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POSTER ABSTRACTS

637.MYELODYSPLASTIC SYNDROMES - CLINICAL AND EPIDEMIOLOGICAL

Hematological Response to Frontline Treatment in Lower Risk Myelodysplastic Syndromes (LRMDS) Is Associated with Better Overall Survival

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Background

The majority of LRMDS patients (pts) (70%) do not progress but unfortunately succumb to complications related to cytopenia, namely anemia and red blood cell transfusion dependency (RBC-TD) or their interplay with co-morbidities. RBC-TD is associated with worse outcome reflecting bone marrow failure and long-term sequela of RBC-TD. There is growing evidence that response to treatment and RBC transfusion independence (TI) are associated with favorable outcome. In lieu of 2 recent randomized clinical trials demonstrating efficacy of luspatercept & imetelstat in LRMDS, we assessed the impact of response to sequential lines of treatment in LR-MDS on overall survival (OS) to guide our treatment choices and to determine whether erythroid stimulating agents (ESA) should still be our 1 st line of therapy.

Methods

We included LRMDS pts (IPSS-R very low & low) from Moffitt Database who received ESA as frontline therapy (FL) and assessed subsequently outcomes with second line (SL) therapy (SOC or clinical trial). We excluded MDS/MPN and del5q pts. We also excluded all pts who eventually progressed to either higher risk MDS or AML to better reflect the majority LRMDS in that disease state. We assessed details of FL and SL. Pts who received FL & SL were then divided into 4 groups based on response to FL and SL therapy: group 1 (no/no), group 2 (no/yes) with response only to SL, group 3 (yes/no) response to FL only, and group 4 (yes/yes) with response to both lines of therapy. Response was defined as hematological improvement (HI) with ≥1.5 g/dl Hgb increase in non-TD pts and RBC-TI in TD pts at baseline for at least for 8 weeks. We compared median OS (mOS) among those groups.

Results

There were 603 LRMDS pts who met eligibility criteria and received ESA as FL (Table-1); 43% were RBC-TD, mean serum EPO was 132 (n=211 pts), 69% received epoetin, 17% darbepoetin and 14% with G-CSF. HI was observed in 42% of pts with no difference among ring sideroblasts (RS) +/- (46% vs 40%, p =.12). Response was higher among non-RBC-TD (52% vs 31%, p< .001). The median time to start ESA was 1.2 mo (0-249). The median time on ESA therapy was 11 mo (.4-213).

331 pts (55%) received SL which included HMA 43% (n= 142), lenalidomide 39% (n=130), luspatercept 7% (n=24), ATG 2% (n=8), investigational agent 4% (n=14), and other 4% (n=13) . The HI rate was 27% (91/331). No difference in HI based on RS nor RBC-TD was observed. The median duration on SL treatment was 6 mo (.1-93).

170 pts (28%) received 3 rd line of therapy with 7% HI, 88 pts (15%) received 4 th line of therapy with 3% HI and 39 pts (7%) had 5 th line of therapy with 2% HI.

Among the 331 pts who received at least FL and SL, pts were divided into 4 groups based on response to (methods, table-2), the mOS was 114 mo among Yes/Yes response group, 103 mo among yes/no group, 97 mo no/yes and 64 mo among no/no (P=.007; Figure-1). Response to FL was significantly associated with better OS after adjusting for RS (HR .74 ,95% CI .55-.99, p=.043).

Conclusions

Only half of patients who receive ESA as FL therapy for LRMDS received any subsequent therapies. Response rates were highest with ESA as FL than any SL therapy. HI with FL and/or SL is associated with improved OS. Lack of response to first line of therapy is associated with worse OS. Responses beyond SL were rarely observed. Identifying and moving agents with high HI rate as FL therapy and or selecting option based on predictors of best chance of response to a specific treatment as FL may lead to better overall survival.

Disclosures Komrokji: *BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Rigel, Taiho, DSI:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Membership on an entity's Board of Directors or advisory committees; *AbbVie, CTI biopharma, Jazz, Pharma Essentia, Servio:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Geron:* Consultancy. **Kuykendall:** *Sierra Oncology:* Research Funding; *AbbVie:* Consultancy; *Blueprint:* Consultancy, Research Funding, Speakers Bureau; *Morphosys:* Consultancy, Research Funding; *BMS:* Consultancy, Research Funding; *Prelude:* Research Funding; *Protagonist Therapeutics, Inc.:* Consultancy, Research Funding; *CTI:* Consultancy; *GSK:* Consultancy; *Imago:* Consultancy; *Incyte:* Consultancy; *Novartis:* Consultancy. **Lancet:** *Jasper Therapeutics:* Consultancy; *Celgene:* Consultancy, Research Funding; *Tegus:* Consultancy; *Servier:* Consultancy; *Jazz:* Consultancy; *Boxer Capital:* Consultancy; *The Dedham Group:* Consultancy; *Globe Life Sciences:* Consultancy; *Peer Voice:* Consultancy; *MD Anderson:* Consultancy; *Novartis:* Consultancy; *BerGenBio / DAVA Oncology:* Consultancy; *Atheneum:* Consultancy; *AbbVie Inc.:* Consultancy; *MEDTalks:* Consultancy. **Padron:** *Gillead:* Membership on an entity's Board of Directors or advisory committees; *CTI:* Membership on an entity's Board of Directors or advisory committees; *Pharmaessentia:* Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Membership on an entity's Board of Directors or advisory committees; *Kura:* Research Funding; *Incyte:* Research Funding; *BMS:* Research Funding. **Sallman:** *Aprea, Jazz:* Research Funding; *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.

