

Real-world Data on Treatments and Clinical and Economic Outcomes for Patients with Myelodysplastic Syndrome (MDS) by Revised International Prognostic Scoring System (IPSS-R) Scores at a Tertiary Care Center

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KEY FINDINGS & CONCLUSIONS

- These real world-data from a tertiary care center confirm the low likelihood of MDS patients achieving and maintaining complete remission
- Few patients received an allogenic stem cell transplant or received second-line therapy, revealing a large unmet need
- Specific genetic profiles may lead to targeted treatments and management of relevant comorbidities
- The healthcare resource utilization and healthcare charges were higher in the high-risk cohort and represent areas for improvement

This study is sponsored by Novartis Pharma AG

Poster presented at the Society of Hematologic Oncology Annual Meeting, held virtually on 8-11 September 2021

INTRODUCTION

- The myelodysplastic syndromes (MDS) include a group of hematopoietic stem cell disorders that are characterized by reduced production of red blood cells, platelets, and mature granulocytes
- The Revised International Prognostic Scoring System (IPSS-R) uses bone marrow blast percentage, karyotype, hemoglobin, platelets, and absolute neutrophil count to classify risk of disease progression as very low-, low-, intermediate-, high-, or very high-risk
- Treatment decisions are largely based on IPSS-R and patient symptoms
- Recent data show mutational profiling may improve the prognostic stratification of MDS
- Minimal real-world evidence exists for this patient population, especially those who failed hypomethylating agent (HMA) therapy
- Primary objectives were to assess treatment patterns and clinical and economic outcomes by risk category

METHODS

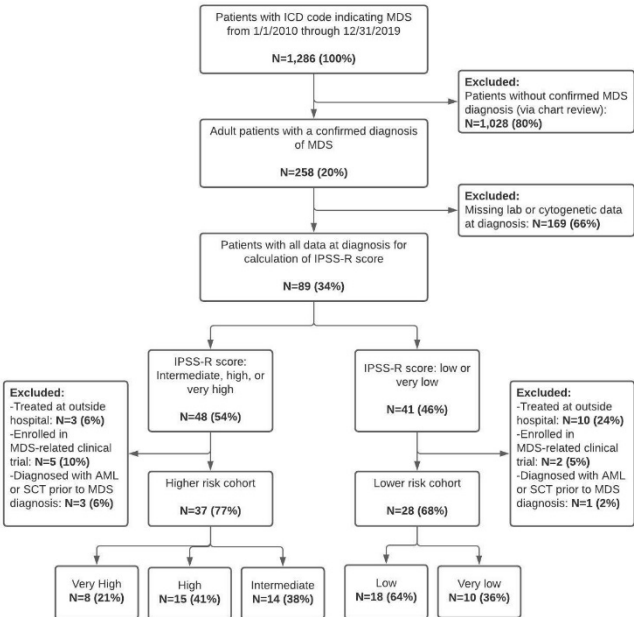
- A retrospective cohort study design was used to assess real-world, patient-level data of adults diagnosed with MDS between 2010-2019 who received initial treatment for MDS at the Huntsman Cancer Institute (HCI)
 - Clinical data were abstracted from the EMR via manual chart review and from discrete fields
 - Healthcare charges were calculated using both pharmacy and medical hospital claims information
 - Patients enrolled in MDS treatment related clinical trial during study period were excluded
- For this analysis, patients with an intermediate to very-high IPSS-R score were categorized in to the “**higher risk (HR)**” cohort; those with low or very low-risk IPSS-R score were categorized to the “**lower risk (LR)**” cohort
- IPSS-R scores were manually calculated based on EMR data by the research team, if EMR data was unavailable, physician documented IPSS-R scores at diagnosis were used

DISCUSSION

- This study was limited by the low number of patients with a calculable IPSS-R score at diagnosis
- These results are from a single academic cancer center and may not be generalizable to a wider population of AML patients
- Future publications will include a combined analysis with another academic cancer center for a total sample size of >350 MDS patients
- Health care charges were not converted to health care costs, which limits direct comparison to published costs in other studies

