References:

[1] Dickens C et al. (2002). Psychosom Med. 64(1), 52–60.
[2] Nagyova I et al. (2005) Patient Educ Couns. 58(1), 55–62.
[3] Sleath B et al. (2008) Arthritis Rheum. 59(2), 186–91.
[4] Suzuki K et al. (2015) PLoS One. 10(3), e0119147.
Acknowledgements: None.
Disclosure of Interest: R. Srumsiri Employee of: Janssen Pharmaceutical KK, Y. Kaneko Paid instructor for: YK has received lecture fees from AbbVie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Pfizer, Janssen, and UCB., J. Mahlich Employee of: Janssen Pharmaceutical KK
DOI: 10.1136/annrheumdis-2017-eular.4542

FRIDAY, 16 JUNE 2017

Rheumatoid arthritis - anti-TNF therapy

FRI0178 RITUXIMAB IS EFFECTIVE IN THE TREATMENT OF RHEUMATOID ARTHRITIS REGARDLESS OF BODY MASS INDEX

D.H. Yoo¹, W. Park², C.H. Suh³, S.C. Shim⁴, S.J. Lee⁵, Y.J. Bae⁵, C. Park⁵, J.H. Koo⁵. ¹Hanyang University Hospital for Rheumatic Diseases, Seoul; ²IN-HA University, School of Medicine, Incheon; ³Ajou University School of Medicine, Suwon; ⁴Chungnam National University Hospital, Daejeon; ⁵Celltrion Inc., Incheon, Korea, Republic Of

Background: High body mass index (BMI) is known to be associated with inadequate clinical response to anti-TNF agents in rheumatoid arthritis (RA) patients.¹ However, there are limited data on the effect of high BMI on the response to rituximab in RA patients, who showed an inadequate response or intolerance to anti-TNF agents.
Objectives: To investigate the impact of BMI on clinical response in the post-hoc analysis of randomized controlled trial that demonstrated clinical equivalence between a biosimilar of rituximab, CT-P10 and innovator rituximab, RTX² (NCT02149121).
Methods: A total of 332 patients who received two courses of either CT-P10 or RTX were included in this analysis. Patients were classified into 3 groups; normal weight (<25kg/m²), overweight (≥25 kg/m² ~<30 kg/m²) and obesity (≥30 kg/m²) as per WHO BMI category. Improvement in disease activity by the Disease Activity Score using C-reactive protein (DAS28-CRP), remission (≤2.6), low disease activity rate (LDA, ≤3.2) and ACR response at Week 24 (Week 24 of 1st course) and Week 48 (Week 24 of 2nd course) and duration of sustained LDA (from the first LDA observed to the last LDA observed up to Week 48) were analysed by BMI categories in the each and combined group of CT-P10 and RTX.
Results: In the pooled group of CT-P10 and RTX, the mean weights were 59 kg in normal weight, 73kg in overweight and 91kg in obesity. All other baseline characteristics were comparable among BMI groups including baseline disease activity based on DAS28; Moderate disease activity, 22.3% vs. 22.8% vs. 25.7%, respectively; High disease activity, 77.7% vs. 77.2% vs. 74.3%, respectively. There was no statistical difference among BMI groups in terms of DAS28 change from baseline and ACR 20/50/70 response (Table). No particular trend was observed in remission and LDA rate by DAS28 at Week 24 and Week 48 among BMI groups (Figure). Mean duration of sustained LDA (months) were also comparable

Table 1. DAS28, ACR responses by BMI subgroups

Parameter	Visit	Normal (N=148)	Over weight (N=114)	Obesity (N=70)
DAS28, mean (SD)	Baseline	5.88 (0.95)	5.81 (0.89)	5.69 (0.78)
	Week 24*	-2.43 (1.12)	-2.13 (1.19)	-2.39 (0.99)
	Week 48*	-2.76 (1.31)	-2.47 (1.32)	-2.74 (1.01)
ACR20, n (%)	Week 24	122 (82.4%)	86 (75.4%)	56 (80.0%)
	Week 48	119 (80.4%)	88 (77.2%)	60 (85.7%)
ACR50, n (%)	Week 24	80 (54.1%)	56 (49.1%)	39 (55.7%)
	Week 48	76 (51.4%)	62 (54.4%)	43 (61.4%)
ACR70, n (%)	Week 24	51 (34.5%)	33 (28.9%)	21 (30.0%)
	Week 48	47 (31.8%)	36 (31.6%)	26 (37.1%)

*Change from baseline.

Figure 1. Remission and LDA by DAS28 by BMI group.

among the groups (4.5 vs. 4.7 vs. 5.0, respectively). Additionally, similar trends in all analyses were observed in each treatment group; CT-P10 and RTX.
Conclusions: The BMI does not affect the clinical response in RA patients with rituximab treatment. Therefore, this result supports that rituximab could be a reasonable therapeutic option for obese RA patients with inadequate response to anti-TNF agents.
References:
[1] Gremese E et al. Arthritis Care Res (Hoboken) 2013;65:94–100.
[2] Yoo DH, et al. American College of Rheumatology 2016; Abstract No. 1635.
Disclosure of Interest: D. H. Yoo Consultant for: Celltrion Inc., W. Park Consultant for: Celltrion Inc., C. H. Suh Consultant for: Celltrion Inc., S. C. Shim Consultant for: Celltrion Inc., S. J. Lee Employee of: Celltrion Inc., Y. J. Bae Employee of: Celltrion Inc., C. Park Employee of: Celltrion Inc., J. H. Koo Employee of: Celltrion Inc.
DOI: 10.1136/annrheumdis-2017-eular.5591

