Objectives: To explore and describe pre-treatment CNS pain response associations with post treatment course of RA disease activity components and patient-physician discrepancy in global disease assessment.

Methods: Patients fulfilling the 2010 ACR/EULAR classification criteria with moderate-severe disease activity (DAS-28>3.2) under stable DMARD treatment were recruited. Patients underwent an fMRI scan, stratified by a whole-brain BOLD positive voxel count threshold of 700 units and randomized to treatment with CZP or placebo in a 2:1 ratio. We descriptively assessed components of RA disease activity (Table 1 + 2). We summarized the mean results and 95% confidence intervals of these measurements at study timepoints and compared the 3 study groups at week 12 using one-way ANOVA and post-hoc Tukey tests.

Results: 156 eligible patients were screened and 139 (99 females, 71%) patients with moderate-high disease activity were randomized. ANOVA and pairwise comparisons showed that PGA-VAS improvement was larger in the CZP-H group whereas more similar to that in placebo in the CZP-L group. PhysGA-VAS however was similarly reduced in both CZP groups. Patients in the CZP-L group constantly rated their pain numerically higher than physicians whereas in the CZP-H group an initially higher discrepancy numerically reduced over time.

Conclusion: These results suggest that improved patient global disease activity assessment could be the main driver of improved DAS-28 LDA rates with CZP treatment in patients with a high CNS pain response. Our findings indicate a potential role of fMRI imaging of the brain to further understand disease activity perception in RA patients.

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Table 1: Baseline patient characteristics.

			Study group		
			Certolizumab-High	Certolizumab-Low	Placebo
N			43	49	47
Age		Mean(SD)	54.3 (10.8)	56.5 (12.2)	52.1 (12.0)
Sex	female	n(%)	34 (79.1)	35 (71.4)	30 (63.8)
	male	n(%)	9 (20.9)	14 (28.6)	17 (36.2)
Disease duration		Mean(SD)	6.0 (8.3)	6.4 (8.6)	6.2 (7.6)
		Median(IQR)	2.0 (1.0-9.0)	3.0 (1.0-8.0)	3.0 (1.0-8.0)
ACPA	Negative	n(%)	15 (34.9)	9 (18.4)	10 (21.3)
	Positive	n(%)	28 (65.1)	40 (81.6)	37 (78.7)
RF	Negative	n(%)	12 (27.9)	13 (26.5)	14 (29.8)
	Positive	n(%)	31 (72.1)	36 (73.5)	33 (70.2)
Tender joints (28)		Mean(SD)	9.3 (6.4)	11.3 (6.7)	9.9 (6.2)
Swollen joints (28)		Mean(SD)	7.0 (4.4)	8.7 (6.3)	8.0 (4.8)
Patient global VAS, mm		Mean(SD)	57.2 (19.9)	59.1 (17.8)	57.6 (22.5)
Physician global VAS, mm		Mean(SD)	46.0 (20.2)	49.5 (19.2)	53.1 (16.2)
Pain VAS		Mean(SD)	53.5 (18.0)	57.1 (17.0)	54.9 (22.7)
ESR		Mean(SD)	23.7 (19.0)	25.2 (17.1)	28.2 (23.2)
CRP		Mean(SD)	6.8 (12.7)	7.9 (8.7)	11.2 (16.5)
DAS28		Mean(SD)	4.7 (1.0)	5.0 (1.1)	4.9 (1.0)

