DALY

Powering the advancement of immunotherapies through research

A clinical study evaluating MB-CART2019.1 as a second-line treatment for patients with relapsed/refractory diffuse large B cell lymphoma

Miltenyi Biomedicine

Evaluating an investigational immunotherapy as a second-line treatment option

The DALY 2-EU Study (EudraCT: 2020-003908-14) is a pivotal phase II, randomized, multi-center, open-label study to evaluate the efficacy and safety of the investigational medicinal product MB-CART2019.1 (IMP, chimeric antigen receptor [CAR] T cell product) compared to standard of care therapy in participants with relapsed/refractory diffuse large B cell lymphoma (R-R DLBCL).

We are currently seeking study participants, and we ask that you consider this clinical study for your patients who:

- Have been diagnosed with relapsed or refractory diffuse large B cell lymphoma after first-line chemoimmunotherapy.
- Are ineligible for high-dose chemotherapy (HDC).
- Are ineligible for autologous stem cell transplantation (ASCT).

Introducing MB-CART2019.1 and the DALY 2-EU Study

MB-CART2019.1 is designed to target B cells in patients with B cell malignancies. It consists of autologous CD4/CD8 enriched T cells transduced to express an anti-CD20-CD19 CAR. The anti-CD20-CD19 CAR transduced T cells will be administered to patients for the treatment of relapsed/refractory diffuse large B cell lymphoma (R-R DLBCL).

CAR T cells have been generated against many cell surface molecules. To date, the most promising clinical outcomes have been reported in patients treated with autologous CAR transduced T cells targeting CD19.[1]

The DALY 2-EU Study is a randomized, open-label clinical study comparing MB-CART2019.1 to 1 of 2 standard of care therapies, lasting up to 3 years. The study is comprised of 2 arms, and participants will have a 50% random chance of receiving either:

- MB-CART2019.1, or
- 1 of 2 standard of care therapies (dependent on country-specific clinical trial protocols):
  - Rituximab with gemcitabine and oxaliplatin (R-GemOx), or
  - Bendamustine with rituximab and polatuzumab vedotin (BR plus P).

Participants from the standard of care arm are allowed to be treated with MB-CART2019.1 upon request by the investigator if at least one of the following criteria is confirmed by the IRC:

- Relapse or progression occurring at any time within 1 year after randomization.
- Failure to achieve partial or complete response at or beyond Week 8 after randomization (after 4 cycles of R-GemOx or 3 cycles of BR plus polatuzumab vedotin) and the start of a new anti-lymphoma therapy is warranted.

The primary objective is to determine the superiority of the treatment with MB-CART2019.1 compared to standard of care therapy as it relates to progression-free survival in a second-line setting.

Study participation at-a-glance

After an initial screening period (up to 4 weeks), all eligible study participants will be randomized to 1 of 2 study treatment groups:

MB-CART2019.1 group

- Leukapheresis: Participants will visit their study location for leukapheresis, a procedure that collects leukocytes from patients' blood. The leukocytes will be sent to a manufacturer for the T cells to be enriched and used to produce their individual study treatment.
- Conditioning with lymphodepletion: Participants will receive lymphodepleting chemotherapy on 3 consecutive days, which is expected to improve the effects of the CAR T cell treatment.
- Treatment: Participants will go to their study location to receive their specific CAR T cell product. They will remain at the hospital for at least 2 weeks so the study team can continuously monitor their health.
- Primary follow-up: Participants will have 17 follow-up visits after they have completed the treatment. Some visits will be completed during their hospital stay.
- Secondary follow-up: Participants will attend 2 visits for additional tests and procedures.

