randomised, double-blind, parallel-group, Phase III study for LBEC0101 (NCT02357069). Patients who were deemed requiring continuous treatment for RA upon the investigator's discretion and agreed to participate in this study were allowed for participation. All patients received LBEC0101 50 mg/ml once a week for 48 weeks with the stable dose of methotrexate regardless of the randomization group in the Phase III study. Efficacy, safety and immunogenicity were assessed up to Week 100. Data were analysed for patients who continued to receive LBEC0101 for 100 weeks (maintenance group) and for those who had received ETN-RP for 52 weeks and then switched to LBEC0101 for 48 weeks (switch group).

Results: A total of 148 patients were enrolled in this study; 70 patients continued to receive LBEC0101 and 78 patients switched to receive LBEC0101 from ETN-RP. DAS28-ESR score in the full analysis set were maintained in both groups from week 52 through week 100 (from 3.068 to 3.103 in maintenance group vs. from 3.161 to 3.079 in switch group). Response rates at week 100 for maintenance and switch groups, respectively, were 79.7% vs. 83.3% for ACR20, 65.2% vs. 66.7% for ACR50% and 44.9% vs. 42.3% for ACR70. The incidences of adverse events were comparable between the groups (70.0% for maintenance group and 70.5% for switch group, respectively). The proportion of patients who newly developed antidrug antibodies was similar between the groups (1.4% for maintenance group and 1.3% for switch group, respectively).

Conclusions: The efficacy and safety of LBEC0101 were comparable in both maintenance and switch groups. The efficacy of LBEC0101 was well sustained over 100 weeks.

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Acknowledgements: HanJoo Baek, HoonSuk Cha, JungYoon Choe, ChanBum Choi, InAh Choi, SeungJae Hong, JinWuk Hur, GeunTae Kim, HyunAh Kim, Jin-seok Kim, Jisoo Lee, SangHeon Lee, SangIl Lee, SeungGeun Lee, ShinSeok Lee, YunJong Lee, JunKi Min, KyungSu Park, SungHwan Park, Won Park, Yong-Beom Park, DongHyuk Sheen, SeungCheol Shim, KichulShin, ChangHee Suh, HyungIn Yang, Bin Yoo and WanHee Yoo.

Disclosure of Interest: Y. W. Song: None declared, H. Matsuno Consultant for: Mochida Pharmaceutical Co., Ltd., AYUMI Pharmaceutical Corporation, Nichi-Iko Pharmaceutical Co., Ltd., Meiji Seika Pharma Co., Ltd., M.-C. Park: None declared, M. Tomomitsu Employee of: Mochida Pharmaceutical Co., Ltd., S. Shin Employee of: LG Chem, Ltd., J. Lee Employee of: LG Chem, Ltd.

DOI: 10.1136/annrheumdis-2018-eular.1316

AB0457

CLINICAL EQUIVALENCE IN EFFICACY BETWEEN ABP 501 AND ADALIMUMAB IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS: A TIPPING POINT SENSITIVITY ANALYSIS

N. Zhang, H. Wang, E. Krishnan. *Biosimilars Development, Amgen Inc., Thousand Oaks, USA*

Background: ABP 501 is the first approved biosimilar to adalimumab. Patient withdrawals from clinical trials can result in missing data, which may lead to loss of statistical power and bias of the treatment difference estimate. Therefore, it is critical to examine the potential effects of missing data and analyse the sensitivity of the results under various assumptions on the mechanism of missing data.

Objectives: To examine and confirm the robustness of the clinical similarity conclusion between ABP 501 and adalimumab reference product (RP) through tipping point sensitivity analyses on ACR20 at week 24, the primary endpoint of the phase 3 study in patients with rheumatoid arthritis.

Methods: The primary analysis for this trial has been previously published. The proportions of patients achieving ACR20/50/70 responses with last observation carried forward imputation at weeks 2, 4, 8, 12, 18 and 24, were similar between ABP 501 and the RP over time. Tipping point sensitivity analyses were used to estimate the difference between ABP 501 and the RP with varying assumptions on the outcomes in patients who withdrew from the study early and those who completed the study.