Table 2: Between group comparisons of disease activity components

	Comparison	Difference	95%CI	P value
Pain-VAS	CZP-L-CZP-H	6.26	-4.87 to 17.38	0.379
	Placebo-CZP-H	8.28	-2.85 to 19.41	0.186
	Placebo-CZP-L	2.02	-8.85 to 12.89	0.899
PGA-VAS	CZP-L-CZP-H	9.49	-1.23 to 20.20	0.094
	Placebo-CZP-H	14.99	4.27 to 25.70	0.003
	Placebo-CZP-L	5.50	-4.97 to 15.97	0.429
PhysGA-VAS	CZP-L-CZP-H	1.59	-8.91 to 12.08	0.932
	Placebo-CZP-H	11.22	0.67 to 21.77	0.034
	Placebo-CZP-L	9.64	-0.54 to 19.81	0.068
PGA-PhysGA Discrepancy	CZP-L-CZP-H	6.90	-0.50 to 14.30	0.073
	Placebo-CZP-H	3.30	-4.14 to 10.74	0.546
	Placebo-CZP-L	-3.60	-10.78 to 3.57	0.461
SJC-28	CZP-L-CZP-H	0.47	-1.26 to 2.19	0.796
	Placebo-CZP-H	1.21	-0.52 to 2.93	0.225
	Placebo-CZP-L	0.74	-0.95 to 2.43	0.554
TJC-28	CZP-L-CZP-H	0.16	-0.28 to 0.61	0.664
	Placebo-CZP-H	0.25	-0.20 to 0.69	0.389
	Placebo-CZP-L	0.08	-0.35 to 0.52	0.889
ESR	CZP-L-CZP-H	6.53	-2.80 to 15.85	0.225
	Placebo-CZP-H	11.77	2.44 to 21.09	0.009
	Placebo-CZP-L	5.24	-3.87 to 14.35	0.363
CRP	CZP-L-CZP-H	0.79	-7.01 to 8.59	0.969
	Placebo-CZP-H	8.24	0.48 to 16.00	0.035
	Placebo-CZP-L	7.45	-0.17 to 15.07	0.057

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Figure 1. Course of disease activity components through trial timepoints. *indicates log-transformed y axis. ** Discrepancy equals Patient global minus physician global assessment.

OP0219 MORTALITY OF RHEUMATOID ARTHRITIS PATIENTS, TREATED TO TARGET AT LOW DISEASE ACTIVITY: 17-YEARS FOLLOW-UP OF THE BEST COHORT

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Background: Rheumatoid arthritis is known to be associated with increased mortality over the years when compared to the general population. In the BeSt study, 508 patients were treated to target (Disease Activity Score ≤ 2.4) for 10 years between April 2000 and August 2012. At the end of the initial study follow-up, the observed mortality in the BeSt cohort was similar to mortality in the general population. In the current study we evaluated the mortality in the BeSt cohort after 17 years follow-up and compared it to the general Dutch population.

Objectives: Evaluate long-term mortality in the BeSt study cohort.

Methods: In the BeSt study 508 patients diagnosed with early RA were randomized to four initial treatment strategies: 1. Sequential monotherapy; 2. Step-up

combination therapy; 3. Initial combination therapy with prednisone; or 4. Initial combination therapy with infliximab. During the 10-year follow-up period treatment was steered at low disease activity (DAS ≤ 2.4) and adjusted every three months when necessary. After 10-years patients were treated and followed-up according to regular care. We explored mortality through the Dutch state registry for mortality (Centrum voor Familiegesciedenis) and treating rheumatologist. Mortality in the BeSt cohort was compared to the general Dutch population (Statistics Netherlands) matched by gender, age and calendar year using the standardized mortality ratio (SMR). Kaplan-Meier curves and the log-rank test were used to compare survival among the initial treatment strategies.

Results: The mean duration of follow-up in non-deceased patients was 17 years (range 16-18). In total, 143 patients died (28%) compared to a total of 105 (21%) expected deaths in the reference population. The overall SMR after 17 years was 1.37 (95% CI: 1.16-1.61). Within the study population, no statistically significant difference in survival-curves was observed between the four initial treatment strategies (log-rank $p=0.76$) (table 1, and figure 1).

Table 1. BeSt study cohort mortality - stratified for initial treatment strategy

	Sequential monotherapy n=126	Step-up combination therapy n=121	Initial combination therapy with prednisone n=133	Initial combination therapy with infliximab n=128
N (%) †	38 (30)	31 (26)	41 (31)	33 (26)
SMR (95% CI)	1.41 (1.03-1.94)	1.20 (0.84-1.70)	1.53 (1.13-2.09)	1.31 (0.93-1.85)

SMR: standardized mortality ratio (number observed deaths/number expected deaths); CI: confidence interval. Conclusion:

Figure 1. Survival curves - stratified for initial treatment strategy

After a mean of 17 years follow-up the mortality was increased in the BeSt study cohort when compared to the general Dutch population. We observed no difference in survival curves among the four treatment strategies.

