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ASTCT®
American Society for
Transplantation and Cellular Therapy

2024 Physician Exchange: Myelodysplastic Syndrome

Recent Advances in MDS

- ## Allo transplant for older MDS patients

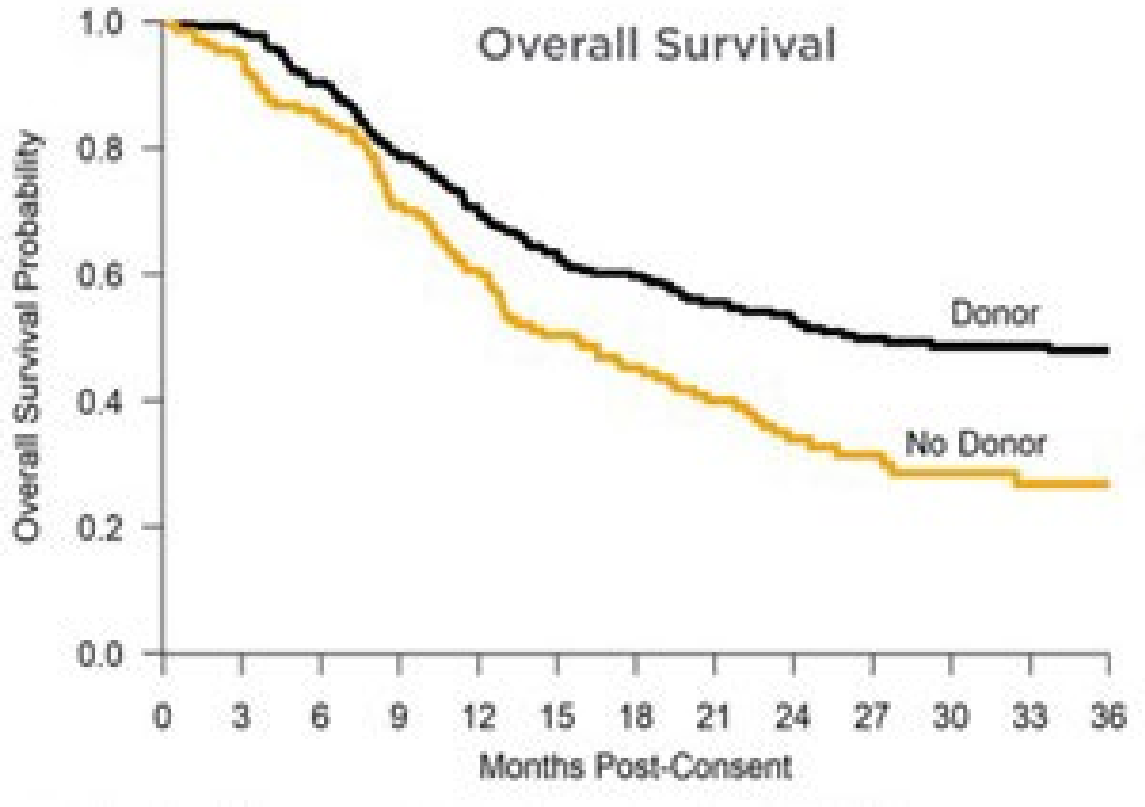
BMT CTN 1102 shows a significant survival advantage with reduced-intensity conditioning HCT over standard care for older patients with MDS.[1]

In a recent study using Connect Myeloid Disease Registry data, the top reason cited that patients with MDS were not referred for HCT consultation was age.[2]

- ## Coverage expansion

CMS recently revised the national coverage determinations for the use of HCT in the treatment of MDS, expanding coverage for bone marrow, peripheral blood, and umbilical cord products based on requests from ASH, ASTCT, NMDP, and CIBMTR.[3]

BMT CTN 1102 Overall Survival



1. Nakamura R, Saber W, Martens MJ, et al. (2021). Journal of Clinical Oncology. DOI: 10.1200/JCO.20.03380.

2. Tomlinson B, de Lima M, Cogle CR, et al. (2023). *Transplantation and Cellular Therapy*. DOI: 10.1016/j.jtct.2023.04.011.

