was considered sufficient to record global data by 6 central readers in all cases. An additional reader assessed only images in DICOM format (n=175). Comparison of active and structural lesion frequencies typical of axSpA was assessed descriptively according to individual and majority of central readers data.

Results: Active lesions typical of axSpA were recorded in about 30% of cases in the cohort. Active or structural lesions typical of axSpA were recorded in about 40% of patients (table 1). Similar data was observed when active sacroiliitis was defined using the ASAS definition of a positive MRI. Structural lesions alone, without any active lesions typical of axSpA, were recorded in 6.6% of cases. Active lesions alone, without any structural lesions typical of axSpA, were recorded in 7.8% of cases. Both active and structural lesions typical of axSpA were recorded in 23.1% of cases. The frequencies of these categories were only slightly lower when majority reader data was analysed.

Abstract OP0249 – Table 1 Contribution of structural MRI lesions to detection of sacroiliitis in the ASAS-CC. (*Individual data from Reader; *majority reader (≥ 4) data)

Variable	Mean% (Range)*	Number (% of Cases)*
Active lesions typical of axSpA	31.5 (24.5-38.5)	79 (28.4%)
Active lesions typical of axSpA but not structural lesions typical of axSpA	7.8 (4.6-11.8)	7 (2.9%)
Structural lesions typical of axSpA	31.4 (23.5-39.9)	68 (28.6%)
Structural lesions typical of axSpA but not active lesions typical of axSpA	6.6 (4.2-12.7)	7 (2.9%)
Active and structural lesions typical of axSpA	23.1 (16.0-29.0)	51 (21.4%)
Active or structural lesions typical of axSpA	39.2 (28.2-48.7)	99 (41.6%)
Active lesions typical of axSpA and meets ASAS definition for positive MRI	30.0 (22.6-37.4)	79 (28.4%)
ASAS positive MRI but not structural lesions typical of axSpA	7.2 (3.4-11.3)	7 (2.9%)
Structural lesions typical of axSpA but not ASAS positive MRI	8.8 (5.0-13.0)	7 (2.9%)
ASAS positive MRI and structural lesions typical of axSpA	22.6 (15.6-28.6)	51 (21.4%)
ASAS positive MRI or structural lesions typical of axSpA	38.4 (27.7-47.9)	99 (41.6%)

Conclusions: Structural lesions typical of axSpA may be observed without any active lesions typical of axSpA in 5%–10% of cases presenting with undiagnosed back pain in the ASAS-CC. This is the same proportion of the cohort for which active lesions typical of axSpA are seen without any structural lesions typical of axSpA. In view of the concomitant presence of both lesions, contextual interpretation seems optimal.

REFERENCE:

[1] Rudwaleit, et al. Ann Rheum Dis 2009;68:777–831.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.7249

FRIDAY, 15 JUNE 2018

Present and future treatments for SLE, Sjögren's and APS

OP0250

A RANDOMISED, DOUBLE-BLIND STUDY TO ASSESS THE SAFETY, TOLERABILITY AND PRELIMINARY EFFICACY OF LENIOLISIB (CDZ173) IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

T. Dörner¹, M. Zeher², U. Laessing³, F. Chaperon³, S. De Buck³, A. Hasselberg³, M.-A. Valentin⁴, S. Ma⁵, M. Cabanski³, C. Kalis³, C. Burkhardt³, P. Gergely³.