Results: The table 1 displays the results of tipping point analyses on the primary endpoint of ACR20 at week 24. There were no scenarios in which the 90% confidence interval (CI) failed to rule out a 12% loss/increase in the ACR20 response.

Abstract AB0457 – Table 1. Tipping point analysis results for RD (90% CI) of ACR20 at week 24

Shift between dropouts and completers in ABP 501	Shift between dropouts and completers in adalimumab RP				
-0.700	-0.700	-0.525	-0.350	-0.175	0.000
	0.002	-0.005	-0.014	-0.019	-0.023
	(-0.063, 0.067)	(-0.072, 0.061)	(-0.080, 0.052)	(-0.085, 0.047)	(-0.088, 0.042)
-0.525	0.013	0.005	-0.003	-0.008	-0.012
	(-0.052, 0.078)	(-0.060, 0.071)	(-0.068, 0.063)	(-0.073, 0.057)	(-0.077, 0.053)
-0.350	0.024	0.016	0.008	0.003	-0.001
	(-0.041, 0.088)	(-0.049, 0.081)	(-0.057, 0.072)	(-0.062, 0.067)	(-0.066, 0.063)
-0.175	0.035	0.027	0.019	0.014	0.010
	(-0.030, 0.100)	(-0.038, 0.093)	(-0.046, 0.084)	(-0.051, 0.079)	(-0.055, 0.075)
0.000	0.048	0.040	0.032	0.026	0.023
	(-0.016, 0.111)	(-0.025, 0.105)	(-0.033, 0.096)	(-0.038, 0.090)	(-0.041, 0.086)

The shift represents the assumed difference in week 24 ACR20 response between patients who dropped out prior to week 24 and those who completed week 24. Among completers, the ACR20 response rate was 77.0% and 74.7% for the ABP 501 and adalimumab groups, respectively.

Conclusions: The tipping point sensitivity analyses support the findings of the key efficacy analyses in the phase 3 RA study and confirm that the effects of missing data would not change the conclusion of clinical similarity between ABP 501 and the RP.

Disclosure of Interest: N. Zhang Shareholder of: Amgen Inc., Employee of: Amgen Inc., H. Wang Shareholder of: Amgen Inc., Employee of: Amgen Inc., E. Krishnan Shareholder of: Amgen Inc., Employee of: Amgen Inc.

DOI: 10.1136/annrheumdis-2018-eular.6855

AB0458

EFFICACY AND B-CELL DEPLETION WITH VERY LOW DOSE RITUXIMAB (BIOSIMILAR) IN SERO-POSITIVE DMARD RESISTANT RHEUMATOID ARTHRITIS: A 24 WEEK STUDY

N.S. Jain¹, S. Pandya², D. Shukla², P. Srivastava². ¹Department of Rheumatology, ²Department of Rheumatology, VS Hospital Ahmedabad, Ahmedabad, India, India

Background: Very Low dose Rituximab (RTX) (100 mg) has been variously used in autoimmune diseases like ITP and rheumatoid arthritis (RA). As cost of treatment is an important issue in resource poor setups, we decided to study efficacy of very low dose RTX in patients with RA.

Objectives: 1) To study clinical efficacy of very low dose RTX in DMARD refractory RA. 2) To study B cell depletion with very low dose RTX

Abstract AB0458 – Table 1. Demographic profile and response to very low dose Rituximab

Demographic Profile	100 mg × 4 doses				100 mg single dose			
	Baseline	Week 12	Week 24	p	Baseline	Week 12	Week 24	p
Total number of patients	14	14	14	-	13	11	11	-
Male:Female		1:6		-		1:3		-
Mean Age		47±12 years		-		49±10 years		-
Mean duration of illness		6.7±4 years (median 5 years)		-		7.1±3 years (median 4.5 yrs)		-
Disease Activity measures								
DAS28(ESR)	5.5±1.1	3.3±1	3.4±0.9	<0.001	5.7±0.7	3.3±0.4	3.4±0.6	<0.001
RAPID3	5±0.8	2.6±1.3	3.3±1.5	<0.001	5.1±1.1	2.9±1.4	2.8±1.6	<0.001
CDAI	26.3±8.5	10±8	8.6±6	<0.001	28.2±7.8	12±6	11±6	<0.001
HAQ	1.7±0.3	0.7±0.5	0.5±0.4	<0.001	1.9±0.4	0.8±0.5	0.7±0.5	<0.001
Mean ΔDAS28 (24 weeks)		2.2±1.5		-		2.3±1		-
Mean CD19	152	28	-	-	78	18	-	-
EULAR Response								
EULAR remission	0	3	4	-	0	1	3	-
EULAR low disease activity	0	4	4	-	0	3	4	-
EULAR good response	0	11	11	-	0	9	9	-

