Index-4 at week 24) and if these features could help elucidate the mechanism of action of ustekinumab in SLE.

**Methods** We examined whole blood RNA and serum at baseline and longitudinally from this trial of 102 seropositive SLE patients, plus age- and sex-matched healthy controls. Targeted proteomic analysis used ELISA, and gene expression analysis used microarray. RNA-Seq was performed on whole blood stimulated in vitro.

**Results** Changes in serum IL-17A, IL-17F and IL-22 were subtle and did not consistently associate with UST response, while no modulation of type I interferon levels was observed. In contrast, durable reduction in IFN-γ protein occurred only in UST-R. These biomarker effects were sustained through Week 48. A non-biased machine-learning algorithm identified a novel 9-gene (PRF1, KLRD1, GZMH, NKG7, GNLY, FGFBP2, TRGC2, TARP, TRGV2) cytotoxic gene-signature (CGS) enriched in baseline blood samples of UST-R vs UST- NR, which was corroborated using a published NK-cell CGS (figure 1). No significant differences in these gene-signatures were observed between placebo responders vs non-responders. In contrast, decreased expression levels were observed over the course of 24 weeks for both signatures only in the UST-R population. After whole-blood stimulation with recombinant IL-12, but not IL-23, expression of representative members of the CGS increased.

**Conclusion** We identified a novel cytotoxic signature in baseline blood samples that associated with UST response in SLE. Targeted biomarker analysis suggests an important role of IL-12 blockade in the mechanism of action of UST in SLE.

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**O10** PREDICTION OF RESPONSE TO RITUXIMAB IN SLE USING A VALIDATED TWO-SCORE SYSTEM FOR INTERFERON STATUS

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**Background** Rituximab (RTX) is used for resistant SLE but clinical response varies. We previously validated two interferon-stimulated gene expression scores (IFN-Score-A and IFN-Score-B) that improved prediction of clinical outcomes in SLE.¹ IFN-Score-A included most commonly reported ISGs and predicted flares and glucocorticoid requirements. IFN-Score-B included ISGs that respond to multiple IFN subtypes and predicted development of SLE in At-Risk individuals. Diagnosis of SLE was associated with both scores, while only IFN-Score-B was elevated in RA. The British Society for Rheumatology Biologics Registry (BILAG-BR) collects samples for RTX-treated patients in the UK. MASTERPLANS is a consortium to identify predictors of drug response.

**Methods** Patients were recruited if they were starting a first cycle of RTX for active SLE (BILAG A or 2xBILAG B) despite previous cyclophosphamide or mycophenolate mofetil. Disease activity was measured using BILAG-2004. Clinical response was defined as improvement by ≥1 grade in active BILAG-2004 systems with no worsening in other systems. Whole blood was collected into TEMPUS tubes and RNA extracted. IFN-Scores were measured using a custom Taqman array as previously described [El Sherbiny et al., 2018]. Multivariate logistic regression was used to test IFN-Scores and baseline clinical covariates as predictors of BILAG response at 6 months.

**Results** Samples were available from 147 patients, of whom 84 had complete baseline and 6 month clinical data available and were included in this analysis. 40/84 (47.6%) patients had BILAG response at 6 months. In univariate and multivariate analysis, high IFN-Score-B expression was significantly associated with clinical response (see table 1).

**Conclusions** This preliminary analysis suggests that assessment of IFN activity has a role in predicting response to RTX. A novel IFN score (Score B) was more predictive than classic ISGs (Score A). These results add to a body of work showing that IFN-Score-B predicts clinically significant outcomes independently of overall IFN activity. Future work will analyse this biomarker in a larger cohort of patients and integrate with other putative clinical and biological predictors of response.

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