Real-world data in a German healthcare survey demonstrate a high medical need of patients with lower risk MDS and ringsideroblasts #410

Kaivers J.[1], Garz A.-K.[2], Kellermann L.[3], Frank M.[3], Ludäscher M.[3], Schackert N.[2], Gattermann N.[1], Germing U.[1]

[1]Universitätsklinikum Düsseldorf, Klinik für Hämatologie, Onkologie und klinische Immunologie, Düsseldorf, Germany, [2]Celgene I A Bristol Myers Squibb Company, Munich, Germany, [3]Oncology Information Service, Freiburg, Germany

Introduction

- Real-world data on clinical characteristics and management of patients (pts) with lower risk MDS (LR-MDS) in general and especially those with ringsideroblasts (LR-MDS-RS+) are sparse. This representative healthcare survey presents the clinical reality in diagnostics and treatment of MDS in 2019. Results were compared with data of a survey from 2010 in order to reveal changes in general MDS patients´ characteristics and the clinical routine care over the last decade.

Methods

- In 2019 data on 619 patients with MDS were collected anonymously and retrospectively in a representative sample of 49 centres in Germany. The standardized data sheet contained all relevant diagnostic and therapeutic procedures. A patient cohort collected with the same method in 2010 (n=607) was used as a comparative cohort. The selection of centers and collection of patient samples was done in two steps. First, german centers involved in the treatment of MDS (ICD D46.0) were identified and contacted. Second, we defined a patient sample reflecting the general prevalence of MDS patients per center-type and regional population densities.

Results

General prevalence of MDS patients per center-type:

- During the last 10 years an increase towards community care was observed. In the 2010 cohort, 30% were treated in university hospitals (UH), 29% in non-university hospitals (NUH) and 39% in community practices (CP). In the 2019 cohort only 10% of the patients were treated in UH, 28% in NUH, and 61% in CP (p< 0.001) (Tab. 1).

	2019 (n= 619)	2010 (n= 607)
University hospitals	64 (10%)	180 (30%)
Non-university hospitals	170 (28%)	179 (29%)
Community practices	378 (61%)	236 (39%)
n.a.	7 (1%)	12 (2%)

Tab. 1: Distribution according to centers of care (2019 vs. 2010, p<0.001)

General patient characteristics:

- The majority of MDS pts required active treatment (83 % of pts in 2019 vs. 79% of pts in 2010) (data not shown). The following analysis were focused on actively treated pts. Pts with active treatment had a median age of 75 years (yrs) in 2019 vs. 71 yrs in 2010 (Fig. 1).

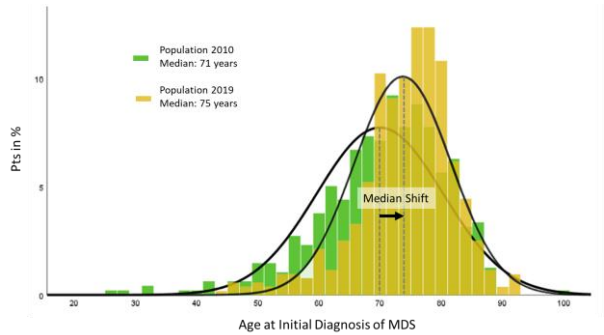

Fig. 1: Development of median age between 2010 and 2019

- There were significantly more pts with an ECOG performance status of 2 or higher in 2019 than in 2010 (p< 0.001) (Tab. 2). Anemia is the first clinical manifestation in ~80% of MDS pts (Table 2).

Treatment pattern – focus anemia treatment:

- Recently, the international MDS working group (IWG) defined criteria to categorize pts with low, intermediate, and high transfusion burden. We find that especially the WHO subtype MDS with RS is characterized by a HTB (Fig. 2). Of note, the frequency of pts with the WHO subtype MDS-RS increases with age (Fig. 3).

	TM MDS 2019			TM MDS 2010		
	Total N=516	< 75 yrs n=251 (49%)	≥ 75 yrs n=265 (51%)	Total N=477	< 75 yrs n=303 (63%)	≥ 75 yrs n=174 (37%)
Gender Male	296 (57%)	131 (52%)	165 (63%)	265 (56%)	166 (55%)	99 (57%)
Age Median (mean)	75 (73,7)	69 (67,6)	79 (79,4)	71 (69,9)	66 (64,3)	79 (79,7)
ECOG 0 1 2 3 4 N.a.	82 (16%) 207 (40%) 166 (32%) 8 (2%) 0 (0%) 53 (10%)	55 (22%) 101 (40%) 65 (26%) 4 (2%) 0 (0%) 26 (10%)	27 (10%) 106 (40%) 101 (38%) 4 (2%) 0 (0%) 27 (10%)	67 (14%) 293 (63%) 80 (17%) 7 (2%) 0 (0%) 30 (4%)	47 (16%) 194 (66%) 36 (12%) 3 (1%) 0 (0%) 23 (4%)	20 (12%) 99 (57%) 44 (25%) 4 (2%) 0 (0%) 7 (4%)
Thrombocytopenia (< 100.000/µl) No Yes N.a.	325 (63%) 177 (34%) 14 (3%)	154 (62%) 86 (34%) 11 (4%)	171 (65%) 91 (34%) 3 (1%)	231 (48,5%) 231 (48,5%) 15 (3%)	136 (45%) 156 (52%) 11(3%)	95 (55%) 75 (43%) 4 (2%)
Neutropenia (< 1800/µl) No Yes N.a.	271 (53%) 175 (34%) 70 (14%)	116 (46%) 94 (38%) 41 (16%)	155 (59%) 81 (31%) 29 (11%)	294 (62%) 161 (33%) 22 (5%)	186 (61%) 106 (35%) 11 (4%)	108 (62%) 55 (32%) 11 (6%)
Anemia (Hb < 10 g/dl) No Yes N.a.	107 (21%) 398 (77%) 11 (2%)	54 (22%) 188 (75%) 9 (3%)	53 (20%) 210 (79%) 2 (1%)	72 (15%) 394 (83%) 11 (2%)	51 (17%) 244 (80%) 8 (3%)	21 (12%) 150 (86%) 3 (1%)

