nitrofurantoin, and 27% had not received any of the included drugs at the end of the 5-year follow-up for ILD and respiratory failure. MTX treatment was not associated with an increased risk of lung disease (≥1 redeemed prescription(s) compared to no prescriptions), HR 1.00 (95% CI 0.78 to 1.27) for ILD and 0.54 (95%CI 0.43 to 0.67) for respiratory failure at 5-year follow-up (Table). The SIR was 3-4 times increased for ILD in MTX-treated RA patients, but this was no different from the RA population in general compared to the background population.

Conclusion: RA patients had an increased risk of ILD compared to the general population, but that risk was not further increased in patients treated with MTX compared to non-MTX treated.

Disclosure of Interests: None declared

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**OP0233**

**EFFICACY, SAFETY, AND PHARMACODYNAMIC EFFECTS OF THE BRUTON’S TYROSINE KINASE INHIBITOR, FENEBRUTINIB (GDC-0853), IN MODERATE TO SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS IN A PHASE 2 CONTROLLED STUDY**


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**Background:** Fenebrutinib (GDC-0853, FEN) is an oral, non-covalent, and selective inhibitor of Bruton’s tyrosine kinase (BTK) in clinical development for autoimmune diseases.

**Objectives:** This was a randomized, placebo-controlled, multi-center study to evaluate the efficacy, safety, and pharmacodynamic effects of FEN in patients with moderate-to-severe systemic lupus erythematosus (SLE) activity.

**Methods:** Patients who met SLICC or revised ACR SLE criteria, had ≥1 seroactivity of strong BTK target and pathway inhibition. FEN had an acceptable safety profile. Several disease activity subgroups were suggestive of a greater treatment effect on SRI-4 compared to PBO.

**Disclosure of Interests:** None declared

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**OP0234**

**MBS2320, A NOVEL SELECTIVE MODULATOR OF IMMUNE METABOLISM, IN PATIENTS WITH SEVERE RHEUMATOID ARTHRITIS: SAFETY, TOLERABILITY AND EFFICACY RESULTS OF A PHASE 2 STUDY**

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**Background:** Despite the availability of several treatment options for Rheumatoid Arthritis (RA), many patients are classed as ‘non-responders’ who show little or no improvement. Hence, there remains a need for new therapies with a differentiated mechanism of action, to be used alone or in combination. MBS2320 is a selective modulator of immune metabolism displaying distinctive dual pharmacology: strong anti-inflammatory activity as well as a broader spectrum of osteoprotection than TNFa inhibition in preclinical models.

**Objectives:** To evaluate the safety, tolerability and efficacy of MBS2320 in patients receiving a stable dose of methotrexate (MTX).

**Methods:** Patients with active RA on a stable dose of MTX were randomised 2:1 to receive MBS2320 (80mg) or matching placebo once daily for 4 weeks. Subject to a satisfactory safety and tolerability assessment, patients were escalated to a dose of 120 mg qd or remained on 80 mg qd for a further 8 weeks. Safety, efficacy, pharmacokinetics and pharmacodynamics were evaluated.

**Results:** 121 patients were randomised (Safety analysis set) to MBS2320 or matching placebo and 96 completed the study. Sixteen subjects were excluded from the efficacy analysis set due to evidence of poor compliance or absence of efficacy evaluations. Enrolled patients were mostly female (86.8%), white and with a mean (range) age at baseline (BL) of 52 (19-69) years.

The study population had hard-to-treat, severe, active and erosive disease as indicated by high BL DAS28-CRP and DAS28-ESR, low Week-12 placebo ACR50 and DAS28-CRP responder rates (2.5% and 5% respectively) and a low ratio of synovitis-to-erosion volume despite treatment with DMARD(s).

**Disclosure of Interests:** None declared

There were no serious treatment emergent adverse events (TEAEs). 15 patients (19%) randomised to MBS2320 withdrew due to TEAEs, predominantly of nausea. TEAEs were typically reported soon after dosing, were mostly mild in severity and resolved without treatment. Onset of TEAEs reduced as the study proceeded.

