PROTEOMIC ANALYSIS COMPARING THE MODE OF ACTION OF UPADACITINIB BETWEEN NON-BIOLOGIC-DMARD-IR AND BIOLOGIC-DMARD-IR PsA PATIENTS IDENTIFIES DISTINCT PATHOGENIC PATHWAYS IN THE SELECT-PsA 1 AND SELECT-PsA 2 PHASE 3 STUDIES

T. Sornasse1, J. Anderson2, K. Kato2, A. Lertratanakul2, I. McInnes3, C. performed in silico with a commercial distributed software. Functional pathway prediction was performed in silico with a commercial distributed software. Log10 (x+1) prior to the analysis. Functional pathway prediction was performed in silico with a commercial distributed software. Mixed Linear Model was used to identify pBM modulated by UPA compared to Baseline, and those differentially modulated between responders (R) and non-responders (NR) according to ACR50, PASDAS Minimal Disease Activity, and PASI75 at week 12. Correlation of disease activity measures with relative non-responders (NR) according to ACR50, PASDAS Minimal Disease Activity, and PASI75 in DMARD-IR patients was associated with the down modulation of multiple pBM predicted to be linked to IFN, IL10, IL17, IL22, and IL27 pathways; while favorable clinical response in bio-IR patients was associated with the down modulation of multiple pBM predicted to be linked to the IL17L, IL23, and IL1 pathways.

Conclusion: UPA effects in both DMARD-IR and bio-IR PsA patients likely stem from the direct and indirect inhibition of multiple biological pathways belonging to the adaptive and innate immune systems. Responder/Non-Responder analysis suggests a possible shift from a TH1 biased biology in DMARD-IR PsA patients to a more TH17 biased biology in bio-IR PsA patients. This apparent change in the disease biology of PsA patients after inadequate response to prior therapy could be attributed to the actual alteration of the disease biology, treatment outcome-based patient selection, or both. Considering the clinical efficacy of UPA in both DMARD-IR and bio-IR PsA patients, this observation highlights the importance of targeting multiple pathways with drugs such as UPA for the treatment of a broad range of PsA patients.

REFERENCES:
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