Other factors associated with higher IRR were sex (being woman), type of biological treatment (TNF inhibitors), concomitant therapy (methotrexate), smoking, comorbidities (Charlson Index) and time of evolution of rheumatic disease. No differences were found between pathologies.

Table. Results of the Poisson regression model. Factors associated with risk of incidence of a first adverse event since biological therapy initiation.

	CRUDE IRR (IC95%)	P	ADJUSTED IRR (IC95%)	P
AGE AT THE BEGINNING OF BIOLOGICAL TREATMENT (REF. ADULTS)				
YOUNG	0.78 (0.55-1.11)	0.175	1.04 (0.71-1.53)	0.829
ELDERLY ADULTS	1.61 (1.36-1.91)	<0.001	1.47 (1.20-1.80)	<0.001
ELDERLY	1.99 (1.44-2.76)	<0.001	1.90 (1.32-2.75)	0.001
WOMEN	1.32 (1.19-1.47)	<0.001	1.41 (1.23-1.61)	<0.001
TNF INHIBITOR	0.84 (0.74-0.96)	0.009	0.67 (0.57-0.79)	<0.001
DIAGNOSIS (REF. RA)				
AS	0.80 (0.70-0.91)	0.001	1.04 (0.87-1.26)	0.651
PSA	0.97 (0.86-1.10)	0.642	1.08 (0.92-1.28)	0.327
CORTICOSTEROIDS	1.31 (1.18-1.47)	<0.001	1.10 (0.96-1.26)	0.186
METHOTREXATE	1.42 (1.27-1.59)	<0.001	1.35 (1.19-1.54)	<0.001
OTHER DMARDS	1.16 (1.04-1.30)	0.009	1.16 (1.01-1.32)	0.038
SMOKING (REF. NO)				
SMOKER	1.16 (1.02-1.32)	0.028	1.19 (1.02-1.39)	0.029
FORMER SMOKER	1.61 (1.32-1.97)	<0.001	1.59 (1.23-2.07)	<0.001
COPD	1.37 (0.97-1.94)	0.072	1.12 (0.76-1.66)	0.571
DIABETES	1.31 (1.07-1.59)	0.008	1.30 (1.02-1.65)	0.034
CHARLSON INDEX	1.15 (1.08-1.21)	<0.001	1.10 (1.02-1.19)	0.009
TIME OF EVOLUTION OF DISEASE	1.01 (1.00-1.01)	0.074	1.01 (1.00-1.02)	0.021

Conclusion: A mix of clinical and patient factors seem to explain the appearance of a first AE after biological therapy initiation, with age being one of those explanatory variables.

REFERENCE

- [1] Ishchenko A, Lories RJ. Safety and Efficacy of Biological Disease-Modifying Antirheumatic Drugs in Older Rheumatoid Arthritis Patients: Staying the Distance. *Drugs Aging* 2016; 33:387-398

Disclosure of Interests: Paloma Vela-Casasempere Grant/research support from: UCB, Abbvie, Pfizer, Roche, Bristol-Myer-Squibb (another research, not BIOBADASER related), Consultant for: UCB, Lilly, Pfizer, Roche, Bristol-Myer-Squibb, Speakers bureau: Roche, UCB, MSD, Pfizer, GSK, BMS, Lilly, Carlos Sánchez-Piedra: None declared, Carolina Perez-Garcia: None declared, Sara Manrique Arijá Speakers bureau: ABBvie, MSD, Janssen, Lilly, Roche, Pfizer, Novartis., María del Carmen Castro Villegas Paid instructor for: MSD, Abbvie, Pfizer, Janssen, Lilly, Roche, Blanca Garcia-Magallon: None declared, Javier Manero: None declared, Silvia Gomez-Sabater: None declared, Rocio Caño-Alameda: None declared, Fernando Sánchez-Alonso: None declared, Federico Diaz-Gonzalez Grant/research support from: MSD, Abbvie, Roche, Novartis, Consultant for: Lilly, Novartis, Pfizer, Amgen, Biogen, Celgene, Speakers bureau: MSD, Lilly, Janssen, BMS, Roche, Juan Jesus Gomez-Reino: None declared

