| | Mavrilimumab total[a] (n=442) |
|---|---|
| **Demographics** | |
| Age, years, median (min–max) | 52 (19–79) |
| Sex, % female | 85.1 |
| **BL disease characteristics** | |
| Years since RA diagnosis, mean (SD) | 7.91 (6.85) |
| MTX dose, mg/week, mean (SD) | 15.00 (6.84) |
| DAS28-CRP, mean (SE) | 5.77 (0.04) |
| Concomitant pulmonary disease, n (%)[b] | |
| Asthma<br>COPD<br>Other | 17 (3.8)<br>8 (1.8)<br>21 (4.8) |
| Ever smoked, n (%) | 134 (30.3) |
| Current smokers, n (%) | 76 (17.2) |
| RF and ACPA positive, n (%) | 359 (81.2) |
| **BL pulmonary function** | |
| % predicted $FEV_1$, mean (SD) | 93.9 (14.7) |
| % predicted FVC, mean (SD) | 94.0 (14.6) |
| % predicted DLCO, mean (SD) [n] | 72.4 (9.3) [48] |
| Borg dyspnoea score, mean (SE) | 0.4 (0.0) |
| **Efficacy results** | |
| Borg dyspnoea score, mean (SE) [N] | |
| Week 12[c,d] | NA |
| Week 74 | 0.3 (0.0) [279] |
| Week 134 | 0.3 (0.0) [58] |
| >20% reduction from BL to 80% predicted $FEV_1$, n/N (%) | |
| Week 12[c,d] | 2/298 (0.7) |
| Week 74 | 8/231 (3.5) |
| Week 104 | 11/178 (6.2) |
| Week 130 | 1/29 (3.4) |
| >20% reduction from BL to 80% predicted FVC, n/N (%) | |
| Week 12[c,d] | 2/298 (0.7) |
| Week 74 | 7/239 (2.9) |
| Week 104 | 3/177 (3.4) |
| Week 130 | 0/32 (0.0) |

[a]Mavrilimumab total=all patientswho received mavrilimumab in either of the two randomised studies or in the OLE study. [b]Clinically significant uncontrolled pulmonary disease was an exclusion criterion for all three studies. [c]Between weeks 12 and 24, 3(3.8%), 8(9.4%), 12(14.8%) and 37 (45.7%) pts receiving mavrilimumab 150 mg, 100 mg, 30 mg eow, and placebo, respectively, transferred from NCT01706926 to the OLE study because of lack of efficacy. [d]Between Weeks 12 and 24, 2 (2.9%) and 0 (0.0%) pts receiving mavrilimumab 100 mg and golimumab 50 mg, respectively, transferred from NCT01715896 to the OLE study because of lack of efficacy.
ACPA, anti-citrullinated protein antibody; BL, baseline; COPD, chronic obstructive pulmonary disease; DAS28–CRP, disease activity score 28 C-reactive protein; DLCO, diffusing capacity of the lung for carbon monoxide; eow, every other week; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; MTX, methotrexate; NA, not available; OLE, open-label extension; pts, patients; RA, rheumatoid arthritis; RF, rheumatoid factor; SD, standard deviation; SE, standard error

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## FRI0217 IMPACT OF RITUXIMAB IN COMBINATION WITH LEFLUNOMIDE AND RITUXIMAB RETREATMENT WITH TWO DIFFERENT DOSAGES ON PATIENT-REPORTED OUTCOMES: RESULTS FROM A MULTICENTER RANDOMIZED PLACEBO CONTROLLED INVESTIGATOR INITIATED CLINICAL TRIAL IN ACTIVE RHEUMATOID ARTHRITIS (AMARA-STUDY)

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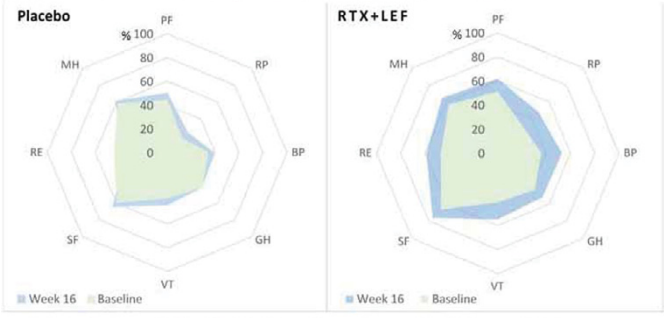
**Background:** Use of biologicals such as Rituximab (RTX) in Rheumatoid Arthritis (RA) is effective and often only licensed in combination with Methotrexate (MTX). In cases of contraindications to or intolerances of MTX other cDMARDs are frequently used without robust data from RCTs. In addition, different strategies of retreatment of RTX are available.

