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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 = 2.4. 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.¹ MID are not applied for improvement from baseline mean SF-36 T-scores >47, which are considered at least as good as the standard US population, hence no improvement is expected.² 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.