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OP0107

ETANERCEPT WITHDRAWAL AND RE-TREATMENT IN PATIENTS WITH INACTIVE NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AT 24 WEEKS: RESULTS OF RE-EMBARK, AN OPEN-LABEL, PHASE IV TRIAL

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Background: In the RE-EMBARK trial (NCT02509026), etanercept (ETN)-treated patients with non-radiographic axial spondyloarthritis (nr-axSpA) who achieved inactive disease (defined as Ankylosing Spondylitis Disease Activity Score with C-reactive protein [ASDAS CRP] <1.3) in Period 1 (P1)¹ discontinued ETN for ≤40 weeks.

Objectives: To assess the proportion of patients with inactive disease after P1 who experienced disease flare (ASDAS with erythrocyte sedimentation rate [ASDAS ESR] ≥2.1) within 40 weeks of ETN withdrawal and to estimate time to flare following ETN withdrawal.

Methods: RE-EMBARK was a multicenter, open-label, Phase IV trial of ETN in patients with active nr-axSpA (meeting Assessment in SpondyloArthritis international Society criteria and with ASDAS CRP ≥2.1) and an inadequate response to ≥2 nonsteroidal anti-inflammatory drugs (NSAIDs) while taking a stable dose of 1 NSAID for ≥2 weeks before the first ETN dose. All patients received ETN (50 mg/week) plus NSAID for the first 24 weeks (P1). At week 24, patients with inactive disease discontinued ETN for ≤40 weeks (Period 2 [P2]). Those who experienced flare during P2 were re-treated with ETN for 12 weeks in Period 3 (P3). Kaplan-Meier (KM) analysis and Cox proportional hazard models were used to 1) estimate the probability of experiencing flare within a given time period, and 2) compare data between RE-EMBARK and the EMBARK trial (NCT01258738) of patients with nr-axSpA who met RE-EMBARK P2 entry criteria (achieved inactive disease after 24 weeks of ETN treatment) and continued treatment for a further ≤40 weeks.

Results: Of the 209 patients in P1 (mean age, 33 years; women, 46%; white, 89%), 119 (57%) entered P2. The proportion of patients experiencing ≥1 flare increased from 22% (25/112) at P2 week 4 to 67% (77/115) at P2 week 40. Overall, 75% (86/115) of patients in P2 experienced flare and 50% experienced flare within 16 weeks (95% CI: 13-24 weeks, KM analysis). Conversely, data from the comparator EMBARK trial suggested that <25% of patients receiving continuous ETN treatment over 40 weeks experienced flare. Cox proportional hazard model analysis showed an 85% relative risk reduction of experiencing flare during P2 in patients with inactive disease who continued ETN treatment vs those who discontinued. By P3 end 62% (54/87) of patients re-treated with ETN re-achieved inactive disease; 50% of patients who re-achieved inactive disease in P3 did so within 5 weeks (95% CI: 4-8 weeks, KM analysis). The observed trend of clinical improvement (P1), worsening (P2), and improvement (P3) was reflected in other clinical measures (Figure) plus measures of joint damage (Spondyloarthritis Research Consortium of Canada Sacroiliac Joint magnetic resonance imaging score) and quality of life (EQ-5D visual analog scale score); mean (standard deviation) score changes from each study period baseline-end were -6.1 (11.7) [P1], +1.5 (4.4) [P2], -2.0 (8.8) [P3] and +27.7 (26.7) [P1], -26.4 (30.5) [P2], +32.1 (26.3) [P3], respectively. There were no unexpected safety signals.

Conclusion: For patients with nr-axSpA who achieved inactive disease with ETN and then discontinued treatment, a quarter maintained treatment-free inactive disease for 40 weeks and 50% maintained an ASDAS ESR score of <2.1 for ≥16 weeks. Re-starting ETN allowed 62% of patients who flared to re-achieve inactive disease within 12 weeks.

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Figure: Clinical Assessments by RE-EMBARK Study Period

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OP0108

RANDOMIZED CONTROLLED TRIAL OF ORAL CORTICOSTEROIDS IN AXIAL SPONDYLOARTHROPATHY: MODIFIED COBRA REGIME

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Background: There is an unmet need of anti-inflammatory agents in AxSpA after NSAID failure. This is especially true for patients with persisting high disease activity and not having access to anti-TNFα. In this regard, corticosteroids may be helpful as a short-term measure. However, current guidelines recommend against oral corticosteroids citing insufficient evidence of efficacy.¹ Also, there is an assumption that the dose required for benefit is much higher than RA, and thus untenable. It is unclear whether starting with a high dose followed by rapid taper would be effective (like the COBRA regime in RA).²

Objectives: To study the efficacy of the COBRA regime of oral corticosteroids in axial SpA over 24 weeks.

