91 Lisocabtagene Maraleucel (liso-cel), a CD19-Directed Chimeric Antigen Receptor (CAR) T Cell Therapy, Versus Standard of Care (SOC) with Salvage Chemotherapy (CT) Followed By Autologous Stem Cell Transplantation (ASCT) As Second-Line (2L) Treatment in Patients (Pts) with Relapsed or Refractory (R/R) Large B-Cell Lymphoma (LBCL): Results from the Randomized Phase 3 Transform StudyClinically Relevant Abstract

Program: Oral and Poster Abstracts

Type: Oral

Session: 704. Cellular Immunotherapies: Cellular Therapies for Lymphomas

Hematology Disease Topics & Pathways:

Adults, Biological, Clinical Trials, Cytokine Release Syndrome, Lymphomas, Neurotoxicity, Clinical Research, B Cell Lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, Therapies, Lymphoid Malignancies, Adverse Events, Study Population

Author(s): Manali Kamdar, Scott R. Solomon, Jon E. Arnason, Patrick B. Johnston, Bertram Glass, Veronika Bachanova, Sami Ibrahimi, Stephan Mielke, Pim G.N.J. Mutsaers, Francisco J. Hernandez-Ilizaliturri, Koji Izutsu, Franck Morschhauser, Matthew A. Lunning, David G. Maloney, Alessandro Crotta, Sandrine Montheard, Alessandro Previtali, Lara Stepan, Ken Ogasawara, Timothy Mack, Jeremy S. Abramson

Background:

Pts with LBCL primary refractory to or relapsed ≤ 12 mo after first-line (1L) therapy may have poor outcomes with SOC, including salvage CT and ASCT, which underscores a critical unmet need. Liso-cel is an autologous CD19-directed, defined composition, 4-1BB CAR T cell product administered at equal target doses of CD8+ and CD4+ CAR+ T cells. In the TRANSCEND NHL 001 study (NCT02631044) in pts with R/R LBCL (≥ 2 prior lines of therapy), liso-cel treatment resulted in an ORR of 73% (CR rate, 53%), 2% grade ≥ 3 cytokine release syndrome (CRS), and 10% grade ≥ 3 neurological events (NE) (Abramson et al. Lancet 2020). Here we present a prespecified interim analysis of TRANSFORM (NCT03575351; SOC vs liso-cel as 2L therapy in pts with R/R LBCL).

Methods:

TRANSFORM is a pivotal, global, randomized, multicenter, phase 3 study comparing efficacy and safety of SOC (Arm A; R-DHAP, R-ICE, or R-GDP per investigator choice followed by BEAM + ASCT) vs liso-cel (Arm B). Pts were adults (aged ≤ 75 years), eligible for ASCT, and with LBCL primary refractory to or relapsed ≤ 12 mo after 1L therapy. Key inclusion criteria were ECOG

PS ≤ 1 and adequate organ function (LVEF ≥ 40%; serum CrCl > 45 mL/min); pts with secondary CNS lymphoma were allowed. Key exclusion criteria were prior gene or anti-CD19–targeted therapy, and active infection. Pts in Arm A were to receive 3 cycles of CT. Responding pts (CR or PR) were to proceed to BEAM + ASCT. Pts in Arm B were to undergo lymphodepletion with fludarabine/cyclophosphamide followed by liso-cel at a target dose of 100 × 106 CAR+ T cells. Bridging therapy with an Arm A CT regimen was allowed. Crossover to receive liso-cel was allowed in Arm A for pts not achieving CR or PR after 3 cycles of CT or not in CR after ASCT, or demonstrating PD at any time.

Primary endpoint is event-free survival (EFS) based on independent review committee per Lugano 2014 criteria, defined as time from randomization to death from any cause, PD, failure to achieve CR or PR by 9 weeks after randomization, or start of new antineoplastic therapy, whichever occurred first. Key secondary endpoints included in the testing strategy are CR rate, PFS, and OS. P value significance threshold for endpoints to reject the null hypothesis was ≤ 0.012.

Results:

A total of 184 pts were randomized, with 92 pts in each arm. Baseline characteristics were well balanced between both arms (Table). Of 91 treated pts in Arm A (1 pt withdrew consent), 43 received BEAM + ASCT, of which 28 achieved CR with CT. Fifty pts crossed over to receive liso-cel. In Arm B, 90 pts received liso-cel infusion; 58 pts (63%) received bridging therapy. Two Arm B pts were not infused (1 each due to manufacturing failure and rapid progression). Median EFS and PFS were significantly longer, and CR rate was significantly improved for Arm B vs Arm A. For Arms A and B, respectively, median EFS was 2.3 vs 10.1 mo (HR, 0.349; P < 0.0001), median PFS was 5.7 vs 14.8 mo (HR, 0.406; P = 0.0001), and CR rate was 39% vs 66% (P < 0.0001). OS data were immature at the time of this analysis with a median follow-up of 6.2 mo (range, 0.9–20.0), but a numerical trend favored Arm B (HR, 0.509; 95% CI, 0.258–1.004; P = 0.0257). Cellular kinetics in Arm B showed a median tmax of 10 d (range, 6–22). No new liso-cel safety signals were detected in the 2L setting. In Arm B, any-grade CRS was reported in 49% of pts, with grade 1 in 37% and grade 2 in 11%. Only 1 pt had grade 3 CRS (onset at Day 9, which resolved in 2 days). Any-grade NEs were reported in 12% of pts and were also primarily low grade (grade 3, 4%). No grade 4 or 5 CRS or NEs were reported. In Arm B, 24% of pts received tocilizumab, 17% received corticosteroids, and none received vasopressors. The most common TEAEs in both arms were cytopenias. Prolonged cytopenias in Arm B (ie, grade ≥ 3 at 35 d after infusion) were reported in 43% of pts; the majority recovered within 2 mo after infusion.

Conclusion:

In the TRANSFORM study, liso-cel demonstrated statistically significant and clinically meaningful improvement in the primary endpoint, EFS, as well as in key secondary efficacy endpoints (CR rate and PFS) compared with SOC as 2L therapy in pts with LBCL primary refractory to or relapsed ≤ 12 mo after 1L therapy. Safety results in the 2L setting were

consistent with the liso-cel safety profile in 3L or later LBCL, and no new safety concerns were identified. Liso-cel improved outcomes vs SOC and exhibited a favorable safety profile, providing support for liso-cel as a potential new SOC for 2L treatment in pts with R/R LBCL.