RESULTS

Figure 1. Patient Flow Diagram



AML: Acute myeloid leukemia; SCT: Stem cell transplant

Table 1. Baseline Patient Characteristics

Variables	LR (n=28)	HR (n=37)	All (n=65)
Age, mean (SD)	69 (10.9)	67 (11.7)	68 (11.4)
Sex, n (%)			
Male	15 (54)	16 (43)	31 (48)
Female	13 (46)	21 (57)	34 (52)
Ethnicity, n (%)			
Caucasian/White	25 (89)	34 (92)	59 (91)
Asian/Pacific Islander	2 (7)	1 (3)	4 (5)
Hispanic/Latino	1 (4)	1 (3)	2 (3)
Unknown	0 (0)	1 (3)	1 (2)
Insurance Type, n (%)			
Commercial	6 (21)	13 (35)	19 (29)
Medicare	19 (68)	16 (43)	35 (54)
Medicaid	1 (4)	2 (5)	3 (5)
Uninsured	1 (4)	6 (16)	7 (11)
Other/Unknown	1 (4)	0 (0)	1 (2)
Region, n (%)			
Utah	25 (89)	27 (73)	52 (80)
Non-Utah	3 (11)	10 (27)	13 (20)
MDS diagnosis year, n (%)			
2017-2019	12 (43)	19 (51)	31 (48)
2014-2016	13 (46)	14 (38)	27 (42)
2010-2013	3 (11)	4 (11)	7 (11)

Table 1. Baseline Patient Characteristics (continued)

Variables	LR (n=28)	HR (n=37)	All (n=65)
Comorbidities from medical histories, n (%)			
AIDS	0 (0)	0 (0)	0 (0)
Autoimmune disorders	2 (7)	3 (8)	5 (8)
Cerebrovascular disease	0 (0)	3 (8)	3 (5)
Chronic pulmonary disease	0 (0)	3 (8)	3 (5)
Congestive heart failure	1 (4)	4 (11)	5 (8)
Dementia	0 (0)	0 (0)	0 (0)
Diabetes with complications	3 (11)	0 (0)	3 (5)
Diabetes without complications	2 (7)	3 (8)	5 (8)
Hemiplegia or paraplegia	1 (4)	0 (0)	1 (2)
Mild liver disease	1 (4)	0 (0)	1 (2)
Moderate/Severe liver disease	1 (4)	0 (0)	1 (2)
Myocardial Infarction	4 (14)	1 (3)	5 (8)
Peripheral vascular disease	1 (4)	0 (0)	1 (2)
Renal disease	9 (32)	1 (3)	10 (15)
Rheumatologic disease	0 (0)	2 (5)	2 (3)
BMI, mean (SD)	25.3 (4.1)	28.7 (6.5)	27.2 (5.8)
WHO classification, n (%)			
MDS with single lineage dysplasia (MDS-SLD)	0 (0)	2 (5)	2 (3)
MDS with multilineage dysplasia (MDS-MLD)	8 (30)	8 (22)	16 (25)
MDS with ring sideroblasts (MDS-RS), NOS	2 (7)	2 (5)	4 (6)
MDS-RS-SLD	1 (4)	0 (0)	1 (2)
MDS-RS-MLD	0 (0)	0 (0)	0 (0)
MDS with excess blasts (MDS-EB), NOS	1 (4)	1 (3)	2 (3)
MDS-EB-1	0 (0)	2 (5)	2 (3)
MDS-EB-2	0 (0)	4 (11)	4 (6)
MDS with isolated del(5q)	2 (7)	4 (11)	6 (9)
MDS, unclassified (MDS-U)	7 (26)	8 (22)	15 (23)
Refractory cytopenia of childhood (provisional)	0 (0)	0 (0)	0 (0)
Unknown	6 (22)	6 (16)	12 (19)
ECOG performance status, n (%)			
Grade 0	4 (15)	4 (11)	8 (13)
Grade 1	7 (26)	9 (24)	16 (25)
Grade 2	1 (4)	2 (5)	3 (5)
Grade 3+	2 (7)	2 (6)	4 (7)
Unknown	13 (48)	20 (54)	33 (52)
Blast count, median (IQR)	2.0 (1.0-3.3)	7.0 (3.0-11.1)	3.4 (2.0-9.2)
Cytogenetic Risk Category at Diagnosis			
Very good	1 (4)	0 (0)	1 (2)
Good	11 (41)	11 (30)	22 (34)
Normal	9 (33)	10 (27)	19 (30)
Intermediate	3 (11)	7 (19)	10 (16)
Poor	1 (4)	8 (22)	9 (14)
Very Poor	0 (0)	1 (3)	1 (2)
Unknown	2 (7)	0 (0)	2 (3)
Absolute neutrophil count, median (IQR)	2.0 (1.0-4.1)	1.2 (0.5-3.0)	1.7 (0.8-3.6)
Hemoglobin, median (IQR)	10.3 (8.5-11.4)	8.4 (7.5-10.3)	9.5 (8.0-10.9)
Platelets, median (IQR)	110 (81-285)	76 (42-149)	83 (55-213)
Secondary MDS, n (%)			
Yes	1 (4)	7 (19)	8 (12)
No	22 (79)	29 (78)	51 (78)
Unknown	5 (18)	1 (3)	6 (9)