DOI: 10.1136/annrheumdis-2019-eular.1369

SAT0169 RISK OF SERIOUS INFECTIONS IN OFFSPRING ACCORDING TO TNFI SUBTYPES

Evelyn Vinet¹, Yvan St-Pierre², Cristiano Moura², Jeffrey Curtis³, Sasha Bernatsky¹. ¹McGill University, Divisions of Rheumatology and Clinical Epidemiology, Montreal, Canada; ²McGill University Health Centre Research Institute, Montréal, Canada; ³University of Alabama at Birmingham, Birmingham, United States of America

Background: TNFi subtypes have differential trans-placental passage; infliximab and adalimumab (both monoclonal immunoglobulins) have the highest transfer, reaching higher fetal than maternal blood levels, while certolizumab (a pegylated Fab fragment) and etanercept (a fusion protein) display the lowest passage (less than 0.25% and 4-7% respectively). Thus, some TNFi subtypes could cause immunosuppression in the offspring. However, to date, there is no data on the risk of serious infections according to TNFi subtypes.

Objectives: We evaluated serious infections in a large group of children born to mothers with chronic inflammatory diseases who used TNFi during pregnancy. Our comparators were unexposed offspring born to affected and unaffected mothers. We determined if the risk of serious infections differed according to TNFi subtypes.

Methods: We identified all women with ≥ 1 hospitalization for delivery after a diagnosis of rheumatoid arthritis (RA), ankylosing spondylitis (AS),

psoriasis (PsO), psoriatic arthritis (PsA), or inflammatory bowel diseases (IBD), and a randomly selected group of unaffected mothers, matched $\geq 4:1$ for age, year of delivery, and state of residence, using MarketScan database (2011-2016). Only women continuously enrolled within MarketScan for ≥ 12 months prior to delivery and with available child linkage were included. We defined TNFi exposure based on ≥ 1 filled prescription and/or infusion procedure code during pregnancy and/or the preconception period. We further refined TNFi exposure based on potential for high (infliximab, adalimumab, golimumab) versus low (certolizumab, etanercept) placental transfer. We ascertained serious infections in the offspring based on ≥ 1 hospitalization with infection as a primary diagnosis, in the first year of life. We performed multivariate analyses, adjusting for maternal demographics, disease type, co-morbidities, pregnancy complications, and drugs (corticosteroids, DMARDs, non-TNFi biologics).

Results: We identified 16,490 offspring of mothers with RA (4,142), AS (381), PsO/PsA(5,743), and IBD (6,731), as well as 164,553 children born to unaffected matched mothers. Among offspring whose mothers had inflammatory diseases, 1,611 (9.8%) were exposed to TNFi during pregnancy, 338 (2.0%) were unexposed during pregnancy but exposed in the preconception period, and 14,541 (88.2%) were unexposed both during the pregnancy and preconception periods. The percent of serious infections in offspring of inflammatory disease mothers with no TNFi exposure (2.1%; 95% CI 1.9, 2.3) was similar to those with TNFi exposure (2.3%; 95% CI 1.6, 3.0), while the percent of serious infections in children born to unaffected mothers was 1.6% (95% CI 1.6, 1.7). In offspring exposed to TNFi with high placental transfer, the percent of serious infections was 2.3% (95% CI 1.6, 3.3), while for TNFi with low transfer, it was 1.7% (95% CI 1.0, 3.1).

In multivariate analyses, we did not observe an increased risk of serious infections in TNFi exposed offspring versus unexposed offspring of mothers with inflammatory diseases (OR 1.0; 95% CI 0.7, 1.5). Results were similar when we restricted TNFi exposure to the third trimester (OR 1.1; 95% CI 0.7, 1.7). In multivariate analyses of children exposed to TNFi with high versus low placental transfer, our point estimate was consistent with increased risk, but the confidence interval was wide, including the null value (OR 1.43; 95% CI 0.66, 3.08).