Methods: Prospective open labelled study. Biologic naïve, conventional DMARD refractory, sero-positive RA patients ACR 2010 criteria) with high disease activity (DAS 28 ESR) were included after informed consent.

Arm 1: Total 4, weekly 100 mg doses (total dose 400 mg) of a RTX biosimilar were infused.

Arm 2: Single 100 mg RTX infusion.

Efficacy was assessed using standard outcome measures for RA (including RAPID3) at week 24. B cell depletion (CD19 levels in peripheral blood by flow cytometry) was studied at baseline, week 1 and week 12.

Results: Total number of patients in Arm 1=14 and in Arm 2=13.

In Arm 1: 28% (4/14) achieved EULAR remission while 78% (11/14) had EULAR good response. In Arm 2: 70% (9/13) had EULAR good response. All patients achieved complete B-cell depletion (defined as <0.01%) at week 1 after just single dose of 100 mg RTX remained so at 6 weeks only to start rising again at week 12. There were no adverse events noted. Steroid doses were reduced in most patients at follow up visits with delta change in steroid dose- 2.2 mg/day. Results comparable with other studies using both low dose and conventional dose of RTX. Limitations of the study includes small sample size and short follow-up.

Conclusions: Very Low dose RTX is efficacious in conventional DMARD refractory RA patients. Single dose (100 mg) is as good as 400 mg upto week 24. Complete B cell depletion can be achieved even with 100 mg RTX as early as week 1.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6390

AB0459 REMISSION RATE OF TOCILIZUMAB IN CONTROLLED TRIALS AND OBSERVATIONAL STUDIES: SYSTEMATIC REVIEW OF RHEUMATOID ARTHRITIS

Q. Kucuksahin¹, L. Kılıç², Z. Aşlar³, C. Beş⁴, V. Yazısız⁵, A. Yazıcı⁶, D. Solmaz⁷, T. Kaşifoğlu⁸, U. Kalyoncu². ¹Rheumatology, YILDIRIM BEYAZIT UNIVERSITY; ²Rheumatology, Hacettepe University; ³Rheumatology, Numune Education and Research Hospital, Ankara; ⁴Rheumatology, Medical Science University Bakırköy Sadi Konuk Hospital, İstanbul; ⁵Rheumatology, Akdeniz University, Antalya; ⁶Rheumatology, Kocaeli University, Kocaeli; ⁷Rheumatology, İzmir Katip Çelebi University, İzmir; ⁸Rheumatology, Eskişehir Osmangazi University, Eskişehir, Turkey

Background: In concept, the state of remission constitutes a clinical condition in which no active disease is present. Target of rheumatoid arthritis (RA) is achieve to remission. Tocilizumab (TOC) is a humanised monoclonal antibody that binds to the interleukin-6 receptor

Objectives: The aim of this study was to assess the remission rate of TOC for the treatment of RA patients in randomised controlled trials (RCTs) and longitudinal observational studies (LOS).

Methods: In January 2017, a systematic Review (SR) was performed in PUBMED MEDLINE. Publications were identified using the MeSH terms: ("rheumatoid arthritis and Tocilizumab") with a limitation to "humans", "all adults: 19 +years", "English" and "clinical trials". All available studies describing the retention rate of TOC were recruited to SR. Retention rate of TOC were calculated according to route (SC or IV), dosage (4 mg/kg vs 8 mg/kg), monotherapy or combination with methotrexate. Of the 662 publications identified by the literature search, 42 were recruited in the analysis. Retention rates of TOC at 12–16 weeks, 24–32 weeks, 48–52 weeks, 2. Years, 3. Years and 5. years were analysed. Open label extension period of RCTs included to LOS. The causes of withdraw of TOC were recorded as inefficacy, adverse event, and others.