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OP0220

ASSESSING THE EFFECT OF INCREASED BODY MASS INDEX ON RESPONSE TO TNF INHIBITORS IN ESTABLISHED RHEUMATOID ARTHRITIS: RESULTS FROM THE METEOR DATABASE

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Background: Rheumatoid arthritis (RA) is associated with increased body mass index (BMI)- 60% of patients are either overweight or obese. Obesity in RA has been shown to predict reduced response to biologic therapy including tumour-necrosis-factor inhibitors (TNFi) [1]. However, it is not clear whether increased BMI influences response to all TNFi drugs in RA.

Objectives: 1. To explore whether BMI is associated with response to TNFi in patients with established rheumatoid arthritis (estRA), including those newly-starting on these drugs.

Methods: Participants with estRA (>1year since diagnosis) taking biologic medications, registered on METEOR (international database of RA patients), 2008-2013, were included. EULAR response, DAS28 remission (including components), and treatment regimens were recorded at baseline, 6, and 12 months. WHO definitions of overweight (BMI ≥ 25) and obese (BMI ≥ 30) were explored as predictors of TNFi response (good EULAR response and DAS28 remission) using normal BMI as comparator. Logistic and linear regression models (controlling for age, gender, smoking, and baseline outcomes) and sensitivity analyses were performed. Subgroup analyses were performed for grouped TNFi and individual TNFi (infliximab, IFX; adalimumab, ADA; etanercept, ETN).

Results: 247 patients with estRA were taking a biologic at 6 months, and 231 patients were taking a biologic at 12 months. Obese patients taking any biologic were significantly less likely to achieve DAS28 remission (OR 0.33 [95%CI 0.12-0.80]) or good EULAR response (OR 0.37 [95%CI 0.16-0.81]) after 6 months, compared to those of normal BMI; this was also demonstrated in those co-prescribed methotrexate (DAS28 remission: OR 0.23 [95%CI 0.07-0.62]; good EULAR response: OR 0.39 [95%CI 0.15-0.92]). These associations did not remain statistically significant at the 12 months assessment.

Regarding specific anti-TNF therapies, RA patients treated with monoclonal antibody (-mab) TNFis (IFX/ADA/ GOL) were significantly less likely to achieve good EULAR response at 6 months if they were obese RA (n=38), compared to those of normal weight (n=44) (OR 0.17 [95%CI 0.03-0.59]). A similar non-significant difference was demonstrated for DAS28 remission, and 12-month remission. Specifically, obese individuals were significantly less likely to achieve good EULAR response at 6 months with IFX (OR 0.09 [95%CI 0.00-0.61]; n=20), and significantly less likely to achieve DAS28 remission at 6 months when newly-starting ADA (OR 0.14 [95%CI 0.01-0.96]; n=17), compared to those of normal weight. There were no significant differences in remission outcomes between individuals of different BMI taking ETN. A small number of individuals stopped taking their respective biologic after 6months; reason for cessation was not recorded.

Similar outcomes were seen in patients already established on anti-TNF therapy, with overweight and obese individuals less likely overall to be in DAS28 remission at all time points.

Conclusion: In established RA, obesity is associated with reduced treatment response to -mab TNFi. No association between increased BMI and response to ETA was observed. Using BMI to direct biologic drug choice could prove to be a simple and cost-effective personalised-medicine approach to prescribing.

References:

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OP0221

HAVE 5-YEAR SURVIVAL RATE AND MORTALITY CHANGED IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS IN THE PAST TWENTY YEARS?-RESULTS FROM THE IORRA COHORT

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Background: The mortality of patients with rheumatoid arthritis (RA) had been reported as being worse than that of the general population [1, 2], but is expected to have improved over time because the progress in treatment of RA during the past twenty years has been actively adopted to RA management [3, 4]. However, the change in the mortality still remains controversial in patients with early RA [5, 6].

Objectives: To investigate whether the vital prognosis of patients with early RA has changed in the past twenty years.

Methods: The IORRA cohort is a large observational cohort established in 2000 at the Institute of Rheumatology, Tokyo Women's Medical University. Essentially, all Japanese patients diagnosed with RA at our institute were registered and clinical parameters were assessed biannually. As there is no National Death Registry in Japan, we obtained death report from residual families who responded to our mail query to patients who failed to conduct the subsequent IORRA survey, from physicians of affiliated hospitals and from police in case they found dead