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POSTER ABSTRACTS

637.MYELODYSPLASTIC SYNDROMES - CLINICAL AND EPIDEMIOLOGICAL

Performance of the Molecular International Prognostic Scoring System (IPSS-M) in Hypomethylating Agent-Treated Patients with Myelodysplastic Syndromes

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Background: Patients with myelodysplastic syndromes (MDS) undergo risk stratification with various prognostication tools, such as the International Prognostic Scoring System (IPSS) and Revised IPSS (IPSS-R). Recently, the Molecular IPSS (IPSS-M) was developed incorporating genomic data in addition to clinical and cytogenetic characteristics. Though IPSS-M has been shown to improve prognostication in all MDS patients at baseline, its utility in specifically patients undergoing hypomethylating agent (HMA) therapy remains unknown. Here, we assess the efficacy of IPSS-M in HMA-treated patients with MDS.
Methods: We retrospectively evaluated all untreated patients with MDS seen at a single tertiary cancer center from July 2017 to July 2021 and identified those who later received HMA therapy. Patient characteristics and bone marrow (BM) data, including morphology, cytogenetics, and mutations, were assessed at diagnosis. Genomic DNA was extracted from whole BM aspirate samples and subject to 81-gene target PCR-based sequencing using a next-generation sequencing platform. Survival data was updated in July 2023.
Results: Out of 799 untreated MDS patients, 455 patients (57%) eventually underwent treatment with HMA. At diagnosis, the median age was 69 (range: 22-90) with 289 (64%) male patients. Patients were generally high risk, with therapy-related MDS in 160 (35%), complex cytogenetics in 167 (37%), and *TP53* mutations in 168 (37%). By IPSS-R, 259 patients (58%) had high- or very high-risk disease, and 340 patients (75%) had higher-risk disease (moderate high-, high-, and very high-risk) by IPSS-M. A total of 291 patients (64%) were treated with HMA monotherapy, and lower-risk MDS patients received more cycles of HMA ($p < 0.001$).
By IPSS-R, the median overall survival was 60.0 months (95% CI: 46.0, not estimable (NE)) in very low-, 87.4 months (95% CI: 59.9, NE) in low-, 36.2 months (95% CI: 30.0, 58.1) in intermediate-, 23.7 months (95% CI: 19.6, 34.8), in high-, and 12.8 months (95% CI: 11.0, 16.7) in very high-risk patients ($p < 0.0001$) with a concordance index of 0.669. Figure 1 depicts the reclassification of patients between IPSS-R and IPSS-M. Risk stratification by IPSS-M (Figure 2) provided similar results: not reached (95% CI: 56.8, NE) in very low-, 60.0 months (95% CI: 49.8, NE) in low-, 40.8 months (95% CI: 22.8, NE) in moderate low-, 44.2 months (95% CI: 27.8, NE) in moderate high-, 33.4 months (95% CI: 22.8, 44.5) in high-, and 16.6 months (95% CI: 13.8, 19.4) in very high-risk patients ($p < 0.0001$). The concordance index of IPSS-M in all HMA-treated MDS patients was 0.648. When analyzing patients with MDS who were more likely to undergo HMA as per standard-of-care treatment (those with IPSS-M moderate low-, moderate high-, high-, and very high-risk disease), the IPSS-M remained statistically significant ($p < 0.0001$) though less discerning in the patients with moderate-risk MDS, as seen by the concordance index of 0.620.
Conclusions: In this group of MDS patients treated with HMA, the IPSS-M did not provide additional prognostic power over the IPSS-R though median overall survival remained inversely proportional to IPSS-M risk category. Concordance indices for survival remained below 0.7, likely due to the overlapping curves in moderate-risk patients by IPSS-M. Further development and validation of prognostic scoring systems in patients treated with HMA are warranted.

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Figure 1. Restratification of IPSS-R to IPSS-M Categories in MDS Patients Treated with HMA.