- There were more females in the HR cohort
- One-third of patients in LR cohort had a diagnosis of renal disease
- Patients in HR cohort had a higher proportion of MDS with excess blasts
- The HR cohort was more profoundly cytopenic in all 3 cell lineages
- A higher proportion of patients in the HR cohort had secondary MDS

Table 2. Somatic Variants Identified on Myeloid Next-Generation Sequencing (NGS) Panel

Gene, N (%)	LR (n=23)	HR (n=35)	All (n=58)
<i>DNMT3A</i>	5 (22)	6 (17)	11 (19)
None	2 (9)	6 (17)	8 (14)
<i>ASXL1</i>	3 (13)	4 (11)	7 (12)
<i>TP53</i>	2 (9)	5 (14)	7 (12)
<i>IDH2</i>	4 (17)	2 (6)	6 (10)
<i>RUNX1</i>	4 (18)	2 (6)	6 (10)
<i>SRSF2</i>	3 (13)	3 (9)	6 (10)
<i>JAK2</i>	2 (9)	2 (6)	4 (7)
<i>STAG2</i>	2 (9)	2 (6)	4 (7)
<i>U2AF1</i>	3 (13)	1 (3)	4 (7)
<i>SF3B1</i>	4 (18)	0 (0)	4 (6)
<i>BCOR</i>	1 (4)	2 (6)	3 (5)
<i>CEBPA</i>	1 (4)	2 (6)	3 (5)
<i>EZH2</i>	2 (9)	1 (3)	3 (5)
<i>GATA2</i>	1 (4)	2 (6)	3 (5)
<i>KMT2A</i>	2 (9)	1 (3)	3 (5)
<i>NRAS</i>	1 (4)	2 (7)	3 (5)
<i>TET2</i>	2 (9)	1 (3)	3 (5)
<i>ASXL2</i>	0 (0)	2 (6)	2 (3)
<i>ETNK1</i>	1 (4)	1 (3)	2 (3)
<i>ZRSR2</i>	1 (4)	1 (3)	2 (3)

- Includes patients that received any NGS testing (n=58)
- Includes genes that were altered in at least 2 patients
- DNMT3A* was the most commonly altered gene
- TP53* was commonly altered, with a slightly higher proportion seen in the HR cohort

Table 3. Treatment Patterns

Variables	LR (n=28)	HR (n=37)	All (n=65)
First-line MDS-related therapy			
Days to treatment initiation, median (IQR)	291 (75-579)	32 (11-55)	37.5 (19-345)
Azacitidine, n (%)	14 (50)	22 (59)	36 (55)
Days of therapy, median (IQR)	165 (90-408)	39 (7-103)	73 (7-219)
Number of cycles, median (IQR)	5.5 (4-13)	2 (1-5)	4 (1-7)
Decitabine, n (%)	1 (4)	1 (3)	2 (3)
Lenalidomide, n (%)	2 (7)	2 (5)	4 (6)
Other [‡] , n (%)	0 (0)	2 (5)	2 (3)
None [§] , n (%)	11 (39)	10 (27)	21 (32)
Second-line MDS-related therapy, n (%)			
Decitabine	0 (0)	1 (3)	1 (2)
Cytarabine	0 (0)	1 (3)	1 (2)
Lenalidomide	1 (4)	1 (3)	2 (4)
Other [‡]	1 (4)	0 (0)	1 (2)
Transplant, n (%)			
Stem cell transplant	5 (18)	13 (35)	18 (28)
Post treatment	4 (80)	9 (69)	13 (72)
After CR, PR, or SD	2 (50)	8 (89)	10 (77)
After DP, IR	2 (50)	1 (11)	3 (23)
Pre-treatment	0 (0)	2 (15)	2 (11)
No treatment	1 (20)	2 (15)	3 (17)

CR: Complete response; PR: partial remission; SD: Stable disease; DP: Disease progression; IR: Incomplete response

[‡]Ruxolitinib, hydroxyurea (first-line); enasidenib (for second-line)