**Objectives:** To demonstrate efficacy on patient-reported outcomes (PROs) of RTX in combination with leflunomide (LEF) in a multicenter investigator-initiated placebo (PLA)-controlled RCT in Germany.

**Methods:** A total of 189 patients with active RA (DAS28>3.2 and at least 3 SJC and 3 TJC) despite stable LEF treatment were screened for a 52-weeks double-blind placebo controlled RCT. Patients were randomized to receive either two-times 1000mg RTX i.v. followed by a retreatment at week 24 with two-times 1000 (RTX-RTXhigh) or 500mg (RTX-RTXlow) or two times PLA at baseline, followed by a retreatment of RTX of either two-times 1000 (PLA-RTXhigh) or 500mg (PLA-RTXlow) at week 24. Adult patients who had inadequate response to more than one antiTNF or failed more than three cDMARDs were excluded. PROs (HAQ, FACIT-F, SF36) were measured at each visit until week 52. Treatment effects on PROs were determined by differences from baseline to week 16, 24 and week52.

**Results:** Of 189 screened patients 148 were randomized (mean age 56 years; mean proportion of RF-and antiCCP-positivity 58.4% and 55.7% in the RTX-group; 74% female). DAS28 at baseline was 5.55 for RTX and 5.53 in the PLA-group. All baseline-characteristics were well balanced between treatment groups. An improvement in HAQ from baseline to week 16 was seen with a mean delta of -0.23 in the RTX-group (MCID) vs. -0.11 for PLA. In the RTX-group, retreatment until week 52 resulted in stable HAQ-values compared to week24 independent from its dosage. FACIT-F values increased in the RTX-group from baseline to weeks 16, 24 and 52 by 11.87, 12.3 and 14.25, respectively. All physical and mental domains of the SF36 showed a pronounced increase of levels at week 16 compared to baseline in the RTX-group (Figure 1). A total of 372 adverse events (AE) were observed during the one-year studyperiod, only 14 classified as severe (10 in RTX and 4 in PLA). 43 serious adverse events were reported, 28 of them in the RTX-group during the placebo-controlled period.

**Figure 1:** SF36 domains at baseline and week 16 after placebo or RTX+LEF treatment




PF: physical functioning; RP: physical role limitations; BP: pain; GH: general health; VT: energy/vitality; SF: social functioning; RE: emotional role limitations; MH: mental health

**Conclusions:** Efficacy of LEF plus RTX was demonstrated not only by measurements of disease activity (as presented previously) but also by measurements of PROs (HAQ, FACIT-F, SF36). This treatment regime showed equal effect sizes compared to the combinational therapy of MTX plus RTX. The treatment with LEF plus RTX illustrated an acceptable safety profile.

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## FRI0218 SHARED EPITOPE POSITIVITY IS RELATED TO EFFICACY OF ABATACEPT IN RHEUMATOID ARTHRITIS

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**Background:** Abatacept, a soluble fusion protein composed of the extracellular domain of CTLA-4 molecule and the Fc portion of human IgG1, is approved therapy for RA by the mechanism of binding to CD80/86 (B7–1/B7–2) on antigen presenting cell (APC), and blocking the B7:CD28 interaction. Meanwhile, it is suggested that HLA-DRB1 shared epitope (SE) associates with the production of ACPA through MHC molecule-based antigen presentation. Moreover, the association between the efficacy of abatacept and the positivity for anti-cyclic citrullinated peptide antibody (ACPA) was reported. Thus, we speculated that there may be correlation between the efficacy of abatacept and patients' HLA-DRB1 SE positivity, so we investigated correlation between the clinical efficacy of abatacept in RA patients and their HLA-DRB1 genotype.

**Objectives:** To identify the relation between the efficacy of abatacept on patients with rheumatoid arthritis (RA) and their HLA-DRB1 phenotype including whether having shared epitope (SE).

**Methods:** HLA-DRB1 phenotype of 72 patients treated with abatacept was identified, and divided into 2 group, SE (HLA-DRB1 0101, 0401, 0404, 0405,