Standard of care group

- Leukapheresis: Participants who wish to be considered for crossover treatment will undergo leukapheresis. Their leukocytes will be cryopreserved at the manufacturing site.
- Treatment: Participants will receive either R-GemOx or BR plus P. They will receive a maximum of 6–8 cycles in either 14- or 21-day cycles, depending on their treatment.
- Crossover (if applicable): Participants selected for crossover treatment will sign a new consent form and transition to the MB-CART2019.1 treatment schedule, starting at lymphodepletion.
- Primary follow-up: Participants will attend 4 visits after they have completed their last treatment cycle.
- Secondary follow-up: Participants will attend 2 visits for additional tests and procedures.

All study participants in the CAR T group who complete the secondary follow-up period will be asked to continue their participation in a 13-year long-term follow-up study.

1 Jae H. Park, Mark B. Geyer, Renier J. Brentjens; CD19-targeted CAR T-cell therapeutics for hematologic malignancies: interpreting clinical outcomes to date. Blood 2016; 127 (26): 3312–3320. doi: https://doi.org/10.1182/blood-2016-02-629063

For more information about this clinical study or to refer a patient, please contact the Principal Investigator who provided you with this fact sheet.

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Patient eligibility requirements for the DALY 2-EU Study

Please consider referring your patients who meet the following key inclusion/exclusion criteria. For a complete list of study eligibility criteria, please contact the Principal Investigator who provided you with this fact sheet.

Key inclusion criteria

1. Histologically proven DLBCL and associated subtypes according to the World Health Organization (WHO) 2016 classification.
2. Relapsed or refractory disease after first-line chemoimmunotherapy.
3. Participants must have received adequate first-line therapy containing at least the combination of an anthracycline-based regimen and rituximab (anti-CD20 monoclonal antibody). Local therapies (e.g., radiotherapies) will not be considered as a line of therapy if performed during the same line of treatment.
4. Participants deemed ineligible to receive HDC followed by ASCT based on the treating physician's assessment and who meet the following criteria:

Either

- Age ≥18 years and
  - Prior ASCT (as first-line consolidation), or
  - Haematopoietic cell transplantation-specific comorbidity index (HCT-CI) >3.

Or

- Age ≥65 years and one or more of the criteria below:
  - Impaired cardiac function (left ventricular ejection fraction [LVEF] <50%), or
  - Impaired renal function (estimated glomerular filtration rate [eGFR] <60 mL/min) calculated according to the modified Modification of Diet in Renal Disease (MDRD) formula, or
  - Impaired pulmonary function (diffusing capacity for carbon monoxide or forced expiratory volume in 1 second less than 80%) or dyspnoea on slight activity, or
  - Eastern Cooperative Oncology Group (ECOG) performance status >1.

Or

- Age ≥70 years.

Key exclusion criteria

1. Contraindications for rituximab with gemcitabine and oxaliplatin (R-GemOx), bendamustine with rituximab plus polatuzumab vedotin (BR plus P), cyclophosphamide and fludarabine as judged by the treating physician.
2. Prior chimeric antigen receptor therapy or other genetically modified T cell therapy.
3. ECOG performance status >2.
4. Absolute neutrophil count <1,000/µL (unless secondary to bone marrow involvement by DLBCL as demonstrated by bone marrow biopsy).
5. Platelet count <50,000/µL (unless secondary to bone marrow involvement by DLBCL as demonstrated by bone marrow biopsy).
6. Absolute lymphocyte count <100/µL.
7. Participants who have central nervous system (CNS) lymphoma involvement in present or past medical history.

All eligible study participants will receive the following at no cost:

- All study-related medicine:
  - MB-CART2019.1, or
  - Rituximab with gemcitabine and oxaliplatin (R-GemOx), or
  - Bendamustine with rituximab and polatuzumab vedotin (BR plus P).
- All study-related assessments and procedures.
- Close care and monitoring from our team of medical professionals.
- Reimbursement for study-related expenses may also be available. Participants will need to speak to a member of our study team for more details.

Consider referring your patients to the DALY 2-EU Study

Thank you for considering this clinical study for your patients with relapsed/refractory diffuse large B cell lymphoma (R-R DLBCL). For more information or to refer a patient, please contact:

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