particularly nausea. There were no significant effects on clinical laboratory tests, vital signs, ECG or physical examination.

Multiple doses of MBS2320 (75 mg) were also generally well tolerated by subjects with RA when co-administered with MTX. There were no clinically significant findings or trends in the laboratory tests, vital signs or ECG data, and no clinically significant findings on physical examination. No SAEs were reported. The majority of TEAEs were mild in severity with diarrhoea and nausea reported most frequently.

In healthy subjects, MBS2320 was steadily absorbed following doses of 50 to 375 mg MBS2320. Systemic exposure (AUC) increased in a dose-proportional manner across all doses and was unaffected by food. In RA patients there was no indication of a PK interaction between MTX and MBS2320 in either direction.

In patients with RA, serum CTX-1, P1NP and osteocalcin increased following 14 days of treatment, while TRAP5b was decreased or unchanged. Median CRP was decreased relative to baseline in after 7 days' treatment with MBS2320, and remained low on Day 14.

Conclusion: MBS2320 was well tolerated for up to 14 days when administered to healthy volunteers and to patients with RA receiving MTX. Systemic exposure was dose-proportional with no evidence of a pharmacokinetic interaction with MTX. Evaluation of biomarkers of bone turnover and inflammation in RA patients showed changes consistent with those expected of an agent with the potential to directly protect the bone and simultaneously ameliorate inflammation.

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THU0187 EFFICIENCY OF TREATMENT SEQUENCES CONTAINING TOFACITINIB FOR RHEUMATOID ARTHRITIS IN SPAIN

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Background: The availability of oral janus kinase inhibitors, as tofacitinib, has extended the treatment pathways for management of patients with rheumatoid arthritis (RA)

Objectives: To assess the cost-effectiveness of tofacitinib as second-line treatment compared to treatment sequences containing standard biological therapies in patients with moderate to severe RA after failure to disease-modifying antirheumatic drugs (DMARDs) from the Spanish National Health System perspective.

Methods: A patient-level microsimulation model was used to compare the lifetime cost and quality-adjusted life-years (QALY) for treatment sequences initiating with tofacitinib (5mg BID) followed by biological therapies versus sequences of biological treatments excluding tofacitinib. The sequences were selected by a panel of experts based on clinical practice in Spain. Concomitant treatment with methotrexate (MTX) was considered along all the therapies in the treatment sequences.

Model parameters included age, weight, initial Health Assessment Questionnaire (HAQ) score and clinical response to short and long treatment. Efficacy was measured by means of HAQ score changes using mixed-treatment-comparisons (for the first 6 months) and data from long-term extension trials (for later periods).

Serious adverse event (SAE) information derived from literature.

The estimation of total cost for sequences included: drugs acquisition (public ex-factory prices with mandatory deduction or reference prices) and parenteral administration, disease progression and SAE management.

Local unitary costs (€, 2018) were applied. Additional comparisons were explored testing other potential sequences.

Results: The base case results showed that sequences initiating with tofacitinib provided greater outcomes than the correspondent sequences excluding tofacitinib. In scenario 1 tofacitinib+MTX→Rituximab+MTX→sc Tocilizumab+MTX→Etanercept+MTX→Certolizumab+MTX provided 13.99 QALYs versus 13.92 QALYs for adalimumab+MTX→Rituximab+MTX→sc Tocilizumab+MTX→Etanercept+MTX→Certolizumab+MTX. In scenario 2 tofacitinib+MTX→Adalimumab+MTX→Rituximab+MTX→sc Tocilizumab+MTX→Etanercept+MTX provided 13.75 QALYs versus 13.62 QALYs for Baricitinib+MTX→Adalimumab+MTX→Rituximab+MTX→sc Tocilizumab+MTX→Etanercept+MTX.

Tofacitinib-containing sequences provided lower total costs than the alternative sequences (−€5,783 and −€13,975 for the pairwise comparisons previously described), resulting, therefore, dominant options versus sequences excluding tofacitinib.

On the probabilistic sensitivity analyses, sequences initiating with tofacitinib resulted cost-effective in 64.0% (scenario 1) and 56.9% (scenario 2) of the 1,000 iterations performed, because incremental cost-effectiveness ratio fell below a €25,000/QALY gained willingness to pay threshold.

Conclusion: These results suggest that the inclusion of tofacitinib could be a dominant strategy for treatment of moderate to severe RA patients after DMARDs failure in Spain.

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THU0188 INHIBITION OF STRUCTURAL JOINT DAMAGE WITH UPADACITINIB AS MONOTHERAPY OR IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: 1 YEAR OUTCOMES FROM THE SELECT PHASE 3 PROGRAM

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Background: Long-term prevention of structural joint damage is a key treatment goal in the management of RA¹. Upadacitinib (UPA), a JAK1-selective inhibitor, inhibited the progression of structural joint damage at 6 months as monotherapy in methotrexate (MTX)-naïve RA patients (pts)² and in combination with MTX in pts with inadequate response (IR) to MTX³.

Objectives: To evaluate the progression of structural joint damage (radiographic) through Week 48 in pts with moderately to severely active RA treated with UPA monotherapy or in combination with MTX.

Methods: Radiographic progression was assessed in 2 phase 3 randomized controlled trials (RCTs), as previously described^{2,3}. MTX-naïve pts were randomized to UPA 15 or 30mg QD or MTX monotherapy [SELECT-EARLY, N=945], while MTX-IR pts were randomized to UPA 15mg QD or adalimumab (ADA) 40 mg eow or placebo (PBO), with continuous background MTX [SELECT-COMPARE, N=1629]. Both RCTs specifically enrolled pts at high risk for progression of joint damage (high disease activity including elevated hsCRP, presence of baseline erosions and ACPA and/or RF positivity^{2,3}). The mean changes (Δ) from baseline