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https://doi.org/10.1136/annrheumdis-2018-EWRR2018.65

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Investigating IL-6 Intracellular Signalling in Peripheral Blood Cell Subsets in Patients at Early and Later Stages of Rheumatoid Arthritis (RA).

L. Ouboussad, L. Hunt, C. Wong, P. Emery, M. McDermott, A. Aslam, M. Buch

1 Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, 2 NIHR- Leeds Biomedical Research Centre (NIHR-LBRC), Leeds Teaching Hospitals NHS Trust, Chapel Allerton Hospital, Leeds, United Kingdom

Introduction: Rheumatoid arthritis (RA) is a chronic, inflammatory arthritis that evolves along an immunological and inflammatory disease continuum. The era of targeted biological therapies has been transformative; however, a significant unmet need is the effective tailoring of therapy to deliver optimal treatment responses. In addition, the concept of a window of opportunity is well-recognised whereby early commencement of treatment confers improved outcomes compared to delayed treatment. The importance of pro-inflammatory cytokines TNF and IL-6 in particular, is well recognised; but high, homogeneous response in early RA (ERA) compared to later RA remains unexplained.

Objectives: The present project focuses on measuring the phosphorylation of STAT3 (p-STAT3) levels as an indication of the activation of IL-6/JAK-STAT signalling pathway at different disease stages (early and established/later). The main aim is to evaluate the variation in cell-subset IL-6 signalling and its association with response to treatment which included IL-6 targeted therapy (Tocilizumab-TCZ) as well as other bDMARD.

Methods: Phosphorylation of IL-6/JAK-STAT key transcription factor STAT3 (p-STAT3) was measured using multiparameter phosphoflow cytometry (phosflow) in T-, B- cells and monocytes isolated from peripheral blood of RA patients. Patients cohorts represented groups at different stages of RA: Treatment-naïve Early RA (ERA group) n=20. Later RA group (LRA n=20) refractory RA patients failing to respond to one or more biologics. Healthy control group (HC n=20) and additional comparable group of 20 early RA patients treated with methotrexate (MTX).

Results: Our previous data evaluating IL-6 pathway (JAK-STAT and also, PI3K/Akt and MAPK/ERK) in T-, B- cells and monocytes isolated from peripheral blood of RA patients. Patients cohort represented groups at different stages of RA: Treatment-naïve Early RA (ERA group) n=20. Later RA group (LRA n=20) refractory RA patients failing to respond to one or more biologics. Healthy control group (HC n=20) and additional comparable group of 20 early RA patients treated with methotrexate (MTX).

Conclusions: Our results are in line with previous findings (2,3), there was a difference in p-STAT3 levels at baseline between early and later RA, and differential response to stimulus with IL-6. Investigation of early vs later RA biologic response profiles will enable us to better understand the multiple cytokine networks, their interaction, and how disease duration and therapy alters this.


Disclosure of Interest: None declared