2116 Matching-Adjusted Indirect Comparison (MAIC) of Lisocabtagene Maraleucel (liso-cel) Vs Axicabtagene Ciloleucel (axi-cel) and Tisagenlecleucel in Relapsed/Refractory (R/R) Large B-Cell Lymphoma (LBCL)

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Introduction

Chimeric antigen receptor T cell therapies have shown encouraging, durable responses in patients with R/R LBCL, yet no head-to-head clinical trials comparing options exist to date. We conducted 2 separate pair-wise MAICs to compare treatment effects of liso-cel vs both axi-cel and tisagenlecleucel.

Methods

MAICs were used to estimate population-adjusted relative treatment effects associated with liso-cel (TRANSCEND NHL 001 [TRANSCEND]; NCT02631044; N = 256) vs axi-cel (ZUMA-1; NCT02348216; N = 101) and vs tisagenlecleucel (JULIET; NCT02445248; N = 111). Outcomes of interest included efficacy (overall and complete response rates [ORR/CRR], overall survival [OS], and progression-free survival [PFS]) and safety (cytokine release syndrome [CRS] by Lee criteria, neurological events [NEs], aphasia, encephalopathy, infections, hypogammaglobulinemia, and prolonged cytopenia).

Individual patient data (IPD) from TRANSCEND were adjusted to match the marginal distribution (eg, mean, variance) of clinical factors among patients from ZUMA-1 and JULIET. Patients from TRANSCEND were removed from the IPD set if they did not satisfy eligibility criteria specified in the comparator trial for each MAIC. IPD for patients who remained in the TRANSCEND data set were weighted using a method-of-moments propensity score model. Baseline characteristic and

outcome definitions were aligned with those in ZUMA-1 or JULIET. Clinically relevant prognostic factors (identified from literature, TRANSCEND data, and 5 independent clinical experts) were adjusted collectively in a stepwise fashion by ranked order. Key matched and adjusted variables in 1 or both comparisons included: disease histology, Eastern Cooperative Oncology Group performance status (ECOG PS), central nervous system (CNS) involvement, prior allogeneic/autologous hematopoietic stem cell transplant (HSCT), tumor burden, International Prognostic Index score, response to last therapy, bulky disease, and age. Efficacy outcomes in patients without bridging therapy were evaluated; however, ZUMA-1 and TRANSCEND treatment protocols differed in bridging therapy use (not allowed in ZUMA-1) and time to product availability (median, 17 vs 24 days, respectively).

Results

After aligning definitions of baseline characteristics among trials, substantial differences were noted for ECOG PS of 2, tumor burden, active CNS involvement, number of prior lines of therapy, prior allogeneic HSCT, and history of hematologic comorbidities between studies. Overall, TRANSCEND included a larger sample size and broader patient population vs comparator trials, allowing for successful MAIC adjustments.