Results: Of the 34 studies, 13 (38%) were RCTs and 21 (62%) were LOSs. Totally 12 043 patients (9834 (81%) female) were pooled to analysis that 6190 patients (51%) were from RCTs. The mean age was 53 years and mean disease duration was 9 years. Seropositivity was 73.6% for rheumatoid factor and 72.2% for ACPA. Overall, 5493 (54.6%) of patients were biologic-naïve. TOC was used as monotherapy (2469/6077, 35.4%), or concomitant with methotrexate (8037/11429, 70.3%). Available baseline DAS-28 score, CDAI, SDAI, and HAQ-DI score were 6.2, 32.1, 33.3, and 1.49 respectively. Remission rate of TOC according to study type were shown in table 1.

Abstract AB0459 – Figure 1

Conclusions: These systematic literature results show that treatment with TOC has a high likelihood of inducing a clinically important benefit in terms of different remission criteria. Remission achieved both RCTs and real life results. Moreover, remission rate of TOC in LOSs was comparable with other biologic DMARDs, as well.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3874

AB0460 LONG-TERM DRUG SURVIVAL OF ETANERCEPT VS OTHER TNF INHIBITOR THERAPIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

P. Emery¹, B. Vlahos², P. Szczypa³, M. Thakur⁴, H.E. Jones², J. Woolcott², P. V. Santos Estrella², A. Gibofsky⁵, C. Rolland⁶, G. Citera⁷, L. Marshall². ¹Leeds Musculoskeletal Biomedical Research Centre LTH, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, UK; ²Pfizer, Collegeville, USA; ³Pfizer Ltd, Walton Oaks; ⁴Pfizer, Sandwich, UK; ⁵Weill Medical College, New York, USA; ⁶Envision Pharma Group, Horsham, UK; ⁷Consultorios Reumatológicos, Buenos Aires, Argentina

Background: TNF α inhibitors have profoundly altered outcomes for patients with rheumatoid arthritis (RA) since they were introduced >15 years ago, by reducing disease activity and radiographic progression and improving quality of life. As a chronic disease, RA often requires life-long treatment, understanding drug survival in real-world settings can be beneficial in optimising disease management.

Objectives: To compare the long-term drug survival of adalimumab (ADA), certolizumab pegol (CZP), etanercept (ETN), golimumab (GLM), and infliximab (IFX) in patients with RA based on systematic literature review (SLR).

Methods: In this SLR, the goal was to identify full-text articles containing registry data or systematic reviews on TNF α inhibitors, following Cochrane dual-reviewer methodology. Searches were conducted in November 2017 with no date restriction, using Embase[®], MEDLINE[®], the Cochrane Central Trials Register and Database of Systematic Reviews, other Cochrane Library databases, and PubMed. Outcomes extracted included drug survival data that were analysed and reported using Kaplan-Meier or Cox regression methods.

Results: Of 3688 non-duplicated publications initially identified, 3299 were excluded based on titles or abstracts and 344 based on full-text screening, leaving 26 publications published between 2005 and 2017 included in the analysis. The number of studies (range of sample size) for each drug were ADA: 15 (25–2349), ETN: 17 (20–3892), IFX: 21 (26–2898), GLM: 4 (2–88) and CZP: 1 (N/A). Among the analysed studies, the mean disease duration in years (range) was ADA: 10.7 (8.2–15.1); ETN: 15.9 (5.0–18.5); IFX: 14.2 (8.5–19.3); CZP: 10.3 (N/A); GLM: 8.9 (8.1–11.5) and mean baseline DAS28 (range) was ADA: 5.0 (4.2–5.9), ETN: 5.2 (4.3–6.3), IFX: 5.3 (4.1–6.4); CZP: 4.7 (N/A) and GLM: 4.7 (4.1–5.1). Trends for survival rates of first-line ETN were slightly higher than ADA at time points ≥ 36 months; ADA and ETN had higher survival rates than IFX at >48 months (figure 1).