3. Press release. (Mar. 22, 2024). *Business Insider*.

Recent Advances in MDS

- ## ASTCT evidence-based guidelines

ASTCT published an evidence-based review on HCT in the management of MDS, reinforcing HCT as the only curative treatment option.[1]

- ## IPSS-M risk classification

Molecular risk stratification is now available for MDS, improving previous IPSS-R categorizations, with many patients more at-risk than previously indicated.[2]

- ## Molecular prognostication tools support new transplant considerations

Specific mutations like RAS-pathway mutations, RUNX1, ASXL1, and TP53 have emerged as indicators for heightened risk of post-transplant relapse.[3]

- Guide decisions regarding the optimal timing of transplant
- Intensity of conditioning regimens
- Potential inclusion of patients in clinical trials focusing on high-risk disease
- Post-transplant maintenance strategies
- Germ line predisposition should significantly influence the process of donor selection

1. DeFilipp Z, Ciurea SO, Culter C, et al. (2023). *Transplantation and Cellular Therapy*. DOI: 10.1016/j.jtct.2022.11.014.

2. Bernard E, Tuechler H, Greenberg PL, et al. (2022). *NEJM Evidence*. DOI: 10.1056/EVIDoa2200008.

3. Mina A, Greenberg PL & Deeg HJ. (2024). *Blood*. DOI: 10.1182/blood.2023023005.

Challenging MDS Cases

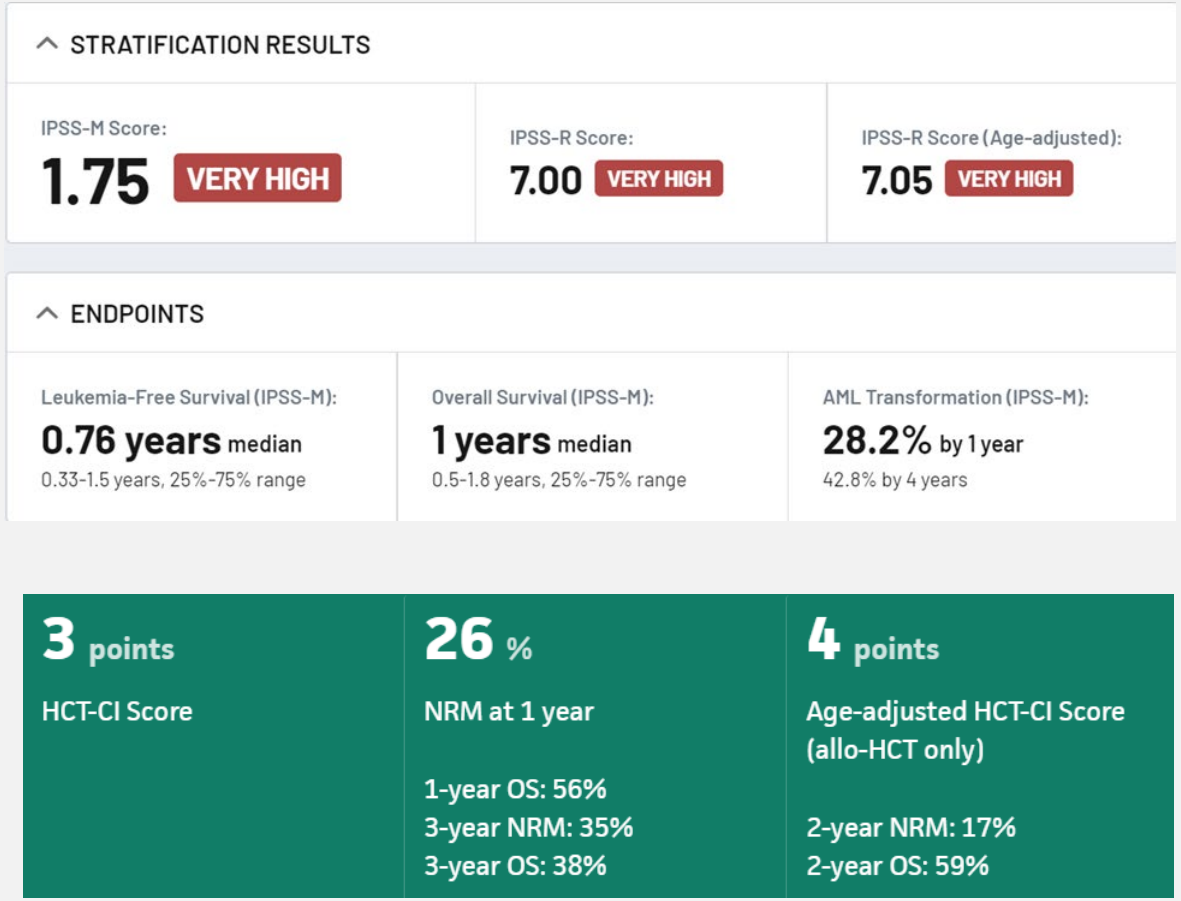
MDS Case 1 | MDS Case 2 | MDS Case 3

Age: 73
Sex: Female
Race/Ethnicity: Black, African
Diagnosis: Very high risk MDS
Diagnosis Date: 4 months ago