¹Department Medicine/Rheumatology and Clinical Immunology Charité Universitätsmedizin, Charité Research Organisation GmbH, Berlin, Germany;

²Medical University of Debrecen, Ungarn, Hungary; ³Novartis Institutes for Biomedical Research; ⁴NOVARTIS, BASEL, Switzerland; ⁵Novartis Institutes for Biomedical Research, Cambridge, USA

Background: Primary Sjögren's syndrome (pSS) is a systemic and progressive autoimmune disease characterised by lymphoid infiltration and progressive alteration of exocrine glands secretory function. Ectopic germinal center-like structures harbour plasma cells that generate autoantibodies leading to immune complex formation. Leniolisib (CDZ173) is an oral low molecular weight compound that selectively inhibits the lipid kinase PI3K δ . In animals, leniolisib blocks PI3K δ -dependent B cell functions, disrupts germinal centre formation and immune cell trafficking, supporting the rationale for a PI3K δ -targeted therapy in pSS

Objectives: To evaluate the safety, tolerability, pharmacokinetics (PK) and preliminary clinical efficacy of multiple oral doses of leniolisib, after 12 weeks of treatment, in pSS patients

Methods: Double-blind, randomised, placebo-controlled, parallel-design study recruited 30 seropositive pSS patients with moderate to severe disease activity as determined by EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) ≥ 6 , EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) ≥ 5 and stimulated

whole salivary flow rate >0 mL/min. Patients were randomised in a 2:1 ratio to receive leniolisib (70 mg b.i.d) or placebo. The primary outcome was change in ESSPRI at week 12. Secondary outcomes included PK, changes in ESSDAI, the Short Form-36 (SF-36), Multidimensional Fatigue Inventory (MFI) and global Visual Analogue Scales (VAS) completed by patients and physicians. Additional assessments included lacrimal gland function and biomarkers relevant to pathway and disease

Results: Overall safety and tolerability profile of leniolisib was acceptable, but appeared less favourable than placebo. In particular, rash occurred more frequently in the leniolisib group (11/20 patients) compared to placebo (1/10 patients). There was a slight improvement (not statistically significant) in ESSPRI scores (dryness, pain and fatigue) favouring leniolisib. Similar trends were observed in secondary endpoints (SF-36/mental and physical, MFI, VAS completed by patients and physicians). After 12 weeks of treatment, there was a slight improvement (not statistically significant) in the lacrimal gland function in the leniolisib group compared to placebo. The observed PK profile was as expected based on healthy volunteer data. Biomarker results suggest a strong and sustained target and pathway engagement, as evidenced by inhibition of phosphorylated Akt in *ex-vivo* stimulated B cells, significant decrease in serum CXCL13 and reduced frequency of circulating Follicular T helper-like cells. There was a trend of decreasing autoantibody levels in leniolisib-treated patients

Conclusions: Leniolisib had an acceptable safety and tolerability profile, but caused rashes a known class effect of PI3K inhibitors. Target and pathway engagement were confirmed, however no clear efficacy signal for leniolisib was seen based on ESSPRI and ESSDAI in this Proof-of-Concept study at the studied dose.

Disclosure of Interest: T. Dörner: None declared, M. Zeher: None declared, U. Laessing: None declared, F. Chaperon: None declared, S. De Buck: None declared, A. Hasselberg: None declared, M.-A. Valentin Shareholder of: Novartis stock option, Employee of: Novartis, S. Ma: None declared, M. Cabanski: None declared, C. Kalis: None declared, C. Burkhardt: None declared, P. Gergely: None declared

DOI: 10.1136/annrheumdis-2018-eular.3111

OP0251

ATTAINMENT OF LOW DISEASE ACTIVITY AND REMISSION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH HIGH DISEASE ACTIVITY IN THE ATACEPT PHASE IIB ADDRESS II STUDY AND ITS LONG-TERM EXTENSION

E. Morand¹, J.T. Merrill², D.A. Isenberg³, A.H. Kao⁴, C. Vazquez-Mateo⁴, S. Wax⁴, P. Chang⁴, K. Pudota⁴, C. Aranow⁵, D. Wallace⁶. ¹Monash University, Melbourne, Australia; ²Oklahoma Medical Research Foundation, Oklahoma, USA; ³University College London, London, UK; ⁴EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica; ⁵Feinstein Institute for Medical Research, Manhasset; ⁶Cedars-Sinai Medical Center, David Geffen School of Medicine, UCLA, Los Angeles, USA