Conclusion: When we compared the risk of serious infections in offspring exposed to TNFi with high versus low placental transfer, we observed a potential trend for an increased risk, although the confidence interval was wide and included the null value. Our findings stress the need to further study this issue.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.5820

SAT0170 A NOVEL FORMULATION OF CT-P13 FOR SUBCUTANEOUS ADMINISTRATION: 30 WEEK RESULTS FROM A PART 2 OF PHASE I/III RANDOMIZED CONTROLLED TRIAL IN PATIENTS WITH RHEUMATOID ARTHRITIS

Rene Westhovens¹, Piotr Wiland², Marek Zawadzki², Delina Ivanova³, Alfredo Berrocal⁴, Elias Chalouhi⁵, Éva Balázs⁶, Sergii Shevchuk⁷, Larisa Eliseeva⁸, Mykola Stanislavchuk⁹, Roman Yatsyshyn¹⁰, Sangjoon Lee¹¹, Jeehye Suh¹¹, Seung Lee¹¹, Yunah Kim¹¹, Daehyun Yoo¹². ¹KU Leuven, Leuven, Belgium; ²Medical University, Dpt of Rheumatology, Wrocław, Poland; ³Diagnostic-Consultative Center Aleksandrovskaya EOOD, Sofia, Bulgaria; ⁴Bio Ciencias Peru S. R.L., Lima, Peru; ⁵Clinica Internacional Sede Lima, Lima, Peru; ⁶Dr. Bugyi István Hospital, Szentes, Hungary; ⁷Clinic of SRI of invalid Rehab. ESTC of VNMU n.a. M.I. Pyrokhov, Vinnytsia, Ukraine; ⁸Siberian State Medical University of Roszdraz, Tomsk, Russian Federation; ⁹National Pirogov Memorial Medical University, Vinnytsia, Ukraine; ¹⁰Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine; ¹¹Celltrion, Inc., Incheon, Korea, Rep. of (South Korea); ¹²Hanyang University Medical Center, Seoul, Korea, Rep. of (South Korea)

Background: CT-P13 subcutaneous (SC) formulation showed comparable efficacy and safety with CT-P13 intravenous (IV) formulation in rheumatoid arthritis (RA)¹ and Crohn's disease² preliminary studies (Part 1).

Objectives: The purpose of this study was to demonstrate non-inferiority (NI) of efficacy and compare safety profiles of CT-P13 SC to CT-P13 IV in RA patients over 30 weeks of Part 2.

Methods: In this randomized, controlled, double blinded, phase I/III study, RA patients received CT-P13 IV 3 mg/kg at Weeks 0 and 2 and were randomized at Week 6 to receive CT-P13 SC 120 mg every 2 weeks or CT-P13 IV 3 mg/kg every 8 weeks. From Week 30, all patients received CT-P13 SC 120 mg every 2 weeks. The primary efficacy endpoint, change of DAS28 (C-reactive protein [CRP]) from baseline to Week 22, was analyzed by using an analysis of covariance (ANCOVA). Non-inferiority is to be concluded if the lower bound of the 95% CI for the

treatment difference in the change of DAS28 (CRP) from baseline to Week 22 is greater than the pre-specified NI margin of -0.6.

Results: A total of 362 patients were enrolled, of whom 348 were randomly assigned at Week 6 into 2 treatment arms in a 1:1 ratio (169 and 179 patients in SC 120 mg and IV 3 mg/kg arms, respectively). The mean change of DAS28 (CRP) from baseline to Week 22 was similar between the arms. The lower limit of two-sided 95% CI (0.03) was greater than the pre-specified NI margin (-0.6) which indicated NI of SC 120 mg compared to IV 3 mg/kg (Table 1). Additional efficacy including ACR responses were similar between two treatment arms up to Week 22 with slightly higher response rate trend observed in SC 120 mg arm at Week 30 (Figure 1). The safety profiles which occurred after study drug administration at Week 6 in SC 120 mg arm were generally comparable to IV 3 mg/kg arm. All of injection site reactions were grade 1 or 2 in intensity. Majority of administration-related reactions (ARRs) were grade 1 or 2 in intensity except 1 patient in IV 3 mg/kg arm who experienced grade 3 ARR and was withdrawn from the study due to this event (Table 2).

