AUTOLOGOUS CAR-T CELLS TARGETING CXCR5 IN PATIENTS WITH RELAPSED/REFRACTORY B-NHL: TICARA PHASE I STUDY

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Background: B-cell non-Hodgkin lymphomas (B-NHL) often relapse or become refractory after initial treatment. CD19-directed CAR-T cell therapies have revolutionized second line therapy but are limited by mechanisms of resistance such as antigen loss, T cell exhaustion, and anti-CAR immunity in a substantial fraction of patients. Furthermore, the lymph node microenvironment—particularly T follicular helper (Tfh) cells—can display a barrier to durable remission. CXCR5, a chemokine receptor expressed on malignant B cells and Tfh cells but not on B cell precursors or plasma cells, presents an attractive target for next-generation CAR-T therapy. MDC_CAR_CXCR5_001 is an autologous humanized CXCR5-directed CAR-T cell product developed at the Max Delbrück Center for Molecular Medicine, Berlin (Bunse et al., 2021) and designed to deplete both malignant B cells and their supportive microenvironment. Preclinical studies demonstrated more potent eradication of B-NHL by anti-CXCR5 CAR-T cells than anti-CD19 CAR-T cells and no unexpected on-target/off-tumor toxicities.
Objectives: This trial aims to evaluate the safety and determine the maximum tolerated dose of a single infusion of autologous MDC_CAR_CXCR5_001 cells. Secondary objectives include pharmacokinetic profiling and preliminary assessment of efficacy. CAR-T cell attributes, cytokine profiling, immunogenicity, and minimal residual disease monitoring will be assessed as exploratory endpoints.
Study Design: This is a single-arm, monocentric Phase I trial enrolling adult patients with relapsed/refractory CXCR5-positive B-NHL. Patients receive lymphodepleting chemotherapy followed by a single infusion of autologous MDC_CAR_CXCR5_001. Four

escalating dose levels (0.5×10^7 to 5×10^8 cells) are evaluated using a Bayesian optimal interval (BOIN) design.

Trial Status: Clinical study initiation is planned for January 2026 with a 15-month enrolment period and 12 months of follow-up. Up to 24 patients are expected to be evaluable for the primary endpoint. The trial is conducted at Charité-Universitätsmedizin Berlin as a first-in-human Investigator-Initiated-Trial and aims to establish proof-of-concept for CXCR5-targeted CAR-T therapy in r/r B-NHL.