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OP0118

EFFECT OF WITHDRAWING ETANERCEPT OR METHOTREXATE ON PATIENT-REPORTED OUTCOMES IN RHEUMATOID ARTHRITIS PATIENTS IN REMISSION ON COMBINATION THERAPY: RESULTS FROM THE SEAM-RA TRIAL

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Background: Limited studies have assessed the effect of withdrawal of either methotrexate (MTX) or etanercept (ETN) on patient-reported outcomes (PROs) in rheumatoid arthritis (RA).

Objectives: To evaluate the baseline and change in PROs following withdrawal of MTX or ETN in RA patients with sustained remission receiving combination ETN+MTX.

Methods: Adult patients with RA on ETN+MTX and in remission (SDAI ≤ 3.3) for ≥ 12 months (including a 24-week, open-label, run-in period) were randomized to a 48-week double-blind period to receive ETN 50mg weekly (N=101), oral MTX 10-25 mg weekly (N=101) or continue ETN+MTX (N=51). The primary endpoint was maintenance of SDAI remission without disease worsening (DW) at week 48 between ETN and MTX groups. Patients who experienced SDAI >11 at any time after randomization, or SDAI >3.3 and ≤ 11 during 2 consecutive or on 3 non-consecutive visits were considered to have DW and resumed ETN+MTX. PROs assessed were patient global assessment of disease activity (PtGA, 0-100mm), patient joint pain (PtJP, 0-100mm), Health Assessment Questionnaire-Disability Index (HAQ-DI), and the 36-item short-form health survey (SF-36) component and domain scores. A 2-sample t-test was used to compare the treatment differences between groups. A subgroup analysis for patients with DW was also performed (DW analysis set) and compared PROs between ETN vs MTX arms (ETN+MTX not shown given the small sample size).

Results: Of the 253 patients randomized, 121 (47.8%) experienced DW and were included in the DW analysis set. Baseline demographics were generally balanced between the 3 treatment groups. Most patients were women (76.3%), White (87.0%), and with a mean age of 55.6 years. The mean (SD) MTX dose was 16.3 (4.69) mg and the mean (SD) duration of RA was 10.3 (7.8) years. At week 48, a significantly greater proportion of patients on ETN vs MTX monotherapy maintained SDAI remission (49.5% vs 28.7%; $P=0.004$) after therapy withdrawal. In the overall population, PtGA and PtJP scores were very low at baseline (PtGA-MTX: 4.4, ETN: 4.5, ETN+MTX: 3.5; PtJP-MTX: 4.9, ETN: 5.5, ETN+MTX: 3.5) and showed some worsening over the study period in all treatment groups, with a mean change at week 48 ranging from 5.0 to 10.0 units for PtGA and 3.7 to 8.1 units for PtJP. Patients on ETN had less worsening, with a nominally significant treatment difference observed between ETN and MTX monotherapy groups for PtGA at almost all timepoints, and for PtJP at weeks 12 and 36 (Figure). Mean HAQ-DI (MTX: 0.32; ETN: 0.26; ETN+MTX: 0.28) and SF-36 scores (physical component [PCS]-MTX: 52.1, ETN: 52.7, ETN+MTX: 52.3; mental component [MCS]-MTX: 55.5, ETN: 55.8, ETN+MTX: 57.1) at baseline show that patients had low disability and excellent health-related quality of life compared with normative values for the general non-RA population. HAQ-DI scores were well maintained at weeks 24 and 48 (change from baseline at week 48-MTX: 0.14; ETN: 0.15; ETN+MTX: 0.21). The SF-36 PCS, MCS, and domain scores decreased minimally from baseline with treatment differences that were not nominally significant between groups. Among patients with DW during the study, those on ETN showed less PtGA and PtJP worsening from baseline than those on MTX at weeks 12, 36, and 48 (Figure). Other PROs (HAQ-DI [change from baseline at week 24-ETN: 0.34; MTX: 0.21; at week 48-ETN: 0.15; MTX: 0.15], SF-36 PCS, MCS, and domain scores) showed a similar degree of worsening in both the MTX and ETN arms.

