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ORAL ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

TRANSCEND FL: Phase 2 Study Primary Analysis of Lisocabtagene Maraleucel as Second-Line Therapy in Patients with High-Risk Relapsed or Refractory Follicular Lymphoma

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Background: Results with CD19-directed CAR T cell therapy in patients (pts) with second-line (2L) R/R follicular lymphoma (FL) and high-risk features, such as progression of disease within 24 months (POD24) from diagnosis or double refractory to

anti-CD20 antibody plus alkylator, have not been previously reported. TRANSCEND FL (NCT04245839), a global, phase 2, open-label, single-arm, multicohort, pivotal study, assessed efficacy and safety of the anti-CD19 CAR T cell therapy lisocabtagene maraleucel (liso-cel) in pts with second line or later (2L+) R/R indolent NHL. Some data from the primary analysis were previously reported, including safety in 2L+ R/R FL, and focused on efficacy in third line or later R/R FL (Morschhauser F, et al. *Hematol Oncol* 2023;41[S2]:877–880). Here, we report primary analysis results in the cohort of pts with 2L high-risk R/R FL.
Methods: Eligible pts in the 2L R/R FL cohort had biopsy-confirmed FL before enrollment and must have had POD24 with treatment $\leq$ 6 months from original FL diagnosis and/or must have had high tumor burden as defined by modified Groupe d'Etude des Lymphomes Folliculaires (mGELF) criteria. All pts received 1 prior combination systemic therapy with an anti-CD20 antibody and alkylator. Eligible pts received liso-cel (100×10^6 CAR$^+$ T cells) after lymphodepleting chemotherapy (LDC). Bridging therapy was allowed with reconfirmation of PET-positive disease before LDC. The primary endpoint was ORR per independent review committee (IRC) by PET/CT using Lugano 2014 criteria. Secondary endpoints included CR rate, duration of response (DOR), PFS, OS, safety, and cellular kinetics. Pharmacodynamic endpoints were exploratory.
Results: At data cutoff (January 27, 2023), 23 of 25 leukapheresed pts received liso-cel and were evaluable for safety and efficacy per IRC; 1 received nonconforming product and 1 reached CR after bridging therapy and no longer met eligibility criteria. Median (range) age was 53 y (34-69), 74% had stage III/IV disease, and 35% were high-risk per FL International Prognostic Index (FLIPI). Sixty-five percent of pts had POD24 from initiation of first-line combination chemoimmunotherapy (52% had POD24 from diagnosis), 70% met mGELF criteria (mGELF only, 48%; mGELF and POD24 from diagnosis, 22%), and 48% were double refractory to anti-CD20 antibody plus alkylator. Median (range) on-study follow-up was 18.1 months (1.0-26.8). In efficacy-evaluable pts, the ORR and CR rate were both 95.7% (95% CI, 78.1-99.9; 1-sided $P < 0.0001$; Table).
With a median follow-up of 16.8 months and 17.8 months, respectively, median DOR and PFS were not reached; 12-month DOR and PFS were 89.8% and 91.3%, respectively. The most common grade (gr) $\geq$ 3 treatment-emergent AEs (TEAE) were cytopenias; neutropenia was most frequent (52%). Cytokine release syndrome (CRS) occurred in 12 (52%) pts (no gr $\geq$ 3). Median (range) time to onset and resolution of CRS was 6 days (2-9) and 3 days (2-7), respectively. Neurological events (NE) occurred in 4 (17%) pts, with 1 (4%) gr 3 and no gr 4-5 (Table). Median (range) time to onset and resolution of NEs was 8.5 days (6-11) and 2.5 days (1-4), respectively. Three (13%) pts received tocilizumab/steroids for CRS/NEs. Prolonged cytopenia (gr $\geq$ 3 laboratory values at Day 29) occurred in 3 (13%) pts; all recovered to gr $\leq$ 2 by Day 90. No gr $\geq$ 3 infections were reported. One TEAE death occurred in the context of IRC-assessed disease progression due to gr 5 macrophage activation syndrome (MAS). Liso-cel showed rapid expansion with median (range) time to maximum transgene levels of 10 days (7-11). Persistence of liso-cel transgene was detected up to Month 12 in 5 of 18 (28%) pts. B-cell aplasia (< 3% CD19$^+$ B cells in peripheral blood lymphocytes) after liso-cel infusion was rapid and maintained in $\geq$ 95% of pts through Month 2.
Conclusions: This is the first report of outcomes in 2L high-risk R/R FL with CD19-directed CAR T cell therapy. In this population, liso-cel achieved very high CR rates (22 of 23 pts); deep and durable remissions, with follow-up ongoing; and a favorable safety profile with low rates of severe (gr $\geq$ 3) CRS, NEs, and prolonged cytopenia, and no severe infections. These data support liso-cel as a potential new treatment option in pts with 2L R/R FL at high-risk for treatment failure.

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Table. Summary of efficacy and safety

Efficacy	Patients with 2L FL (n = 23)
ORR, n (%)	22 (95.7)
95% CI; 1-sided *P* value	78.1–99.9; < 0.0001
CR rate, n (%)	22 (95.7)
95% CI; 1-sided *P* value	78.1–99.9; < 0.0001
PR, n (%)	0
Stable disease, n (%)	0
PD, n (%)	1 (4.3)
DOR, median (95% CI)	NR (19.3–NR)
Probability of continued response at 12 months, % (SE)	89.8 (6.866)
PFS, median (95% CI)	NR (20.2–NR)
PFS rate at 12 months, % (SE)	91.3 (5.875)
Safety	**Patients with 2L FL (n = 23)**
AEs of special interest, n (%)	
Any-grade CRS[a]	12 (52.2)
Grade 1	7 (30.4)
Grade 2	5 (21.7)
Grade 3	0
Grade 4 or 5	0
Any-grade NEs[b]	4 (17.4)
Grade 1	3 (13.0)
Grade 2	0
Grade 3	1 (4.3)
Grade 4 or 5	0
Prolonged cytopenia[c]	3 (13.0)
Grade ≥ 3 infection	0
MAS	1 (4.3)
Hypogammaglobulinemia	1 (4.3)

[a]CRS was graded based on Lee 2014 criteria; [b]NEs were defined as investigator-identified neurological AEs related to liso-cel and were graded per the NCI CTCAE, version 5.0; [c]Defined as grade ≥ 3 laboratory abnormalities of neutropenia, anemia, or thrombocytopenia on Day 29. NR, not reached; SE, standard error.

Figure 1

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