OP0016 COMPARATIVE EFFECTIVENESS AT 1 YEAR OF DIFFERENT ANTI-TNF DRUGS AS FIRST BIOLOGIC DMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS – RESULTS FROM THE NATIONWIDE SWEDISH REGISTER

C. Turesson^{1,2}, T. Frisell³, M. Dehlin⁴, D. Di Giuseppe³, N. Feltelius⁵, A. Kastbom⁶, J. Askling³ on behalf of ARTIS study group. ¹Department of Rheumatology, Skåne University Hospital; ²Rheumatology, Department of Clinical Sciences, Malmö, Lund University, Malmö; ³Department of Medicine, Karolinska Institutet, Stockholm; ⁴Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, Gothenburg University, Gothenburg; ⁵Medical Products Agency, Uppsala; ⁶Rheumatology/AIR, Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden

Background: Treatment with TNF inhibitors is part of the management of patients with severe rheumatoid arthritis (RA). There is limited data on the comparative effectiveness of different TNF inhibitors from clinical trials and observational studies of patients treated in clinical practice.

Objectives: To compare effectiveness of different TNF inhibitors in a large, population representative, sample of bionative patients with RA.

Methods: The study was based on the Swedish Rheumatology Quality register, in which clinical data are prospectively recorded at treatment initiation and at subsequent visits. Patients with RA initiating a TNF inhibitor as their first ever biologic DMARD in 2010–2014 were included and followed through 2015. The proportion remaining on drug at 1 year (± 90 days) after starting therapy was compared. Furthermore, effectiveness at 1 year was assessed as the proportions with EULAR good response, remission (DAS28 < 2.6), HAQ improvement (> 0.2) and swollen and tender joint counts of 0, all corrected for drug survival (1). The relative response was estimated with log-binomial regression, adjusting for potential confounders and using the largest group (etanercept) as reference.

Results: A total of 5568 patients were included. There was a significant difference in the adjusted chance of drug survival across TNF inhibitors (Table). Patients treated with certolizumab or infliximab were less likely to remain on treatment compared to those started on etanercept. The chance of achieving each of the clinical response measures was significantly lower for those initiating infliximab compared to patients treated with etanercept. There were no significant differences in these outcomes compared to etanercept for any of the other TNF inhibitors.

Conclusions: Patients with RA starting infliximab as their first biologic DMARD were less likely to remain on treatment with significant improvement at 1 year compared to those initiating etanercept. There was a similar trend for certolizumab vs. etanercept, but there were no consistent differences in clinical effectiveness between etanercept and adalimumab or golimumab. Treatment context may affect these patterns.

References:

[1] Kristensen A&R 2006; 54: 600–6.

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OP0017 LACK OF PLACENTAL TRANSFER OF CERTOLIZUMAB PEGOL DURING PREGNANCY: RESULTS FROM CRIB, A PROSPECTIVE, POSTMARKETING, MULTICENTER, PHARMACOKINETIC STUDY

X. Mariette¹, A. Flynn², F. Förger³, A. Moltó⁴, R.-M. Flipo⁵, A. van Tubergen⁶, L. Shaughnessy⁷, J. Simpson⁷, M. Teil⁸, E. Helmer⁹, M. Wang⁷, E. Chakravarty¹⁰. ¹Université Paris-Sud, le Kremlin-Bicêtre, France; ²University of Utah, Salt Lake City, United States; ³Inselspital, University of Bern, Bern, Switzerland; ⁴Groupe Hospitalier Cochin, AP-HP, Paris; ⁵Centre Hospitalier

Abstract OP0016 – Table 1. Status at the 1-year evaluation visit among patients with RA initiating a TNF inhibitor as their first ever biologic DMARD

	Etanercept N=1651	Infliximab N=1366	Adalimumab N=1004	Certolizumab N=921	Golimumab N=626	P
Observed percentage						
On drug	70.6	66.4	69.2	65.2	68.0	
EULAR good response*	28.0	23.9	25.9	24.3	27.8	
DAS28 remission*	25.9	21.3	26.0	22.4	27.7	
HAQ improvement*	28.0	24.5	29.0	25.0	24.8	
28 Joint counts = 0*	23.3	16.8	20.4	19.0	21.6	
Adjusted [†] relative risk (95% CI)						
On drug	Ref.	0.94 (0.89–1.00)	0.98 (0.92–1.04)	0.90 (0.84–0.96)	0.97 (0.90–1.04)	0.02
EULAR good response*	Ref.	0.82 (0.70–0.96)	0.95 (0.80–1.12)	0.84 (0.70–1.01)	0.96 (0.79–1.17)	0.10
DAS28 remission*	Ref.	0.83 (0.70–0.98)	1.02 (0.85–1.21)	0.89 (0.74–1.08)	1.00 (0.82–1.23)	0.12
HAQ Improvement*	Ref.	0.82 (0.70–0.96)	1.04 (0.89–1.21)	0.86 (0.73–1.03)	0.86 (0.71–1.05)	0.02
28 Joint count = 0*	Ref.	0.74 (0.61–0.89)	0.91 (0.75–1.11)	0.85 (0.69–1.04)	0.91 (0.73–1.13)	0.03

*LUNDEX corrected (1). [†]Sex, age, disease duration, RF, co-treatment (methotrexate, glucocorticoids.)

