Samsung Bioepis, Sanofi, UCB, Consultant of: Galapagos, Gilead, Janssen, Lilly, Merck Sharp & Dohme, Maya H Buch Speakers bureau: AbbVie, Consultant of: AbbVie, Eli Lilly, Gilead, Merck Serono, Pfizer, Roche, Sanofi, Grant/research support from: Gilead, Pfizer, Roche, UCB, Yusuf Patel: None declared, Raimón Sanmartí Speakers bureau: AbbVie, Bristol Myers Squibb, Gebro, Janssen, Lilly, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, Consultant of: AbbVie, Bristol Myers Squibb, Gebro, Lilly, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, Grant/research support from: Bristol Myers Squibb, Merck Sharp & Dohme, Pfizer, Sara Marsal Speakers bureau: Bristol Myers Squibb, Celgene, Pfizer, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol Myers Squibb, Celgene, Galapagos, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, UCB, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Sanofi, UCB, M.T. Nurmohamed Speakers bureau: AbbVie, Bristol Myers Squibb, Eli Lilly, Roche, Sanofi, Consultant of: AbbVie, Celgene, Celltrion, Eli Lilly, Janssen, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Mundipharma, Novartis, Pfizer, Roche, Sanofi, Hedley Griffiths Consultant of: AbbVie, Gilead, Janssen, Novartis, Peter Peichl: None declared, Bettina Bannert: None declared, Adrian Forster: None declared, Melanie Chartier Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Yedid Elbez Consultant of: Bristol Myers Squibb, Christiane Rauch Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Vadim Khaychuk Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Karissa Lozenski Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb
DOI: 10.1136/annrheumdis-2021-eular.955

AB0208

DO LOW CONCENTRATIONS OF CITRATE IN AN ADALIMUMAB FORMULATION IMPACT THE INCIDENCE AND/OR INTENSITY OF INJECTION SITE PAIN? DATA FROM PHASE I AND III STUDIES ASSESSING THE LOCAL TOLERANCE OF GP2017 (ADALIMUMAB BIOSIMILAR, SDZ-ADL) IN HEALTHY VOLUNTEERS, RHEUMATOID ARTHRITIS, AND PSORIASIS PATIENTS

P. Wiland¹, A. Blauvelt², L. Lemke³, O. Von Richter³, A. Balfour⁴, F. Furlan⁵, N. Gaylis⁶. ¹Medical University, Department of Rheumatology and Internal Medicine, Wrocław, Poland; ²Oregon Medical Research Center, Research Excellence & Personalized Patient Care, Portland, United States of America; ³Hexal AG (A Sandoz company), Clinical Development Biopharmaceuticals, Holzkirchen, Germany; ⁴Hexal AG (A Sandoz company), Clinical Development Biostatistics, Holzkirchen, Germany; ⁵Hexal AG (A Sandoz company), Global Medical Affairs, Holzkirchen, Germany; ⁶Arthritis and Rheumatic Disease Specialties, 21097 NE 27th Court Suite 200, Aventura, United States of America

Background: Adalimumab (ADL) is typically self-administered every 2 weeks (W) as a subcutaneous (s.c.) injection by patients (pts) for diverse indications, including rheumatoid arthritis (RA), psoriatic arthritis (PsA), and psoriasis (PsO). Conflicting evaluations of local tolerance to formulations containing citrate buffer have created insecurities among health care professionals and pts.^{1,2}

Objectives: To evaluate local tolerance of SDZ-ADL (GP2017), a biosimilar ADL with low citrate concentration (1.2 mM),³ in 466 healthy volunteers (HV) and 408 pts (RA: 177 and PsO: 231 including PsA: 52) from four phase I pharmacokinetic (PK) and two phase III confirmatory studies.

Methods: HV evaluated their injection site pain (ISP) using a Visual Analogue Scale (VAS) of 0–100 mm. HV received a single 40 mg/0.8 mL s.c. injection and pts received SDZ-ADL every 2W during 48–51W duration of study. Injection site reactions (ISR) as well as adverse events (AEs) were assessed by investigators during the clinical studies. Details of study designs have been reported previously.^{4–7}

Results: Overall, 456 (97.9%) HV experienced no ISR. Ten HV experienced ISR. These were mostly of mild intensity; only 1 (0.2%) had an ISR of moderate intensity. 96.6% of HV experienced no pain (VAS score 0–4 mm)⁸ at 1-hour post-dose (Figure 1). In the phase III studies, a low number of ISR/ISP events were observed, which decreased during the course of study. Detailed results are provided in Table 1. No ISR/ISP led to treatment or study discontinuation in any study.

Conclusion: The proportion of HV and pts experiencing ISR and ISP after administration of SDZ-ADL was low, with no events leading to treatment or study discontinuation. These results call into question the clinical impact of citrate and its concentration in ADL formulations on the incidence and intensity of ISP.

