Median DLCO values for pre- and post RTX were 71.0% (60.0-77.0) and 63.0% (47.0-74.0), respectively ($p=0.061$). Median pre and post-RTX FVC were 74.0% (61.0-99.0) and 84.0% (63.0-100.0), respectively ($p=0.28$). After a median of 2.7 years, 11 (55.0%) patients had stable disease, 2 (10.0%) patients had regression of RA-ILD and 7 (35.0%) patients had progressive disease. Sex, age, seropositivity and radiographic patterns were not associated with progression. In total, 23 adverse events were detected in 11 (42.3%) patients. Five of them were serious infections requiring hospitalization, mostly pneumonia. Other adverse events were simple infections and surgeries such as arthroplasty. RTX was stopped in 4 (15.4%) patients due to infections secondary to hypogammaglobulinemia in 2, malignancy in 1 and allergic reaction in 1.

Conclusion: RTX seems to achieve stabilization/improvement of RA-ILD with fewer adverse events. However, given that RA-ILD develops post-RTX, it is not a panacea; therefore, we need more effective treatment modalities in the case of RA-ILD.

Table 1. Characteristics of 26 patients with RA-ILD treated with rituximab

Age at first RTX infusion, median (IQR), years	61.2 (57.1-65.1)
RA disease duration at first RTX, median (IQR), years	10.1 (4.3-29.7)
ILD disease duration at first RTX, median (IQR), years	1.9 (0.1-4.5)
Age at RA diagnosis, median (IQR), years	51.1 (40.0-60.6)
Age at ILD diagnosis, median (IQR), years	58.3 (53.9-63.3)
Male patient, n (%)	16 (61.5)
RF positivity, n (%)	25 (96.2)
ACPA positivity, n (%)	20 (90.9)
CRP levels, mg/L, mean (SD)	40.3 (58.9)
ESR levels, mean (SD)	37.7 (18.2)
Smoking status, n (%)	16 (64.0)
Prior TNF inhibitor treatment, n (%)	5 (19.2)
DAS28 at first RTX infusion, mean (SD)	5.3 (1.5)
Radiographic pattern, n (%)	
UIP	7 (26.9)
NSIP	8 (30.8)
OP	2 (7.7)
Indeterminate	8 (30.8)
Others	1 (3.8)
Follow-up duration, median (IQR), years	2.5 (1.2-3.7)

RA-ILD= Rheumatoid arthritis-related interstitial lung disease, RTX= rituximab, RA= rheumatoid arthritis, RF= rheumatoid factor, ACPA= anti-citrullinated protein antibody, TNF= tumor necrosis factor, CRP= C-reactive protein, ESR= erythrocyte sedimentation rate, UIP= usual interstitial pneumonia, NSIP= non-specific interstitial pneumonia, OP= organizing pneumonia

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.731

POS0598

COMPARISON OF INJECTION SITE REACTIONS AND INJECTION SITE ERYTHEMA BETWEEN YLB113 AND ETANERCEPT REFERENCE PRODUCT FROM PHASE 3 ACTIVE COMPARATOR STUDY (STUDY NO. YLB113-002)

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Background: YLB113 is an etanercept biosimilar approved in all indications of its etanercept Reference Product (RP). Therapeutic equivalence in terms of clinical efficacy, safety and immunogenicity was previously demonstrated in a pivotal multicenter, double-blind, randomized, parallel-group, active-control, comparative study (YLB113-002) in rheumatoid arthritis (RA) subjects.^{1,2} Similar incidence of treatment emergent adverse events (TEAEs) was seen in both treatment arms except for injection site reactions (ISRs) and injection site erythema (ISE), both of which were less frequent in subjects treated with YLB113.

Objectives: This post-hoc analysis was performed to further evaluate the differences in the incidence of ISRs and ISE during the 24 week treatment when the subjects with RA were treated with 50 mg of YLB113 or RP given once a week as a SC injection along with methotrexate.

