Estimating Long-term Survival in a Cohort of Allogeneic Hematopoietic Stem Cell Transplant Patients

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INTRODUCTION

• Allogeneic hematopoietic cell transplantation (HCT) is a common treatment for many hematologic diseases.
• Most deaths occur in the first 2 years after HCT due to relapse, graft-versus-host disease, infections, malignancies, or other toxicities.1,2
• Among patients who are alive and recurrence free at 2 years after HCT, survival of 10 years is between 80% and 92%.3
• Advances in transplantation practices have led to improved outcomes and more long-term HCT survival.

As survival outcomes continue to improve and new treatments emerge, understanding and quantifying the full lifetime benefit of HCT in terms of mean overall survival (OS) is clinically relevant.

In this analysis, we estimate the mean OS of a cohort of HCT patients.

METHODS

Systematic Literature Review

• The systematic literature review was performed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.
• The scope was defined in terms of Population, Intervention, Comparators, Outcomes, and Study design (PICOS criteria; Table 1).
• Using extensive search terms for the indication and study designs, studies were identified using the EMBASE, MEDLINE, and Cochrane databases.
• The literature search was conducted on July 19, 2018 and included studies published between database inception January 1, 1999 and July 19, 2018.
• Relevant congress abstracts published between January 2013 and June 2018 were also identified.

To ensure inclusion and exclusion criteria were used to review identified citations.

No treatment limitations were imposed to ensure inclusion of all relevant evidence, and the study designs were limited to prospective and retrospective observational studies; case reports were included regardless of sample size.

Two independent reviewers screened all citations and full-text articles; any discrepancies were resolved by a third independent reviewer.

Table 1. PICOS Criteria

<table>
<thead>
<tr>
<th>Element</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Outcome</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>Patients with PTLD after HCT</td>
<td>Non-human</td>
<td>Not fulfilling inclusion criteria</td>
<td></td>
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<tr>
<td>Intervention</td>
<td>Non-pharmacological, non-interventional, single center</td>
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<tr>
<td>Comparator</td>
<td>Real-world treatment</td>
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<td>Therapies</td>
<td>Real-world treatment</td>
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<td>Treatment sequences</td>
<td>Real-world treatment</td>
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<tr>
<td>Outcomes</td>
<td>Real-world treatment</td>
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<tr>
<td>Measures</td>
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<td>Study Design</td>
<td>Real-world treatment</td>
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<tr>
<td>Restrictions</td>
<td>Real-world treatment</td>
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</tbody>
</table>

Data Source

• We retrieved only 2 published articles that met the inclusion criteria from the literature review: Uhlin et al, 2014 and Wingard et al, 2011 (Table 2).
• Data from Uhlin et al, 2014 was used to estimate the percentage of patients alive at 2 years after HCT, which was 60%.
• For 2-year survivors, the data set for OS was taken from Wingard et al, 2011 and the age-adjusted life tables for the general UK population.

Long-term Survival Model

• Extracted data were incorporated into a long-term survival model using a step-wise approach.
• Short-term survival (up to 2 years after HCT) using data reported by Uhlin et al, 2014.
• Longer-term survival (more than 2 years after HCT) using data reported by Wingard et al, 2011 and the age-adjusted life tables for the general UK population.

CONCLUSIONS

• The mean OS for a cohort of HCT patients was estimated to be 25.9 years.
• This estimate helps to understand and quantify the full lifetime survival benefit to HCT patients, including the tail end of the survival curve and the potential added benefits of future treatments after HCT.
• The parametric models revealed a narrower range for the estimated mean OS, minimizing the uncertainty of the results.
• Since the first 2 years after HCT have the highest mortality rate, new treatments that can improve survival during this time may change the impact on the lifelong benefit of the therapy.

RESULTS

3. Base-case Survival Scenario

• Weibull
• Exponential
• Gamma
• Log-logistic
• Log-normal

Figure 2.

Figure 3C. Best-case Survival Scenario

Scenarios

• For a cohort of HCT patients who received their transplant at age 23.5, the estimated mean OS for the base-case survival scenario was 25.9 years after HCT (Figure 3A).
• The estimated mean OS for the worst-case survival scenario was 21.9 years when using excess mortality from Wingard et al, 2011 for the rest of the patients’ lives (Figure 3B).
• The estimated mean OS for the best-case survival scenario was 31.7 years when hazards used from general UK population after 15 years (Figure 3C).

Summary of Survival Scenarios

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients selected out of 31,818 (318 centers worldwide)</th>
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</thead>
<tbody>
<tr>
<td>Uhlin et al, 2014</td>
<td>9,393 patients alive at 2 years after HCT</td>
</tr>
<tr>
<td>Wingard et al, 2011</td>
<td>10,652 patients selected out of 31,818 total transplant records</td>
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</table>

REFERENCES


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DISCLOSURE

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