Prevalence of HCQ Retinopathy Stratified by Cumulative Dose (g)

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.328

OP0134

NOVEL INTERFERON GENE EXPRESSION SCORES PREDICT REFRACTORY SEVERE CUTANEOUS DISEASE FOLLOWING RITUXIMAB THERAPY IN SLE

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Background: We developed and validated two continuous interferon-stimulated gene (ISG) expression scores (IFN-Score-A and IFN-Score-B) that predict clinical outcomes in SLE. IFN-Score-A includes ISGs typically present in a global interferon signature while IFN-Score-B includes additional ISGs potentially responsive to multiple IFN subtypes [1].

We have previously shown that these scores associate with treatment response following rituximab (RTX) therapy within the British Isles Lupus Assessment Group (BILAG) Biologics Register (BILAG-BR), a UK wide study of patients treated with RTX for active SLE following cyclophosphamide and/ or mycophenolate mofetil treatment failure. Specifically, multivariable analysis showed higher baseline IFN-Score-B independently predicted BILAG response at 6 months post treatment [2]. We also showed that response of cutaneous lupus to RTX can be poor even when other organs respond well, and that interferons are enriched in the skin of patients with SLE where dysregulated keratinocytes are a source of IFN κ [3]. MASTERPLANS is a consortium aimed at identifying therapeutic biomarkers in SLE.

Objectives: To investigate how IFN-Score-A and -B associated with skin disease and response to RTX.

Methods: Pre-treatment whole blood samples were collected in TEMPUS tubes from subjects undergoing first RTX treatment within BILAG-BR. IFN-Scores were derived using a custom Taqman array as previously described [1]. Clinical response was defined as improvement in BILAG-2004 disease activity, with a maximum of one domain showing persistent BILAG-2004 grade B disease, and no new BILAG grade A or B disease flares at 6 months. The mucocutaneous domain of BILAG was then analysed separately.

Results: 147 patients were studied, of whom 90 had follow up data available. Baseline BILAG-2004 grade A/B disease activity predominantly affected the mucocutaneous domain in 74/147 (50.3%), musculoskeletal in 61/147 (41.5%) and renal domain 66/147 (37.4%).

At 6 months 59/90 (65.6%) achieved an overall treatment response. Responders showed significantly higher mean IFN-Score-B compared with non-responders (-1.8 vs -2.4, $p = 0.04$). Among those with active grade A/B BILAG-2004 mucocutaneous disease at baseline, 38/50 (76%) showed improvement within this domain at 6 months. However, among overall non-responders, 7/31 (22.6%) had new or residual BILAG-A mucocutaneous disease at 6 months post RTX, indicating it to be a substantial component of overall treatment failure. In contrast, persistent grade A musculoskeletal disease was seen in 9.7% of non-responders. BILAG-A mucocutaneous disease is characterised by severe manifestations including extensive rashes covering > 18% of body surface area, severe bullous lupus or panniculitis and disabling deep mucosal ulceration. Neither IFN-Score-A nor IFN-Score-B were significantly associated with the severity of mucocutaneous disease at baseline. However, individuals with persistent or new BILAG-A mucocutaneous disease at six months following RTX displayed significantly lower baseline IFN-Score-B than those with improving or residual less severe disease (-3.0 vs -2.1, $p = 0.04$) after RTX.

Conclusion: Low IFN score-B status identified an endotype of severe mucocutaneous SLE which was resistant to RTX therapy in the BILAG-BR cohort. We previously showed that high IFN-score-B independently predicts overall therapeutic response to rituximab. Further work will aim to refine IFN status as overall and organ specific biomarkers in SLE.

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Acknowledgements: We would like to thank the Medical Research Council, National Institute of Health Research, UK for funding the MASTERPLANS project

Disclosure of Interests: Lucy Marie Carter: None declared, Adewonuola Alase: None declared, Zoe Wigston: None declared, Antonios Psarras: None declared, Agata Burska: None declared, Md Yuzaif Md Yusof: None declared, Elizabeth Hensor: None declared, John Reynolds: None declared, Miriam Wittmann Consultant of Abbvie, Celgene, Janssen, L'Oreal, Novartis and Pfizer, Ian N. Bruce Speakers bureau: GlaxoSmithKline, UCB Pharma, Consultant of: AstraZeneca, Eli Lilly, GlaxoSmithKline, ILTOO Pharma, MedImmune, Merck Serono, Grant/research support from: Genzyme Sanofi, GlaxoSmithKline, Edward Vital Consultant of: Roche, GSK and AstraZeneca, Grant/research support from: Roche, GSK and AstraZeneca

DOI: 10.1136/annrheumdis-2021-eular.1098

OP0135

SAFETY AND EFFICACY OF SUBCUTANEOUS BELIMUMAB AND INTRAVENOUS RITUXIMAB COMBINATION IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: A PHASE 2, RANDOMISED, PLACEBO-CONTROLLED 68-WEEK STUDY

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