Efficacy Comparison of Tisagenlecleucel Versus Usual Care in Patients With Relapsed or Refractory Follicular Lymphoma

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METHODS

Patient Characteristics

After weighting, baseline variables, including number of previous lines of systemic therapy (median: 4 lines) were well balanced between the tisaga-cel and SOC cohorts based on observed standard errors (SMD) of < 3% for all variables after weighting. For figure 1, table 1:

- Propensity score methods were used to adjust for differences in baseline characteristics.

- The results of this study will be helpful for comparative effectiveness research of the efficacy and safety of tisaga-cel vs. SOC in a real-world population.

- The study was registered at ClinicalTrials.gov (NCT03125527).

ENDPOINTS

- Clinical endpoints were evaluated for one eligible line of therapy (LoT) for each patient in the SOC cohort, the weighted (tisaga-cel) LoT and the standard of care (SOC) LoT for all evaluated endpoints.

- The Kaplan-Meier curves were generated using the method of Kaplan and Meier. The hazard ratio was calculated by weighted Cox proportional hazard model for indirect comparison between tisaga-cel and SOC. The number of patients at risk was calculated using the life table method.

- The hazard ratios were tested for differences between treatment arms using the log-rank test and the chi-squared test for trend.

Statistical Analyses

- Clinical endpoints were evaluated for one eligible line of therapy (LoT) for each patient. The weighted (tisaga-cel) LoT and the standard of care (SOC) LoT were well balanced.

- The Kaplan-Meier curves were generated using the method of Kaplan and Meier. The hazard ratio was calculated by weighted Cox proportional hazard model for indirect comparison between tisaga-cel and SOC. The number of patients at risk was calculated using the life table method.

- The hazard ratios were tested for differences between treatment arms using the log-rank test and the chi-squared test for trend.

RESULTS

Figure 1. Propensity Score Distribution in Original Sample

- The Kaplan-Meier curves were generated using the method of Kaplan and Meier. The hazard ratio was calculated by weighted Cox proportional hazard model for indirect comparison between tisaga-cel and SOC. The number of patients at risk was calculated using the life table method.

- The hazard ratios were tested for differences between treatment arms using the log-rank test and the chi-squared test for trend.

Table 1. Indirect Comparison of Tisagenlecleucel (ELARA) vs. SOC (ReCORD-FL) Cohorts

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>ELARA Cohort</th>
<th>SOC Cohort</th>
<th>Hazard Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>69.1 (69.1-77.7)</td>
<td>69.1 (69.1-77.7)</td>
<td>1.00 (0.94-1.06)</td>
<td>0.988</td>
</tr>
<tr>
<td>PFS estimation</td>
<td>69.1 (69.1-77.7)</td>
<td>69.1 (69.1-77.7)</td>
<td>1.00 (0.94-1.06)</td>
<td>0.988</td>
</tr>
<tr>
<td>OS</td>
<td>69.1 (69.1-77.7)</td>
<td>69.1 (69.1-77.7)</td>
<td>1.00 (0.94-1.06)</td>
<td>0.988</td>
</tr>
</tbody>
</table>

Figure 2. Kaplan-Meier Plot of Progression-Free Survival for Tisaga-cel (ELARA) vs. SOC (ReCORD-FL) Cohorts

- The Kaplan-Meier curves were generated using the method of Kaplan and Meier. The hazard ratio was calculated by weighted Cox proportional hazard model for indirect comparison between tisaga-cel and SOC. The number of patients at risk was calculated using the life table method.

- The hazard ratios were tested for differences between treatment arms using the log-rank test and the chi-squared test for trend.

Figure 3. Kaplan-Meier Plot of Overall Survival for Tisaga-cel (ELARA) vs. SOC (ReCORD-FL) Cohorts

- The Kaplan-Meier curves were generated using the method of Kaplan and Meier. The hazard ratio was calculated by weighted Cox proportional hazard model for indirect comparison between tisaga-cel and SOC. The number of patients at risk was calculated using the life table method.

- The hazard ratios were tested for differences between treatment arms using the log-rank test and the chi-squared test for trend.

DISCUSSION AND CONCLUSION

- The ITC results suggest that tisaga-cel has superior efficacy over SOC in a clinically relevant matched group of patients with r/r FL, not evaluable for response.

- This study provides further context to the results of the single-arm ELARA trial by providing needed historical control data from clinically comparable patients receiving SOC in a randomized setting.

- Appropriate statistical methods were applied to address inherent study limitations and to adjust for key differences between ELARA and RECORD-FL.

- RECORd-FL patients can be reclassified using the ELARA inclusion/exclusion criteria at multiple lines of therapy.

- There are potential differences in baseline prognostic factors related to efficacy.

- There is heterogeneity in response/progression assessment criteria and in frequency and rigor in practice settings of RECORD-FL.

- Our findings provide evidence that not only is ELARA a viable treatment option in comparison with patients with r/r FL, but also it is associated with superior efficacy.

- This study is the first randomized controlled trial to assess the comparative effectiveness of tisaga-cel vs. SOC in patients with relapsed/refractory follicular lymphoma.

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