Régional Universitaire de Lille, Lille, France; ⁶Maastricht University Medical Center, Maastricht, Netherlands; ⁷UCB Pharma, Raleigh, United States; ⁸UCB Pharma, Slough, United Kingdom; ⁹UCB Pharma, Brussels, Belgium; ¹⁰Oklahoma Medical Research Foundation, Oklahoma City, United States

Background: There is a need for effective and safe treatment during pregnancy in women affected by chronic active inflammatory diseases, such as rheumatoid arthritis. Adequate disease control is crucial to ensure the best fetal and maternal health, and reduce adverse pregnancy outcomes.^{1,2} Anti-TNFs are an effective therapeutic option, but because most cross the placenta, they are often stopped during pregnancy.^{3,4} Certolizumab pegol (CZP), due to its Fc-free molecular structure, has no active placental transfer compared to other anti-TNFs.^{5,6}

Objectives: To accurately measure the potential level of placental transfer of CZP from mothers to infants using a highly sensitive, CZP-specific assay.

Methods: CRIB (NCT02019602) was a pharmacokinetic (PK) study of pregnant women (≥ 30 weeks [wks] gestation) receiving commercial CZP (maintenance dose) for an approved indication; last dose was within 35 days prior to delivery. Blood samples were collected from the mothers, umbilical cords, and infants at delivery, and infants again at Wks 4 and 8 post-delivery. CZP concentration was measured with a sensitive, CZP-specific electrochemiluminescence immunoassay validated in plasma (LLOQ=0.032 $\mu\text{g/mL}$; 10-fold lower than assay used in prior CZP PK studies^{6,7}).

Results: 21 CZP-treated pregnant women were screened; 16 entered the study (Table). Maternal CZP plasma levels at delivery were within the expected therapeutic range (median [range]: 24.4 [5.0–49.4] $\mu\text{g/mL}$). Of the 16 infants delivered, 2 samples were excluded: 1 due to missing data, 1 due to implausible PK data. 13/14 infants had no quantifiable CZP levels at birth ($< 0.032 \mu\text{g/mL}$); 1 infant had a minimal CZP level of 0.042 $\mu\text{g/mL}$ (infant/mother plasma ratio: 0.09%); no infants had quantifiable levels at Wks 4 and 8 (Figure). 3/15 umbilical cord samples had quantifiable CZP levels (maximum: 0.048 $\mu\text{g/mL}$); 1 umbilical cord collapsed and was excluded. No anti-CZP antibodies were detected in mothers, umbilical cords, or infants. The infants of CZP-exposed mothers had a safety profile consistent with that of unexposed similar-age infants.

Table: Baseline characteristics of mothers and infants

Median (min, max), unless stated otherwise	All mothers (n=16) [a]
Age, years	31 (18, 40)
Mother's indication for CZP treatment, n	
Rheumatoid arthritis	11
Crohn's disease	3
Psoriatic arthritis	1
Axial spondyloarthritis/ankylosing spondylitis	1
Median (min, max), unless stated otherwise	All infants (n=16)
Female, n (%)	10 (62.5)
Gestational age at birth, weeks	39.9 (37.7, 41.7)
Weight at birth, kg	3.3 (2.6, 4.0)

Figure: Plasma CZP concentrations in mothers and infants (n=14 mother-infant pairs [b])

[a] Mothers who entered the study; [b] 2/16 infant samples were excluded: 1 due to missing data, and 1 due to implausible PK data (ie. data not consistent with a paediatric CZP PK model, based on the expected range of clearance, volume of distribution, and subsequent elimination half-life); [c] ± 24 hours; [d] ± 7 days (2 samples not collected); [e] ± 7 days. Min: minimum; Max: maximum; BLQ: below the LLOQ ($< 0.032 \mu\text{g/mL}$); LLOQ: lower limit of quantitation.

Conclusions: Using a highly sensitive assay, CZP levels were below LLOQ in 13/14 infant blood samples at birth, and all samples at Wks 4 and 8. This indicates no to negligible placental transfer of CZP from mothers to infants, suggesting lack