Determination of Time to Treatment Initiation in Metastatic Cancers

BACKGROUND

- Timeliness of delivery of care in cancer is recognized as an important determinant of clinical outcomes.
- There have been few studies of time to treatment initiation (TTI) in patients with advanced cancers.
- Studies of TTI among patients with non-small-cell lung cancer (NSCLC) and melanoma are limited, and existing studies are sample-specific, utilizing different definitions and methodologies.
- The objective of this work was to explore the determinants of TTI among cancer patients treated with systemic therapy in the Flatiron Health network.

METHODS

Study Design

- This was a retrospective cohort study of patients newly diagnosed with metastatic NSCLC, metastatic/recurrent HNSCC, or metastatic melanoma in the United States from January 1, 2014 to June 30, 2019.
- Patients were included in the study cohort if they satisfied the following criteria:
  - Had no diagnosis of metastatic cancer in the 1 year prior to the index date.
  - Had a diagnosis of metastatic NSCLC, metastatic/recurrent HNSCC, or metastatic melanoma on or after the index date.
- Exclusion criteria included:
  - Patients with no diagnosis of metastatic cancer in the 1 year prior to the index date.
  - Patients who had a diagnosis of metastatic NSCLC, metastatic/recurrent HNSCC, or metastatic melanoma on or after the index date.
- The definition of metastatic disease was based on ICD-9 and ICD-10 codes.
- The date of diagnosis was defined as the date of the first diagnosis of metastatic NSCLC, metastatic/recurrent HNSCC, or metastatic melanoma.
- The index date was the date of metastasis diagnosis for metastatic NSCLC, metastatic/recurrent HNSCC, or metastatic melanoma.
- The date of death was defined as the date of the death event.
- The date of treatment initiation was defined as the date of the first systemic treatment for metastatic NSCLC, metastatic/recurrent HNSCC, or metastatic melanoma.
- The date of follow-up was the date of the last record in the Flatiron Health database.

Statistical Methods

- Determinants of TTI were examined with a generalized linear mixed model with a binomial distribution and logit link function.
- A random effect for Practice was used to account for clustering within the Flatiron Health network.
- The outcome of interest was TTI, defined as the time from diagnosis to treatment initiation.
- Significant determinants were identified with a p-value < 0.05.

RESULTS

- A total of 17,392 patients were included in the study, of whom 7,092 (40.6%) had NSCLC, 3,129 (18.0%) had HNSCC, and 1,440 (8.6%) had melanoma.
- The median TTI for the unrestricted population was 363.8 (366.1) days and 490.0 (480.7) days for the restricted sample.
- Table 1 presents the Patient Demographic and Clinical Characteristics of the study population.
- Table 2 presents the Kaplan-Meier Estimates for Median Time to Treatment Initiation.
- Table 3 presents the Variants Associated With Time to Treatment From Generalized Linear Mixed Model.

LIMITATIONS

- This study is limited by the retrospective nature of the data and the reliance on administrative claims data, which may be limited in terms of accuracy and completeness.
- The results should be interpreted with caution because HNSCC of the small subset of patients included in this study.
- The study population consists of patients treated within the Flatiron network, a select population of patients that may not be representative of the general population.
- There may exist selection biases and unmeasured confounding in the Flatiron data set. Certain prognostic factors outside of ECOG performance status should continue to be explored.

CONCLUSIONS

- Significant determinants of TTI among patients treated with systemic therapy depend on the cancer type.
- Older age at diagnosis (P = 0.002), lower Charlson Comorbidity Index score (P = 0.046), and a history of smoking (P = 0.016) were significantly associated with lower TTI among patients with NSCLC.
- Female gender was found to be a significant determinant of higher TTI among patients with melanoma (P = 0.004).
- Among the melanoma population, no specific determinants of TTI were found (Table 3).

Table 1. Patient Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.4 (11.9)</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>0.356 (0.192)</td>
</tr>
<tr>
<td>Race (White)</td>
<td>0.424 (0.228)</td>
</tr>
<tr>
<td>Race (Black)</td>
<td>0.849 (0.449)</td>
</tr>
<tr>
<td>Race (Asian)</td>
<td>0.323 (0.167)</td>
</tr>
<tr>
<td>Race (Other)</td>
<td>0.164 (0.092)</td>
</tr>
<tr>
<td>Smoking status</td>
<td>0.016 (0.009)</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>0.012 (0.012)</td>
</tr>
<tr>
<td>ECOG performance status</td>
<td>0.006 (0.002)</td>
</tr>
<tr>
<td>Treatment type</td>
<td>0.004 (0.002)</td>
</tr>
</tbody>
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Table 2. Kaplan-Meier Estimates for Median Time to Treatment

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Median TTI (95% CI)</th>
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<tbody>
<tr>
<td>NSCLC</td>
<td>363.8 (366.1) days</td>
</tr>
<tr>
<td>HNSCC</td>
<td>490.0 (480.7) days</td>
</tr>
<tr>
<td>Melanoma</td>
<td>363.8 (366.1) days</td>
</tr>
</tbody>
</table>

Table 3. Variants Associated With Time to Treatment From Generalized Linear Mixed Model

- Significant predictors of TTI included age, gender, Charlson Comorbidity Index, and smoking status.
- The results support the importance of age, gender, and smoking status as significant determinants of TTI.

References

- Pardoll DM. Science. 2012;337(6092):121-123.