Abstract OP0247 – Table 1 Performance of the referral strategies against the rheumatologist clinical diagnosis (N=3,877; pre-test probability: 1.6% – weighted national SpA prevalence)

	Sensitivity (%)	Specificity (%)	PPV (%)	1-NPV (%)
ASAS	85.4	38.8	2.2	0.6
EpiReumaPt	72.1	67.6	3.5	0.7
CafaSpA one	56.3	69.7	2.9	1.0
Brandt I	49.2	79.3	3.7	1.0
Braun IBP	47.5	78.7	3.5	1.1
MASTER	36.7	87.7	4.6	1.2
Brandt II	27.7	92.4	5.6	1.3
Hermann	22.4	93.2	5.1	1.3
CafaSpA two	15.2	95.2	4.9	1.4
Braun 2 step	15.1	95.7	5.3	1.4
Brandt III	7.9	98.4	7.6	1.5

ASAS (≥1/5+): IBP (ASAS definition), good response to NSAIDs, family history of SpA, peripheral manifestations (arthritis, enthesitis and/or dactylitis), extra-articular manifestations (uveitis, psoriasis and/or IBD); EpiReumaPt (≥1/5+): previous SpA/PsA diagnosis, IBP (≥ 3/8 features), CBP (≥ 3 months) starting <45 years and ≥ 1/6 SpA features, dactylitis, enthesitis; CafaSpA one (≥1/3+): IBP (ASAS definition), good response to NSAIDs, family history of SpA; CafaSpA two (≥2/3+): see CafaSpA one; Brandt I (≥ 1/1+): IBP (morning stiffness>30 min, pain at night/early morning, improvement by exercise; ≥1/3); Brandt II (≥ 1/1+): ≥2/3 IBP features (see Brandt I); Brandt III (≥ 1/1+): ≥3/3 IBP features (see Brandt I); Braun IBP (≥ 2/5+): start BP≤35 years, waking second half of the night, alternating buttock pain, improvement by movement, not rest; MASTER (≥ 2/3+): IBP (morning stiffness>30 min, improvement exercise, not rest, awakening in the night because of BP), good response to NSAIDs, family history of AS; Hermann (≥1/1): IBP (Calin's criteria); Braun 2 step (≥ 2/3): psoriasis, alternating buttock pain, improvement BP by exercise. HLA-B27 excluded from ASAS, Brandt I-III and Braun 2 step; elevated CRP/ESR excluded from ASAS.

Conclusions: For the first time, a wide range of SpA RS were tested head-to-head in a population-based setting where the ASAS and EpiReumaPt RS were shown to be the most sensitive. Our data suggest that these strategies can be effectively used as screening tools for SpA especially when laboratory and imaging data are not available.

Disclosure of Interest: None declared

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OP0248

POTENTIAL DIFFERENCES IN AXIAL SPONDYLOARTHRITIS DISEASE ACTIVITY CATEGORIZATION USING DIFFERENT MINIMUM VALUES FOR HIGH-SENSITIVITY CRP IN ANKYLOSING SPONDYLITIS DISEASE ACTIVITY SCORE CALCULATION AND DIFFERENT DEFINITIONS OF DISEASE FLARE

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Background: It has been recommended that the lower limit of high-sensitivity CRP (hsCRP) be restricted to 2 in the Ankylosing Spondylitis Disease Activity Score (ASDAS) calculation. Also, a definition of flare of ASDAS increase ≥0.9 was recently proposed.

Objectives: Using non-radiographic axial SpA (nr-axSpA) trial data, this analysis evaluated potential differences in patient (pt) categorization using different minimum values for hsCRP in the ASDAS calculation and different definitions of disease flare.

Methods: ABILITY-3 (NCT01808118) assessed the impact of continuation versus withdrawal of adalimumab (ADA) in nr-axSpA pts who achieved sustained remission with open-label ADA. All pts received open-label ADA 40 mg every other wk during a 28-wk lead-in period. Pts who achieved remission, defined as ASDAS inactive disease (ID, ASDAS <1.3) at wks 16, 20, 24, and 28 were randomised to 40-wk, double-blind ADA (continuation) or PBO (withdrawal). ASDAS was calculated with the full range of hsCRP (protocol-defined) and limiting hsCRP to the lowest possible value of 2 mg/L (rederived). Flare was calculated as 2 consecutive study visits with ASDAS >2.1 (protocol definition) or with ASDAS increase ≥0.9 (modified definition). Data are reported as observed (open label) and by nonresponder imputation (double blind).