Methods: Safety analysis set (263 in YLB113 arm and 254 in RP arm) was considered for this analysis.

Local reactions at the site of injection were assessed at each of eight study visits. The number of subjects who experienced ISRs and ISE were statistically compared for YLB113 and RP. The risk difference and 95% confidence interval (CI) were computed between arms to understand the magnitude of difference in the incidence of events. The statistical significance of between group difference was tested using chi-square test.

Results: The result of this analysis showed a statistically significant difference in the incidences of ISRs and ISE between subjects who received YLB113 and RP. The risk difference between YLB113 and RP arms for ISR was -9.98% (95% CI, WALD -14.81%, -5.15%) and, for ISE it was -7.94% (95% CI, WALD -11.96%,

-3.92%; Table 1). This could be possibly explained by the absence of latex in the syringe needle cap of YLB113.³

Table 1. Differences in ISRs and ISEs between YLB113 and Reference Product (RP)

Event	YLB113 N=263	RP N=254	YLB113 vs RP Risk Diff (95%CI, WALD)	P-value (Chi-Square)
	No of subjects with events [n(%)]	No of subjects with events [n(%)]		
Injection-site reactions	10 (3.8%)	35 (13.8%)	-9.98% (-14.81%, -5.15%)	<0.0001
Injection-site erythema	5 (1.9%)	25 (9.8%)	-7.94% (-11.96%, -3.92%)	0.0001

Conclusion: YLB113 has shown statistically significant lower incidences of ISRs (P-value <0.0001) and ISEs (P value 0.0001) compared to RP. This property may translate to a better acceptability by patients.

REFERENCES:

- [1] EULAR Abstract AB0416 (2019). Ann Rheum Dis, volume 78, supplement 2, year 2019, page A1670.
- [2] Yamanaka H, Kamatani N, Tanaka Y, et al. A Comparative Study to Assess the Efficacy, Safety, and Immunogenicity of YLB113 and the Etanercept Reference Product for the Treatment of Patients with Rheumatoid Arthritis. *Rheumatol Ther*. 2020;7(1):149-163.

- [3] Viatris Etanercept Summary of Product Characteristics May 2020.

Disclosure of Interests: Dimitris Stefanidis Employee of: Viatris GmbH Sr. Director, Global Medical Affairs Lead, Immunology Biosimilars, Unmesh G Employee of: Viatris, Juan Sánchez-Bursón: None declared, Chirag Shah Shareholder of: As an employee, Shareholder of Lupin LTD, Employee of: Employee of Lupin LTD, Dhananjay Bakhle Shareholder of: As part of Employee Stock Options Plan from Lupin LTD, Employee of: Employee of Lupin LTD

DOI: 10.1136/annrheumdis-2021-eular.829

POS0599

DISEASE ACTIVITY IN PATIENTS WITH RA BY SEROSTATUS AND TREATMENT LINE, FOLLOWING TREATMENT WITH ABATACEPT: RESULTS FROM AN INTERNATIONAL OBSERVATIONAL STUDY

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Background: RF and anti-citrullinated protein antibodies (ACPAs) are associated with a severe and aggressive disease course in patients with RA.¹ Abatacept is a selective co-stimulation modulator for the treatment of RA.² ASCORE (Abatacept SubCutaneOus in Routine Clinical Practice; NCT02090556) was a 2-year, observational, prospective, multicentre study of SC abatacept for the treatment of RA in routine clinical practice.³

Objectives: To determine if serostatus and treatment line impacted disease activity in patients enrolled in the ASCORE study.