Background: Low disease activity (LDA) and remission are consummate goals of SLE treatment.¹ Lupus Low Disease Activity State (LLDAS) is associated with reduced damage accrual,² and has been shown to be a feasible clinical trial endpoint.³ In the Phase IIb ADDRESS II study,⁴ atacept improved SRI-6 response rates and flare prevention at Week (Wk) 24 vs placebo (PBO), in patients with High Disease Activity (HDA; SLEDAI-2K ≥ 10) at Screening, with an acceptable safety profile.

Objectives: Post-hoc analysis of ADDRESS II and its long-term extension to describe 48-wk rates of LDA and remission in patients with HDA at Screening.

Methods: Pts were randomised 1:1:1 to weekly subcutaneous PBO or atacept 75 or 150 mg for 24 wks in ADDRESS II. Completers entered the extension study at the same dose, except PBO patients who switched to atacept 150 mg (PBO/atacept 150 mg). This analysis includes: LDA (SLEDAI-2K ≤ 2); LLDAS (SLEDAI-2K ≤ 4 without major organ activity, no new disease activity vs previous visit, Physician's Global Assessment [PGA] ≤ 1 , prednisone-equivalent ≤ 7.5 mg/day, and stable immunosuppressants); and remission (clinical SLEDAI-2K=0, PGA <0.5 , prednisone ≤ 5 mg/day) per definitions proposed by DORIS.¹

Results: Of 306 ADDRESS II pts, 158 (52%) had HDA at entry; 42.4% achieved SRI-6, 23.4% LDA, 15.8% LLDAS and 10.8% remission at Wk 24. At Wk 48, 52.5% achieved SRI-6, 26.6% LDA, 19.0% LLDAS and 10.8% remission. Among the 83 HDA patients with an SRI-6 response at Wk 48, LDA, LLDAS, and remission represented increasingly stringent subsets (49.4% [n=41] attaining LDA, 34.9% [n=29] LLDAS, and 20.5% [n=17] remission). LDA, LLDAS and remission rates were higher in patients treated with atacept 150 mg vs 75 mg and PBO/atacept 150 mg (table 1; figure 1).

Abstract OP0251 – Figure1. LDA, LLDAS and remission in patients with HDA at screening (a. LDA; b. LLDAS; c. remission)

Abstract OP0251 – Table 1 LDA, LLDAS and remission at Wk 48 of patients with HDA at screening

Endpoint	Statistics	PBO/Atacicept 150 mg* (n=52)	Atacicept 75 mg (n=55)	Atacicept 150 mg (n=51)
LDA	Attainment, n (%)	10 (19.2)	12 (21.8)	20 (39.2)
	OR [95% CI]		1.17 [0.46–3.00]	2.71 [1.11, 6.60]**
LLDAS	Attainment, n (%)	5 (9.6)	12 (21.8)	13 (25.5)
	OR [95% CI]		2.62 [0.85–8.06]	3.22 [1.05, 9.82]**
Remission	Attainment, n (%)	1 (1.9)	7 (12.7)	9 (17.6)
	OR [95% CI]		7.44 [0.88–62.71]	10.93 [1.33, 89.78]**

*PBO pts who switched to atacicept 150 mg after Week 24; **p<0.05; CI, confidence interval; OR, odds ratio

Conclusions: At 48 wks, patients entering the ADDRESS II study with HDA who received atacicept 150 mg were more likely to attain LDA, LLDAS and remission than those treated with 75 mg or PBO/atacicept 150 mg. These endpoints were more stringent and discriminatory than SRI-6, confirming LLDAS, LDA, and remission to be robust and meaningful endpoints for SLE trials, and adding further support for future studies of atacicept in SLE.

