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POSTER ABSTRACTS

903.HEALTH SERVICES AND QUALITY IMPROVEMENT -MYELOID MALIGNANCIES

Validation of the Charlson Comorbidity Index Model in Acute Myeloid Leukemia Treated with a Hypomethylating Agent and Venetoclax

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1. Introduction

The Charlson comorbidity index (CCI) model is a scoring model that combines comorbidities and age; it has been shown to predict mortality in patients with acute myeloid leukemia (AML). However, treatment-specific comorbidity score thresholds associated with increased patient mortality remain unclear, particularly for newer treatment approaches. The aim of this study is to identify and update CCI score thresholds for patients undergoing treatment with venetoclax and a hypomethylating agent (decitabine or azacitidine; VEN + HMA) to refine the selection of treatment candidates in the first-line and salvage settings.

2. Methods

We analyzed 183 patients with newly diagnosed or relapsed or refractory AML treated with HMA + VEN from January 1, 2018 to April 18, 2023 at VCU Massey Comprehensive Cancer Center. We recorded baseline patient-related and disease characteristics, including Charlson comorbidity index (CCI) scores at the time of initial diagnosis, dates of regimen initiation, and survival. We used the D'Agostino & Pearson method for normality testing and the Mann-Whitney test for between-group comparisons. Categorical comparisons used Fischer's exact test. We applied the Bonferroni correction if multiple comparisons were made. We analyzed survival by the Kaplan-Meier method with significance determined by the log-rank test. The event for calculating the overall survival (OS) was the date of death. Patients were otherwise censored at the date of last contact.

3. Results

We analyzed 100 (54.6%) patients in the first-line setting treated with HMA + VEN. Starting from a CCI score threshold of 4, we incrementally analyzed CCI cohorts (e.g., $\leq$4 vs >4; $\leq$5 vs >5, and so on) until we reached a significant survival difference between cohorts at a CCI score threshold of 6. CCI score thresholds of 4 and 5 were not significant ($p = 0.946$ and $p = 0.840$, respectively). In patients treated with first-line HMA + VEN, those with a CCI score threshold of $\leq$6 had significantly improved overall survival compared with patients with a CCI score of >6: (8.8 m. vs 3.4 m., $p = 0.013$, Figure A). Next, we analyzed 89 (48.6%) patients in the relapsed or refractory setting; six (3.3%) patients received HMA + VEN as both first-line and as salvage therapy. We observed a significant survival difference at the first model increment analyzed: patients with a CCI score of 4 or lower had a median overall survival of 9.4 m compared to 5.2 months for CCI scores greater than 4 ($p = 0.048$, Figure B).

In light of these findings, we conducted an exploratory analysis to account for any significant between-group differences independent of the assigned CCI score. In the first-line setting, patients with CCI scores $\leq$6 were significantly younger compared to those with scores >6 (71 vs 75 y., $p = 0.002$). The median ECOG score was 2 in both groups at the specified CCI score threshold of 6 ($p = 0.939$). There was no difference in the proportion of ELN 2022 adverse-risk disease between the $\leq$6 and >6 cohorts (55.4% vs 61.8%, $p = 0.669$), and there was no significant difference in the receipt of allogeneic stem cell transplant (3.0% vs 0%, $p = 0.547$). In the salvage setting, we observed that age was also significantly different between the $\leq$4 and >4 cohorts (54 y. vs 70 y., $p < 0.0001$), and there was no significant difference in the ECOG scores at the time of relapse in the $\leq$4 vs >4 cohorts (1 vs 1, $p = 0.769$) or in the proportion of ELN 2022 adverse-risk disease (54.4% vs 61.9%, $p = 0.522$).

4. Discussion

This study validates new Charlson comorbidity index score thresholds for patients treated with HMA + VEN. We did not identify any significant confounding factors outside of the variables analyzed in the CCI model; age was the only significant

finding, which is accounted for in the CCI scoring model. In the first-line setting, we identified a novel lower CCI score threshold of 6 that predicts superior survival in patients treated with HMA + VEN. In the salvage setting, the CCI score threshold appears lower at 4, which likely reflects a selection for patients able to tolerate multiple lines of therapy due to a decreased comorbidity burden. These CCI score thresholds can be used as a predictive guide and a clinical tool to assess fitness for lower-intensity venetoclax-based therapies in AML.

