Abstract: P1134

Title: BISPECIFIC ANTI-CD20/19 CAR-T – ZAMTOCABATAGENE AUTOLEUCEL FOR RELAPSED/REFRACTORY DLBCL – INTERIM ANALYSIS RESULTS OF DALY-II-USA STUDY

Abstract Type: Poster Presentation

Session Title: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

DALY II USA is the first multicenter trial of fresh, bispecific targeted CD20/CD19, chimeric antigen receptor (CAR) T-cell therapy for patients (pts) with R/R diffuse large B-cell lymphoma (DLBCL). While CD19 CAR T-cell therapy is an established treatment for pts with R/R DLBCL, relapse remains a clinical challenge. One proposed mechanism of resistance is either loss of epitope, recognition or downregulation of the CD19 receptor. To improve outcomes, dual targeting of B-cell receptor has been proposed. Reported here is the preplanned interim futility analysis after treatment of 22 evaluable pts.

Aims:

To assess safety and efficacy of dual CAR-T therapy with zamtocabtagene autoleucel (zamto-cel) administered fresh in R/R DLBCL

Methods:

Eligible pts were >18 y, ECOG PS 0-1, with R/R DLBCL after ≥2 prior lines of systemic therapy. No bridging chemotherapy was allowed. Apheresis material was shipped fresh without cryopreservation to a central manufacturing site. A fixed 12-day process of CAR-T production was performed using the CliniMACS Prodigy® (Miltenyi Biotec). A single infusion of $2.5x10^6$ cells/kg fresh zamto-cel was administered after lymphodepletion which was initiated during manufacturing to facilitate a fresh infusion. Evaluation of response rate is the primary objective of this study.

Results:

As of 1 Sep 2022, 28 pts have enrolled (All treated) with 22 evaluable per protocol. Most (69%) of treated patients presented advanced disease with IPI score of at least 3 and abnormal baseline LDH and 28% were previously treated with CD19 and or CD79 targeting agents. Six pts were not included in the primary efficacy analysis. One received a frozen product and 5 received a non-conforming fresh product. Per Independent Radiology Committee (IRC) 18 (82%) of 22 evaluable pts had either complete (CR - 46%) or partial response (PR – 36%) exceeding preplanned futility threshold. Response rate in evaluable set was similar to that in all-treated population (Tbl. 1). Post progression biopsy were available in 5 pts. There was no isolated CD19 loss, but 1pt had dual target loss CD19+CD20 in relation to the pre-treatment status. PFS at 6 months for evaluable pts were 64% and 61% for all treated. The treatment was well tolerated. Among all 28 treated pts., there were no grade 3-4 CRS events and only two transient and reversible Grade 3 ICANS (9%). There were no treatment related mortality.

Summary/Conclusion:

Prespecified efficacy threshold of zamto-cel was exceeded in the interim analysis Treatment demonstrated a favorable safety profile, with promising ORR and PFS in advanced DLBCL population often pre-treated with agents not available in the previous similar studies. We also demonstrate the feasibility of a rapid manufacturing process with 100% fresh infusion in eligible pts.

Table 1: Objective Response Rate per IRC and per Site

	Evaluable Set (n=22)	**All Treated (n=28)**		
	IRC	**Per Site**	**IRC**	**Per Site**
ORR	**18 (82%)**	**17 (77%)**	**22 (79%)**	**20 (71%)**
CR	10 (46%)	11 (50%)	14 (50%)	13 (46%)
PR	8 (36%)	6 (27%)	8 (29%)	7 (25%)
SD	1 (4%)	2 (9%)	1 (4%)	2 (7%)
PD	3 (14%)	3 (14%)	5 (17%)	5 (18%)

IRC – Independent Radiology Committee

Keywords: CAR-T, CD20, CD19, Diffuse large B cell lymphoma