Abstract: S158

Title: CHARACTERISTICS ASSOCIATED WITH RESPONSE TO LISOCABTAGENE MARALEUCEL (LISO-CEL) IN PATIENTS (PTS) WITH R/R CLL/SLL: EXPLORATORY ANALYSES FROM TRANSCEND CLL 004

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Background:

In the phase 1/2 TRANSCEND CLL 004 (NCT03331198) study, at the primary analysis data cut (09/29/2022), liso-cel treatment at a target dose of 100 × 106 CD19-directed CAR+ T cells resulted in a complete response/remission (CR)/CR with incomplete marrow recovery (CRi) rate (CR rate) of 18%, an overall response rate (ORR) of 47% (CR/CRi and partial response/remission [PR]/nodular PR [nPR]), and a manageable safety profile in the full efficacy-evaluable population of pts with R/R CLL/SLL (n = 87; Siddiqi et al, *Lancet* 2023). For the subgroup of pts whose disease previously progressed on a Bruton tyrosine kinase inhibitor and failed venetoclax (primary efficacy analysis set [PEAS]), the CR rate was 18% (primary endpoint; $P = 0.0006$) and ORR was 43%. In a subsequent data cut (02/28/2023), with a longer median follow-up of 23.5 months, the CR rate and ORR improved to 19% and 48% in the full efficacy-evaluable population and 20% and 44% in the PEAS, respectively (Siddiqi et al, *Blood* 2023).

Aims:

Assess pretreatment characteristics associated with achieving CR or overall response (OR) in pts with R/R CLL/SLL from TRANSCEND CLL 004 at the primary analysis data cut (09/29/2022).

Methods:

Exploratory analyses were based on the primary analysis data cut available at the time of this analysis; the median follow-up was 21.1 months in pts who received monotherapy with conforming product at a target dose level of 100 × 106 CAR+ T cells. Informed consent was obtained. Response was based on independent review committee evaluation per 2018 International Workshop on CLL criteria. Post hoc univariable analyses were performed to evaluate correlations between selected key clinically relevant demographic features, disease characteristics/high-risk cytogenetics, disease stage/risk scores, and biomarker lab tests with CR and OR endpoints. For CR analyses, pts who achieved a best overall response (BOR) of CR/CRi (CR group) were compared with pts who achieved a BOR of PR/nPR/stable disease (SD)/progressive disease (PD)/nonevaluable (NE) (non-CR group). For OR analyses, pts who achieved a BOR of CR/CRi/PR/nPR (OR group) were compared with nonresponders (SD/PD/NE [NR group]).

Results:

In total, 87 pts (BOR of CR/CRi, n = 16; PR/nPR, n = 25; SD/PD, n = 40; NE, n = 6) were included. Lower beta-2 microglobulin (B2M) at screening was observed in pts achieving CR. Rai stage 0–II at screening and lower sum of the product of perpendicular diameters (SPD) of the lymph nodes before lymphodepleting chemotherapy (LDC) showed similar trends towards achieving CR. Pretreatment characteristics correlated with achieving OR included absence of bulky disease, lower SPD, and BALL risk score 0–1 (all before LDC). There was no apparent correlation between achieving response (CR/OR) and age, sex, mutated *TP53*, deletion of 17p, unmutated immunoglobulin heavy-chain variable region (IGHV), or presence of complex karyotype (all at screening). Descriptive statistics are summarized in the **Table**. Potential relationships of other characteristics and response as well as safety endpoints, including cytokine release syndrome and neurological events, will be explored.

Summary/Conclusion:

Preliminary results of exploratory analyses from TRANSCEND CLL 004 suggest that lower disease burden at

baseline as indicated by lower SPD, lower B2M, and absence of bulky disease were correlated with increased likelihood of achieving a response in pts with R/R CLL/SLL. Liso-cel is effective in treating pts with R/R CLL/SLL regardless of the presence or absence of high-risk disease features such as mutated *TP53,* deletion of 17p, unmutated IGHV, and complex karyotype.

Table. Pretreatment characteristics in relation to achieving CR or OR

Characteristic (continuous variable)	CR group	Non-CR group	OR group	NR group
B2M at screening, mg/L, median (IQR), n = 75	3.1 (2.6–3.8), n = 15	4.2 (2.9–6.3), n = 60	3.7 (2.8–4.5), n = 37	4.4 (2.8–6.2), n = 38
SPD before LDC, cm^2, median (IQR), n = 79	24.8 (17.7–34.0), n = 14	40.9 (17.1–104.0), n = 65	25.0 (13.8–36.2), n = 37	59.3 (25.4–115.1), n = 42
Age at screening, years, median (range), n = 87	64 (60–78), n = 16	66 (49–82), n = 71	64 (50–78), n = 41	66 (49–82), n = 46
Characteristic (categorical variable)	**CR rate, % (Clopper–Pearson 95% CI)**		**ORR, % (Clopper–Pearson 95% CI)**	
Rai staging at screening				
Low/intermediate risk (Rai stage 0–II), n = 37	29.7 (15.9–47.0)		56.8 (39.5–72.9)	
High risk (Rai stage III–IV), n = 44	11.4 (3.8–24.6)		38.6 (24.4–54.5)	
Bulky disease (largest lymph node ≥ 5 cm) before LDC				
Presence, n = 41	14.6 (5.6–29.2)		31.7 (18.1–48.1)	
Absence, n = 38	21.1 (9.6–37.3)		63.2 (46.0–78.2)	
BALL risk score before LDC				
Low risk (0–1), n = 31	29.0 (14.2–48.0)		61.3 (42.2–78.2)	
Intermediate risk (2–3), n = 35	17.1 (6.6–33.6)		48.6 (31.4–66.0)	
High risk (4), n = 11	9.1 (0.2–41.3)		18.2 (2.3–51.8)	
Sex				
Male, n = 60	18.3 (9.5–30.4)		46.7 (33.7–60.0)	
Female, n = 27	18.5 (6.3–38.1)		48.1 (28.7–68.1)	
Mutated *TP53* at screening				
False, n = 50	16.0 (7.2–29.1)		50.0 (35.5–64.5)	
True, n = 38	22.2 (10.1–39.2)		41.7 (25.5–59.2)	
Deletion of 17p at screening				
False, n = 51	13.7 (5.7–26.3)		45.1 (31.1–59.7)	
True, n = 34	26.5 (12.9–44.4)		47.1 (29.8–64.9)	
Unmutated IGHV at screening				
False, n = 19	21.1 (6.1–45.6)		63.2 (38.4–83.7)	
True, n = 41	22.0 (10.6–37.6)		41.5 (26.3–57.9)	
Presence of complex karyotype at screening				
False, n = 34	17.6 (6.8–34.5)		52.9 (35.1–70.2)	
True, n = 52	19.2 (9.6–32.5)		44.2 (30.5–58.7)	

CI, confidence interval; IQR, interquartile range.

Keywords: Cellular therapy, Chronic lymphocytic leukemia, CAR-T