

# Prognostic and Predictive Value of IPSS-R in Assessing Overall Survival (OS) in a Phase III Study of Rigosertib in Second-line Higher-risk (HR) MDS Patients

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## INTRODUCTION

ONTIME was a randomized (2:1) study of rigosertib vs best supportive care (BSC) in 299 pts with HR-MDS who had relapsed after, failed to respond to, or progressed during hypomethylating agents (HMAs). This study showed a trend favoring RIG in the overall ITT analysis and a significant effect of RIG in the subgroup of pts with very high risk (VHR) per the revised International Prognostic Scoring System (IPSS-R).

## METHODS

We examined the utility of the IPSS-R and correlation between baseline disease characteristics and OS in 93 rigosertib and 41 BSC pts with IPSS-R VHR.

## RESULTS

This first clinical study using IPSS-R in second-line HR-MDS pts showed a effect (p<0.01) of rigosertib on median OS vs BSC not only in the overall group of pts with IPSS-R VHR, but also in several subgroups defined by baseline disease characteristics (see table).

## CONCLUSION

IPSS-R is a useful prognostic tool for second-line MDS pts. After HMA failure, MDS pts with IPSS-R VHR and certain subgroups identified by baseline disease characteristics showed an OS advantage when treated with rigosertib compared to BSC. Such characteristics should be considered in the design of future second-line studies in MDS patients with IPSS-R VHR.

Median (months) OS by Baseline Disease Characteristics in Patients with IPSS-R VHR

Characteristic	Rigosertib		BSC		Log-rank p-value	Hazard ratio (Rigosertib / BSC) (95% CI)
	N	OS	N	OS		
All patients with IPSS-R VHR	93	7.6	41	3.2	0.0050	0.56 (0.37-0.84)
Primary HMA failure*	55	8.1	21	2.6	0.0055	0.48 (0.28-0.81)
FAB classification of RAEB-t	23	5.8	9	3.4	0.0031	0.26 (0.10-0.68)
ECOG performance status 0 or 1	79	8.9	30	3.6	0.0006	0.44 (0.28-0.71)
Bone marrow blast 20-30%	24	5.9	9	3.4	0.0020	0.25 (0.10-0.64)
Hemoglobin < 9 g/dL	63	6.9	21	2.3	< 0.0001	0.30 (0.17-0.54)
Platelet count ≥ 40 ×10 <sup>9</sup> /L	37	10.1	13	4.4	0.0009	0.27 (0.12-0.62)
Neutrophil count ≥ 0.8 × 10 <sup>9</sup> /L	24	8.5	12	2.7	0.0038	0.29 (0.12-0.70)
FAB classification of CMML	1	9.2	5	4.7	< 0.0001	--

\* Failed to respond to or progressed during HMA treatment (Prébet T, Gore SD, Esterni B, et al. Outcome of high-risk myelodysplastic syndrome after azacitidine treatment failure. J Clin Oncol 2011; 29:3322-27.)  
 FAB, French/American/British classification system; RAEB-t, refractory anemia with excess blasts in transition; ECOG, Eastern Cooperative Oncology Group; CMML, chronic myelomonocytic leukemia