Methods: This was a double blind placebo controlled randomized trial. Patients with active axial SpA (BASDAI ≥ 4) despite NSAIDs were randomized to either

receive oral prednisolone or placebo as per COBRA regime, started on oral prednisolone at a dose of 60 mg, rapidly tapered weekly to reach a dose of 10 mg by 6 weeks and subsequently maintained on a low dose of 5 mg till 24 weeks. Primary end point was 50% improvement in BASDAI at week 24. Secondary end points were improvement in ASDAS and BASFI. Analysis was by intention-to-treat. Trial Registration# CTRI/2018/01/011342

Results: This study enrolled 65 patients (62 males) who were randomized to corticosteroid (n=32) or placebo (n=33) with mean $\pm$ SD age 28.5 ± 8.4 years and BASDAI 5.4 ± 1.0 . Primary end point was reached in 12 (37.5%) and 3 (9%) patients treated with steroids and placebo respectively ($p=0.007$). On repeated measures analysis by general linear model, there was a significant difference between the two-groups in BASDAI ($p=0.03$) (Figure-1). Patients in the corticosteroid group had significant improvement in BASDAI, ESR, CRP, ASDAS ESR and ASDAS CRP at 24 weeks (Table-1). Clinically important improvement in ASDAS CRP was achieved by significantly higher number of patients in steroid group (17 (55%) vs 6 (18%), $p=0.002$). Major improvement in ASDAS ESR and ASDAS CRP was also higher in the steroid group (Figure-2). At 24 weeks, patients in the steroid group had significant reduction in IL-6 levels compared to that in placebo group ($p=0.007$, data for 41 patients). Patients in the steroid group had more weight gain and facial puffiness, however no serious adverse events were noted in both the groups.

Figure 1. Change in mean BASDAI

Table 1. Changes in disease indices and inflammatory markers at 24 weeks

Changes in Parameters (24 weeks-baseline)	Placebo	Corticosteroid	P value
ESR, Median (IQR)	0 (-11 to 21)	-13 (-37 to 4)	0.01
CRP mg/L	0 (-8.8 to 13)	-9 (-22.7 to 0)	0.03
Median (IQR)			
BASDAI (mean $\pm$ SD)	-0.51 $\pm$ 1.6	-1.88 $\pm$ 2.5	0.03
BASMI (mean $\pm$ SD)	-0.25 $\pm$ 0.8	-0.56 $\pm$ 0.9	0.23
BASFI (mean $\pm$ SD)	-0.35 $\pm$ 2.3	-1.48 $\pm$ 3.1	0.28
BAS-G (mean $\pm$ SD)	-1.02 $\pm$ 2.7	-1.86 $\pm$ 2.5	0.32
ASDAS-ESR (mean $\pm$ SD)	-0.13 $\pm$ 1.0	-1.11 $\pm$ 1.1	0.001
ASDAS-CRP (mean $\pm$ SD)	-0.24 $\pm$ 1.1	-1.17 $\pm$ 1.3	0.006

Figure 2. Clinically important and Major improvement at 24 weeks

Conclusion: Oral prednisolone given by COBRA regime was associated with significant improvement in disease activity scores in axial SpA at 24 weeks. This extends and supports results from a previous short term study.³ Thus, corticosteroids may be an option for patients not having access to biologics, atleast for the short-term.

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OP0109 CO-MEDICATION WITH A CONVENTIONAL SYNTHETIC DMARD IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IS ASSOCIATED WITH IMPROVED RETENTION OF TNF INHIBITORS: RESULTS FROM THE EUROSPA COLLABORATION

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Background: Axial spondylarthritis (axSpA) patients treated with a tumour necrosis factor inhibitor (TNFi) may receive a concomitant conventional synthetic disease-modifying anti-rheumatic drug (csDMARD), although the value of combination therapy remains unclear.

Objectives: Describe the proportion and phenotype of patients with axSpA initiating their first TNFi as monotherapy compared to TNFi+csDMARD combination therapy, and to compare the 1-year TNFi retention between the two groups.

Methods: Data from 13 European registries was collected. Two exposure treatment groups were defined: TNFi monotherapy at baseline (=TNFi start date) and TNFi+csDMARD combination therapy. TNFi retention rates were assessed with Kaplan-Meier curves for each country and combined. Hazard ratios (HR, 95% CI) for discontinuing the TNFi were obtained with Cox models: (i) crude; adjusted for (ii) country, and (iii) country, sex, age, calendar year, disease duration and BASDAI. Participating countries were dichotomized into two strata, depending on their 1-year retention rate being above (stratum A) or below (stratum B) the average retention rate across all countries.

Results: 22,196 axSpA patients were included with 34% on TNFi+csDMARD combination therapy. Baseline characteristics are presented in table 1. Overall, the crude TNFi retention rate was marginally longer in the combination therapy group (80% (79-81%)) compared to the monotherapy group (78% (77-79%)) and was primarily driven by differences in stratum B (fig. 1). TNFi retention rates varied significantly across countries (range:-11.0% to +11.3%), with a clear distinction between the 2 strata. The HRs for discontinuation over 1-year (reference=TNFi monotherapy) in the 3 models were: (i) 0.88 (0.82-0.93), (ii) 0.87 (0.82-0.92), (iii) 0.88 (0.82-0.93).

Conclusion: Considerable differences were observed across countries in the use of combination therapy and TNFi retention in axSpA patients. The overall 1-year TNFi retention was higher with csDMARD co-therapy compared to TNFi monotherapy. TNFi monotherapy had a 12-13% higher risk of treatment discontinuation.

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