[§]Supportive care or growth factor was received by 10 (91%) LR and 8 (80%) HR patients with no first-line treatment

- Median follow-up of patients with no first-line treatment was: 580 days
- HR cohort initiated therapy sooner and received fewer cycles
- HR cohort was more likely to undergo stem cell transplant

Table 4. Treatment Response to First-line Therapy

Physician-documented First-line Treatment Response, n (%)	First-line treatment HMA (n=38)	Other [‡] (n=6)	Total (n=44)	Received HMA [‡] LR (n=15)	HR (n=23)
Complete response	2 (5)	0 (0)	2 (5)	1 (7)	1 (4)
Marrow complete remission	3 (8)	0 (0)	3 (7)	0 (0)	3 (13)
Partial remission	2 (5)	0 (0)	2 (5)	1 (7)	1 (4)
Stable disease	16 (42)	1 (17)	17 (39)	7 (47)	9 (39)
Treatment failure	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Disease progression	11 (29)	1 (17)	12 (27)	5 (33)	6 (26)
Death	1 (3)	0 (0)	1 (2)	0 (0)	1 (4)
Unknown	3 (8)	4 (67)	7 (16)	1 (7)	2 (9)
Days to best response, median (IQR)	113 (48-115)	NA	113 (48-115)	144.5 (113-176)	64 (48-114)

[‡]Ruxolitinib, hydroxyurea, lenalidomide

[§]Only HMA monotherapy was observed in this patient population

- Days to best response includes patients with a complete or partial response
- There was low response to treatment, especially among patients not treated with a HMA

Table 5. Healthcare Resource Utilization

Encounter Type	LR (n=28)	HR (n=37)	All (n=65)
MDS-related, median per patient per month (IQR)			
Hospital admissions	0 (0)	0 (0)	0 (0)
Days in the hospital	0 (0)	0 (0)	0 (0)
Office visits	2 (4)	3 (5)	3 (4)
All-cause, median per patient per month (IQR)			
Hospital Admissions	0 (0)	0 (0)	0 (0)
Days in the hospital	0 (1)	0 (0)	0 (0)
Office visits	7 (6)	13 (11)	9 (10)

- There were higher rates of healthcare resource utilization in the HR cohort

Figure 2. Progression-free Survival

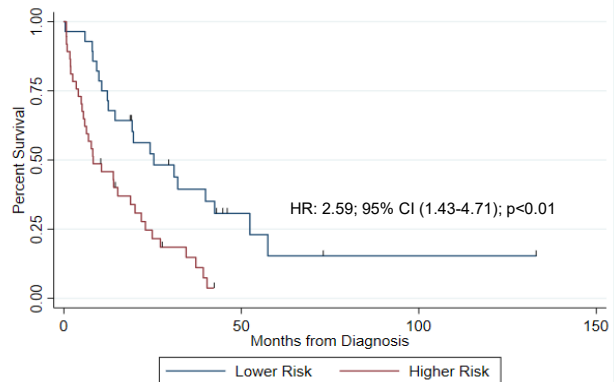
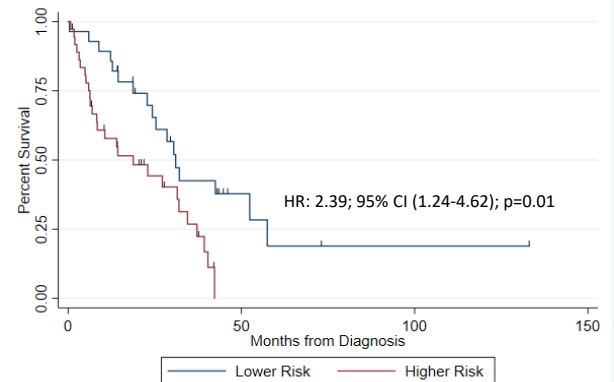


Figure 3. Overall Survival



- Includes all study patients (n=65)
- Median PFS from diagnosis of 25 and 8 months for LR and HR cohorts, respectively
- Median follow-up to AML progression, death, or last visit: 432 days

- Includes all study patients (n=65)
- Median OS from diagnosis of 31 and 19 months for LR and HR cohorts, respectively
- Median follow-up to death or last visit: 580 days

Acknowledgements

This investigation was supported by the University of Utah Population Health Research (PHR) Foundation, with funding in part from the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR002538 (formerly 5UL1TR001067-05, 8UL1TR000105 and UL1RR025764)

Research reported in this publication was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number UL1TR002538. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health