Conclusion: In patients with sustained SDAI remission on ETN+MTX, mental and physical health as measured by SF-36 was comparable with that of the non-RA population. Withdrawal of ETN (MTX monotherapy) resulted in a greater worsening of PtGA and PtJP than withdrawal of MTX (ETN monotherapy), and

patients on ETN monotherapy restored these scores close to baseline towards the end of the treatment period. These findings demonstrate that ETN monotherapy has a greater effect on maintaining overall patient assessment of disease and joint pain compared with MTX monotherapy.

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OP0119

SHOULD WE USE BDMARDS IN FIRST INTENTION IN EARLY RHEUMATOID ARTHRITIS?: RESULTS AT 5 YEARS FROM THE ERA LOUVAIN BRUSSELS COHORT

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Background: Early effective treatment has led to major improvements in patients with rheumatoid arthritis (ERA). Low disease activity and remission are achieved earlier and in higher frequency when the initial treatment in rheumatoid arthritis includes a combination of methotrexate (MTX) with a bDMARD compared to MTX alone.

Objectives: The aim of this study is to retrospectively analyse and compare the benefit of a treatment with methotrexate (MTX) alone or combined with a bDMARD as an induction therapy during 5 years of follow-up in early rheumatoid arthritis (ERA) patients.

Methods: We included ERA patients from the UCLouvain Brussels cohort who met the ACR/EULAR 2010 classification criteria and were naïve to DMARDs. Treatments were initiated based on the decision of a senior rheumatologist. bDMARDs induction therapy was usually limited to 6 or 12 months. We collected patient characteristics at baseline and clinical response was analysed at 6 months, 1 year, 3 years and 5 years.

Results: Data from 470 eligible ERA patients were collected. The average age of the population is 48.9 years; 70.5% of the patients are women; 27.3% are smokers and 68.8% are positive for anti-citrullinated protein antibody (ACPA).

281 patients (59.8 %) initiated MTX as a monotherapy (MTX group) compared to 189 patients (40.2%) who received a bDMARD (Bio group). At baseline, the disease activity is the main factor that favors the initiation of bDMARDs (DAS28-CRP 5.2 vs 4.5, $p < 0.001$) followed by HAQ (1.32 vs 1.15, $p = 0.009$), ACPA positivity (77.8% vs 62.5%, $p = 0.0006$), rheumatoid factor positivity (71.5% vs 60.2%, $p = 0.0134$). Other parameters such as age, gender, smoking habits or baseline erosion were similar between groups.

391 patients were followed up to 5 years. We then divided each of the two groups into two subgroups according to the last treatment they received at 5 years. Figure 1 shows the percentage of DAS28-CRP remission during time in each of the four groups (MTX->MTX (n=134), MTX->BIO (n=103); BIO->MTX (n=95), BIO->BIO (n=59);

Figure 1. DAS28-CRP remission rate during time in each of the four groups (MTX->MTX (n=134), MTX->BIO (n=103); BIO->MTX (n=95), BIO->BIO (n=59).

At 12 months, DAS28-CRP response rate was statistically significantly higher in MTX->MTX and BIO->MTX groups compared to the two other groups. As expected, the remission rate was rescued in the group MTX->Bio after 12 months.

Interestingly, ERA patients initially treated by a bDMARD followed by a MTX maintenance therapy experienced a stable and sustained rate of remission.

Conclusion: Longterm remission is an achievable goal in ERA followed in daily clinic. Our results suggest that a bDMARD induction therapy followed by MTX maintenance therapy could be a good option in severe case of ERA.

REFERENCES:

- [1] Smolen JS and al. D. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying anti-rheumatic drugs: 2019 update. *Ann Rheum Dis.* 2020 Jan 22.

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OP0120

DURATION OF CLINICAL EFFICACY FOLLOWING TREATMENT WITH VIB4920 IN SUBJECTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

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Background: VIB4920 binds CD40 ligand and functionally neutralizes its engagement with CD40¹. We reported results through Day 85 of a Phase 1b, randomized, double-blind, placebo-controlled study (NCT02780388) in subjects with moderate to severe rheumatoid arthritis (RA) who had an inadequate response to methotrexate (MTX) or other disease modifying anti-rheumatic drugs (DMARDs) or tumor necrosis factor (TNF)-inhibitors¹. We showed that at the end of the 12-week treatment period (Day 85), subjects treated with 1000 or 1500 mg VIB4920 (once every 2 weeks) had a clinically meaningful and statistically significant greater reduction in disease activity compared to placebo.

