O13 INNATE IMMUNITY TRANSCRIPTIONAL PROFILES AS POTENTIAL PREDICTIVE BIOMARKERS FOR TREATMENT RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS: INSIGHTS FROM A LONGITUDINAL STUDY

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Background Systemic Lupus Erythematosus (SLE) is a prototypic, systemic autoimmune disease that can affect many organs. Current treatment of SLE is largely empirical, while the existing immunosuppressive treatments fail to induce remission in over 40% of patients.

Methods Whole blood transcriptome samples were obtained from 95 patients with moderate to severe SLE at baseline, 1 month and 6 months after initiation of treatment with cytotoxic agents (cyclophosphamide, mycophenolate mofetil), mycophenolate mofetil/anti-CD40 antibody, rituximab or belimumab. Disease activity was assessed using the SLEDAI-2K. Response to treatment was defined as achievement of Low Disease Activity State (LLDAS) or remission at 6 months. Differentially expressed genes (DEGs) were identified using the DEseq2. Weighted correlation network analysis (WGCNA) was applied to detect modules of co-expressed transcripts. Abundances of cell types were assessed by CIBERSORTx.

Results 95 patients were enrolled in our study. Most of the patients were women (93.7%) with a mean [SD] age at SLE diagnosis of 42.9 [13.6] years and a mean disease duration [SD] at sampling of 5.1 [7.2] years. Cyclophosphamide was the most frequently used immunosuppressive agent (n=46), followed by belimumab (n=24) and rituximab (n=21). 43 patients responded to treatment. Transcriptional disturbances related to type I interferon signaling (p=0.04, r= 0.15) and leukocyte chemotaxis (p=0.005, r=0.21) positively correlated with response to treatment at 6 months. Enrichment of processes linked to complement activation and PI3KK/Akt pathway distinguishes active Lupus Nephritis (LN) responders from LN non-responders at baseline. Gene expression signatures indicative of cell cycle checkpoint regulation and humoral immunity emerged as potential determinants of resistant disease 6 months after treatment initiation. Marked reduction in the naïve B cell compartment uniquely characterized successful response induction, while the neutrophilic fraction exhibited a statistically significant reduction upon treatment, irrespective of the 6-month outcome.

Conclusions Baseline transcriptional signatures related to innate immunity correlated with 6-month response to treatment in SLE. Disturbances linked to cell cycle regulation decisively shaped the transcriptional landscape of 'resistant' disease.

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O14 RITUXIMAB OBJECTIVE OUTCOME MEASURES TRIAL IN SLE (ROOTS): OUTCOMES OF RANDOMISED AND RESCUE RITUXIMAB THERAPY IN A DOUBLE-BLIND RANDOMISED PLACEBO-CONTROLLED TRIAL

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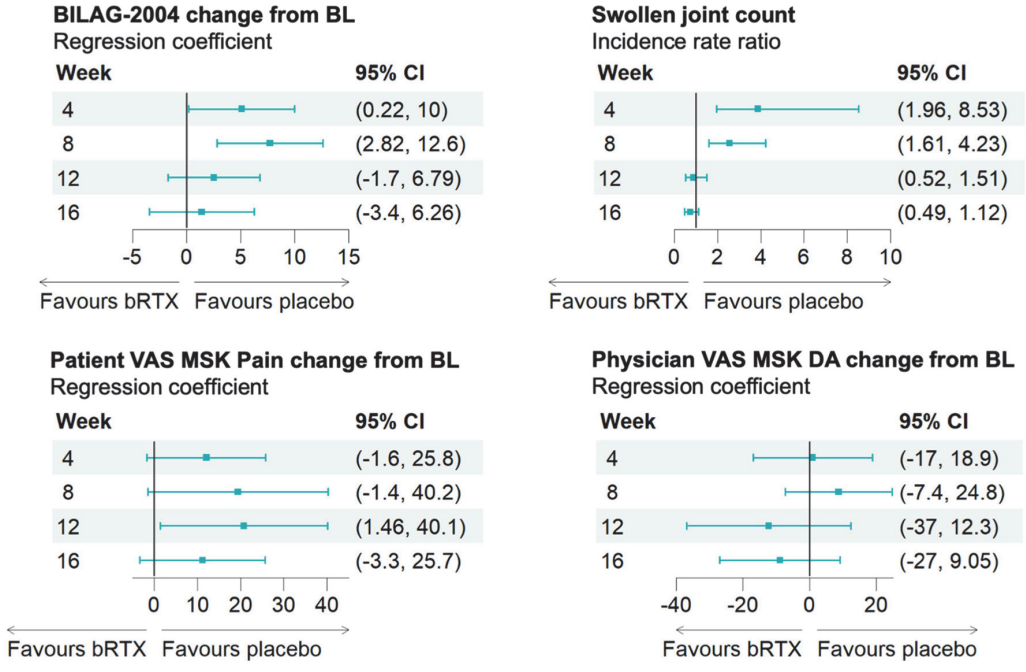
Objective (i) Assess a novel musculoskeletal SLE trial design with objective eligibility and endpoints and a low-glucocorticoid standard of care; (ii) further validate Lupus Arthritis and Musculoskeletal Disease Activity Score (LAMDA) and



Abstract O14 Figure 1 Efficacy during randomised phase (n=25)