0.8]) relative to PBO. Adverse events (AEs; ≥1) occurred in 95.5% of BEL and 94.2% of PBO pts, and 25.9% of BEL and 29.9% of PBO pts had ≥1 serious AE.

Conclusions The addition of BEL to commonly used ST for the treatment of LN significantly improved renal responses with no unexpected safety signals.

REFERENCE

1. Brad H Rovin, Frédéric Houssiau, Richard Furie, Ana Malvar, Y K Onno Teng, Gabriel Contreras, Xueqing Yu, Beulah Ji, David Roth, Christi Kleoudis, Susan Makowiak, Anuradha Madan, Jennifer Gilbride, Yulia Green. Belimumab (BEL) improves renal outcomes in active lupus nephritis (LN): a phase 3 randomized, placebo (PBO)-controlled trial. *J Am Soc Nephrol.* 2020;31:54.

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Trial Registration NCT0163933. GSK Study BEL114054

507 RNASEQ GENE EXPRESSION CONFIRMS THE IMPORTANCE OF GWAS ASSOCIATED RISK GENES IN LUPUS NEPHRITIS

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Background The era of GWAS studies identified over 90 SLE risk loci, while the genetic risk factors associated with lupus nephritis (LN) require further study. The absence of strong associations might reflect uncertainty about future LN status or insufficient coverage within the array. To highlight the importance of previously identified risk genes and pathways predisposing to LN, we investigated PBMC RNAseq data from a cohort of SLE patients followed for several years with and without biopsy-proven LN.

Methods PBMC RNAseq data, including some longitudinal data, from 46 LN samples (30 patients) and 44 samples from SLE patients without LN (28 patients) were studied. The analysis of differentially expressed genes was performed using the limma R package. The reported LN genetic loci were collected from published data. The regularized logistic regression was used to select the most important genes.

Results Comparing LN and non-LN samples, 109 genes were differentially expressed between groups (logFC 1.5, 5% FDR). The functional analysis identified genes related to glomerular membrane formation (COL4A3, COL9A3, MMP9), WNT signaling (WNT1, WNT7A, TPBG), and cell adhesion (FBLN7, ADAM23, TNFAIP6). To find the most informative genes to distinguish LN patients, we used 3 models based on: (1) differentially expressed genes, (2) GWAS reported genes, (3) a combination of the above. All models were based on the same 67 (70%) training and 23 (30%) testing sample sets and efficiently segregated LN patients (AUC 0.9, 0.8, and 0.9). Despite the equal efficiency of the first and the third model, the inclusion of IKZF1 and PRPF18 genes reduced the number of required predictor genes.

Conclusion LN might be an initial presentation of SLE disease or can have a late-onset. The analysis of longitudinal samples helps classify SLE patients correctly and may be of predictive value. Polymorphism in IKZF1 was reported in association with several autoimmune diseases and found to relate to Th and dendritic cell activation. The PRPF18 gene encodes a pre-mRNA splicing factor. Interestingly, another polymorphism at that locus is highly associated with darker skin color in the African-American population, a group with high risk for severe lupus. As a limitation of our study is the relatively small number of participating SLE patients, additional patient data will be needed to confirm these results.

508 C3D-IMAGING IN LUPUS NEPHRITIS

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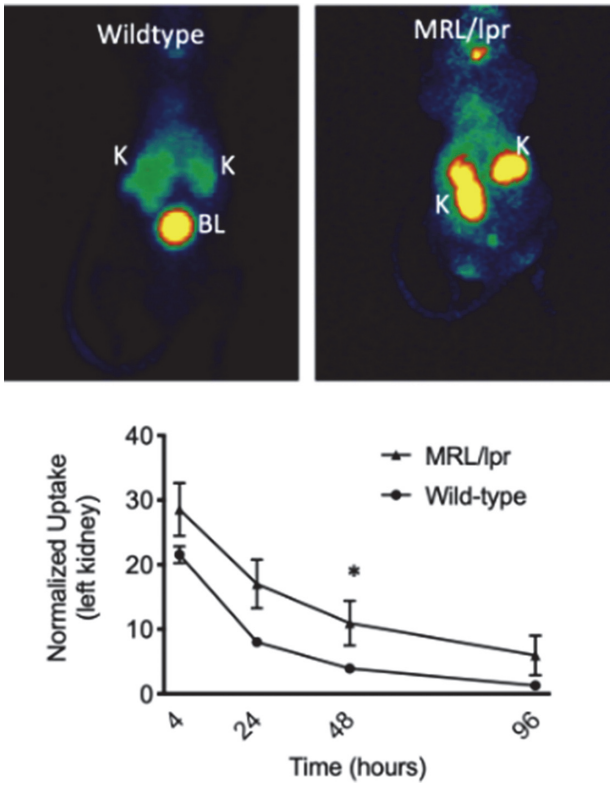
Background We have developed a positron emission tomography (PET)-based imaging probe for detecting inflammation in the kidneys. After immune-complexes deposit in the glomeruli of patients with lupus nephritis (LN), circulating C3 is cleaved and covalently fixed to tissue surfaces. Kidney biopsies are routinely immunostained for deposited C3 fragments as a marker of immunologic activity. Although generally safe, biopsies are invasive procedures, and they are also subject to sampling error. Our new method is based on non-invasive detection of C3d deposits in an animal model of LN and can be translated for use in patients. Furthermore, it will not be limited by the small size of the biopsy or require an invasive procedure.



Abstract 508 Figure 1 C3d-PET of MRL/lpr and wild-type mice. 16-week-old animals were injected with ^{124}I labeled anti-C3d antibody and PET imaging was performed at various timepoints. The kidneys of the MRL/lpr mice revealed higher uptake and retention of ^{124}I-labeled antibody. *P < 0.05. "K" indicates kidney, "BL" indicates bladder.