REFERENCES:

- [1] Van Vollenhoven, et al. Ann Rheum Dis 2017.
- [2] Franklyn, et al. Ann Rheum Dis 2016.
- [3] Morand, et al. Ann Rheum Dis 2018 (in press).
- [4] Merrill, et al. Arthritis Rheum 2017.

Disclosure of Interest: E. Morand Grant/research support from: AstraZeneca/Medimmune, Janssen, UCB and BMS, Consultant for: EMD Serono, AstraZeneca/Medimmune, and Janssen, J. T. Merrill Grant/research support from: GSK and BMS (investigator-initiated studies), Consultant for: EMD Serono, Lilly, GSK, Anthera and Biogen; • Clinical Trial Data Management/Analysis/QA Services for Celgene and Xencor, D. A. Isenberg Consultant for: EMD Serono (consulting fees have been passed to a local arthritis charity), A. H. Kao Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), C. Vazquez-Mateo Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), S. Wax Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), P. Chang Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), K. Pudota Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), C. Aranow Grant/research support from: EMD Serono Research and Development Institute, Inc., D. Wallace Consultant for: Merck KGaA

DOI: 10.1136/annrheumdis-2018-eular.2618

OP0252 ORGAN DAMAGE PROGRESSION AND LONG-TERM SAFETY OF BELIMUMAB (BEL) IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): AN EXTENSION OF PIVOTAL PHASE 3 BLISS STUDIES

B.F. Van Vollenhoven¹, S.V. Navarra², R.A. Levy³, M. Thomas⁴, A. Heath³, T. Lustine³, A. Adamkovic³, J. Fettiplace⁵, M.L. Wang³, B. Ji⁵, D. Roth³.
¹Amsterdam Rheumatology and Immunology Center ARC, Amsterdam, Netherlands; ²University of Santo Tomas Hospital, Manila, Philippines; ³GSK, Collegeville, PA, USA; ⁴Kerala Institute of Medical Sciences, Trivandrum, Kerala, India; ⁵GSK, Stockley Park, UK

Background: Non-United States completers of the Phase 3 BLISS-52 (BEL110752) and BLISS-76 (BEL110751) studies could continue treatment with BEL.

Objectives: To evaluate long-term safety, tolerability and organ damage progression in patients with SLE treated with BEL.

Methods: In this multicentre, open-label long-term study (BEL112234/ NCT00712933), patients received intravenous BEL every 4 weeks, plus standard SLE therapy. Safety was assessed at each visit. Organ damage (Systemic Lupus International Collaborative Clinics/American College of Rheumatology Damage Index [SDI]) was assessed as a safety endpoint every 48 weeks. The study continued until BEL was commercially available in each patient's country and included an 8 week follow-up period.

Results: In total, 738 patients entered the long-term study and were treated for up to 9 years (3352 patient-years). Of these, 735 (99.6%) received ≥ 1 dose of BEL; the mean (SD) number of infusions was 56.4 (27.02). The incidence of adverse events (AEs) remained stable or declined over time (table 1). The most common AEs were headache (n=205, 27.9%), nasopharyngitis (n=155, 21.1%), diarrhoea (n=143, 19.5%), arthralgia (n=136, 18.5%) and influenza (n=134, 18.2%). Sixty-nine patients (9.4%) experienced an AE resulting in discontinuation of BEL or study withdrawal. Eleven deaths occurred, one of which (cardiogenic shock) was possibly related to BEL. Three serious AEs of suicide attempt/ideation (0.4%) occurred. The mean (SD) SDI score was 0.6 (1.02) at baseline (prior to the first dose of BEL). At Year 8 87.7% of patients had no change in SDI score from baseline, indicating low organ damage accrual (figure 1).

^aNumber of patients; ^bincluded opportunistic infections, tuberculosis, herpes zoster (recurrent and disseminated) and sepsis; ^ctwo deaths during post-treatment follow-up.

Conclusions: BEL displayed a stable safety profile with no new safety signals. There was minimal organ damage progression.