Background The two Apolipoprotein L1 (APO1) risk variants (RV), G1 and G2, are enriched in African populations due to resistance to Trypanosoma brucei, a parasite endemic in West Africa. This improved fitness comes with the cost of propensity toward renal disease by multiple causes including SLE. In Ghana, up to 60% of individuals are heterozygous and 30% are variant homozygous. However, APO1 variant phenotypes have never been described in a Ghanaian SLE cohort. Further it remains unclear whether RV associated nephritis progression is driven by accelerated inflammation or intrinsic renal disease. Accordingly, we evaluated APO1 genotype-phenotype traits in the context of SLE activity in 101 Ghanaian patients seeking care at Korle bu Teaching Hospital in Accra, Ghana.

Methods 101 Ghanaian patients meeting at least 4 clinical criteria for SLE were stratified by APO1 genotype PCR/sequencing as follows: ancestral (G0/G0), RV heterozygotes (RV/G0), and RV homozygotes (RV/RV). DNA was extracted from saliva. Clinical endpoints including demographics, ACR criteria, SLEDAI score, and SLICC damage index were recorded at time of blood draw. Based on cytokines known to fluctuate with SLE activity in African Americans, a 12 cytokine array was performed on sera to determine active inflammatory pathways. Interferon signature as measured by the WISH cell assay was completed.

Results The frequencies of the G0, G1, and G2 alleles were 63.3%, 24.2%, and 12.5% respectively. Subjects were 100% female, and 32.1 years of age with a disease duration of 2.9 years. There were no differences in demographics across the genotypes. The RV associated with higher BP: 107.4/72.3, 108.5/72.1, and 120.6/83.4 in the G0/G0, RV/G0, and RV/RV groups respectively (p = 0.013 systolic; 0.003 diastolic). Among those with nephritis, RV/RV associated with increased creatinine and proteinuria with creatinine values of 0.9, 1.1, and 2.5, and average (3 visit) urine dipstick values of 1.0, 1.2, and 3.3 in the G0/G0, RV/G0, and RV/RV groups respectively (creatinine: p = 0.03; urine dipstick p = 0.01). RV/RV carriers were on higher doses of prednisolone (17.2 mg) compared to G0/G0 or RV/G0 carriers (11.2 mg; 11.8 mg respectively). SLEDAI scores were comparable across the genotypes, however RV/RV associated with elevated SLICC damage index: G0/G0 or RV/G0: 0.95 vs RV/RV: 1.7; driven by renal, CVD, and neurologic manifestations G0/G0: 0.46, RV/G0: 0.39, RV/RV: 1.25; p = 0.03 Despite more damage, RV/RV individuals had lower dsDNA titters (10.7 IU/mL) than G0/G0 (57.1 IU/mL) and RV/G0 (95.6 IU/mL) carriers (p = 0.03). Cytokine scores were also lower in RV/RV carriers compared to G0/G0 and RV/RV, for example serum IL8 levels were 34.6 pg; 33.2 pg, and 13.8 pg (IL-8: p = 0.04). Both G0/G0 and RV/G0 individuals exhibited more elevated IFN signatures than RV/RV individuals (245.7, 81.3, and 24.3 respectively, p = 0.04).

Conclusions Taken together, the APO1 RV associated with increased blood pressure, creatinine, proteinuria, and SLICC damage score in this Ghanaian SLE cohort. Paradoxically, RV homozygotes exhibited lower dsDNA titers and lower cytokine profiles than G0/G0 or RV/G0 patients. This suggests that RV homozygotes may have an intrinsic propensity toward organ damage independent of SLE activity.