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Figure. Patient-reported outcomes over 3 years of BKZ treatment

Full analysis set (N=254). Weeks 0 and 48 refer to the BEAGLE and OLE baseline, respectively. All patients received BKZ 160 mg during the OLE after completing BKZ 160 mg or 320 mg in BEAGLE. SF-36 PCS, MCS and ASQoL were recorded to Week 144. Arrows indicate improvement; positive change from baseline represents improvement in SF-36 PCS and MCS; negative change from baseline represents improvement for all other outcomes. MID/MCII/MCID thresholds: BASDAI total score MCII = 0.7; fatigue (BASDAI Q1) MCID = 1.1; morning stiffness (mean of BASDAI Q5+6) MCID = 1.7; BASFI MCII = 0.4; total spinal pain MCID = 1.6; SF-36 PCS score MID = 2; ASQoL total score MCID = -2.1. SF-36 MID values are appropriate for groups with baseline mean T-scores of 30–40; for higher T-score ranges, MID values tend to be higher. MCII are not applied for improvement for baseline mean SF-36 T-scores >47, which are considered at least as good as the standard US population, hence no improvement is expected. Since mean SF-36 MCS at baseline was 54.3, the MID was not applied here. ASQoL: Ankylosing Spondylitis Quality of Life questionnaire; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASDAI50: BASDAI 50% improvement from baseline; BASFI: Bath Ankylosing Spondylitis Functional Index; BKZ: bimekizumab; MCII: minimum clinically important improvement; MCID: minimum clinically important difference; MI: multiple imputation; MID: minimally important difference; NRI: non-responder imputation; NRS: numeric rating scale; OLE: open-label extension; SF-36 MCS: 36-Item Short-Form Survey Mental Component Summary; SF-36 PCS: 36-Item Short-Form Survey Physical Component Summary.

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POS0920

TARGETED SERUM PROTEOMIC ANALYSIS FOLLOWING UPADACITINIB TREATMENT IN ANKYLOSING SPONDYLITIS SHOWS ROBUST SUPPRESSION OF INNATE AND ADAPTIVE IMMUNE PATHWAYS WITH TISSUE REPAIR MODULATION

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Background: Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients with active ankylosing spondylitis (AS) with an inadequate response (IR) to nonsteroidal anti-inflammatory drugs (NSAID) therapy in the SELECT-AXIS 1¹ trial.

Objectives: To identify pathways modulated by UPA in AS patients with emphasis on those associated with response to treatment.

Methods: A subgroup of patients from the SELECT-AXIS 1 study, with available baseline and at least one follow up plasma sample during the placebo-controlled period, were selected for analysis (PBO, n=65; UPA 15 mg QD, n=63). The levels of 92 inflammation related protein biomarkers (BioMs) were analyzed using the Olink® platform; change from baseline were expressed as Log₂ Fold Change; a repeated measure mixed linear model identified BioMs differentially modulated by UPA. Relationship between change in BioMs and change in clinical disease activity measures were derived using Pearson's correlation (ASDAS-CRP, BASDAI, and CRP) and Spearman's correlation (MRI Spine SPARCC). Pathway analysis was performed with Ingenuity® Pathway Analysis (Qiagen Inc.).

Results: Treatment with UPA 15 mg QD reduced the levels of BioMs associated with IFN, IL6, T Cells, M1 or "inflammatory" Macrophages, and Dendritic Cells (DC); and increased those of BioMs associated with tissue repair and hematopoiesis. The type of pathways, inferred *in silico* based on BM data, suggests that UPA exerts broad inhibitory activity directly on multiple JAK1-dependent upstream pathways (IL1, IL23, IL17, IL18, and TNFα), resulting in the inhibition of key functional pathways such as leukocyte activation and mobility, inflammatory response, and damage to connective tissue. Improvement in ASDAS-CRP, BASDAI, and MRI spine SPARCC correlated with increase in BioMs associated with tissue repair (FGF5, DNER [Delta/Notch Like EGF Repeat Containing]) and hematopoiesis (FLT3LG, and SCF/KITLG), while improvement in ASDAS-CRP and CRP correlated with decrease in CCL23, CSF1, IL-6, and MMP1; and reduction in only CRP correlated with decrease in IFN- and of TNFα-related BioMs (Data tables will be presented).