Objectives: To assess the duration of clinical efficacy following the last dose of VIB4920 in subjects with moderate to severe RA.

Methods: Subjects in the Phase 1b study (Ph1b) continued to have monthly safety and efficacy assessments between Days 85 and 169, the end of a 12-week follow-up. To estimate the subsequent duration of meaningful clinical improvement, we conducted an observational one-visit study (OS) (EudraCT 2019-002351-42) with the primary endpoint of time from last dose of VIB4920

to start of a new DMARD or biologic therapy or increase in dose of DMARD that was ongoing at Day 169 (ie, rescue therapy).

Results: At Day 169 of the Ph1b (3 months after the last dose), clinical responses achieved at Day 85 were maintained in the 1000 and 1500 mg cohorts (Figure). Of 24 subjects, 16 (6/12 treated with 1000 mg and 10/12 with 1500 mg) participated in the OS. The median (range) time from Day 169 (last visit) in the Ph1b to the OS was 21.8 (21.2 to 23.1) months in the 1000 mg group and 33.7 (32.3 to 34.8) months in the 1500 mg group. All subjects had taken DMARDs (primarily methotrexate [MTX]) for at least part of this time (Table). Rescue therapy was started in 1/6 (16.7%) subject in the 1000 mg group and 3/10 (30.0%) subjects in the 1500 mg group (Table); median time to rescue could not be estimated due to the limited number of rescues. Two subjects were on no DMARDs at the OS. All subjects, except for 1 in the 1000 mg group, who was rescued with adalimumab, and 2 in the 1500 mg group (no rescue), had active disease (DAS28-CRP ≥ 2.6) at the OS. The median DAS28-CRP at the OS was higher than at Day 169 of the Ph1b but lower than at the Ph1b baseline visit (Table). Two subjects who received 1500 mg and met DAS28-CRP criteria for low disease activity (< 3.2) at Day 169 also met these criteria at the OS without receiving any rescue therapy after a median of nearly 37 months after last treatment. Results from the Patient and Physician Global Assessment VAS showed trends similar to the DAS28-CRP.

Conclusion: Blocking CD40L with VIB4920 led to prolonged clinical benefit in patients with RA when added to stable background DMARD therapy. The exact duration of benefit could not be defined in this study, but most patients did not require rescue therapy during a prolonged follow-up period, and some patients maintained low disease activity or discontinued DMARDs, suggesting a possible long-term benefit of VIB4920. Interpretation of these data is limited because the OS did not include placebo-treated subjects from the Ph1b. The duration of clinical response needs to be confirmed in prospective, double-blind, placebo-controlled studies.

REFERENCES:

- [1] Karnell JL et al. *Sci Transl Med.* 2019 Apr 24;11(489).

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Summary of Results

	VIB4920 1000 mg N = 6	VIB4920 1500 mg N = 10
Subjects who received ≥ 1 DMARD at any time between Day 169 of Ph1b and OS	6 (100%)	10 (100%)
Hydroxychloroquine (HCQ)	1 (16.7%)	0
MTX	5 (83.3%)	9 (90.0%)
Leflunomide	1 (16.7%)	2 (20.0%)
Adalimumab	1 (16.7%)	0
Etanercept	0	1 (10.0%)
Rescue therapy		
HCQ, Adalimumab	1 (16.7%)	0
MTX	0	2 (20%)
MTX, Leflunomide, Etanercept	0	1 (10%)
DAS28-CRP [median (min, max)]		
Ph1b Baseline	5.4 (4.7 – 6.3)	4.7 (4.3 – 5.7)
Ph1b Day 169	2.9 (1.1 – 4.2)	2.3 (1.1 – 3.4)
OS	3.7 (1.1 – 5.5)	3.9 (2.3 – 5.6)

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