



# The 65th ASH Annual Meeting Abstracts

## POSTER ABSTRACTS

### 637.MYELODYSPLASTIC SYNDROMES - CLINICAL AND EPIDEMIOLOGICAL

#### Evaluation of the Molecular International Prognostic Scoring System (IPSS-M) in Patients (Pts) with Myelodysplastic Syndromes/Neoplasms (MDS) with Missing Molecular Data

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# Introduction

The IPSSM incorporates molecular features to improve outcome prediction for pts with MDS. However, IPSSM requires assessment of 31 genetic mutations to classify pts into 6 risk groups. Importantly, IPSSM accounts for missing data and provides best, average, and worst IPSSM scores. Here, we used a large cohort of pts with MDS to analyze the performance of IPSSM if molecular data were missing to better understand the performance of the tool in this frequently encountered clinical setting.

# Methods

For this study, we combined data from a publicly available dataset (Kewan et al. 2023 Nat com) with our multicenter VALIDATE database to increase sample size. Only pts with available molecular data were included and IPSSM was calculated twice: a. using *TP53* mutation ( *TP53*<sup>MT</sup>) only and assuming that all other molecular mutations are missing (missing molecular data [IPSSM<sup>MM</sup>]) and b. using the full molecular panel (available molecular data [IPSSM<sup>AM</sup>]). *TP53*<sup>MT</sup> were included in all IPSSM calculations given frequency and significant impact on survival. Time-to-event analysis from the time of diagnosis was conducted using Kaplan-Meier estimator. The performance of different scores was evaluated by Harrell's c-index. This study was supported by an independent research grant from AbbVie.

# Results

Of 2,789 pts, 2,489 had molecular data and were included. Median age was 72 years (IQR: 65-78). MDS with excess blast 1/2 (42%) was the most common subtype. Overall, 39% of pts treated with HMA and 15% of underwent transplantation. In total, 16% of pts had complex karyotypes. The most prevalent mutations were *SF3B1* (21%), *ASXL1* (20%), *TP53* (15%), *SRSF2* (15%), *DNMT3A* (12%), and *RUNX1* (10%), 39% of the pts had >1 gene mutation.

Based on IPSSR, pts were classified as very low (13%), low (47%), intermediate (13%), high (13%), and very high (14%) risk. First, we calculated IPSSM score assuming that all molecular data were missing (IPSSM<sup>MM</sup>) except *TP53*<sup>MT</sup>. Accordingly, pts were classified as very low (4%), low (33%), moderate low (19%), moderate high (14%), high (17%), and very high (14%) risk. IPSSM<sup>MM</sup> resulted in the re-stratification of 1623 (66%) pts of which 1104 (68%) pts were up-staged, and 519 (32%) pts were down-staged. When applying actual molecular data (IPSSM<sup>AM</sup>), pts were classified as very low (14%), low (30%), moderate low (12%), moderate high (10%), high (17%), and very high (17%) risk. When compared with IPSSR, IPSSM<sup>AM</sup> resulted in re-stratification of 1218 pts (50%) of which 868 pts (71%) were upstaged (**Panel A**). When comparing IPSSM<sup>MM</sup> with IPSSM<sup>AM</sup>, 1243 pts (51%) were assigned to the same risk group and 1186 pts (49%) were assigned to different risk groups. Amongst reclassified pts, 431 (36%) were upstaged and 755 (64%) were down staged. Only 109 pts (5%) were reclassified with more than one shift.

Median follow-up time was 24 (IQR:10-77) months (mo) with a median overall survival (OS) of 50 mo (95% CI: 47-55). The probability of OS based on IPSSM<sup>MM</sup> and IPSSM<sup>AM</sup> risk groups was significantly different (p-value: <0.0001 for both), **Panel B**. Median OS (mo) based on IPSSM<sup>MM</sup> vs. IPSSM<sup>AM</sup> were as follows: very low (not reached vs. 125), low (103 vs. 82), moderate low (63 vs. 58), moderate high (46 vs. 43), high (27 vs. 24), and very high (13 vs.15). Median OS based on IPSSR were: very low (not reached), low (78), intermediate (36), high (24), and very high (14). The median LFS (n=1100 pts) based on IPSSM<sup>MM</sup> vs. IPSSM<sup>AM</sup> were as follows: very low (41 vs. 78), low (63 vs. 54), moderate low (39 vs. 33), moderate high (26 vs. 29), high (18 vs. 15), and very high (11 vs. 13).