REFERENCES:

- [1] Nash et al. *Rheumatol Ther.* 2016;3:257–70.
- [2] NHS. Regional medicines optimisation committee briefing, best value biologicals: adalimumab update 6. July 2019. <https://www.sps.nhs.uk/wp-content/uploads/2019/07/Adalimumab-RMOC-Briefing-6.pdf>.

- [3] https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761071b1.pdf.
- [4] Blauvelt A, et al. *Br J Dermatol.* 2018;179:623–31.
- [5] Wiland P, et al. *BioDrugs* 2020;34:809–23.
- [6] Richter OV, et al. *Expert Opin Biol Ther.* 2019;19:1057–64.
- [7] Richter OV, et al. *Expert Opin Biol Ther.* 2019;19:1075–83.
- [8] Hawker GA, et al. *Arthritis Care Res.* 2011;63:240–52.

Figure 1. Proportion of HV with ISP in phase I PK studies

Table 1. ISP and ISR results from phase I PK and phase III confirmatory studies

Phase I PK studies					
Study	101 (N=73)	102 (N=108)	103 (N=178)	104 (N=107)	Pooled studies (N=466)
VAS scores (mm) at 1-hour post-dose					
Mean (SD)	0.89 (2.07)	0.07 (0.52)	1.03 (1.71)	1.03 (2.49)	0.79 (1.84)
Median	0	0	1	0	0
ISR scores at 1-hour post-dose, n (%)					
None	73 (100)	106 (98.2)	178 (100)	99 (92.5)	456 (97.9)
Mild	0 (0)	1 (0.9)	0 (0)	8 (7.5)	9 (1.9)
Moderate	0 (0)	1 (0.9)	0 (0)	0 (0)	1 (0.2)
Phase III confirmatory studies					
	ADACCESS^{5*} (PsO and PsA pts)	ADMYRA^{6*} (RA pts)			
	W0–17 (N=231)	W0–51 (N=168; including pts re-randomised to continue SDZ-ADL after W17)	W0–24 (N=177)	W0–48 (N=177; all pts continued SDZ-ADL after W24)	
Dosage	Induction 80 mg W0, then 40 mg EoW s.c.	40 mg EoW s.c.	40 mg EoW s.c.	40 mg EoW s.c.	
Study duration, W	17	51	24	48	
AEs - ISR, n (%)	15 (6.5), 34	9 (5.4), 26	7 (4.0), 11	7 (4.0), 12	
Mild	14 (6.1), 30	9 (5.4), 26	7 (4.0), 11	7 (4.0), 12	
Moderate	1 (0.4), 4	0	0	0	
AEs - ISP (reported as ISR), n (%)	3 (1.3)	1 (0.6)	2 (1.1)	2 (1.1)	

*ADACCESS and ADMYRA were switch studies, therefore, only pts exposed to SDZ-ADL throughout the study period are included here. EoW, every other week, N, number of HV or pts

Disclosure of Interests: Piotr Wiland Speakers bureau: Celltrion, Celgene, Eli Lilly, Novartis, Pfizer, Sandoz, Sanofi-Aventis, Consultant of: Celltrion, Celgene, Eli Lilly, Novartis, Pfizer, Sandoz, Sanofi-Aventis, Andrew Blauvelt Speakers bureau: AbbVie, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Evimmune, Forte, Galderma, Incyte, Janssen, Leo, Novartis, Pfizer, Rapt, Regeneron, Sandoz, Sanofi Genzyme, Sun

Pharma, and UCB Pharma., Consultant of: AbbVie, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Evomune, Forte, Galderma, Incyte, Janssen, Leo, Novartis, Pfizer, Rapt, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, and UCB Pharma., Lena Lemke Employee of: Hexal AG, Oliver von Richter Employee of: Hexal AG, Alison Balfour Employee of: Hexal AG, Fabricio Furlan Employee of: Hexal AG, Norman Gaylis: None declared

DOI: 10.1136/annrheumdis-2021-eular.1045

AB0209

SERIOUS INFECTIOUS COMPLICATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICS

E. Aronova¹, G. Gridneva¹, A. Kudryavtseva¹, G. Lukina², ¹V.A. Nasonova Research Institute of Rheumatology, Moscow, Moscow, Russian Federation; ²Moscow Clinical Scientific Center named after Loginov A. S., Moscow, Moscow, Russian Federation

Objectives: To study infectious complications of therapy with biologics, analyze the frequency of withdrawal of bDMARDs due to infectious complications.

Methods: The ambispective analysis included data on 505 cases of prescribing biologics with different mechanism of action in 188 patients with rheumatoid arthritis (160 women, 28 men).