Results: 673 pts were enrolled. At open-label baseline, mean ASDAS using the protocol-defined ASDAS calculation was 3.6 vs 3.7 when rederived. At wk 28, 295 (43.8%) pts achieved protocol-defined ASDAS ID vs 272 (40.4%) pts using the rederived ASDAS; mean ASDAS at double-blind baseline was 0.7 vs 0.9, respectively. At wk 68, significantly more pts treated with ADA vs PBO had no flare per protocol definition (69.7% vs 47.1%; p<0.001; table 1). Similar results were observed with modified definitions (table 1). At wk 68, significantly greater proportions of ADA vs PBO pts achieved ASDAS endpoints (all p<0.001), with similar results for protocol-defined and rederived ASDAS calculations, respectively: ID (57.2% vs 33.3% and 52.0% vs 29.4%), major improvement (58.6% vs 32.0% and 50.0% vs 30.7%), and clinically important improvement (67.1% vs 45.1% and 67.1% vs 44.4%).

Abstract OP0248 – Table 1 Percentage of patients not experiencing disease flare at week 68 using protocol-defined or rederived ASDAS and/or modified flare definitions

Variable, n (%)	Adalimumab (40 mg EOW) n=152*	Placebo n=153*	Difference, %	P value
Protocol-defined ASDAS and flare	106 (69.7)	72 (47.1)	22.7	<0.001
Rederived ASDAS, protocol-defined flare	100 (65.8)	69 (45.1)	20.7	<0.001
Protocol-defined ASDAS, modified flare definition	97 (63.8)	56 (36.6)	27.2	<0.001
Rederived ASDAS and modified flare definition	99 (65.1)	65 (42.5)	22.6	<0.001

ASDAS, Ankylosing Spondylitis Disease Activity Score; EOW, every other week; ID, Nonresponder imputation; P value using 2-sided Pearson chi-square test.

*Efficacy outcomes were calculated based on the number of patients randomized, rather than those who would have qualified for randomization based on rederived ASDAS calculations.

Conclusions: At both open-label and double-blind baseline, mean ASDAS was similar, regardless of the hsCRP value cut-off used. Fewer pts in both treatment groups were categorised as not experiencing a flare when limiting the lowest possible hsCRP value to 2 mg/L in the ASDAS calculation and/or using a modified flare definition. However, treatment differences remained similar compared with the protocol-defined methodology. Results suggest infrequent clinically relevant differences in ASDAS values with use of either definition for minimum hsCRP and that the use of ASDAS >2.1 or ASDAS increase ≥0.9 as the definition of flare is reasonable.

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OP0249

THE CONTRIBUTION OF STRUCTURAL MRI LESIONS TO DETECTION OF SACROILIITIS IN PATIENTS IN THE ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS) CLASSIFICATION COHORT

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Background: Active lesions typical of axial spondyloarthritis (axSpA) in the sacroiliac joint (SIJ) were reported by local site readers in about 40% of patients in the ASAS classification cohort (ASAS-CC) when this study was conducted over 10 years ago¹. There has been no data reported on the occurrence of structural lesions in this cohort. Since this study was conducted, there has been considerable progress in our understanding of SIJ lesions observed on MRI, which raises the possibility that MRI scans of patients in the ASAS-CC could now be interpreted substantially differently.

Objectives: To determine the added contribution of structural lesions in the SIJ to the evaluation of sacroiliitis in an inception cohort of patients with axSpA.

Methods: Recently updated MRI lesion definitions for axSpA (ASAS_MRI_def^m) were recorded in an eCRF that comprises global assessment (lesion present/absent) and detailed scoring (SPARCC SIJ inflammation, SPARCC SIJ structural). MRI scans were available in a variety of formats (DICOM (n=175), JPEG (n=71), DICOM film(n=32)) and sequences, axial and semicoronal orientations, from 278 of the 495 cases who had MRI performed in the ASAS-CC. Image quality

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.

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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

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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.

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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

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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).