Conclusion: Treatment of NSAID-IR AS patients with UPA 15 mg QD resulted in the coordinated decrease in multiple BioMs associated with the innate and adaptive immune responses, and in the increase in BioMs generally associated with tissue repair and hematopoiesis. *In silico* pathway prediction indicates that treatment with UPA directly inhibits JAK1-dependent and indirectly JAK1-independent pathways, resulting in the down modulation of functional pathways related to inflammation and tissue damage which are known to be dysregulated in AS². Based on this observation and on the correlation of change in BioMs with change in clinical measures, we hypothesize that both increase in BioMs associated with tissue repair and hematopoiesis, and decrease in BioMs associated with inflammation may contribute to the clinical activity of UPA in AS patients.

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POS0921

EFFICACY AND SAFETY OF ACETEMETACIN IN THE TREATMENT OF 1215 ACTIVE ANKYLOSING SPONDYLITIS PATIENTS: DATA FROM A PROSPECTIVE COHORT MANAGED BY SMART-PHONE SPONDYLOARTHRITIS MANAGEMENT SYSTEM

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Background: Biological DMARDs have widely used in the treatment of AS in last two decades, but NSAIDs still serves as a cornerstone in the treatment.

Given the wide use of Acemetacin in AS and relative lack of clinical evidence on the selection of NSAIDs in the treatment of AS, the investigation on acemetacin treating AS is of great significance.

Objectives: Our study aims to investigate efficacy and safety of acemetacin in the treatment of AS.

Methods: Data on efficacy and safety is available in 1215 patients from the Chinese Ankylosing Spondylitis Imaging Cohort (CASPIC), which is collected through the Smart-phone SpondyloArthritis Management System (SpAMS)^[1]. Patients' self-assessments are completed online at baseline and every subsequent clinic visit. Physician-reported assessments, laboratory tests, and treatments were recorded by rheumatologists at every clinic visit.

Results: 1215 patients with AS were registered, of whom 992 were treated with acemetacin and 123 were treated with other NSAIDs. The results showed that total back pain and BASFI were significantly improved after three-month treatment of acemetacin, while comparing to other NSAIDs ($P=0.027$ and 0.015 , respectively). After six-month treatment, patients taking acemetacin showed greater improvement in PGA ($P=0.013$), total back pain ($P=0.049$), night back pain ($P=0.047$), BASFI ($P=0.042$), ASDAS ($P=0.007$) and CRP ($P=0.032$) compared to those taking other NSAIDs. During the follow-up periods, no serious adverse events were reported. Mild abnormal liver function occurred in nine patients (9/992) treated with acemetacin and in six patients treated with other NSAIDs (6/123). See Table 1 for details.

Conclusion: Acemetacin showed better efficacy and acceptable safety profile in the treatment of active ankylosing spondylitis comparing with other NSAIDs.

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Table 1. The comparison of two groups at 0, 3 and 6 months after treatment

	Baseline		3 months		6 months	
	95%CI	P	95%CI	P	95%CI	P
PGA	-0.13(-0.49, 0.24)	0.494	-0.28(-0.74, 0.18)	0.235	-0.59(-1.06, -0.11)	0.013*
Total back pain	-0.03(-0.37, 0.32)	0.889	-0.50(-0.94, -0.06)	0.027*	-0.44(-0.88, -0.002)	0.049*
Night back pain	0.01(-0.36, 0.38)	0.956	-0.30(-0.75, 0.16)	0.203	-0.46(-0.91, -0.006)	0.047*
BASFI	-0.30(-0.59, 0.004)	0.053	-0.55(-0.99, -0.11)	0.015*	-0.34(-0.67, -0.01)	0.042*
ASDAS	-0.10(-0.29, 0.08)	0.287	-0.15(-0.46, 0.16)	0.342	-0.41(-0.70, -0.11)	0.007*
CRP	-4.39(-8.87, 0.10)	0.055	0.91(-10.39, 12.21)	0.874	-7.86(-15.03, -0.68)	0.032*

