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OP0129

EFFECTIVENESS OF COBRA-SLIM WITH OR WITHOUT EARLY ACCESS TO A TEMPORARY 6-MONTH COURSE OF ETANERCEPT IN EARLY RA: PRIMARY OUTCOME OF THE 2-YEAR, PRAGMATIC, RANDOMISED CARERA2020 TRIAL

Keywords: Randomized control trial, Rheumatoid arthritis, Treat to target

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Background: EULAR recommends methotrexate (MTX), combined with short-term glucocorticoids as first-line treatment for early Rheumatoid Arthritis (RA). In the CareRA trial, the COBRA-Slim regimen (MTX 15 mg/w + step-down prednisone 30, 20, 12.5, 10, 7.5, 5 mg/d), including a treat to target (T2T) approach starting with addition of leflunomide and only at a later stage bDMARDs, provided the best balance between efficacy, safety and cost-effectiveness. The potential advantage of temporary bDMARD use earlier in the T2T setting needs further investigation.

Objectives: To determine the long-term effectiveness of accelerated access to a temporary course of etanercept compared to addition of leflunomide in patients with early RA who insufficiently respond to initial COBRA-Slim induction therapy.

Methods: DMARD-naïve patients with a recent diagnosis of RA (≤1 year ago) were included in the 2-year, open-label, multicentre, pragmatic randomised controlled superiority trial Care in Early RA 2020 (CareRA2020). All patients started the COBRA-Slim induction regimen. Patients were classified as insufficient responders if, even despite MTX dose increase, they did not achieve DAS28-CRP ≤3.2 between week 8 and week 32 or if DAS28-CRP was ≥2.6 at week 32 regardless of MTX dose. Insufficient responders were randomised to either Standard COBRA-Slim (addition of leflunomide 10 mg/d) or COBRA-Slim Bio-induction (addition of etanercept 50 mg/w for 24 weeks). Additional treatment adaptations followed the T2T principle. Primary outcome was the difference in DAS28-CRP over time, determined via a linear mixed model including random intercepts and a random slope for time, adjusting for baseline DAS28-CRP and seropositivity. Missing data were imputed with the Expectation-Maximisation algorithm.

Results: In total, 276 patients were included, of which 155 (56%) were classified as sufficient and 121 (44%) as insufficient responders. Of the insufficient responders, 9 patients were not randomised by investigator decision, 2 were randomisation errors, 55 were randomised to Standard COBRA-Slim, and 55 to COBRA-Slim Bio-Induction. The mean ± SD area under the DAS28-CRP curve over 104 weeks was 232 ± 66 for the initial sufficient responders, 310 ± 82 for the Standard COBRA-Slim group, and 316 ± 73 for the COBRA-Slim Bio-induction group. Both randomisation groups had comparable DAS28-CRP scores over time (β = -0.095, 95% CI (-0.299 to 0.108), p=0.351). At the end of the trial, 82% (127/155), 9% (5/55), and 36% (20/55) of patients were on csDMARD monotherapy in the initial sufficient responders, Standard COBRA-Slim, and COBRA-slim Bio-induction group, respectively. Moreover, 6% (9/155) sufficient responders, 58% (32/55) in the Standard COBRA-Slim, and 45% (25/55) in the COBRA-Slim Bio-induction group were treated with a b- or tsDMARD.

Conclusion: More than half of the CareRA2020 participants achieved remission with COBRA-Slim induction therapy. DAS28-CRP over 104 weeks was not superior with COBRA-Slim Bio-induction versus the Standard COBRA-Slim T2T regimen in initial insufficient responders. However, compared to the Standard COBRA-Slim group, more patients in the Bio-induction group were treated with csDMARD monotherapy and less with advanced therapies at the end of the study.

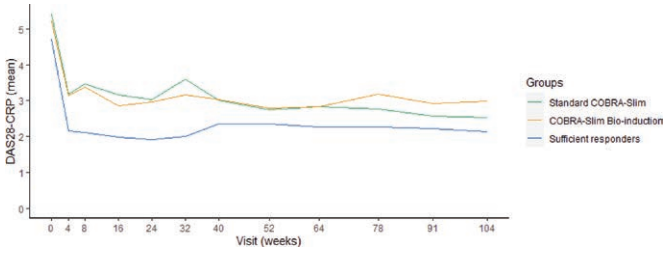

Figure 1. Disease activity evolution during the CareRA2020 trial

Table 1. Baseline characteristics of patients included in the CareRA2020 trial

	Sufficient responders (n=155)	Standard COBRA-Slim (n=55)	COBRA-Slim Bio-induction (n=55)
Sex (female)	66% (103)	75% (41)	69% (38)
Age (years)	54.5 ± 14.0	53.4 ± 13.1	52.5 ± 12.9
Symptom duration (months)	5.0 (3.0 - 9.0)	3.0 (2.0 – 6.0)	4.0 (2.0 – 6.0)
Disease duration (days)	6.0 (1.0 – 20.0)	6.0 (2.0 – 15.0)	7.0 (0.5 – 19.0)
RF and/or ACPA positivity	77% (119)	76% (42)	75% (41)
Erosions present	27% (42)	15% (8)	18% (10)
HAQ (0-3)	1.1 ± 0.7	1.6 ± 0.6	1.5 ± 0.8
PhGA	51.7 ± 19.5	59.5 ± 20.9	55.4 ± 21.0
DAS28-CRP	4.7 ± 1.3	5.4 ± 1.1	5.2 ± 1.3

Expressed in proportions %(n), mean ± SD, or median (IQR).

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