FRI0179 MINIMAL TO NO TRANSFER OF CERTOLIZUMAB PEGOL INTO BREAST MILK: RESULTS FROM CRADLE, A PROSPECTIVE, POSTMARKETING, MULTICENTER, PHARMACOKINETIC STUDY

M.E.B. Clowse¹, F. Förger², C. Hwang³, J. Thorp⁴, R.J.E.M. Dolhain⁵, A. van Tubergen⁶, L. Shaughnessy⁷, J. Simpson⁷, M. Teil⁸, N. Toubanc⁹, M. Wang⁷, T.W. Hale¹⁰. ¹Duke University Medical Center, Durham, United States; ²Inselspital, University of Bern, Bern, Switzerland; ³Keck Hospital of USC, Los Angeles; ⁴University of North Carolina at Chapel Hill, Chapel Hill, United States; ⁵University Medical Centre Rotterdam, Rotterdam; ⁶Maastricht University Medical Center, Maastricht, Netherlands; ⁷UCB Pharma, Raleigh, United States; ⁸UCB Pharma, Slough, United Kingdom; ⁹UCB Pharma, Brussels, Belgium; ¹⁰Texas Tech University School of Medicine, Amarillo, United States

Background: Women with active chronic rheumatic inflammatory conditions (RA, PsA, AxSpA) often face uncertainty regarding the safety of the use of biologics during breastfeeding.¹ Limited and non-validated data exist on the potential transfer of anti-TNFs into breast milk.² CRADLE (NCT02154425) was the first sponsored study to evaluate certolizumab pegol (CZP) concentrations in breast milk, and to estimate the Average Daily Infant Dose (ADID) of maternal CZP.
Objectives: To determine the concentration of CZP in breast milk and calculate the ADID of maternal CZP.
Methods: CRADLE was a pharmacokinetic study of lactating mothers (≥6 weeks postpartum) receiving commercial CZP. Decision to treat with CZP and breastfeed was independent of study participation. At steady state (≥3 CZP doses), breast milk samples were collected on Days 0, 2, 4, 6, 8, 10, 12, 14 (±28) from each mother across 1 dosing period. CZP was detected using a highly sensitive, CZP-specific electrochemiluminescence immunoassay validated in milk (lower limit of quantification [LLOQ]=0.032 µg/mL; 10-fold lower than previous assays). CZP stability in milk was confirmed.
Results: 18 CZP-treated mothers were screened: 17 entered the sampling period; 16 on CZP 200 mg Q2W; 1 on CZP 400 mg Q4W (7 RA; 5 SpA; 5 CD; Table A). Samples from 4/17 mothers had no measurable CZP in breast milk; 13/17 had quantifiable levels for at least 1 time point (highest concentration: 0.076 µg/mL; Table B). Estimated ADID ranged 0–0.0104 mg/kg/day; median Relative Infant Dose (RID; calculated post hoc³): 0.15%. Infants of CZP-exposed mothers had a

Table A: Baseline characteristics of mothers and infants

Mean (SD), unless otherwise stated	All mothers (N=18) [a]
Age, years	33.7 (4.2)
Weight, kg	68.9 (9.6)
BMI, kg/m ²	23.6 (3.0)
Indication for CZP treatment, n [b]	
Rheumatoid arthritis	7
Psoriatic arthritis	3
Axial spondyloarthritis/ankylosing spondylitis	2
Crohn's disease	5
Infant age at mother's first sample, n (%)	All infants (N=17)
≤6 months	13 (76.5)
>6 months–≤12 months	2 (11.8)
>12 months–≤18 months	2 (11.8)

[a] Includes 1 screen failure; [b] n=17.

Table B: Concentrations of CZP (µg/mL) in breast milk

Mother no.	0	2	4	6	8	10	12	14	28
5	0.056	0.069	0.074	0.076	0.076	0.069	0.069	0.06	–
1	0.067	0.061	0.066	0.065	0.062	0.056	0.052	0.041	–
9	0.039	0.04	0.047	0.045	0.042	0.043	0.038	0.035	–
3	BLO	0.032	0.049	0.053	0.037	0.037	0.033	0.033	–
16	0.04	0.033	0.036	0.037	0.043	BLO	BLO	BLO	–
11	BLO	BLO	0.051	0.038	0.042	BLO	0.033	BLO	–
2	BLO	BLO	0.035	0.037	0.041	BLO	0.043	BLO	–
15	BLO	BLO	0.041	0.034	0.033	BLO	0.037	BLO	–
10	BLO	BLO	BLO	0.033	0.042	0.042	BLO	BLO	–
8	BLO	BLO	0.035	0.034	0.043	BLO	BLO	BLO	–
12	BLO	BLO	0.034	0.037	0.033	BLO	BLO	BLO	–
6	BLO	BLO	0.044	0.048	BLO	BLO	BLO	BLO	–
7	BLO	BLO	BLO	BLO	BLO	0.035	BLO	BLO	–
4	BLO	BLO	BLO	BLO	BLO	BLO	BLO	BLO	–
13	BLO	BLO	BLO	BLO	BLO	BLO	BLO	BLO	–
14	BLO	BLO	BLO	BLO	BLO	BLO	BLO	BLO	–
17	BLO	BLO	BLO	BLO	BLO	BLO	BLO	BLO	–

BLO: below the lower limit of quantification; LLOQ: lower limit of quantification.

Less than 3xLLOQ (<0.096 µg/mL)
Less than 2xLLOQ (<0.064 µg/mL)
BLO (<0.032 µg/mL)
CZP plasma C_{trough} from the RAPID2 study: 15.7 µg/mL