LSO-092 SAFETY, EFFICACY AND PHARMACODYNAMICS OF CENERIMOD IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: TWO RANDOMISED, DOUBLE-BLIND PHASE 2 CLINICAL TRIALS

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Background Two Phase 2 studies investigating once-daily cenerimod, a selective sphingosine 1-phosphate 1 receptor modulator, in adults with SLE were recently completed: CARE (NCT03742037) and ID-064A203.

Methods The CARE study was previously described.1 Adults with moderate to severe SLE were randomised to placebo or cenerimod (0.5, 1, 2 or 4 mg). At Month (M) 6, patients receiving cenerimod 4 mg were re-randomised to placebo or cenerimod 2 mg for M7-12; patients from other groups continued their initial treatment to M12. The primary endpoint was change from baseline to M6 in SLEDAI-2K score modified to exclude leukopenia (mSLEDAI-2K).

ID-064A203, performed in Japan, randomised adults with moderate to severe SLE to 2 or 4 mg cenerimod for 3 months with end-of-study at M9. The primary endpoint was occurrence of treatment-emergent adverse events (AEs), serious AEs and AEs of special interest. The secondary endpoint was change from baseline to each post-baseline assessment (PBA) until M9 in total lymphocyte count. Exploratory endpoints included change from baseline to each PBA until M9 in mSLEDAI-2K, physician's global assessment and biomarkers.

In both studies, patients continued their SLE background therapies, and oral corticosteroid (OCS) dose should have been maintained stable for ≥15 days before randomisation. It was preferable for OCS dose to be maintained stable until M3 in ID-064A203, and to the end of M6 in CARE.

Results Results from ID-064A203 will be available in 2023.

CARE results were presented;1 the primary endpoint was not met after adjustment for multiplicity (nominal p=0.0291 for cenerimod 4 mg versus placebo), although reduction in disease activity at M6 was observed.

Conclusions These Phase 2 clinical trials increase our knowledge of the efficacy, safety and pharmacodynamics of cenerimod in SLE. Two Phase 3 trials of 4 mg cenerimod in patients with SLE are underway (OPUS, NCT05648500, NCT05672576).

Short oral presentation session 17: miscellaneous conditions associated with SLE

LSO-093 GUT MICROBIOTA ANALYSIS IN KOREAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background In recent years, many studies have demonstrated an important role of gut microbiota in the development of various illnesses including autoimmune diseases. A number of evidence have also been found that alterations of gut microbiota affect the host immune system, resulting in changes in autoimmunity, which contributes significantly to the development of systemic lupus erythematosus (SLE). Therefore, we aimed to elucidate discover the gut microbiotas influential to SLE and investigate their association with disease activities.

Methods Fecal samples were provided in the same protocol from 38 patients with SLE in Ajou Lupus Cohort and 52 age and sex-matched healthy controls (HCs). The components of the gut microbiota in feces were investigated via 16S rRNA next-generation sequencing, and alpha and beta diversities were evaluated. Clinical, laboratory, and medication data of SLE patients were obtained through medical records, and the correlation between disease activity and gut microbiota was also analyzed.

Results The gut microbiota of SLE group exhibited a significant decrease in species richness in the beta diversity analysis by NMDS plots compared to controls. Taxonomic composition differences between the two groups were also found at phylum, genus, species levels. At the species level, the relative abundance of 7 kind of bacteria was significantly higher and another 7 bacterial taxa were significantly lower in the SLE group compared with HCs, suggesting that reduction in Faecalibacterium prausnitzii and Prevotella copri (p=0.001 and p=0.001, respectively) played an important role in SLE. In clinical correlation analysis, there was a significant positive correlation between complement 3/4 and Faecalibacterium prausnitzii (r=0.44 and r=0.49, respectively), and total lymphocytes and Prevotella copri (r=0.45).

Conclusions The composition of gut microbiota was different between SLE patients and HCs in Korean population. Among them, Faecalibacterium prausnitzii and Prevotella copri, which are significantly reduced in SLE patients, are expected to provide potential targets for new treatment.

LSO-094 ANALYSIS OF MICROBIOTA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Previous studies have reported that gut dysbiosis is observed in systemic lupus erythematosus (SLE) and linked to the diseases. However, the relation with the pathogenesis remains unclear. We explored gut microbiota in patients with SLE and investigated the association with the onset and activity of disease and clinical findings