Methods: Eligible patients, aged ≥ 18 years, with active moderate-to-severe RA (ACR/EULAR 2010 criteria) who were IV abatacept-naïve and initiated SC abatacept 125mg once weekly, were enrolled into two cohorts: biologic (b) DMARD-naïve patients and those with ≥ 1 prior bDMARD treatment failure. This *post hoc* analysis assessed the mean change in disease activity (CDAI, SDAI and DAS28 [ESR]) from baseline (BL) at 6, 12, 18 and 24 months in response to treatment with abatacept. Patients were stratified by BL serostatus (all patients, RF/ACPA double positive [+/+] RA; RF/ACPA single positive [+/-; RF+/ACPA- or RF-/ACPA+] RA and RF/ACPA double negative [-/-] RA) and by line of therapy (all patients, patients receiving abatacept as a first-line or $\geq$ second-line therapy and those receiving abatacept following 1 or ≥ 2 prior bDMARDs). Overall patient data, as well as data for patients who were +/- or those who had 1 or ≥ 2 previous bDMARDs, are not shown. Estimates of mean difference are from *t*-test.

Results: Among 2892 eligible patients in ASCORE, 1748 patients with RF/ACPA status available at BL were included in this analysis (1079 +/+ RA, 326 +/- RA and 343 -/- RA). After 6 months, patients with +/+ RA on first-line abatacept therapy had better improvements in CDAI and SDAI scores from BL than patients on $\geq$ second-line abatacept therapy (mean difference [95% CI]: -3.4 [-5.6, -1.1]; $p=0.0032$ and -3.9 [-6.5, -1.3]; $p=0.0035$, respectively); better improvements in SDAI were also seen after 12 months (mean difference [95% CI]: -3.5 [-6.5, -0.5]; $p=0.0207$). Changes in CDAI and SDAI scores were comparable after 18 and 24 months. At 6 and 12 months, patients with +/- RA on first-line therapy had better improvements from BL in DAS28 (ESR) than those on $\geq$ second-line therapy (mean differences [95% CI]: -0.5 [-0.8, -0.2]; $p=0.0002$ and -0.4 [-0.7, -0.0]; $p=0.0317$, respectively); changes were comparable at 18 and 24 months (Figure 1). For patients on $\geq$ second-line therapy, at 18 months those with +/- RA had better improvements from BL in DAS28 (ESR) than those with -/- RA (mean difference [95% CI]: -0.7 [-1.2, -0.1]; $p=0.0232$). For patients not stratified by line of therapy, changes in DAS28 (ESR) were comparable between the +/- and -/- RA subgroups over time, with the exception of 6 months where patients with -/- RA had better improvements from BL compared with patients with +/- RA (mean difference [95% CI]: -0.3 [-0.6, -0.0]; $p=0.0495$).

Conclusion: In this real-world, *post hoc* analysis, patients with +/- RA who received abatacept as a first-line therapy had greater early improvements in disease activity compared with patients who received abatacept as a $\geq$ second-line therapy. Improvements in disease activity at 24 months were comparable between patients who were +/- and those who were -/-. Larger studies are needed to further corroborate these findings.

REFERENCES:

- Katchamart W, et al. *Rheumatol Int* 2015;35:1693–1699.
- Malmström V, et al. *Nat Rev Immunol* 2017;17:60–75.
- Alten R, et al. *Ann Rheum Dis* 2019;78(Suppl 2):A1639.

Figure 1. Mean change from BL in DAS28 (ESR) for patients with RA treated with abatacept

p values are for the mean difference between abatacept as a first-line and abatacept as a $\geq$ second-line therapy, determined by *t*-test.
+/+ RF/ACPA double positive; +/- RF/ACPA double negative; ACPA-anti-citrullinated protein antibody.

Acknowledgements: Professional medical writing and editorial assistance was provided by Rachel Rankin, PhD, at Caudex and was funded by Bristol Myers Squibb. This study was funded by Bristol Myers Squibb.

