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POSTER ABSTRACTS

637.MYELODYSPLASTIC SYNDROMES - CLINICAL AND EPIDEMIOLOGICAL

Characteristics and Outcomes of Younger Adult Patients (Pts) with Myelodysplastic Syndromes (MDS): A Multicenter Retrospective Study

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Introduction:
MDS are primarily diseases of the elderly, with median age at diagnosis of 72 years. Focused data on clinical and molecular characteristics, as well as outcomes, in younger pts under age 60 years are limited. We conducted this multicenter retrospective study to describe pt characteristics, cytogenetic and molecular profiles, treatment modalities, and outcomes in younger pts with MDS, including adolescent and young adults (AYA).

Methods:
The study included pts diagnosed with MDS between 2002-2023 at 7 academic centers. We compared baseline characteristics, treatment, and outcomes of AYA (18-39 years) and younger adult (YA) pts (40-59 years). Responses were assessed using the modified IWG 2006 response criteria which included complete remission (CR), marrow CR (mCR), and hematologic improvement (HI). Wilcoxon rank sum test and Fisher's exact (and Chi-square) test were used to compare pt and disease characteristics for continuous and categorical variables, respectively. Overall survival (OS) was estimated using the Kaplan-Meier method and compared using log-rank test.

Results:
A total of 173 pts were identified (AYA, N=50; YA, N=123). Median age at diagnosis was 50 years (range, 18-59), with 51% females. Baseline characteristics are shown in Table 1. Therapy-related MDS (t-MDS) was observed in 40 pts (23%) with the remaining classified as *de novo* MDS (N=133; 77%). Inherited bone marrow failure syndromes were documented in 15 pts (9%), with Shwachman-Diamond Syndrome (N=4) and Fanconi anemia (N=4) being the most frequent. Using the WHO 2016 classification, the most common subtypes of MDS in both the AYA and YA cohorts were MDS with multilineage dysplasia (38% vs 19%), MDS with excess blasts-2 (MDS-EB) (24% vs 29%), and MDS-EB-1 (16% vs 20%). Similarly, using the WHO 2022 classification, the most common subtypes were MDS with low blasts (50% vs 21%), MDS with increased blasts-2 (MDS-IB-2) (24% vs 24%), and MDS-IB-1 (16% vs 18%). Stratifying pts using the IPSS-R cytogenetic (CG) risk group, the most common CG

risk category identified was good CG (34% vs 52%, *p*=0.012). Poor/very poor CG were present in 34% and 37% of the AYA and YA groups, respectively. *STAG2* and *NRAS* mutations occurred more frequently in the AYA pts compared to the YA group, while the YA cohort was enriched for the following mutations: *TP53*, *DNMT3A*, *SF3B1*, *SRSF2*, and *TET2* (Figure 1).
In the AYA population, 18 pts (38%) had very low/low, 10 (21%) intermediate, and 20 pts (42%) had high/very high risk MDS using IPSS-R. In the YA population, 32 pts (26%) had very low/low, 32 (26%) intermediate, and 57 pts (47%) had high/very high risk MDS using IPSS-R. Twenty-seven percent of pts with very low to intermediate-risk MDS using IPSS-R were upstaged to moderate high to very high-risk MDS using IPSS-M. The majority of pts (AYA: 75%; YA: 63%, *p*=0.5) were transfusion independent at baseline. Single-agent hypomethylating agents were the most frequently used frontline therapy, used in 17 AYA pts (34%) and 58 YA pts (48%), with more AYA pts receiving upfront allogeneic stem cell transplantation (Allo-SCT) compared to YA pts (28% vs 5%). After frontline therapy (Table 1), an additional 14 AYA (28%) and 52 YA (42%) pts received Allo-SCT. In pts with IPSS-R intermediate to very high-risk, response rates (HI+CR+mCR+mCR with HI) to frontline therapies were 46% and 54.5% in the AYA and YA groups, respectively.
After median follow-up of 24 months [range, 1-218], median OS was numerically longer in the AYA versus YA group (155 vs 53 months, *p*=0.2). AML transformation occurred in 24% and 20% of the pts in the AYA and YA groups, respectively. Median OS was significantly longer in *de novo* compared to t-MDS pts (56 vs 27 months, *p*=0.03). Median OS among Allo-SCT compared to non-SCT pts were not reached vs 155 months (*p*=0.9) in the AYA group and 53 vs 54 months (*p*=0.4) in the YA group. IPSS-R (very low+low vs intermediate vs high+very high) was able to distinguish differences in OS in the YA (133 vs 53 vs 17 months, *p*=0.0002) and AYA (155 vs not reached vs 18 months, *p*=0.006) pts, with the exception of the intermediate-risk group in the AYA cohort.
Conclusions: In this study, d *e novo*MDS was seen in the majority of younger pts with MDS (both AYA and YA). Mutations in *STAG2* and *NRAS* were more common in the AYA pts, while YA pts had MDS more enriched for *TP53, DNMT3A, TET2* and splicing mutations. This study is still ongoing with a plan to compare the abovementioned groups to older pts (≥60 years) with MDS.