Disclosure of Interests: None declared

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POS0922

NON-STEROIDAL ANTI-INFLAMMATORY DRUG USE IS ASSOCIATED WITH DISEASE ACTIVITY AND REDUCED SIGNIFICANTLY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH TUMOR NECROSIS FACTOR INHIBITORS; DATA FROM A REAL LIFE EXPERIENCE

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs) is the first line treatment option in axial spondyloarthritis (axSpA) patients suffering from pain and stiffness. However there is only limited data regarding the concomitant use of NSAIDs during tumour necrosis factor inhibitor (TNFi) treatment.

Objectives: To evaluate longitudinal concomitant NSAIDs use with the TNFi treatment and the determinant of the ASAS-NSAID index in patients with axSpA.

Methods: In total 429 axSpA patients (253 [59%] male; 272 [63%] with AS and 157 [37%] with non-radiographic (nr)-axSpA) who have followed up one year were included in this observational study. The data regarding disease activity and serum CRP levels were collected on 12, 24 and 52nd week. At each visit NSAID usage, type, dosage and frequency were recorded in order to calculate ASAS-NSAID index. The longitudinal relationship between NSAID-index and other factors tested by using generalized estimating equations (GEE) which is a technique for longitudinal data analysis allowing the use of all available data even deviated from normality.

Results: At baseline 127/138 (92%) patients starting TNFi and 239/291 (82%) conventionally treated patients were using NSAID. Both the rate ($p=0.007$) and the median (IQR) ASAS-NSAID index were higher in biologic treatment group (100 [50] vs 70.8 [89.4]; $p<0.001$). During follow-up ASAS-NSAID index was decreased significantly in patients treated with TNFi (median 100 to 8.0; $p<0.001$), however ASAS-NSAID index was not changed in conventionally treated patients

($p=0.154$) (Figure 1). In univariate longitudinal analysis revealed that ASAS-NSAID index was significantly associated with BASDAI, ASDAS, BASFI scores and patient global assessment of disease activity, serum levels of CRP and education. We established two multivariable models (Table 1) to assess the associated factors/covariates with ASAS-NSAID index over time (one with ASDAS and the other BASDAI+CRP as disease activity index) and showed that BASDAI and patient global assessment of disease activity were independent determinants of NSAID dosage in biologic treated patients. However, in multivariate analysis there was no significant predictor for NSAID index in conventional treatment group.

Conclusion: Our results showed that NSAID prescription was significantly higher in axSpA patients who have TNFi indication. NSAID use was decreased significantly over time with TNFi and still independently determined by disease activity. However, it is stable in conventionally treated axSpA patients.

Table 1. The factors associated with ASAS-NSAID index in biologic treated patients

	Model 1			Model 2		
	B	95%CI	p	B	95% CI	p
BASFI	-0.55	-4.384; 4.275	0.980	0.943	-3.795; 5.682	0.696
BASMI	0.951	-1.511; 3.413	0.449	-0.098	-2.430; 2.234	0.934
PGA	0.535	0.210; 0.860	0.001	0.759	0.432; 1.086	0.000
CRP	-0.068	-0.220; 0.084	0.380			
BASDAI	5.718	2.487; 8.949	0.001			
ASDAI+CRP				1.771	-6.571; 10.113	0.677

PGA: Patient global assessment

Disclosure of Interests: None declared

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POS0923

INFLUENCE OF BASELINE DEMOGRAPHICS ON IMPROVEMENTS IN DISEASE ACTIVITY MEASURES IN PATIENTS WITH ANKYLOSING SPONDYLITIS RECEIVING UPADACITINIB: A POST HOC SUBGROUP ANALYSIS OF SELECT-AXIS 1

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Background: Upadacitinib (UPA), an oral Janus kinase inhibitor, has demonstrated efficacy and safety through 14 weeks in the SELECT-AXIS 1 study in biologic disease-modifying antirheumatic drug-naïve patients with active ankylosing spondylitis (AS).¹