Initial CBC: WBC 2 × 10^9/L, ANC 0.8 X10^9/L, Hgb 6g/dL, Plts 60k
Bone marrow biopsy: Presence of trilineage dysplasia, increased myeloblasts 7%, abnormal megakaryocytes. These findings are consistent with a diagnosis of MDS with increased blasts (MDS-EB1)

Cytogenetics: -7
Molecular testing: DNMT3A 20%
IPSS-R: 7
IPSS-M: 1.75

Performance status: ECOG 1, KPS 80%, used to walk 30 min 3x/week before diagnosis
Co-morbidities: HTN, Type II DM on oral therapy, dyslipidemia, creatinine stable at 1.4, FEV1 82%, DLCO2 adj 72%; HCT CI 3
Treatment: Hypomethylating agent
Response: After 4 cycles of azacitidine, having prolonged neutropenia ANC 0.7 X10^9/L, improved thrombocytopenia 90k and anemia Hgb 8g/dL, decreased bone marrow blasts 4%
Transfusion Dependency: 5 PRBC transfusions since diagnosis
Complications: Fatigue, dyspnea with exertion
Social: Lives 3 hours from nearest transplant center. Retired on Medicare. Children are grown and live out of state, pt worries about being burden to husband and family
Preliminary Donor Search Findings: No siblings, 2 haploidentical children. A few 8/8 and many available 7/8 unrelated donors



MDS Case 1 | MDS Case 2 | MDS Case 3

Age: 68

Sex: Male

Race/Ethnicity: White, non-Hispanic

Diagnosis: MDS with low blasts

Diagnosis Date: New diagnosis

Initial CBC: WBC 2.8 × 10^9/L, ANC 1.2 X10^9/L, Hgb 6g/dL, Plts 80k

Bone marrow biopsy: Presence of dysplastic changes primarily in the erythroid lineage, dysplastic megakaryocytes, absence of significant dysplasia in the granulocytic lineage with 4% myeloblasts. These findings are consistent with a diagnosis of MDS with low blasts

Cytogenetics: Normal karyotype

Molecular testing: MDS NGS panel showed ASXL1, SRSF2, UTAF1 mutated

IPSS-R: 4

IPSS-M: 1.25

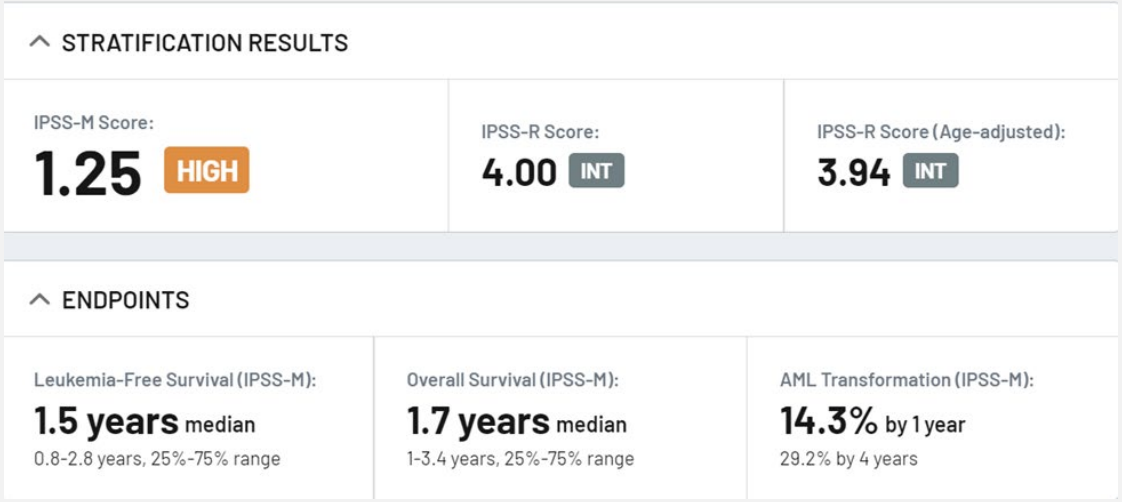
Co-morbidities: 40 pack-year smoker, no longer actively smoking, mild COPD, Type II DM on oral medications, HTN