Disclosures Abaza: *Rigel:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Biomea:* Research Funding; *Novartis:* Research Funding; *BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Kite:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Servier:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Astellas:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Curis:* Research Funding; *Biosight:* Research Funding; *ALX Oncology:* Research Funding. **Desai:** *Janssen Research & Development:* Research Funding; *BMS:* Consultancy, Other: Advisory role; *Abbvie:* Consultancy, Other: Advisory role; *Servier:* Consultancy, Other: Advisory role; *Janssen Pharmaceuticals:* Current Employment. **Shallis:** *Gilead Sciences:* Consultancy; *Servier:* Consultancy; *Curio Science:* Consultancy; *Bristol Myers Squibb:* Consultancy; *Rigel:* Consultancy. **Patel:** *AbbVie:* Honoraria; *Kronos Bio:* Research Funding; *Pfizer:* Research Funding; *BMS:* Honoraria. **Sallman:** *AbbVie, Affimed Gmbh, Gilead, Incyte, Intellisphere, LLC, Molecular Partners AG, PGEN Therapeutics, Inc., Takeda, Zentalis; Advisory board for AvenCell, BlueBird Bio, BMS, Intellia, Jasper Therapeutics, Kite, Magenta Therapeutics, NKARTA, Novartis, Orbita:* Consultancy; *Aprea, Jazz:* Research Funding. **Roboz:** *Syndax:* Consultancy; *Pfizer:* Consultancy; *Novartis:* Consultancy; *Mesoblast:* Consultancy; *MEI:* Consultancy; *Takeda:* Consultancy; *Jazz:* Consultancy; *Jasper:* Consultancy; *Janssen:* Consultancy, Research Funding; *GSK:* Consultancy; *Bluebird bio:* Consultancy; *Blueprint:* Consultancy; *BMS:* Consultancy; *AZ:* Consultancy; *Astellas:* Consultancy; *Amgen:* Consultancy; *Agios:* Consultancy; *AbbVie:* Consultancy; *Actinium:* Consultancy. **Carraway:** *Agios:* Consultancy, Speakers Bureau; *Stemline Therapeutics:* Consultancy, Speakers Bureau; *Jazz Pharmaceuticals:* Consultancy, Other: Travel, Accommodations, Expenses , Speakers Bureau; *Celgene:* Research Funding; *AbbVie:* Other; *Syndax:* Other: DSMB; *Genentech:* Consultancy; *Astex Pharmaceuticals:* Other; *Novartis:* Consultancy, Other: Travel, Accommodations, Expenses , Speakers Bureau; *Daiichi:* Consultancy; *BMS:* Consultancy, Research Funding, Speakers Bureau; *Takeda:* Other. **Zeidan:** *Syros:* Consultancy, Honoraria; *Foran:* Consultancy, Research Funding; *Tyme:* Consultancy, Honoraria; *Shattuck Labs:* Research Funding; *Astex:* Research Funding; *Regeneron:* Consultancy, Honoraria; *Schrödinger:* Consultancy, Honoraria; *Zentalis:* Consultancy, Honoraria; *Mendus:* Consultancy, Honoraria; *Orum:* Consultancy, Honoraria; *Notable:* Consultancy, Honoraria; *Lox Oncology:* Consultancy, Honoraria; *BioCryst:* Consultancy, Honoraria; *ALX Oncology:* Consultancy, Honoraria; *Kura:* Consultancy, Honoraria; *Chiesi:* Consultancy, Honoraria; *Gilead:* Consultancy, Honoraria; *Syndax:* Consultancy, Honoraria; *Epizyme:* Consultancy, Honoraria; *Genentech:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria; *Amgen:* Consultancy, Honoraria; *Ionis:* Consultancy, Honoraria; *Takeda:* Consultancy, Honoraria; *BeyondSpring:* Consultancy, Honoraria; *Otsuka:* Consultancy, Honoraria; *Taiho:* Consultancy, Honoraria; *Seattle Genetics:* Consultancy, Honoraria; *Geron:* Consultancy, Honoraria; *Daiichi Sankyo:* Consultancy, Honoraria; *Astellas:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria; *Boehringer-Ingelheim:* Consultancy, Honoraria; *Servier:* Consultancy, Honoraria; *Agios:* Consultancy, Honoraria; *Incyte:* Consultancy, Honoraria; *Jazz:* Consultancy, Honoraria; *Celgene/BMS:* Consultancy, Honoraria; *Pfizer:* Consultancy, Honoraria; *AbbVie:* Consultancy, Honoraria. **Patnaik:** *Kura Oncology:* Research Funding; *CTI Pharmaceuticals:* Membership on an entity's Board of Directors or advisory committees; *StemLine:* Research Funding. **Altman:** *Fujifilm:* Consultancy, Research Funding; *Bristol Myers Squibb:* Consultancy, Research Funding; *Celgene:* Consultancy, Research Funding; *Aptose Biosciences:* Consultancy, Research Funding; *Boehringer Ingelheim:* Consultancy, Research Funding; *Aprea AB:* Consultancy, Research Funding; *Amgen:* Consultancy, Research Funding; *Amphivena:* Consultancy, Research Funding; *Syros:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *MD Education:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Agios:* Consultancy, Research

