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POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Lisocabtagene Maraleucel (liso-cel) in Patients (Pts) with R/R MCL: Subgroup Analyses in Pts with High-Risk Disease Features from the MCL Cohort of the TRANSCEND NHL 001 Study

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Background: Pts with R/R MCL after ≥ 2 prior lines of therapy, including a Bruton tyrosine kinase inhibitor (BTKi), have poor prognosis. Among pts with R/R MCL, several high-risk disease features are associated with a worse prognosis, including *TP53* mutation, high proliferation index (Ki-67 ≥ 30%), blastoid morphology, and secondary CNS involvement. Liso-cel is an autologous, CD19-directed, 4-1BB CAR T cell product administered at equal target doses of $CD8^+$ and $CD4^+$ CAR^+ T cells. In the primary analysis of the MCL cohort from the phase 1, seamless design TRANSCEND NHL 001 study (NCT02631044), liso-cel treatment resulted in a rapid, high rate of durable CRs with a manageable safety profile in pts with heavily pretreated R/R MCL. Here we report the outcomes in pts with R/R MCL from prespecified subgroup analyses based on high-risk disease features.

Methods: Eligible pts had PET-positive R/R MCL after ≥ 2 lines of prior therapy, including a BTKi, alkylating agent, and CD20-targeted agent. Pts received liso-cel at a target dose of 50×10^6 or 100×10^6 CAR^+ T cells after lymphodepleting chemotherapy. Bridging therapy 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. The liso-cel-treated set included all pts who received liso-cel. The efficacy analysis set included all pts in the liso-cel-treated set who had PET-positive disease per IRC at baseline.

Results: Of 104 leukapheresed pts, 88 received liso-cel. Median on-study follow-up was 16.1 mo (range, 0.4-60.5). Median age was 68.5 y (range, 36-86) and median prior systemic lines of therapy was 3 (range, 1-11). Among liso-cel-treated pts, 66 (75%) had Ki-67 ≥ 30% and 15 (17%) had Ki-67 < 30% (Ki-67 was not reported in 7 [8%] pts); 20 (23%) had a *TP53* mutation present and 34 (39%) did not (*TP53* mutation was indeterminate in 4 [5%] pts and not reported in 30 [34%] pts); and 27 (31%) had blastoid morphology and 48 (55%) did not (blastoid morphology was not reported in 13 [15%] pts). Most pts with these high-risk disease features also had disease that was refractory to last therapy, was refractory to prior BTKi, and had a complex

karyotype. A total of 7 (8%) pts had secondary CNS lymphoma, of which 5 had refractory disease, 5 had Ki-67 ≥ 30%, and 1 each had *TP53* mutation and blastoid morphology.

Response rates, PFS, and OS across subgroups were consistent with the overall population, with high ORR and CR rate that was durable and high PFS and OS (Table 1). Although a limited number of pts had *TP53* mutation assessed, pts with *TP53* mutation had a numerically lower median DOR than the overall population, likely due to a higher proportion of objective responders achieving a PR than CR; however, pts with *TP53* mutation who achieved CR had durable responses with 6 of 11 pts in an ongoing response at data cutoff. Among the 7 pts with secondary CNS lymphoma, response rates were high (ORR, 86% [n = 6]; CR rate, 71% [n = 5]), and 3 of 5 pts who achieved CR were in an ongoing response at data cutoff.

Safety outcomes across subgroups were generally consistent with the overall population (Table 2). Most cytokine release syndrome (CRS) and neurological events (NE) were low grade in all subgroups, similar to the overall population (any-grade CRS, 61% [grade 3-4, 1%]; any-grade NEs, 31% [grade 3-4, 9%]; and no grade 5 CRS or NEs). Incidences of other TEAEs of special interest were also similar among subgroups. Of the 7 pts with secondary CNS lymphoma, 5 had low-grade CRS and 3 had low-grade NEs with no grade ≥ 3 CRS or NEs reported; 1 pt had a grade ≥ 3 infection.

Cellular kinetics and B-cell aplasia by subgroup will be presented.

Conclusions: In these subgroup analyses including pts with R/R MCL and high-risk disease features (Ki-67 proliferation index ≥ 30%, *TP53* mutation, blastoid morphology, and secondary CNS lymphoma), liso-cel demonstrated clinically meaningful efficacy across subgroups with durable responses. Efficacy and safety outcomes were generally consistent with the overall study population. While some subgroups were limited by small numbers, these results suggest a favorable benefit/risk profile for liso-cel in pts with R/R MCL and high-risk disease features, a pt population for whom effective treatment options are rarely available.

