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ELEVENTH ANNUAL MEETING

Response to Erythropoiesis-Stimulating Agent Therapy in IPSS-R Lower Risk Myelodysplastic Syndrome Patients Restratified According to IPSS-M

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INTRODUCTION

Erythropoiesis-stimulating agents (ESAs) are commonly used to treat anemic low-risk myelodysplastic syndrome (MDS) patients[1]. Response to these agents is heterogeneous. Our study investigated the impact of type and number of DNA somatic mutations on response to ESAs in a group of low-risk MDS patients revaluated by IPSS-M.

METHOD

A total of 45 lower-risk MDS patients with symptomatic anemia (Hb < 10 g/dL) and IPSS-R very-low, low, intermediate (score < 3.5) were evaluated. Somatic mutations were evaluated by Ion Torrent-NGS with a panel of 40 genes. The response to ESA (min dose 40.000 U sc/week) was assessed using the 2018 International Working Group (IWG) revised response criteria[2]. Patients were categorized as long responders (>24 months) or short responders (<24 months).

RESULTS

All LR MDS IPSS-R patients were re-stratified according to the IPSS-M model. For IPSS-R categories, 23 patients modified their risk category, and 70% were risk-upstaged, while 30% were down-staged for IPSS-R, consistent with previous findings[3].

In the very-low or low IPSS-M categories, 64% of patients achieved erythroid hematologic improvement (HI-E): among them, 41% were long responders, and 21% were short responders. In MDS with moderate low and moderate high IPSS-M categories, only 20% of patients achieved HI-E, 11% were classified as long responders, and 22% as short responders. MDS patients re-stratified to high or very high-risk IPSS-M categories did not achieve a long response to ESA, while 14% achieved a short response.

The median number of mutations in this cohort of patients was 3 +/- 1, and the presence of multiple mutations showed a trend with a decreased response to ESA therapy (p=0,102). The mutational burden, assessed by the dominant clone allele frequency (DCAF), did not significantly differ among the response subgroups (p=0,795)

	Non responder (N=23)	Short responder (N=9)	Long responder (N=13)
IPSS-R			
very low	3 (13%)	3 (33%)	0
low	17 (74%)	5 (56%)	12 (92%)
intermediate	3 (13%)	1 (11%)	1 (8%)
IPSS-M			
(very) low	11 (48%)	6 (67%)	12 (92%)
moderate	6 (26%)	2 (22%)	1 (8%)
(very) high	6 (26%)	1 (11%)	0
N mutations (median)	4 (95%CI:2,4-3,9)	3 (95%CI:2,4-4,0)	2 (95%CI:1,3-2,7)
DCAF% (median)	49,5% (95%CI: 37,4-54,1)	48% (95%CI: 29,5-67,0)	43% (95%CI: 24,8-57,6)

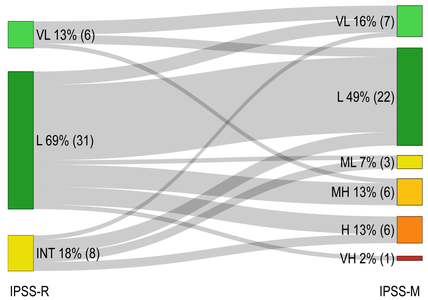


Figure 1: Restratification of patients according to IPSS-M prognostic system

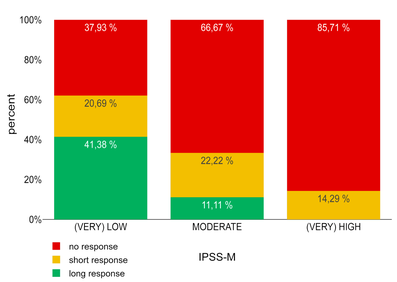


Figure 2: ESA response divided by IPSS-M category

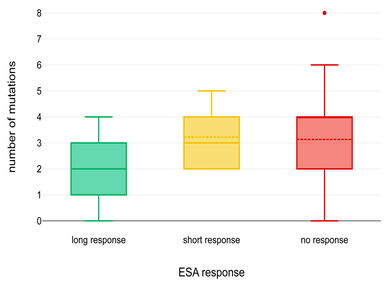


Figure 3: Number of mutations in the different ESA response groups

CONCLUSIONS

Our findings, although analyzed in a limited group of patients, suggest that IPSS-M categories and the number of somatic mutations, but not their VAFs, may impact the rate of response to ESAs.

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