IPSSM<sup>MM</sup> showed comparable performance to IPSSM<sup>AM</sup> with c-index (95%CI): 0.713 (0.697 -0.728) vs. 0.714 (0.699-0.729) for OS and 0.645 (0.622-0.669) vs. 0.623 (0.599-0.647) for LFS. When used as continuous scores, IPSSM<sup>MM</sup> continues to be comparable to IPSSM<sup>AM</sup> for OS (c-index:0.721 vs. 0.730) and LFS (c-index:0.655 vs. 0.641). IPSS-R had a lower c-index for OS (0.688) and LFS (0.622).

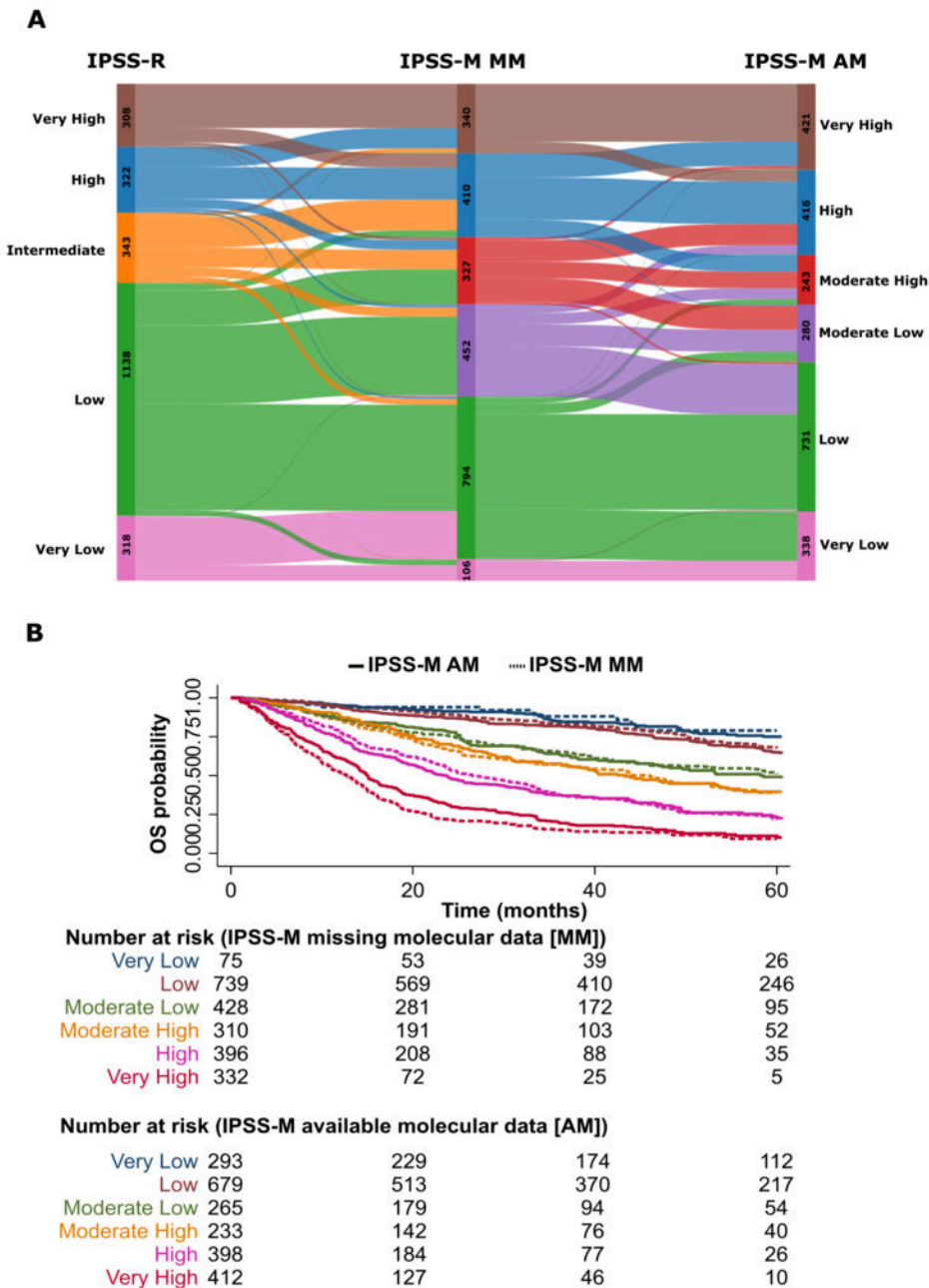
# Conclusions

Our study supports prognostic and clinical value of IPSSM even if most molecular data are missing, confirming that IPSSM adjusts well for missing molecular data and can be used in clinical practice if molecular data are largely missing. While molecular testing remains optimal for accurate risk stratification in MDS, our data suggest that clinical, pathological and cytogenetic data continue to be the main determinant of outcome prediction for pts with MDS.

**Disclosures Stahl:** Kymera: Membership on an entity's Board of Directors or advisory committees; **Rigel:** Membership on an entity's Board of Directors or advisory committees; **GSK:** Membership on an entity's Board of Directors or advisory committees; **Dedham group:** Consultancy; **Haymarket Media:** Other: GME activity ; **Clinical care options:** Other: GME activity ; **Novartis:** Membership on an entity's Board of Directors or advisory committees, Other: GME activity ; **Boston Consulting:** Consultancy; **Curis Oncology:** Other: GME activity ; **Sierra Oncology:** Membership on an entity's Board of Directors or advisory committees. **DeZern:** Sobi: Consultancy; **Novartis:** Membership on an entity's Board of Directors or advisory committees; **Geron:** Membership on an entity's Board of Directors or advisory committees; **Caribou:** Membership on an entity's Board of