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 1 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 changes 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-α, IFN-β, IL-6, 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 (IFNα/β, IFNγ, IL-7, IL-8, IL-5, IL-17, 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 and hematopoiesis. 

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 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 AS.

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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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 1 trial.

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Acknowledgements: AbbVie, Inc was the study sponsor, contributed to the study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of the final version

Disclosure of Interests: Thierry Sornasse Shareholder of: AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: AbbVie, Employee of: AbbVie, Timothy Radstake Shareholder of: AbbVie, Employee of: AbbVie, Dennis Mognongale Speakers bureau: AbbVie, Grant/research support from: AbbVie

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POS0921

EFFICACY AND SAFETY OF ACEMETACIN IN THE TREATMENT OF 1215 ACTIVE ANKYLOSING SPONDYLITIS PATIENTS: DATA FROM A PROSPECTIVE COHORT MANAGED BY SMARTPHONE 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.


Acknowledgements: AbbVie, Inc was the study sponsor, contributed to the study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of the final version

Disclosure of Interests: Thierry Sornasse Shareholder of: AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: AbbVie, Employee of: AbbVie, Timothy Radstake Shareholder of: AbbVie, Employee of: AbbVie, Dennis Mognongale Speakers bureau: AbbVie, Grant/research support from: AbbVie

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