Performance Status: ECOG 1

Prior treatment: Not started

Transfusion Dependency: Received 1 PRBC transfusion

Preliminary Donor Search Findings: Haploidentical child and sibling. Multiple 8/8 matches on the registry



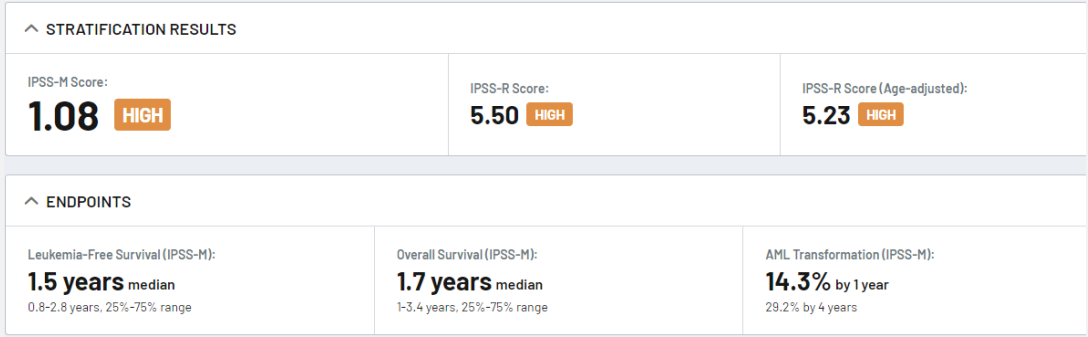
MDS Case 1 | MDS Case 2 | MDS Case 3

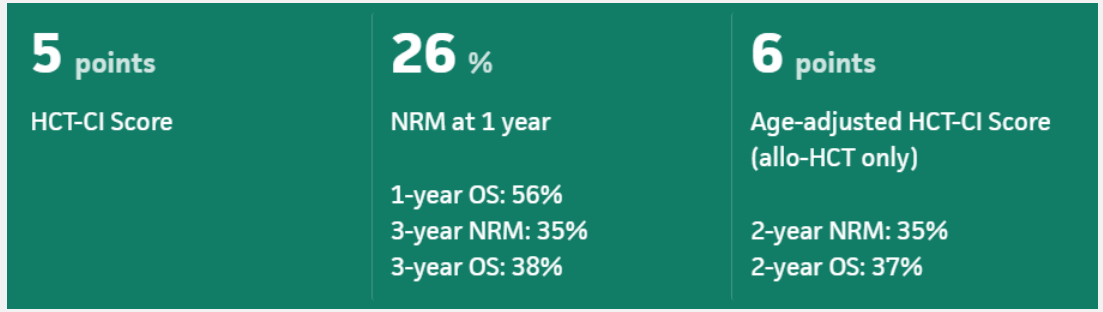
Age: 58
Sex: Male
Race/Ethnicity: Asian American
Diagnosis: High risk MDS
Diagnosis Date: 2 months ago

Bone marrow biopsy: Presence of dysplastic changes affecting multiple lineages with increased blasts (5-9%). These findings are consistent with a diagnosis of MDS with increased blasts (MDS-EB1)
Cytogenetics: (del(7q))/ monosomy 7

Molecular testing: ASXL1, SRSF2 mutated
IPSS-R: 5.5
IPSS-M: 1.08

Performance status: ECOG 3, significant decline since 6 mo ago with significant weight loss
Co-morbidities: chronic venous stasis disease, prior CABG, afib s/p ablation, FEV1 82%, DLCO2 adj 72%, type II DM on oral meds
Prior treatment: On azacitadine since diagnosis
Transfusion Dependency: PRBC to maintain Hgb>7g/dl or if symptomatic
Complications: Confined to chair or bed most hours of the day due to weakness and fatigue
Preliminary Donor Search Findings: unknown, two siblings





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Thank you!