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Table-1	Baseline characteristics of Whole Cohort (n=603)				
Variable	**Total n=603 n (%)**				
Age (years)(median)	72				
Sex (male)	382 (63%)				
Race (white)	561 (93%)				
ECOG PS (0-1)	576 (86%)				
RBC-TD at baseline	260 (43%)				
MDS classification					
WHO 2016		**WHO 2022**		**ICC 2022**	
MDS-SLD	105 (17%)	MDS-LB	130 (22%)	MDS-SF3B1	149 (25%)
MDS-MLD	199 (33%)	MDS-SF3B1	153 (25%)	MDS-del5q	2
MDS-RS	273 (45%)	MDSdel5q	2	MDS-TP53	2
MDS-EB1	10 (2%	MDS-TP53	2	MDS-nos	6 (1%)
MDS-EB2	0	MDS-IB1	4 (1%)	MDS-SLD	56 (9%)
MDS-U	7 (3%)	MDS-IB2	1	MDS-MLD	107 (18%)
		MDS-IB-F	1	MDS-EB1	5 (1%)
		h-MDS	9 (2%)	missing	327 (54%)
		MDS-RS-SF3B1WT	23 (4%)		
		missing	276 (46%)		
Risk stratification					
IPSS-R		**IPSS-M**			
Very low	170 (28%)	Very low	31 (5%)		
low	433 (72%)	Low	171 (28%)		
		Moderate low	68 (11%)		
		Moderate high	22 (4%)		
		High	11 (2%)		
		Very High	0		
		missing	300 (50%)		
Baseline Blood counts		**Somatic Mutations**			
Hgb	9.5	*SF3B1* 157/313 (50%)			
WBC	4.4	*TET-2* (96/309) (30%)			
ANC	2.35	*ASXL-1* (65/319) (20%)			
Platelets	196	*DNMT3A* (39/310) (13%)			

Table-2	Baseline characteristics of the groups based on Response to FL and SL				
	NO/NO (n=163)	NO/YES (n=60)	YES/NO (n=77)	YES/YES (n=31)	P Value
Age (median)	72	73	69.6	68.2	.15
Sex (male)	111 (68%)	36 (60%)	50 (65%)	22 (71%)	.65
Race (white)	151 (93%)	58 (97%)	72 (95%)	31 (100%)	.27
MDS-RS	74 (45%)	31 (52%)	47 (61%)	20 (65%)	.06
SF3B1 MT	41/86	16/26	23/40	16/18	.051
IPSS-R Very low low	 39 (24%) 127 (76%)	 6 (10%) 54 (90%)	 19 (25%) 58 (75%)	 11 (36%) 20 (64%)	.03
RBC-TD	101 (62%)	38 (63%)	36 (47%)	16 (52%)	.1

Figure-1 Median OS based on response to FL and SL therapy

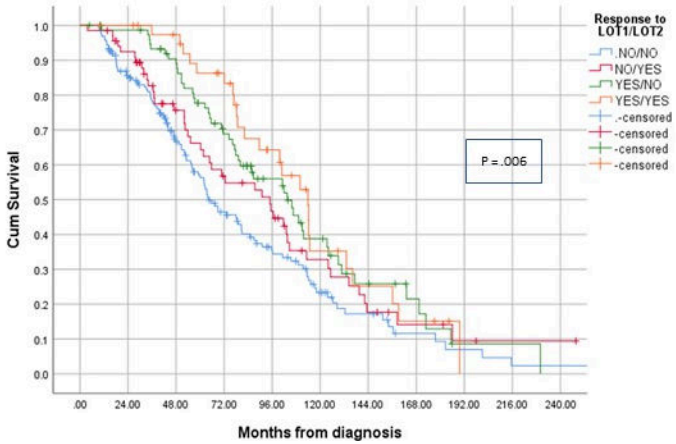

Figure 1