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TARGETING CD38 IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Depletion of long-lived plasma cells (PC) resembles a novel concept for the treatment of antibody-mediated autoimmune diseases, such as systemic lupus erythematosus (SLE). Therapeutic approaches such as autologous stem-cell transplantation and proteasome inhibition are limited by significant treatment-related toxicity. A novel target for PC depletion is CD38, a surface protein that is highly expressed on plasma cells (PCs) but also activated Tcells and most myeloid cells. Daratumumab is a monoclonal antibody targeting CD38 that is licensed for the treatment of multiple myeloma.

Objectives: Here, we aimed to ascertain clinical safety and efficacy of Daratumumab for the treatment of refractory SLE, as well as to gain insights into effects of Daratumumab on the immune system.

Methods: We treated two SLE patients with life- and organ-threatening SLE with four weekly dosis of 16 mg/kg Daratumumab. We performed integrative analyses of clinical, serological and immunological effects over a follow-up period of 6 months. Using flow cytometry and single-cell RNA and T-cell receptor sequencing we followed CD38 expression and composition of peripheral blood leukocytes with a special focus on memory T cells.

Results: Patient 1, a 50-year-old woman, suffered from active biopsy-proven class III lupus nephritis (LN) with nephrotic syndrome, pericarditis, arthritis and skin rash. Upon Daratumumab treatment, her glomerular filtration rate normalized within 3 months and proteinuria gradually declined from 6.4 to 1.9 g/g Creatinine during the 180-day follow-up period. Pericarditis, arthritis and skin rash completely resolved. Patient 2, a 32-year-old woman, presented with auto-immune hemolytic anemia requiring blood transfusions, immune thrombocytopenia and cutaneous vasculitis. Her direct antiglobulin test normalized within 3 months and remained negative in the follow-up with consecutive recovery of the hemolytic anemia. Immune thrombocytopenia stabilized and vasculitic skin lesions completely resolved. Infusions were well tolerated without severe adverse drug reactions. NK cells and Dendritic Cells were transiently depleted, while numbers of T cells, B cells and Monocytes in the peripheral blood remained stable. CD38+ memory T cells that were expanded prior to treatment were virtually undetectable early after treatment. Their single cell transcriptomics demonstrated an upregulation of genes associated with activation, cytotoxicity and type 1 interferon response. CD38+ CD8+ memory T cells showed marked oligoclonality. These prominent clones persisted upon treatment but their transcription profile gradually normalized.

Conclusion: Daratumumab appears to be a safe and effective treatment for refractory SLE. Further investigations are warranted to establish the efficacy in a clinical trial and to gain further insights into the pathophysiologic mechanism of action.

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TREATMENT STATUS FOR OSTEOPOROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: CROSS-SECTIONAL ANALYSIS FROM A LUPUS REGISTRY OF NATIONAL INSTITUTIONS (LUNA)

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Background: Osteoporosis is one of the most important adverse effects of glucocorticoids in patients with systemic lupus erythematosus (SLE). Because osteoporosis is not usually treated by chronic kidney disease (CKD), more attention should be paid to the treatment for osteoporosis in SLE patients with CKD. Many treatment options for osteoporosis have emerged recently, but treatment status in patients with SLE is not elucidated.

Objectives: The purpose of this study is to elucidate the treatment status for osteoporosis in patients with SLE among the CKD stages.

Methods: Using data from lupus registry of nationwide institutions (LUNA), a cross-sectional analysis was performed. We firstly described treatment status for osteoporosis in all enrolled patients. Secondary, treatment status for osteoporosis was compared among CKD stages. Finally, bone damage in Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) was compared among CKD stages.

Results: Of 3,344 patients (median age: 52 years; median [interquartile range] [IQR] 44 [38-57] years) (IQR) of enrolled 917 patients was 44 (34-57) years and 895 patients (88%) were female. CKD stages were: CKD stage 1, 234 (26%); CKD stage 2, 465 (51%); CKD stage 3, 189 (21%); CKD stage 4, 9 (1%); CKD stage 5, 16 (2%). Median (IQR) age, female sex,