TPS7085 Poster Session

ALPHA3: A pivotal phase 2 study of first-line (1L) consolidation with cema-cabtagene ansegedleucel (cema-cel) in patients (pts) with large B-cell lymphoma (LBCL) and minimal residual disease (MRD) after response to standard therapy.

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Background: R-CHOP as 1L therapy for LBCL has a cure rate of ~60%. However, ~10% of pts are refractory (Coiffier, *NEJM* 2002) and ~30% of responders relapse within 2 years (Maurer, *J Clin Oncol* 2014). Autologous CAR T cell therapies have revolutionized treatment of relapsed/refractory (R/R) LBCL and are considered standard 2L treatment due to improved overall survival (OS; Westin, *NEJM* 2023) but may not be an option due to aggressive disease, pt comorbidities, access barriers, and/or manufacturing issues/delays. Identifying responders to 1L therapy at high risk of relapse and rapidly administering an off-the-shelf CAR T cell therapy for remission consolidation may improve outcomes. Presence of circulating tumor DNA–based MRD, measured by PhasED-Seq, at the end of 1L therapy is highly prognostic for relapse (Roschewski, *Hematol Oncol* 2023). Cema-cel is an immediately available, off-the-shelf, HLA-unmatched allogeneic CD19 CAR T cell product made using Cellectis technologies. A phase 1 study of cema-cel in pts with R/R LBCL showed safety and efficacy comparable to that of autologous CAR T cell therapies (Locke, *J Clin Oncol* 2023). We describe the design of the pivotal ALPHA3 phase 2 study of cema-cel, the first randomized, open-label study to assess a CAR T cell therapy as a consolidation strategy in pts with detectable MRD measured by PhasED-Seq after standard 1L immunochemotherapy. **Methods:** ALPHA3 (NCT06500273) will evaluate efficacy and safety of cema-cel with 1 of 2 lymphodepletion (LD) regimens compared to standard-of-care (SOC) observation in pts with LBCL who are in response at the end of 1L therapy but test MRD+. Key eligibility criteria include histologically confirmed LBCL, completion of a full course of standard 1L therapy, ECOG PS 0/1, and adequate organ function. The study will consist of a 2-part seamless design. In Part A (currently enrolling), pts will be randomized to SOC observation or to 1 of 2 treatment arms (cema-cel [120×10^6 CAR T cells] following 3-day LD with fludarabine [30 mg/m^2/day] and cyclophosphamide [300 mg/m^2/day] with/without the anti-CD52 monoclonal antibody, ALLO-647 [30 mg/day]). Part A will conclude with an interim analysis to select the optimal LD regimen. Part B will assess efficacy of the selected regimen vs observation. The primary endpoint is event-free survival per independent review committee (IRC), with hierarchical testing of key secondary endpoints of progression-free survival per IRC and OS. Other secondary endpoints include MRD clearance, safety of cema-cel and ALLO-647, and disease outcomes after subsequent therapy. The study will enroll ~240 pts across ~50 sites at academic- and community-based centers. Site activation is ongoing; sites outside the US are being considered. The study was initiated in June 2024 with accrual into 2026. Clinical trial information: NCT06500273. Research Sponsor: Allogene Therapeutics, Inc.