Table 1. Analysis of Change (decrease) from Baseline of DAS28 (CRP) at Week 22 (ANCOVA)

Treatment	n	DAS28 (CRP) decrease Least Square Mean (Standard Error)	Estimate of Treatment Difference	95% CI of Treatment Difference
SC 120 mg	164	2.22 (0.221)	0.28	(0.03, 0.53)
IV 3 mg/kg	171	1.95 (0.209)		

Note. Country, Week 2 serum CRP concentration (≤ 0.6 mg/dL vs >0.6 mg/dL), and Week 6 body weight (≤ 100 kg vs >100 kg) were considered as covariates.

Table 2. Summary of Safety Results up to from Weeks 6 to 30

		SC 120 mg (N=170)	IV 3 mg/kg (N=178)
Safety, n (%)	Treatment-emergent AEs	62 (36.5)	76 (42.7)
	Administration-related reactions	1 (0.6)	8 (4.5)
	Injection site reactions	11 (6.5)	4 (2.2)
	Infections	34 (20.0)	32 (18.0)

Note. One patient in IV 3 mg/kg arm was analyzed as SC 120 mg arm in Safety Population as receiving CT-P13 SC at Week 14.

Figure 1. The proportion of patients Achieving Clinical Response according to the ACR Criteria up to Week 30

Note. Results at Week 2 and Week 6 were obtained following IV infusion in the Dose-Loading Phase.

Conclusion: The study demonstrated NI of efficacy for CT-P13 SC to the CT-P13 IV. Also, CT-P13 SC showed similar efficacy and safety profiles to CT-P13 IV up to Week 30. CT-P13 SC could provide a favorable benefit to patients with an alternative convenient way of administration.

REFERENCES

- [1] Westhovens R, et al. *Annals of the Rheumatic Diseases* 2018;77(-):315 (suppl2)
- [2] Schreiber, S, et al. *Gastroenterology* 2018;154(6):S-1371

Disclosure of Interests: Rene Westhovens Grant/research support from: Bristol-Myers Squibb, Consultant for: Celltrion, Galapagos-Gilead, Piotr Wiland Speakers bureau: Novartis, Pfizer, Abbvie, Gedeon-Richter, Lilly, Roche and Sandoz, Marek Zawadzki Grant/research support from: Celltrion, Inc., Delina Ivanova Grant/research support from: Celltrion, Inc, PPD, Quintiles, Egis Pharmaceuticals, and Pfizer., Alfredo Berrocal Grant/research support from: Celltrion, Inc., Elias Chalouhi Grant/research support from: Celltrion, Inc., Éva Balázs Grant/research support from: Celltrion, Inc., Consultant for: Merck and Amgen, Sergii Shevchuk: None

declared, Larisa Eliseeva Grant/research support from: Celltrion, Inc., Mykola Stanislavchuk Grant/research support from: AstraZeneca, Celltrion, Galapagos, Genentech, GlaxoSmithKline, Human Genome, Lilly, MedImmune, Pfizer, Roche and UCB, Roman Yatsyshyn Grant/research support from: Celltrion, Inc., SangJoon Lee Shareholder of: Celltrion, Inc., Employee of: Celltrion, Inc., JeeHye Suh Employee of: Celltrion, Inc., SeulGi Lee Employee of: Celltrion, Inc., Yunah Kim Employee of: Celltrion, Inc., DaeHyun Yoo Grant/research support from: Celltrion, Inc., Consultant for: Celltrion, Inc.