Results: Patients in the study group received from 2 to 5 bDMARDs, median (25% -75%) 2 (2-3). Biologics were discontinued 326 times, of which due to the development of serious adverse reactions - 70 times, of which due to the development of infectious complications - 16 times (5% of all cases of discontinuations, 29% of all serious adverse reactions). During treatment with the first bDMARD, infectious complications that required discontinuation of the drug developed in 5.3% of cases (N = 10), with the second bDMARD - in 5.2% of cases (N = 4), no statistical differences were found between these groups. On the background of treatment with the third bDMARD, infectious complications led to the withdrawal of treatment in 14.3% of cases (N = 1), in the fourth - 0%, and in the fifth - 33.4% of cases (N = 1). There was no correlation between the number of sequentially prescribed biologics and the incidence of infectious complications. Most often, serious infections developed during treatment with drugs of the TNF- α inhibitor group (infliximab, etanercept, adalimumab, golimumab, certolizumab pegol) and tofacitinib. Out of 16 cases of infectious complications, 5 were associated with tuberculosis infection.

Conclusion: Infectious complications make up a significant proportion (29%) of all serious adverse reactions leading to the discontinuations of biologics in patients with rheumatoid arthritis. The frequency of discontinuation of bDMARDs due to infectious complications was about 5% and did not change during treatment with both the first and second biologics. It is necessary to remain alert about tuberculosis infection and examine patients before prescribing and during treatment with bDMARDs.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1078

AB0210

COMPARISON OF EFFICACY AND SAFETY OF BIOSIMILAR RITUXIMAB AND ORIGINATOR RITUXIMAB IN REAL CLINICAL PRACTICE

D. Kusevich¹, Y. Olyunin², E. Nasonov^{3,4}, ¹V.A. Nasonova Research Institute of Rheumatology, Laboratory of Osteoarthritis, Moscow, Russian Federation; ²V.A. Nasonova Research Institute of Rheumatology, Laboratory of Early

Arthritis, Moscow, Russian Federation; ³V.A. Nasonova Research Institute of Rheumatology, Scientific Supervisor, Moscow, Russian Federation; ⁴I.M. Sechenov First Moscow State Medical University, Ministry of Health of Russia (Sechenov University), Department of Therapy and Occupational Diseases, Moscow, Russian Federation

Background: Due to the expiration of many originator biologics patents, their biosimilars (BS) have appeared and were put into clinical practice. The introduction of such drugs reduces the cost of treatment and thereby increases its availability. BS rituximab (RTX) Acellbia was developed by the Russian company "BIOCAD". Its effectiveness and safety have been proven in two clinical trials. It was licensed in Russia for the treatment of rheumatoid arthritis (RA) in 2017.

Objectives: To compare efficacy and safety of BSRTX and originator RTX (ORTX) in real clinical practice.

Methods: RA patients fulfilling the EULAR/ACR 2010 criteria and followed-up at the V. A. Nasonova Research Institute of Rheumatology were included. All of them had previously received methotrexate without effect. They were divided into 4 groups. The first and second groups included patients who had not previously received biologics. Treatment with BSRTX was started in the first group, ORTX was administered in the second group. The third and fourth groups included patients who received ORTX with significant improvement. Patients of the third group were switched to BSRTX, in the fourth group treatment with ORTX was continued. ORTX and BSRTX were administered twice 500 mg over 2 weeks. The indication for repeated administration of ORTX and BSRTX was an exacerbation of RA. Patients were examined before the first or regular administration of ORTX or BSRTX and before the planned repeat course of treatment with these drugs. RA activity was evaluated with the DAS28. Adverse events (AE) were recorded. Data were tested for normality using the Kolmogorov-Smirnov test. Continuous variables are presented as mean $\pm$ SD if they obey normal distribution, and as median [quartile interval] if they were not consistent with normal distribution. Mann-Whitney U test was used for comparison between groups.

Results: 127 patients with RA were included. 66 patients had not previously received biologics. BSRTX was started in 35 of them and ORTX - in 31. 61 patients already received ORTHX with clinical improvement. 31 of them were switched to BSRTX, and 30 continued therapy with ORTX. The median interval between the baseline examination and the assessment before the second treatment course in the BSRTX group was 6 [5; 13] months, in the ORTX group - 7 [7; 11] months. In group 1 median DAS28 during follow-up decreased from 5,8 [5,2; 6,9] to 3,9 [3,1; 4,5], in group 2 - from 5,7 [5,2; 6,0] to 4,1 [3,8; 4,6], respectively. These changes were comparable in both groups. The mean duration of the interval between infusion of BSRTX or ORTX and repeated examination - 11,3 $\pm$ 8,2 and 10,1 $\pm$ 4,8 months, respectively. These differences are not significant. In group 3 median DAS28 at the baseline examination was 5,1 [3,9; 5,9], at the second one - 4,3 [3,8; 5,3], in group 4 - 4,6 [3,7; 5,4] and 4,2 [3,5; 5,2] respectively. These values did not differ significantly. The frequency and nature of adverse events during treatment with ORTX and BSRTX did not significantly differ. We did not observe serious AE and unexpected AE.

Conclusion: The results of the present study show that efficacy and safety of BSRTX and ORTX were comparable when they were used as the first biologics and when switching from ORTX to BSRTX. BSRTX can be used in routine clinical practice for the treatment of RA. Disclosure of Interests:

None declared

DOI: 10.1136/annrheumdis-2021-eular.1091