Gastrointestinal disorders were the most frequently reported TEAEs (all causalities) with a higher incidence in patients receiving MBS2320 (68.8%) than placebo (14.6%). Nausea was most frequently reported during Week 1 (27.3% patients), Asthenia and/or fatigue was reported more frequently in the MBS2320 treatment group (53.8% patients) than with placebo (73% patients), with the majority being considered related to study drug. Infections were more frequently reported by patients receiving placebo (22.0%) than those receiving MBS2320 (12.5%). There were no clinically relevant treatment-related trends in the biochemistry, haematology, urinalysis, vital signs or ECG data.

Higher ACR20 response rates were observed in patients receiving MBS2320 versus those receiving placebo at all time points and increased with time. At Week 12, ACR50 response rates with MBS2320 treatment were increased by >4-fold compared with placebo (11.6% vs 2.5%). Greater mean reductions from baseline in DAS28-CRP were also observed in patients receiving MBS2320 versus those receiving placebo at Week 12 (-18.6% vs -8.4%). DAS28-CRP responder rates were more than doubled with MBS2320 treatment compared to placebo (5% vs 14%). These changes were mirrored by improvements in tender joint counts, reduced hsCRP and improvements in Patient Reported Outcomes of pain VAS, Patients’ and Clinicians’ Global Assessments of Disease Activity and Patients’ Global Impression of Change.

Conclusion: MBS2320 was generally well tolerated for up to 12 weeks in this RA study population. Nausea was the most common TEAE, was generally mild in severity and resolved without treatment. In this population of patients with hard-to-treat, severe, active, erosive disease MBS2320 showed evidence of a clinical benefit on both ACR20 responses and DAS28-CRP.

References:

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OP0235 ACHIEVING A LOW DAS IN THE FIRST 4-MONTHS AFTER DIAGNOSIS IS IMPORTANT FOR THE LONG-TERM CHANCE OF ACHIEVING DMARD-FREE REMISSION

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Background: Sustained DMARD-free remission (SDFR) is increasingly achievable in RA. The pathogenesis underlying SDFR-development is unknown and patient-characteristics at diagnosis poorly explain why SDFR will be achieved. This limits substantiated decisions to discontinue DMARD-treatment in clinical practice.

Objectives: To increase the understanding of SDFR, we studied the course of disease activity scores (DAS) over time in relation to SDFR-development. Subsequently, we explored whether DAS-time course could be helpful to identify patients likely to achieve SDFR.

Methods: 761 RA-patients consecutively included in the Leiden Early Arthritis Clinic, treated with initial methotrexate and treat-to-target treatment, were studied (median follow-up 7 years). The course of DAS was compared between patients achieving SDFR within 7 years and those who did not, using linear mixed models, stratified for ACPA. Subsequently, the relation between DAS at 4 months and the probability of achieving SDFR within 7 years was studied with logistic regression. Kaplan-Meier curves were constructed to illustrate cumulative incidence of SDFR for different DAS categories at 4 months, respectively <1.6, 1.6-2.4, 2.4-3.6, >3.6.

Results: Patients achieving SDFR were characterized by a remarkably different DAS response within 4 months after diagnosis. Compared to patients who did not achieve SDFR, the SDFR-group showed a prominently stronger decline in DAS between baseline and 4 months; 1.59 units decline (95%CI, 1.24-1.95) versus 0.96 units (95%CI, 0.85-1.07) decline (p<0.001) (figure 1). Stratification for ACPA yielded a similar and statistically significant effect in ACPA-negative RA. In ACPA-positive RA this effect was absent. Subsequently, the probability of achieving SDFR during 7 years was studied in ACPA-negative RA and it was observed to be lower for patients with higher DAS at 4 months. After 7 years of disease, the cumulative incidence for SDFR in ACPA-negative patients with DAS<1.6 at 4 months was high (71.0%), whilst SDFR was rare among those with DAS>3.6 at 4 months (71%) (figure 2).

Conclusion: In RA-patients treated according to current guidelines, SDFR is predominantly achieved in patients with a strong decline in DAS during the first four months after diagnosis. Especially in ACPA-negative RA, the DAS at 4-months can be useful for later decisions to stop DMARDs.