EHA-6079: Risk Reclassification in Multiple Myeloma: Assessing the Shift from mSMART v3.0 to v4.0

EHA2025 Congress
June 12-15 | Milan, Italy

FELIPE FLORES QUIROZ[1] JORGE HURTADO MARTINEZ[1] SAMUEL BENNION1 MASON BARNES[1] JENNIFER AHLSTROM[1] KARLA MARIANA CASTRO BÓRQUEZ[1] PATRICIA FLORES PÉREZ[1] EDUARDO FRANCO HERNANDEZ[1] ANDREA ROBLES ESPINOZA[1] DIEGO FRANCO HERNÁNDEZ[1] JAY R. HYDREN[1]
1 HealthTree Foundation, South Jordan, Utah, United States of America

HealthTree Foundation

HealthTree Cure Hub® Registry

BACKGROUND

Risk stratification in multiple myeloma (MM) guides treatment decisions by identifying high-risk patients with poorer prognoses. After 2024 IMS Risk Stratification update, the mSMART classification, developed by Mayo Clinic, has evolved from mSMART 3.0 to 4.0, refining high-risk criteria. mSMART 4.0 now requires multiple combinations of specific cytogenetic and genomic abnormalities for high-risk classification, whereas 3.0 labeled single abnormalities as high risk. In addition, it also included clinical features like primary plasma cell leukemia and newly diagnosed patients with extramedullary disease. It also changes the R-ISS staging feature for β2-microglobulin (B2M) levels higher than 5.5 mg/L. This new criteria might focus on better identifying patients with high-risk features, improving the selection of patients that require a more aggressive approach.[1]

AIMS

This study evaluates the concordance between mSMART v3.0 to v4.0 on risk stratification in MM patients, by assessing changes in the classification of high-risk, standard-risk, and specific genetic subgroups, such as double-hit and triple-hit patients.

METHODOLOGY

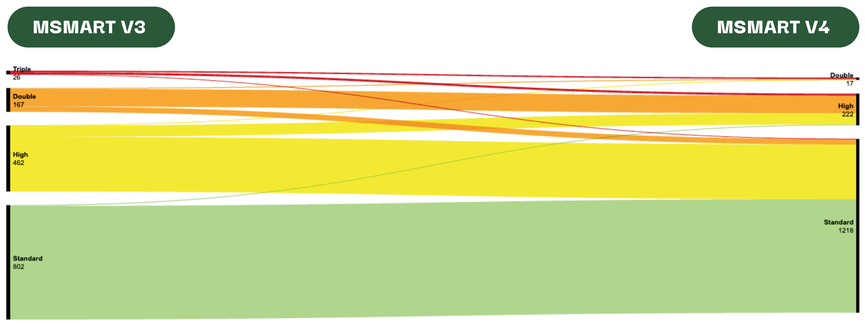
We developed an algorithm that automatically evaluates risk classifications in mSMART v3.0 and v4.0 using the available Electronic Health Records from the HealthTree Cure Hub Registry.[2] This retrospective analysis included a cohort of 274 MM patients, comparing risk categories such as standard risk, high-risk, double-hit, triple-hit, and R-ISS stage 3, based on the updated mSMART v4.0 criteria. Statistical analysis included McNemar's tests to assess changes in classification, with significance set at $p < 0.05$.

RESULTS

A comparative analysis of mSMART versions 3.0 and 4.0 revealed notable shifts in patient risk stratification. While patients initially classified as standard-risk remained unchanged, 84 individuals (77.78%, $p < 0.01$) previously deemed high-risk under version 3.0 were reclassified to standard-risk in version 4.0. Additionally, all patients identified as double-hit in version 3.0 were reassigned to either standard or high-risk categories in version 4.0 ($p < 0.01$), with 26 (66.6%) now categorized as high-risk and 13 (33.3%) as standard-risk. With the removal of triple-hit labeling in the mSMART v4.0, 7 (25%) of patients that were previously categorized as triple-hit were reclassified to double-hit, 20 (71.43%, $p < 0.01$) to high risk and 1 (3.57%) to standard-risk. Notably, 26 patients (54.17%, $p < 0.01$) with R-ISS stage 3 disease were categorized as standard-risk under the updated mSMART guidelines ($p < 0.001$).

MSMART RISK SHIFT FROM V3 TO V4

mSMART Risk Shift	Standard (V4)	High Risk (V4)	Double Hit (V4)
Standard (V3)	796 (99.3%)	6 (0.7%)	0 (0.0%)
High (V3)	383 (82.9%)	78 (16.9%)	1 (0.2%)
Double Hit (V3)	38 (22.8%)	123 (73.7%)	6 (3.6%)
Triple Hit (V3)	1 (3.8%)	15 (57.7%)	10 (38.5%)



Risk Stratification Shift from mSMART V3 to V4 according to RW-EHR data.

CONCLUSION

The transition from mSMART v3.0 to v4.0 has demonstrated a significant 77.8% reduction in the reclassification of high-risk patients, with a marked transition of double-hit patients now categorized as either standard (33.3%) or high-risk (66.6%). In addition, 54.17% of R-ISS stage 3 patients were reclassified as standard-risk. Notably, triple-hit and standard-risk patients in mSMART v3.0 remained at the extreme ends of the risk categories, indicating stability in the reclassification of patients with the highest and lowest risk. The mSMART v4.0 is more selective in finding high-risk patients, possibly addressing prior over classifications tied to genetic abnormalities or R-ISS stage 3 myeloma. Future studies comparing classifications and outcomes between mSMART v3.0 and v4.0 are imperative for understanding the full implications of these changes for prognosis and treatment decisions.

REFERENCES

1. Mikhael et al. Mayo Clin Proc 2013;88:360- 376. v22 //last reviewed Oct 2024
2.Hurtado Martınez, Jorge Arturo, et al. The HealthTree Cure Hub Registry: A Patient-Centered, Multicenter Approach to Advancing Multiple Myeloma Care.

AKNOWLEDGMENTS

Our deepest gratitude to the patients and caregivers who share their data and experiences through HealthTree Cure Hub. Your contributions make this research possible.

CONTACT

For more information or inquiries on clinical research collaboration, please contact our research team:
Reserach@healthtree.org