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SAT0050

PREDICTION OF RESPONSE TO CERTOLIZUMAB PEGOL TREATMENT BY FUNCTIONAL MRI OF THE BRAIN: AN INTERNATIONAL, MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL (PRECEPRA)

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Background: Personalization of RA treatment is not optimal due to lack of predictors. We previously demonstrated in RA patients that central nervous system (CNS) pain response to tender joint compression, measured by using functional MRI (fMRI) of the brain rapidly wanes after 24 hours of anti-TNF administration and that a higher pre-treatment BOLD signal volume seems to predict clinical response to treatment with certolizumab-pegol (CZP)^{1,2}. We therefore hypothesized that the CNS pain response upon compression of a painful joint could predict subsequent anti-TNF treatment response.

Objectives: To compare disease activity after 12-weeks of CZP treatment to that of placebo in DMARD-refractory RA patients based on pre-treatment baseline CNS pain response measured using BOLD fMRI.

Methods: Adult RA patients fulfilling the 2010 ACR/EULAR classification criteria with a DAS28>3.2 under stable DMARD treatment for at least 3 months were eligible. Patients underwent fMRI scanning of the brain at screening for stratification by CNS pain response. Whole brain BOLD-signal-voxel-count of 700 units classifying between low and high, and were randomized to CZP or placebo (2:1). The primary outcome was low disease activity (LDA, DAS28 ≤3.2) after 12 weeks of treatment.

Results: 156 RA patients, inadequate responders to csDMARD, signed the informed consent. 139 patients (46/47, 46/49 and 42/43) (99 females, 71%) with moderate-high disease activity (mean (SD) DAS-28: 4.83 (1.03)) could be included respectively and completed the 12-week study treatment. Geometric mean (SD) numbers of baseline BOLD signal positive voxels were 559 (10), 81 (12) and 2498 (3) in the 3 arms respectively. The mean DAS28 (SD) scores after 12 weeks of study treatment were Placebo: 3.89 (1.29), CZP-L: 3.42 (1.06) and CZP-H: 3.06 (1.04). LDA was achieved in 12/47 patients (25.5 %) in placebo, 22/49 (44.9%) in the CZP-L, and 25/43, (58.1%) in the CZP-H arm. The linear effect term for the ordinal study group variable supported a linear trend of increasing CZP treatment effect with increasing baseline CNS pain response. RR (95% CI) for achieving LDA with each unit increase in treatment category over placebo was 1.79 (1.24 to 2.74, p=0.003).

Conclusion: A higher pre-treatment brain activity in response to pain measured with fMRI predicts the chance of achieving low disease activity with CZP treatment.

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-1 Baseline characteristics of the study population overall and by study groups.

	Overall	Study group		
		Certolizumab-Hq	Certolizumab-Lc	Placebo
	139	43	49	47
mean (SD)	54.3 (11.8)	54.3 (10.8)	56.5 (12.2)	52.1 (12.0)
Female	99 (71.2)	34 (79.1)	35 (71.4)	30 (63.8)
Male	40 (28.8)	9 (20.9)	14 (28.6)	17 (36.2)
Age, years				
Mean(SD)	6.2 (8.1)	6.0 (8.3)	6.4 (8.6)	6.2 (7.6)
Median(IQR)	2.0 (1.0-8.1)	2.0 (1.0-9.0)	3.0 (1.0-8.0)	3.0 (1.0-8.0)
CRP				
Negative	34 (24.5)	15 (34.9)	9 (18.4)	10 (21.3)
Positive	105 (75.5)	28 (65.1)	40 (81.6)	37 (78.7)
ESR				
Negative	39 (28.1)	12 (27.9)	13 (26.5)	14 (29.8)
Positive	100 (71.9)	31 (72.1)	36 (73.5)	33 (70.2)
ESR (28), mean (SD)	10.2 (6.5)	9.3 (6.4)	11.3 (6.7)	9.9 (6.2)
ESR (28), mean (SD)	7.9 (5.3)	7.0 (4.4)	8.7 (6.3)	8.0 (4.8)
Visual analogue scale VAS, mm, mean (SD)	50.0 (20.0)	57.2 (19.9)	59.1 (17.8)	57.6 (22.5)
Global VAS, mm, mean (SD)	49.6 (18.7)	46.0 (20.2)	49.5 (19.2)	53.1 (16.2)
mm, mean (SD)	55.2 (19.3)	53.5 (18.0)	57.1 (17.0)	54.9 (22.7)
ESR, mean (SD)	25.8 (19.9)	23.7 (18.0)	25.2 (17.1)	28.2 (23.2)
ESR, mean (SD)	8.7 (13.0)	6.8 (12.7)	7.9 (8.7)	11.2 (16.5)
ESR/h, mean (SD)	4.8 (1.0)	4.7 (1.0)	5.0 (1.1)	4.9 (1.0)

SD, standard deviation; IQR, interquartile range; ACPA, anti-citrullinated peptide antibodies; RF, Rheumatoid factor; VAS, visual analogue scale; ESR, erythrocyte sedimentation rate; CRP, C reactive protein; DAS-28, disease activity score 28 joints.

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SAT0051

REMISSION IN RHEUMATOID ARTHRITIS PATIENTS: A CLUSTER ANALYSIS TO IDENTIFY AND CHARACTERIZE SUBPOPULATIONS OF PATIENTS

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Background: Disease Activity Score (DAS) is a continuous measure of Rheumatoid Arthritis (RA) activity, used in clinical practice for monitoring disease progression and for documenting treatment response. According to EULAR, the clinical desired target is to achieve a remission state (or failing that, low disease activity). However, the population of RA patients in this state could be heterogeneous.