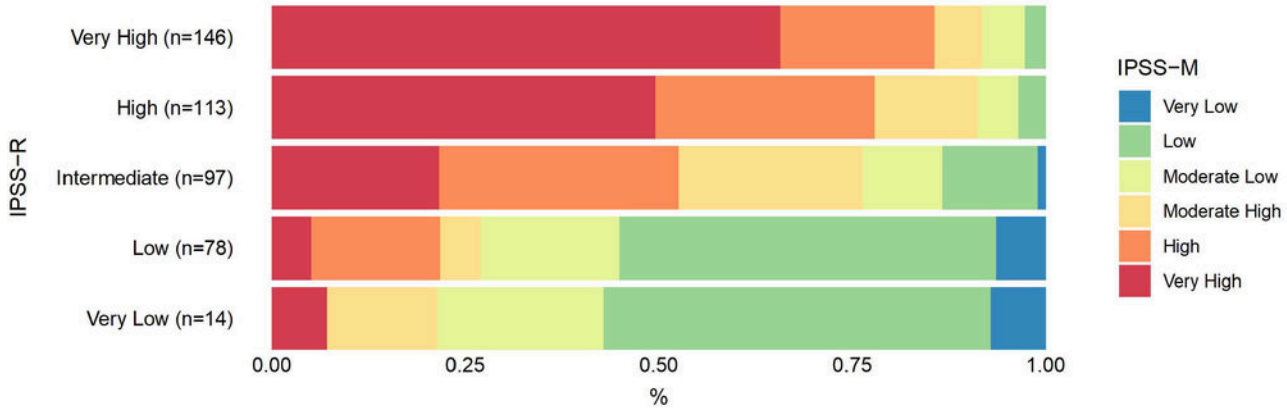

Figure 2. Median Overall Survival in HMA-Treated MDS Patients by IPSS-M Category.

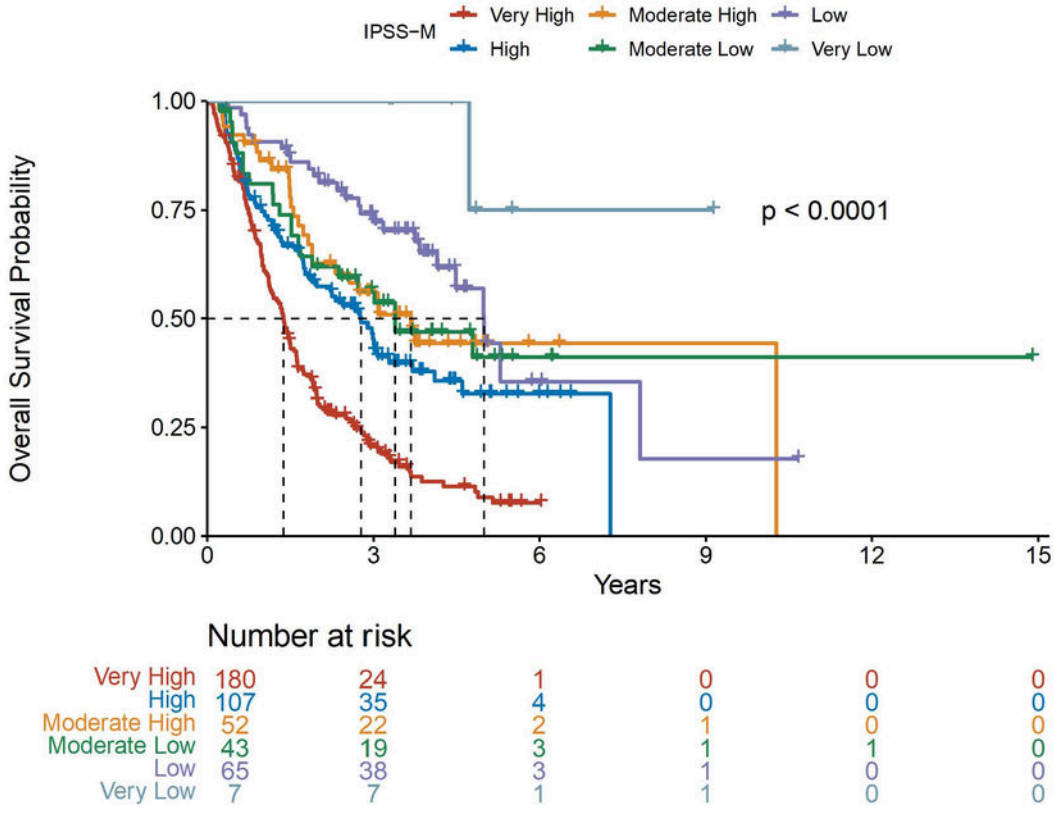

Figure 1

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