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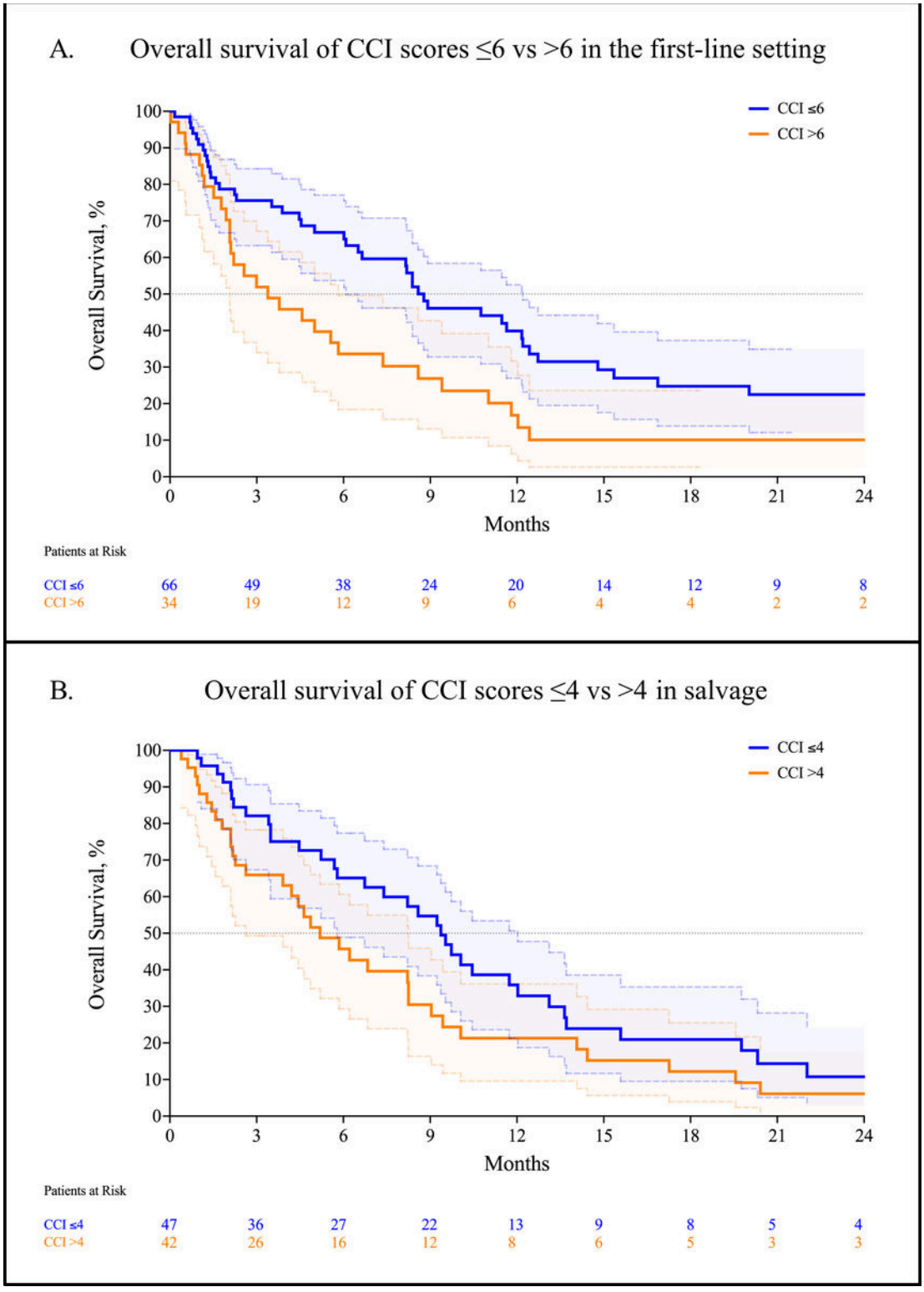

Figure 1

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