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Table 1. Summary of efficacy outcomes by subgroup (efficacy analysis set)

	Overall (n = 83)	Ki-67 proliferation index		*TP53* mutation		Blastoid morphology	
		≥ 30% (n = 62)	< 30% (n = 14)	Yes (n = 19)	No (n = 32)	Yes (n = 27)	No (n = 45)
ORR, % (95% CI)[a]	83 (73.3–90.5)	85 (74.2–93.1)	71 (41.9–91.6)	89 (66.9–98.7)	87.5 (71.0–96.5)	70 (49.8–86.2)	91 (78.8–97.5)
n	69	53	10	17	28	19	41
CR rate, % (95% CI)[a]	72 (61.4–81.6)	76 (63.3–85.8)	57 (28.9–82.3)	58 (33.5–79.7)	84 (67.2–94.7)	63 (42.4–80.6)	82 (67.9–92.0)
n	60	47	8	11	27	17	37
DOR, mo							
Median (95% CI)[b]	15.7 (6.2–24.0)	15.7 (6.7–24.0)	NR (1.5–NR)	6.2 (2.3–NR)	9.7 (3.3–NR)	11.3 (2.3–NR)	15.8 (5.6–NR)
Median FU (95% CI)[c]	22.8 (16.7–23.0)	22.8 (16.6–23.0)	22.6 (0.0–23.0)	16.9 (10.9–22.9)	22.6 (11.7–22.8)	23.0 (16.2–23.3)	17.1 (11.9–22.8)
PFS, mo							
Median (95% CI)[b]	15.3 (6.6–24.9)	15.3 (6.6–24.9)	24.0 (2.4–NR)[d]	7.4 (3.3–NR)	16.6 (4.0–24.0)	7.8 (3.1–NR)	16.6 (6.5–NR)
Median FU (95% CI)[c]	23.5 (17.7–23.8)	18.2 (17.6–24.0)	23.6 (2.6–24.0)	18.0 (5.7–23.8)	23.5 (12.4–24.0)	23.5 (18.2–24.0)	18.0 (12.4–24.0)
OS, mo							
Median (95% CI)[b]	18.2 (12.9–36.3)	18.2 (10.7–NR)	13.5 (2.4–NR)[d]	17.1 (6.6–NR)	15.7 (8.3–36.3)	12.9 (5.6–NR)	20.7 (13.5–36.3)
Median FU (95% CI)[c]	24.0 (23.7–24.2)	23.8 (23.6–24.2)	24.2 (8.4–35.8)	23.7 (11.8–60.5)	23.8 (23.6–24.2)	24.2 (23.7–26.8)	23.8 (18.1–24.0)

Response rates are rounded to whole numbers except those with ".5."
[a]Two-sided 95% exact Clopper-Pearson CIs; [b]Kaplan-Meier method was used to obtain 2-sided 95% CIs; [c]Reverse Kaplan-Meier method was used to obtain the median FU and its 95% CIs; [d]Two pts in the Ki-67 < 30% subgroup received new anticancer therapy shortly after liso-cel and were censored in PFS analyses; these pts' deaths at 1 and 11 mo were included in the OS analyses.
FU, follow-up; NR, not reached.

Table 2. TEAEs of special interest by subgroup (liso-cel–treated set)

	Overall (n = 88)	Ki-67 proliferation index		*TP53* mutation		Blastoid morphology	
		≥ 30% (n = 66)	< 30% (n = 15)	Yes (n = 20)	No (n = 34)	Yes (n = 27)	No (n = 48)
CRS,[a] n (%)							
Any grade	54 (61)	40 (61)	8 (53)	12 (60)	22 (65)	13 (48)	34 (71)
Grade 1–2	53 (60)	40 (61)	7 (47)	12 (60)	22 (65)	13 (48)	33 (69)
Grade 3–4	1 (1)	0	1 (7)	0	0	0	1 (2)
Grade 5	0	0	0	0	0	0	0
NE,[b] n (%)							
Any grade	27 (31)	20 (30)	4 (27)	6 (30)	11 (32)	7 (26)	14 (29)
Grade 1–2	19 (22)	14 (21)	2 (13)	4 (20)	8 (24)	6 (22)	8 (17)
Grade 3–4	8 (9)	6 (9)	2 (13)	2 (10)	3 (9)	1 (4)	6 (12.5)
Grade 5	0	0	0	0	0	0	0
Tumor lysis syndrome, n (%)	2 (2)	0	1 (7)	1 (5)	0	0	1 (2)
Grade ≥ 3 infections,[c] n (%)	13 (15)	7 (11)	5 (33)	6 (30)	4 (12)	6 (22)	5 (10)
Hypogammaglobulinemia, n (%)	6 (7)	6 (9)	0	2 (10)	1 (3)	2 (7)	2 (4)
Prolonged cytopenia,[d] n (%)	35 (40)	26 (39)	5 (33)	8 (40)	16 (47)	10 (37)	19 (40)

All percentages are rounded to whole numbers except those with ".5."
[a]CRS was graded based on the Lee 2014 criteria; [b]NEs were defined as investigator-identified neurological AEs related to liso-cel; [c]Includes grade ≥ 3 TEAEs from the infections and infestations (System Organ Class); [d]Defined as laboratory-based grade ≥ 3 abnormalities of neutropenia, anemia, and/or thrombocytopenia at Day 29.

Figure 1

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