Directors or advisory committees; **Bristol Myers Squibb:** Consultancy; **Appellis:** Consultancy, Membership on an entity's Board of Directors or advisory committees. **Sekeres:** Geron: Membership on an entity's Board of Directors or advisory committees; **Novartis:** Consultancy, Membership on an entity's Board of Directors or advisory committees; **Kurome:** Consultancy, Current holder of stock options in a privately-held company; **BMS:** Consultancy, Membership on an entity's Board of Directors or advisory committees. **Carraway:** AbbVie: Other; **Stemline Therapeutics:** Consultancy, Speakers Bureau; **BMS:** Consultancy, Research Funding, Speakers Bureau; **Novartis:** Consultancy, Other: Travel, Accommodations, Expenses , Speakers Bureau; **Astex Pharmaceuticals:** Other; **Agios:** Consultancy, Speakers Bureau; **Jazz Pharmaceuticals:** Consultancy, Other: Travel, Accommodations, Expenses , Speakers Bureau; **Daiichi:** Consultancy; **Syndax:** Other: DSMB; **Takeda:** Other; **Celgene:** Research Funding; **Genentech:** Consultancy. **Desai:** BMS: Consultancy, Other: Advisory role; **Servier:** Consultancy, Other: Ad-

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**A.** Distribution of patients (n=2,489) based on International Prognostic Scoring System-Revised (IPSS-R), International Molecular Prognostic Scoring System with missing molecular data (IPSS-M MM), and International Molecular Prognostic Scoring System with available molecular data (IPSS-M AM)

**B.** Kaplan-Meier probability estimate of overall survival (OS) for patients stratified by International Molecular Prognostic Scoring System with missing molecular data (IPSS-M MM) and International Molecular Prognostic Scoring System with available molecular data (IPSS-M AM)

**Figure 1**

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