Matching-Adjusted Indirect Comparison (MAIC) of Axicabtagene Ciloleucel (axi-cel) and Epcoritamab (epcor) in Relapsed/Refractory Large B-Cell Lymphoma (LBCL) After at Least Two Prior Systemic Therapies (3L+)

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BACKGROUND

- LBCL accounts for up to 40% of non-Hodgkin lymphoma cases and current standard first-line treatment contains rituximab and cyclophosphamide, commonly a CD20-targeted antibody in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone.
- Given a significant proportion of patients, ranging from 40-50%, are refractory or relapse subsequent to treatment, exploration of alternative treatment options is warranted.2

OBJECTIVES

- To estimate relative treatment effects of axi-cel versus epcor for the treatment of 3L+ LBCL by means of a MAIC.

METHODS

- A pre-specified logistic propensity score model was used to weigh ZUMA-1 (axi-cel) individual patient level data so that mean baseline characteristics matched those observed in EPCORE NHL-1 (epcor).
- Outcomes were then compared across matched populations using weighted statistical tests: logistic regression models for binary outcomes and Cox proportional hazards models for time-to-event outcomes.
- The outcomes of interest were response rates as assessed by independent review committee (IRC), overall survival (OS), progression-free survival (PFS), by IRC, duration of response (DoR), and cytokine release syndrome (CRS).

RESULTS

PATIENT DEMOGRAPHICS AND DISEASE CHARACTERISTICS

- Prior to matching, axi-cel and epcor trial populations differed for most of the included covariates (Table 1).
- Refractory disease in ZUMA-1 was re-categorized to match EPCORE NHL-1 and defined as disease that either progressed during therapy or within 8 months of completion of therapy.
- MAIC convergence was achieved using the full set of covariates, and after MAIC convergence was achieved using the full set of covariates, and after

Table 1. Baseline characteristics in ZUMA-1 before and after matching to EPCORE NHL-1

<table>
<thead>
<tr>
<th>Category</th>
<th>ZUMA-1 Cohorts 1+2</th>
<th>EPCORE NHL-1</th>
<th>Matched ZUMA-1 Cohorts 1 Matched ZUMA-1 Cohorts 2</th>
<th>Matched EPCORE NHL-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECOG PS 0</td>
<td>64.2</td>
<td>64.5</td>
<td>64.2</td>
<td>64.5</td>
</tr>
<tr>
<td>ECOG PS 1</td>
<td>35.8</td>
<td>35.5</td>
<td>35.8</td>
<td>35.5</td>
</tr>
<tr>
<td>Refractory to last therapy</td>
<td>52.2</td>
<td>52.2</td>
<td>52.2</td>
<td>52.2</td>
</tr>
<tr>
<td>Median follow-up (months)</td>
<td>27.1</td>
<td>27.1</td>
<td>27.1</td>
<td>27.1</td>
</tr>
<tr>
<td>Prior auto-SCT</td>
<td>40.9</td>
<td>40.9</td>
<td>40.9</td>
<td>40.9</td>
</tr>
<tr>
<td>b-cell lymphoma subtype</td>
<td>52.5</td>
<td>52.5</td>
<td>52.5</td>
<td>52.5</td>
</tr>
<tr>
<td>TNFR 1</td>
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<td>35.5</td>
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<tr>
<td>TFL</td>
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<td>47.1</td>
<td>47.1</td>
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<tr>
<td>B-cell lymphoma subtype</td>
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</tbody>
</table>

MATCHING-ADJUSTED INDIRECT COMPARISONS

- Results from the MAIC are summarized below and those from the naïve

Table 2. naïve and MAIC-weighted relative treatment effect estimates of axi-cel versus epcor

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Naïve estimates</th>
<th>MAIC estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective response</td>
<td>1.69 (0.97, 2.93)</td>
<td>1.69 (0.97, 2.93)</td>
</tr>
<tr>
<td>Complete response</td>
<td>1.88 (1.13, 3.35)</td>
<td>1.88 (1.13, 3.35)</td>
</tr>
<tr>
<td>Progression-free survival</td>
<td>0.51 (0.31, 0.85)</td>
<td>0.51 (0.31, 0.85)</td>
</tr>
</tbody>
</table>

LIMITATIONS

- While potential prognostic factors adjusted for in the MAIC were based on those observed in the randomized trials, estimates were limited by data availability as variables must be reported from both trials for matching; as such it was not feasible to match on LHD Level or fulky disease at baseline.
- As with any analysis of single-arm or non-comparative studies, estimates may be subject to residual bias given uncertainty about any unmeasured or unmeasured prognostic factors/selection-modifiers not captured in the observed model which may have influenced the outcome of interest.
- No proportion of patients in EPCORE NHL-1 would not have been eligible for ZUMA-1 (39% prior recived prior CAR T therapy) and this difference could not be adjusted for in the MAIC.

CONCLUSIONS

- Based on the available evidence, this analysis suggests that axi-cel demonstrated comparable response rates and more favorable PFS versus epcor among R/R LBCL, possibly extending treatment in the third line or greater setting.
- Axi-cel was associated with a higher risk of grade 3 or higher CRS related to the procedure, however, no risk-benefit profile has improved over time with enhanced toxicity management in clinical practice.3

REFERENCES


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DISCLOSURES

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