of all monitoring tests that captures liver enzyme elevations and what happens after an alanine aminotransferase (ALT) elevation in clinical practice.

Objectives: To assess predictors of ALT elevation in an unselected population of MTX-treated RA patients, describe monitoring of liver enzymes in clinical practice, including the handling and outcome of elevated ALT levels.

Methods: All RA patients starting MTX treatment January, 2005–April, 2013 at a rheumatology clinic, (Uppsala university hospital, Sweden) were identified. Clinical and laboratory data from onset of RA until MTX treatment stopped or the end of the study period September, 2013, were obtained from medical records and supplemented by a telephone interview. Predictors for ALT>1.5 the upper limit of normal (ULN) were identified by multiple regression analysis.

Results: The study comprised 213 RA patients starting MTX therapy. During a mean follow-up (MTX-treatment period) of 4.3 years, 6288 ALT tests were performed. ALT >ULN was observed in 84 (39%) of the patients and 7% of all tests. The strongest predictor for ALT >1.5 x ULN was a pre-treatment ALT elevation (mean observation period 1.5 years before MTX start) (adjusted OR=6.8, 95% CI 2.2–20.5). In the patients with pre-treatment ALT elevation, the mean time to first ALT elevation was shorter than in those without pre-treatment elevation (p<0.001), and all had recurrent elevations during MTX treatment. In all patients with ALT >ULN, re-elevations occurred in 70%, with similar proportions in those without active interventions and in those where e.g. MTX dose reduction was performed (73% vs. 67%; p=0.43). In patients who permanently stopped MTX due to ALT elevation (n=7), ALT >ULN recurred in 5 (71%) after stopping MTX. Two patients were eventually diagnosed with nonalcoholic fatty liver disease. No patient developed signs of hepatic failure.

Conclusions: Pre-treatment ALT elevation is a strong predictor for early and subsequent ALT elevations during therapy. Overall, re-elevations are common, but only a minority of performed ALT tests captures elevations. More individualized or alternative means to follow these patients could be considered to more effectively identify those with MTX-related liver toxicity, and those who despite recurrent ALT elevations could continue MTX treatment without risk for deleterious liver damage.

Disclosure of Interest: None declared