Tab. 2: Patients´ characteristics in 2010 and 2019

	LR-MDS-RS$^-$	LR-MD-RS$^+$	HR-MDS
	N=305 (59%)	N=76 (15%)	N=129 (25%)
Hb level <10,0 g/dl ≥10,0 g/dl n.a.	221 (73%) 55 (18%) 29 (10%)	64 (84%) 6 (8%) 6 (8%)	112 (87%) 7 (5%) 10 (8%)
Transfusion burden defined by IWG criteria 2016			
NTD (0 RBC units/16 wks)	74 (24%)	14 (18%)	39 (30%)
LTB + NTD/LTB LTB (3-7 RBC units/16 wks) NTD/LTB (1-2 RBC units/16 wks)	159 (52%) 103 (34%) 56 (18%)	29 (38%) 25 (33%) 4 (5%)	69 (54%) 47 (36%) 22 (17%)
HTB (≥8 RBC units/16 wks)	72 (24%)	33 (43%)	21 (16%)

Tab. 3: Hb level and transfusion burden of pts in TM MDS 2019. Lower risk MDS: IPSS-R very low, low and intermediar
Higher risk MDS: IPSS-R high and very high.
RS status as determined by morphologic analysis

- Regardless of age, LR-MDS-RS+ pts suffered from hemoglobin (Hb) < 10 g/dl more often than LR-MDS-RS- pts (84% vs. 73% (p< 0.05)). Indeed, Hb-level of LR-MDS-RS+ pts are comparably low to pts with higher risk (HR) MDS with or without RS (84% vs. 87% (p=n. s.)). Strikingly (Tab. 3), 43% LR-MDS-RS+ vs. 24% LR-MDS-RS- vs. 16% HR-MDS pts (p< 0.05) have a high transfusion burden (HTB: ≥8 EK / 16 weeks) as defined by the IWG criteria 2018 (Tab 3). 73% of HTB LR-MDS-RS+ present with sEPO levels ≥ 200 U/l (data not shown).

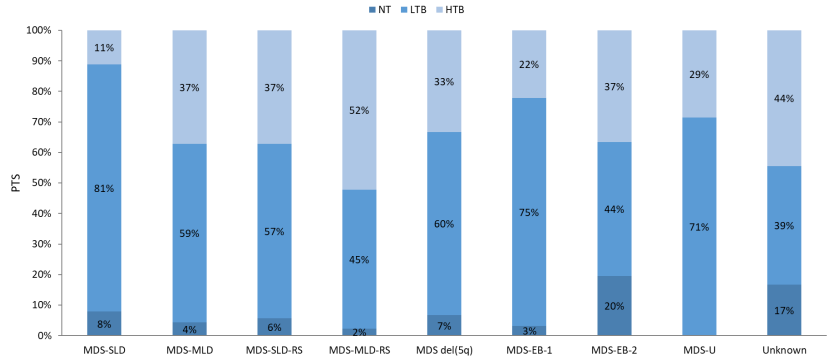

Fig. 2: Transfusion burden according to IWG criteria 2018 and WHO subtype

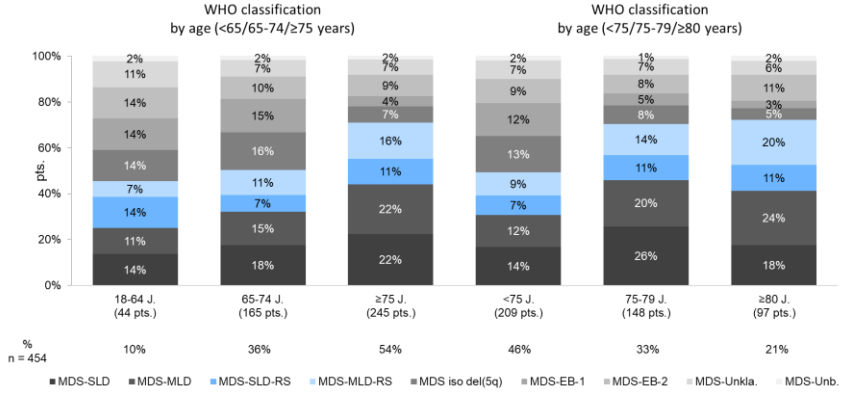

Fig. 3: Correlation of age and ringsideroblastic phenotype

Conclusion

- During the last decade, the percentage of pts in CP increased significantly. Today, actively treated pts are older and less fit than 10 years ago. The predominant threat of LR-MDS remains anaemia. Especially LR-MDS-RS+ pts show an unmet medical need. Their phenotypes behave like HR-MDS with regard to hematopoietic insufficiency and high transfusion dependence. In addition, the majority of HTB LR-MDS-RS+ pts present elevated sEPO levels (≥ 200 U/l, data not shown) and are thus unlikely suitable for EPO-based therapy.