TRANSCEND CLL 004: Minimal residual disease (MRD) negative responses after lisocabtagene maraleucel (Liso-Cel; JCAR017), a CD19-directed CAR T cell product, in patients (pts) with relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL).

Presented Tuesday, June 4, 2019

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Background:
Eradication of MRD in CLL patients may be necessary for deep and durable responses. We assessed safety, pharmacokinetics, and efficacy of liso-cel, an investigational, anti-CD19 CAR T cell product administered as a defined composition of CD4+/CD8+ CAR T cells, in the ongoing phase 1/2 TRANSCEND CLL 004 study.

Methods:
Eligible pts had CLL/SLL, received ≥2 prior lines of therapy (including Bruton's tyrosine kinase inhibitors [BTKi] unless medically contraindicated), and had ECOG PS ≤1. Post lymphodepleting chemotherapy, pts received liso-cel infusion at either dose level (DL)1 = 50×10^6 or DL2 = 100×10^6 total CAR+ T cells. Patients were monitored for dose-limiting toxicities (DLTs). Response was assessed by iwCLL 2008 criteria. MRD was assessed by flow cytometry in blood (10^{-4}) and by NGS in bone marrow (BM; 10^{-6}).

Results:
At data cutoff, 16 pts received liso-cel: DL1, n = 6; DL2, n = 10. 75% of pts had high-risk features (*TP53* mutation, complex karyotype, or del17p); 100% had prior ibrutinib and 50% had prior venetoclax.

Median (range) number of prior lines of therapy was 4.5 (2–11). There was 1 DLT of grade (G) 4 hypertension (DL2). The most common G3/4 treatment-emergent adverse events were cytopenias (thrombocytopenia, 75%; anemia, 69%; neutropenia, 63%; leukopenia, 56%). 1 pt had G3 cytokine release syndrome (CRS); 3 pts had G3 neurological events (NE). Best overall response rate (ORR) in 15 evaluable pts was 87% (13/15). 7 pts (47%) achieved complete remission with/without complete blood count recovery (CR/CRi). ORR at 6 mo was 83% (5/6). 10/15 pts (67%) achieved undetectable MRD (uMRD) in blood by day 30 and in 7/8 pts (88%) in BM. MRD-negative CRs were seen in patients who had failed both BTKi and venetoclax. Median time to peak blood CAR+ T cell level was 16 days (4–30).

Conclusions:

In this study of heavily pretreated pts with standard- and high-risk CLL/SLL and previous ibrutinib treatment, liso-cel-related toxicities (ie, CRS and NEs), were manageable. Pts rapidly achieved CR/CRi and uMRD. Additional follow-up will be presented. Clinical trial information: NCT03331198