# PROTOCOL SYNOPSIS

## Phase II Multicenter Trial of MB-CART2019.1 (Zamtocabtagene Autoleucel) Therapy as Frontline Consolidation for High-Risk Mantle Cell Lymphoma

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| **Co-Principal Investigators:** | Nirav Shah and Michael Jain |
| **Study Design:** | This study is a prospective, multicenter Phase II study with participants receiving MB-CART2019.1 as frontline consolidation for high-risk mantle cell lymphoma (MCL). |
| **Primary Objective:** | The primary objective is to estimate one-year progression free survival (PFS) after frontline consolidation therapy with MB-CART2019.1. |
| **Secondary Objectives:** | The secondary objectives include the assessment of overall and complete response rates (best and at day 90), response duration, non-relapse mortality (NRM), relapse/progression, overall survival, event-free survival, and immune effector cell (IEC)-related toxicities in patients receiving MB-CART2019.1 therapy. |
| **Eligibility Criteria:** | Eligible patients are ≥18 years of age with high-risk MCL, defined as meeting any one of the following criteria: high-risk by Mantle Cell Lymphoma International Prognostic Index Combined (MIPI-c), a simplified Mantle Cell Lymphoma International Prognostic Index (MIPI) score of ≥6.2, tumor protein 53 (TP53) mutation, ≥50% TP53 expression by immunohistochemistry, complex karyotype, Ki67 ≥50%, blastoid or pleomorphic histology with Ki67 ≥30%, leptomeningeal disease at diagnosis or the presence of a NOTCH1 mutation. Patients must have received 2 cycles of appropriate frontline systemic induction therapy and achieved a response of stable disease or better. |
| **Treatment Description:** | Eligible patients will receive a single intravenous infusion of MB-CART2019.1 cells at a dose of 2.5x10^6 cells/kg following lymphodepleting chemotherapy. |
| **Accrual Objective:** | The goal is 52 participants in total who receive MB-CART2019.1 therapy. Additional participants may be screened, consented, registered, and treated in order to reach accrual goals. |
| **Accrual Period:** | The estimated accrual period is 2 years. |
| **Study Duration:** | Participants will be followed for 1-year post-infusion. |

**Long Term Follow-Up:** Assessment of survival annually through 15 years after infusion will be completed using a separate long-term follow-up protocol.

**Pausing Guidelines:** NRM at Day 100 and treatment-limiting toxicity (TLT) at Day 28 will be monitored throughout the study. Safety pausing rules will monitor NRM through 100 days and TLT through 28 days post-CAR T infusion. The Day 100 NRM rate and Day 28 TLT rate are not expected to exceed 10%. If either rate exceeds this threshold, the NHLBI will be notified in order that the Data and Safety Monitoring Board (DSMB) can be advised.

**Correlative Studies:** Samples will be banked pre- and post-infusion for future submitted protocols for use of specimens.