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Table 1: Baseline Patient Characteristics' and Frontline Treatment

Characteristics/Variables, N (%)	AYA (18-39 years) (N=50)	YA (40-59 years) (N=123)	*P* value
Median age (years) [range]	28 [18-39]	54 [40-59]	<0.001
Type of MDS			0.43
De Novo	41 (82)	92 (75)	
Therapy related	9 (18)	31 (25)	
2016 WHO Subtype			0.1
Isolated deletion 5q	1 (2)	5 (4)	
Single-lineage dysplasia (SLD)	5 (10)	4 (3)	
Multilineage dysplasia (MLD)	19 (38)	23 (19)	
RS-MLD	4 (8)	18 (15)	
RS-SLD	0 (0)	5 (4)	
Excess blasts 1	8 (16)	25 (20)	
Excess blasts 2	12 (24)	36 (29)	
MDS unclassifiable	1 (2)	4 (3)	
Unknown	0 (0)	3 (2)	
2022 WHO Subtype			0.01
MDS- isolated del 5q (low blasts)	1 (2)	5 (4)	
MDS-*SF3B1* mutation (low blasts)	1 (2)	10 (8)	
MDS with biallelic *TP53*	2 (4)	16 (13)	
MDS with low blasts	25 (50)	26 (21)	
MDS-IB1	8 (16)	22 (18)	
MDS-IB2	12 (24)	30 (24)	
MDS with fibrosis (MDS-f)	0 (0)	1 (1)	
MDS hypoplastic (MDS-h)	1 (2)	5 (4)	
Unknown	0 (0)	8 (7)	
2022 ICC MDS Subtype			0.02
MDS-*SF3B1*	1 (2)	9 (7)	
MDS-del(5q)	1 (2)	6 (5)	
MDS NOS, without dysplasia	1 (2)	4 (3)	
MDS NOS, with SLD	5 (10)	7 (6)	
MDS NOS, with MLD	21 (42)	24 (20)	
MDS-Excess Blasts	13 (26)	31 (25)	
MDS/AML	7 (14)	15 (12)	
MDS with mutated *TP53*	1 (2)	10 (8)	
MDS/AML with mutated *TP53*	0 (0)	13 (11)	
Unknown	0 (0)	4 (3)	
Median Hemoglobin (g/dL) [range]	8.9 [3.9-15.3]	9.1 [4.6-14.9]	0.58
Median Platelets (10^9/L) [range]	59 [8-306]	80 [5-713]	0.25
Median ANC (10^9/L) [range]	1.4 [0-8.7]	1.4 [0-14.9]	0.63
Median bone marrow blasts (%) [range]	3 [0-18]	5 [0-18]	0.13
IPSS-R			0.079
Very low	1 (2)	12 (10)	
Low	17 (34)	20 (16)	
Intermediate	10 (20)	32 (26)	
High	9 (18)	25 (20)	
Very high	11 (22)	32 (26)	
Unknown	2 (4)	2 (2)	
Frontline therapy			
HMAs alone	17 (34)	58 (47)	
Allo-SCT	14 (28)	6 (5)	
Observation	8 (16)	15 (12)	
Chemotherapy	4 (8)	0 (0)	
HMAs + venetoclax	3 (6)	13 (11)	
ESAs	2 (4)	6 (5)	
Immunosuppressive therapy	1 (2)	1 (1)	
Prednisone	1 (2)	0 (0)	
Lenalidomide	0 (0)	4 (3)	
Clinical trial	0 (0)	15 (12)	
Missing	0 (0)	2 (2)	
Other	0 (0)	1 (1)	
G-CSF	0 (0)	2 (2)	
Allogeneic SCT after frontline therapy (excluding upfront Allo-SCT)	14 (28)	52 (42)	
Total number of Allo-SCT	28 (56)	58 (47)	

Abbreviations: Allo-SCT: allogenic stem cell transplantation; AML: acute myeloid leukemia; ANC: absolute neutrophil count; AYA: adolescent and young adults; ESAs: erythrocyte stimulating agents; G-CSF: granulocyte colony stimulating factor; HMAs: hypomethylating agents; IB: increased blasts; ICC: International Consensus Classification; IPSS-R: revised international prognostic scoring system; MDS: myelodysplastic syndromes; NOS: not otherwise specified; RS: ring sideroblasts; WHO: World Health Organization; YA: younger adult.

Figure 1. Mutation Frequency

Figure 1