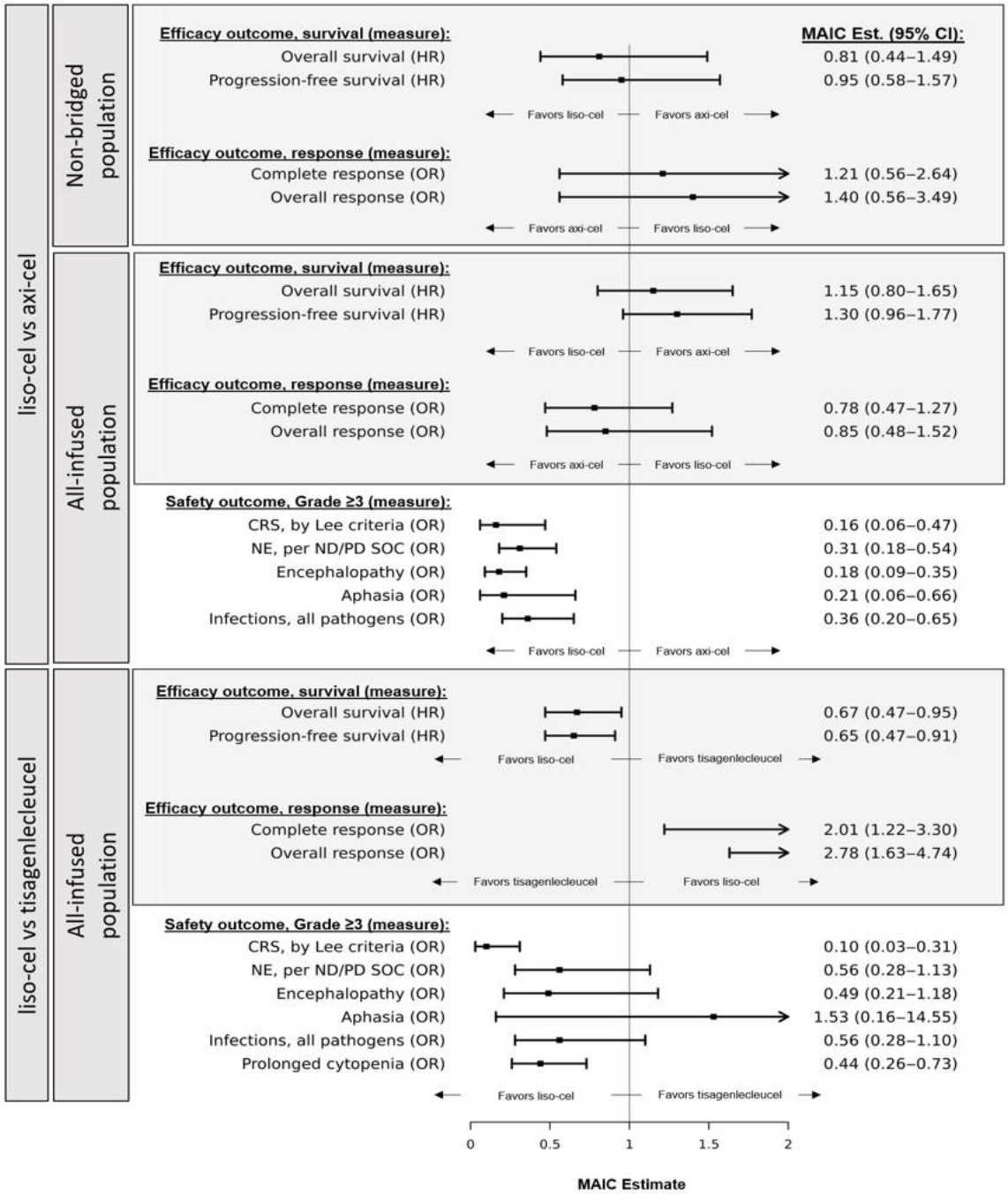
When comparing TRANSCEND to ZUMA-1, MAIC-weighted efficacy outcomes were comparable between trials: odds ratios (ORs [95% CI]) for ORR and CRR with liso-cel vs axi-cel were 0.85 (0.48-1.52) and 0.78 (0.47-1.27), respectively; hazard ratios (HRs [95% CI]) for OS and PFS were 1.15 (0.80-1.65) and 1.30 (0.96-1.77), respectively (Figure). When limited to patients without bridging therapy, differences between trials remained statistically insignificant. MAIC-weighted safety outcomes showed a favorable safety profile for liso-cel, with a statistically significant lower odds of CRS, NEs (including aphasia and encephalopathy), and infections vs axi-cel. ORs (95% CI) for all-grade and grade ≥3 CRS with liso-cel vs axi-cel were 0.06 (0.03-0.13) and 0.16 (0.06-0.47), respectively; ORs for all-grade and grade ≥3 NEs were 0.21 (0.13-0.35) and 0.31 (0.18-0.54), respectively.

When comparing TRANSCEND to JULIET, liso-cel showed a statistically significant higher ORR/CRR and longer OS/PFS than tisagenlecleucel. ORs (95% CI) for ORR and CRR achieved with liso-cel vs tisagenlecleucel were 2.78 (1.63-4.74) and 2.01 (1.22-3.30), respectively; HRs (95% CI) for OS and PFS were 0.67 (0.47-0.95) and 0.65 (0.47-0.91), respectively. Adjusted safety outcomes showed generally comparable profiles with lower ORs (95% CI) for all-grade and grade ≥3 CRS with liso-cel vs tisagenlecleucel: 0.53 (0.32-0.89) and 0.10 (0.03-0.31), respectively.

Conclusions

MAIC-weighted outcomes suggest that liso-cel may provide a more well-balanced overall efficacy and safety profile for the treatment of R/R LBCL, with better efficacy compared with tisagenlecleucel and better safety compared with axi-cel.

Figure. MAIC-Weighted Efficacy and Safety Outcomes



CRS, cytokine release syndrome; Est., estimate; HR, hazard ratio; MAIC, matching-adjusted indirect comparison; ND/PD SOC, nervous system disorders/psychiatric disorders by system organ class; NE, neurological event; OR, odds ratio.