DOI: 10.1136/annrheumdis-2019-eular.612

SAT0171 A RETROSPECTIVE ANALYSIS OF LONG TERM SAFETY UP TO FIVE YEARS OF INFLIXIMAB BIOSIMILAR CT-P13 IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

Tae-Hwan Kim¹, Shin-Seok Lee², Won Park³, Yeong Wook Song⁴, Chang-Hee Suh⁵, Sookyoung Kim⁶, Youngnam Lee⁶, DaeHyun Yoo¹. ¹Hanyang University Hospital for Rheumatic Diseases, Rheumatology, Seoul, Korea, Rep. of (South Korea); ²Chonnam National University Medical School and Hospital, Rheumatology, Gwangju, Korea, Rep. of (South Korea); ³Inha University Hospital, Rheumatology, Incheon, Korea, Rep. of (South Korea); ⁴Seoul National University Hospital, Rheumatology, Seoul, Korea, Rep. of (South Korea); ⁵Ajou University School of Medicine, Rheumatology, Suwon, Korea, Rep. of (South Korea); ⁶Celltrion Healthcare, Incheon, Korea, Rep. of (South Korea)

Background: Long term safety and efficacy of anti-TNF inhibitors in rheumatic diseases is an important aspect of patient treatment. CT-P13 is the first infliximab biosimilar approved by EMA and FDA and has demonstrated comparable efficacy and safety with reference infliximab in rheumatoid arthritis (RA)^{1,2} and ankylosing spondylitis (AS)^{3,4}. However, long term data of infliximab biosimilar to date has been limited to two years^{5,6}.

Objectives: To demonstrate drug survival and long term safety and efficacy of CT-P13 up to 5 years in patients with RA or AS, including patients who switched from reference infliximab to CT-P13.

Methods: Long term data was retrospectively collected from medical records of patients with RA and AS treated with CT-P13 at least once between September 2012 and December 2017 in five referral hospitals in Korea. Patients included both those who were infliximab-treatment naïve at the start of CT-P13 treatment (naïve patient) and those who switched from reference infliximab to CT-P13 (switched patient). Primary endpoints were safety and drug survival up to 5 years analyzed by Kaplan-Meier curve.

Results: Data from 491 patients (154 RA and 337 AS) were collected and analyzed, including 19 and 118 switched patients with RA and AS, respectively. Median disease duration was 64.7 months (range: 4.7 to 265.9 months) for patients with RA and 56.3 months (range: 3.0 to 216.7 months) for patients with AS. The median duration of CT-P13 treatment was 46.8 weeks (range: 0 to 250.6 weeks) and 94.1 weeks (range: 0 to 246.0 weeks) for patients with RA and AS, respectively. The probability of survival at year 5 for patients with RA was 0.42 and 0.53 respectively for naïve and switched patients. The probability of survival at year 5 for patients with AS was 0.64 and 0.72 respectively for naïve and switched patients. Median DAS28-ESR score decreased from 5.80 at baseline to 2.73 at year 5 and median DAS28-CRP score decreased from 5.14 at baseline to 1.29 at year 4 for patients with RA. Median BASDAI score decreased from 6.60 at baseline to 3.00 at year 5 for patients with AS. The most common reason for discontinuation for both patients with RA and AS was lack of efficacy. 31.8% of patients with RA and 29.4% of patients with AS experienced at least one adverse event and the most frequently observed type of adverse event was upper respiratory tract infection for 3.90% in patients with RA and 4.15% in patients with AS.

Conclusion: This is the longest evidence to date of safety and efficacy of infliximab biosimilar CT-P13 treatment in patients with RA or AS. Five year analysis of medical records showed that long term treatment with CT-P13 was safe and efficacious based on drug survival, disease activity measurements, and adverse events. Drug survival was similar between patients who were naïve at the start of CT-P13 treatment and switched from reference to CT-P13.

REFERENCES

- [1] Yoo DH, et al. *Ann Rheum Dis.* 2013;72(10):1613-20.