Disclosure of Interests: Rieke Alten Speakers bureau: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Consultant of: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Grant/research support from: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Xavier Mariette Consultant of: Bristol Myers Squibb, Galapagos, Gilead, GlaxoSmithKline, Janssen, Pfizer, UCB, Rene-Marc Flipo Speakers bureau: AbbVie, Bristol Myers Squibb, Janssen, Lilly, Medac, Merck Sharp & Dohme, Novartis, Pfizer, Roche-Chugai, Grant/research support from: Amgen, Janssen, Novartis, Pfizer, Roberto Caporali Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celltrion, Fresenius Kabi, Galapagos, Gilead, Lilly, Merck Sharp & Dohme, Pfizer, Roche, 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, Karissa Lozenski Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Vadim Khaychuk Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.928

POS0600 IMMUNOGENICITY OF RITUXIMAB BIOSIMILAR GP2013: A RARE EVENT, BUT NOT WITHOUT CONSEQUENCES ...

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Background: The bioequivalence between rituximab (RTX) originator and its biosimilar GP2013 has been demonstrated in rheumatoid arthritis (RA) (1). A recent randomized controlled trial suggested in a selected population a very low immunogenicity of GP2013 in RA (<1%) (2).

Objectives: To study in daily practice the risk of immunogenicity of patients treated with GP2013 for their chronic inflammatory rheumatic disorder.

Methods: Prospective routine care study carried out between September 2018 and August 2020 in the Rheumatology department of Cochin Hospital. We consecutively included patients treated with the biosimilar RTX GP2013, systematically used in the department since March 2018. Samples were taken before each infusion in order to detect anti-RTX antibodies (Ab) and RTX residual concentrations by ELISA (Lisa Tracker Duo Rituximab, LTR005, Theradiag).

Results: We included 159 consecutive patients treated with GP2013 (124 women, 78%) with a mean age of 59 $\pm$ 13 years and a mean disease duration of 18 $\pm$ 11 years. Among these 159 patients, 108 (68%) had RA and 51 had another disease (16 systemic sclerosis (SSc), 15 mixed connective tissue disease (MCTD), 5 systemic lupus (SLE), 5 inflammatory myopathies (MI), 5 undifferentiated polyarthritis, 2 juvenile idiopathic arthritis (JIA) and 3 primary Sjögren's syndromes). 137 patients (86%) were receiving associated disease-modifying therapy (DMARD), mainly methotrexate (111/137 patients, 81%). 120 patients (75%) were in maintenance therapy with originator RTX (cumulative dose of RTX: 3.5 $\pm$ 6g) before the switch to GP2013 in March 2018. Originator RTX was not re-established during the entire treatment period. The other 39 patients (25%) treated with GP2013 were naïve of originator RTX.

The analysis of the first sample, performed before the second GP2013 infusion, identified 8 patients (5 RA, 1 SLE, 1 MCTD and 1 SSc) with positive anti-RTX antibodies (prevalence 5%), with rates varying between 6 and >100ng/mL and undetectable residual RTX concentrations. Among these 8 patients, 6 had previously received originator RTX and 2 were RTX-naïve patients. There was a trend for higher body mass index in patients with positive anti-RTX antibodies (28 $\pm$ 7 vs. 25 $\pm$ 6 kg/m², $p=0.12$), and no association was observed between anti-RTX immunization and age, disease duration, combination with conventional DMARD, mean interval between infusions or cumulative RTX dose.

Among the 8 immunized patients, two groups could be isolated: i) a group of 5 patients (3 RA, 1 SLE, 1 SSc) with low antibody levels (6-22ng/mL) and no significant clinical consequences (absence of treatment discontinuation and loss of efficacy after 13 $\pm$ 4 months of follow-up, only one minor allergic reaction) and ii) a group of 3 patients (2 RA, 1 MCTD) with a high antibody levels ($\geq$ 100ng/mL) and meaningful clinical consequences: one severe allergic reaction during the second GP2013 infusion leading to treatment discontinuation, and a loss of efficacy with incomplete B depletion in 2 patients leading to RTX dose escalation from 500 mg to 1 g. Among the 151 patients not immunized at the time of the first sample, no severe allergic reaction and 6 minor allergic reactions were noted under GP2013.