Abstract: P1126

Title: SUBGROUP ANALYSES IN PATIENTS WITH R/R MCL TREATED WITH LISOCABTAGENE MARALEUCEL BY PRIOR LINES OF THERAPY AND RESPONSE TO BRUTON TYROSINE KINASE INHIBITOR FROM THE TRANSCEND NHL 001 MCL COHORT

Abstract Type: Poster Presentation

Topic: Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

Background:

In the TRANSCEND NHL 001 (TRANSCEND; NCT02631044) MCL primary analysis, the CD19-directed, CAR T cell product lisocabtagene maraleucel (liso-cel) demonstrated a high, durable CR rate with manageable safety in patients with heavily pretreated R/R MCL. In a prior subgroup analysis of patients with high-risk disease features (Palomba et al, *Blood* 2023), liso-cel showed clinically meaningful efficacy, indicating that some patient subgroups with few treatment options may have improved outcomes with this new therapy.

Aims:

To report outcomes by number of prior lines of therapy (LOT) and by response to prior Bruton tyrosine kinase inhibitor (BTKi).

Methods:

Patients had PET-positive R/R MCL after ≥ 2 prior systemic LOTs, including BTKi, alkylating, and CD20-targeted agents, and provided informed consent. Patients received liso-cel (100 × 106 CAR+ T cells) after lymphodepleting chemotherapy. Bridging therapy for anticancer disease control during liso-cel manufacturing was allowed. Primary endpoints were treatment-emergent AEs (TEAE) and ORR by independent review committee (IRC) per Lugano 2014 criteria; secondary endpoints included CR rate, duration of response (DOR), PFS, and OS.

Results:

Eighty-eight patients received liso-cel. Median follow-up was 16.1 months (range, 0.4–60.5). For all patients, CR rate was 72%; median DOR, PFS, and OS were 15.7, 15.3, and 18.2 months, respectively (**Table**). ORR, CR rate, and median DOR, PFS, and OS were similar to all patients for most subgroups, but numerically lower in patients with ≥ 5 prior LOTs and patients refractory to prior BTKi. Grade ≥ 3 TEAEs ranged from 67% to 96% across subgroups, similar to all patients (86%); the most common grade ≥ 3 TEAE was neutropenia (33%–58%). Most cytokine release syndrome (CRS) and neurological events (NE) were grade 1–2 (**Table**) with no grade 5 CRS/NE. Grade ≥ 3 infection (11%–19%) and prolonged cytopenia (32%–50%) in subgroups were similar to all patients (15% and 40%, respectively). Cellular kinetics will be presented.

Summary/Conclusion:

In the TRANSCEND MCL primary analysis cohort, all subgroups benefited from liso-cel and responses were generally comparable to the overall population, with a numerically shorter duration in patients with ≥ 5 prior LOTs and disease refractory to prior BTKi, supporting study of liso-cel in earlier LOTs.

Table

	Overall population	Prior LOT ≥ 2	Prior LOT 3–4	Prior LOT ≥ 5	Refractory to BTKi	Not refractory to BTKi
Efficacy,[a] n	**83**	**81**	**29**	**26**	**45**	**35**
ORR, n (%)	69 (83)	67 (83)	25 (86)	21 (81)	34 (76)	32 (91)
CR rate, n (%)	60 (72)	58 (72)	21 (72)	17 (65)	29 (64)	28 (80)
DOR, median (95% CI)	15.7 (6.2–24.0)	14.5 (5.7–NR)	17.5 (3.3–NR)	6.7 (2.4–15.8)	5.3 (2.3–15.8)	24.0 (7.6–NR)
PFS, median (95% CI)	15.3 (6.6–24.9)	12.3 (6.5–NR)	16.6 (2.6–NR)	7.4 (3.3–12.3)	6.1 (3.1–16.5)	24.0 (8.6–NR)
OS, median (95% CI)	18.2 (12.9–36.3)	17.1 (11.1–36.3)	18.4 (6.7–NR)	13.5 (9.5–17.1)	11.1 (6.1–17.1)	36.3 (15.3–NR)
Safety,[b] n	**88**	**85**	**31**	**26**	**47**	**36**
CRS: grade 1–2 / grade 3–4, n (%)	53 (60) / 1 (1)	52 (61) / 1 (1)	20 (65) / 1 (3)	18 (69) / 0	30 (64) / 0	20 (56) / 1 (3)
NE: grade 1–2 / grade 3–4, n (%)	19 (22) / 8 (9)	19 (22) / 7 (8)	7 (23) / 3 (10)	5 (19) / 2 (8)	12 (26) / 5 (11)	6 (17) / 2 (6)

The original protocol allowed patients with ≥ 1 LOT and was later amended to require ≥ 2 LOTs; 3 patients had 1 prior LOT; 2 patients were efficacy evaluable, and both achieved CR with DORs of 16.8 and 23.3+ months, respectively.
[a]All liso-cel–treated patients with confirmed PET-positive disease per IRC before infusion;
[b]All liso-cel–treated patients.
NR, not reached.

Keywords: Mantle cell lymphoma, Non-Hodgkin's lymphoma, CAR-T, relapsed/refractory