Review on CTL019 and KTEC19, CART-cell Agents used for the Treatment of Large B-cell Lymphoma

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Abstract

Background: Diffuse Large B-cell Lymphoma (DLBCL) consisted of 25-30% of Non-Hodgkin Lymphomas (NHLs) and an aggressive disease. CTL019 and KTEC-19 are CD19-direct genetically-modified-autologous T-cell immunotherapies used in treating adult patients with relapsed or refractory(r/r) large B-cell-Lymphoma after ≥2 systemic therapy.

Hypothesis: To evaluate CTL019 and KTE19, risk/benefit in large B-cell Lymphoma

Methods: CTL019C2201-study, a single-arm, open-label phase-II multicenter for adult patients with r/r DLBCL after ≥2 prior lines of chemotherapy or treated with autologous-hematopoietic-stem-cell transplantation. Of the 160-patient enrolled, 93 were treated with an intravenous infusion of 1-5 x $10^{(8)}$ viable-CTL019 after lymphodepletion. The primary-endpoint was the Objective Response Rate (ORR) at the time of Best Overall Response (BOR). The durability of response, a critical secondary-endpoint was assessed from time of initial response-to-time of relapse or last observation. Zuma-1 study was used to review the efficacy and safety of KTE-C19 approval. Of 135-subject screened in phase I/II, 119 were enrolled and underwent-leukapheresis, 110 received conditioning-chemotherapy and 108-patient with r/r aggressive B-cell NHL received 2x$10^{(6)}$ cells/kg viable-KTE-C19. The prespecify interim-analysis of ORR in 92-patient for futility and for efficacy were conducted based on a null-ORR of ≤20% and an alternative-ORR of ≥40%. The secondary-endpoint included Duration-of-Response (DoR), Progression-Free-Survival (PFS) and safety.

Results: Of the 160-patient enrolled in CTL019C2201, 49 withdrew from the study. The primary efficacy-endpoint BOR (n=68); ORR was 50%, (95%CI:37.6,62.4%), Complete-Response-Rate (CRR) was 32.4% (95%CI:21.5,44.8). The secondary-endpoint, DoR (n=34); median DoR for the overall group and the complete-response were not reached, after median follow-up of 9.4-month and 8.4-month respectively compared to patients with partial-response who had only 3.3-month median DoR. Of 106-patient treated with CTL019, 78-patient (74%) had Cytokines-Release-Syndrome (CRS). Intention-To-Treat (ITT) analysis of all KTE-C19 enrolled patients; ORR was 66% and CRR was 47% (95%CI:37,57). Of 108-patient treated with KTE-C19, 101-patient (94%) had CRS. Deaths and CRS odd-ratio are 1.68 and 0.17 respectively.

Conclusion: KTE-C19 and CTL019 have shown clinical-meaningful in large B-cell Lymphoma and need 15-year follow-up monitoring for Replication-Competent-Lentivirus (RCL) and clonal-mutagenesis.