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# POSTER ABSTRACTS

## 704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

### CD19/BCMA CAR-T Cell Therapy for Refractory Systemic Lupus Erythematosus - Safety and Preliminary Efficacy Data from a Phase I Clinical Study

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Background: Despite significant advances in the treatment of systemic lupus erythematosus (SLE), a subset of patients continue to experience severe progression of their disease despite multiple immunosuppressive and targeted therapies. Furthermore, to date, drug-free remission and seroconversion have been difficult to achieve in SLE. CD19 single-targeted chimeric antigen receptor (CAR) T-cell therapies have shown promising efficacy in SLE but have been unable to attack CD19-negative, long-lived plasma cells, which produce numerous antibodies.This trial aims to study the safety, tolerability and preliminary efficacy of deep B-cell clearance in patients with refractory SLE using autologous anti-CD19 and BCMA CAR-T cells.
Method: The CAR product was manufactured by Shanghai YaKe Biotechnology Ltd. The clinical study was conducted in a dose-escalation format. T cells were enriched from patient's peripheral blood, transfected with lentiviral vectors and expanded. After lymphodepleting chemotherapy with cyclophosphamide/fludarabine (D-4 to D-2), patients receive a single infusion of 1-2x106 CD19 CAR-T cells and BCMA CAR-T cells per kilogram of body weight at D0. On the first day of chemotherapy initiation , all SLE-related immunosuppressants, biologics, etc. were discontinued except for a few patients who were maintained on low-dose prednisolone. Tolerability was assessed by monitoring cytokine release syndrome (CRS), immune-related effector cell neurotoxicity syndrome (ICANS), and infections. Initial efficacy was assessed by attainment of lupus low disease activity state (LLDAS), dsDNA antibody and ANA seroconversion, and discontinuation of all SLE-specific therapies.
Results: As of July 31, 2023, 12 patients with refractory SLE were treated with CD19/BCMA CAR-T cells with a median follow-up of 118.5 (45-524) days. All patients had active severe SLE and had received glucocorticoids, hydroxychloroquine, tacrolimus, total glucosides of paeony, merti-macrolide, leflunomide, azathioprine, methotrexate, cyclophosphamide, immunoglobulin, rituximab, belimumab, and Tetracycline before treatment with CAR-T cells, which were standard treatments that were either ineffective or difficult to withdraw.3 patients received 1x10^6/kg of each of CD19 CAR-T cells and BCMA CAR-T cells, and 9 patients received 2x10^6/kg of each of CD19 CAR-T cells and BCMA CAR-T cells 2x10^6/kg. CAR-T cells were prepared successfully in all patients. BCMA CAR-T achieved expansion in all patients, while CD19 CAR-T did not expand in 1 patient, and expansion of CAR T cells preceded depletion of circulating B cells. All patients developed grade 1 CRS, which manifested as controllable fever, and no ICANS occurred. 11 patients (91.7%) developed grade 4 hematologic toxicity, and 1 patient (8.3%) developed grade 3 hematologic toxicity. Within 6 months of CAR-T treatment, 2 patients were infected with neocoronavirus, 1 patient developed gastrointestinal tract infection, and 1 patient developed pulmonary infection , and all of them recovered after treatment. The SLEDAI-2K score decreased in all patients, from a mean of 18.3 to 1.5. Low-level proteinuria persisted in some patients, possibly due to previously accumulated glomerular filtration impairment. All patients met LLDAS criteria and were able to successfully discontinue all SLE-related medications, including glucocorticoids. peripheral blood B cells recovered at approximately 3 months after CAR-T therapy. To date, no SLE flares have occurred.
Conclusions: These data suggest that CD19/BCMA CAR-T cell therapy is well tolerated and can induce rapid and durable remission in severe refractory SLE.

**Disclosures** No relevant conflicts of interest to declare.

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