

# A Validation of a Post-Hypomethylating Agent Failure (HMAF) Prognostic Model in Myelodysplastic Syndromes (MDS) Patients Treated with Rigosertib versus Best Supportive Care (BSC) in a Randomized Controlled Phase III trial

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## BACKGROUND

- MDS patients for whom hypomethylating agents have failed have poor outcomes. Defining variables that impact the outcome after failure is clinically important.
- As the International Prognostic Scoring System (IPSS) and the revised IPSS (IPSS-R) were developed for newly diagnosed patients, their utility at the time of HMAF is inconsistent.
- A new model was developed to risk-stratify patients after HMAF (Nazha et al, *Haematologica* 2016) and subsequently validated in an independent cohort from the GFM database (Prebet et al, *Haematologica* 2016)<sup>1,2</sup>.
- The purpose of this analysis is to validate the model in a prospective cohort of MDS patients treated homogeneously on the ONTIME trial<sup>3</sup>.

## METHODS

- Clinical data were obtained from MDS patients who enrolled on the ONTIME, phase III, randomized clinical trial that evaluated the efficacy of rigosertib versus BSC in patients with IPSS Int-2 or High risk MDS assessed after HMAF.
- HMAF was defined as failure to achieve a response; relapse after achieving a response, or intolerance to azacitidine or decitabine.
- Response were evaluated by the 2006 IWG criteria.
- Overall survival was calculated from the time of HMAF (time of randomization) to death or last follow up.

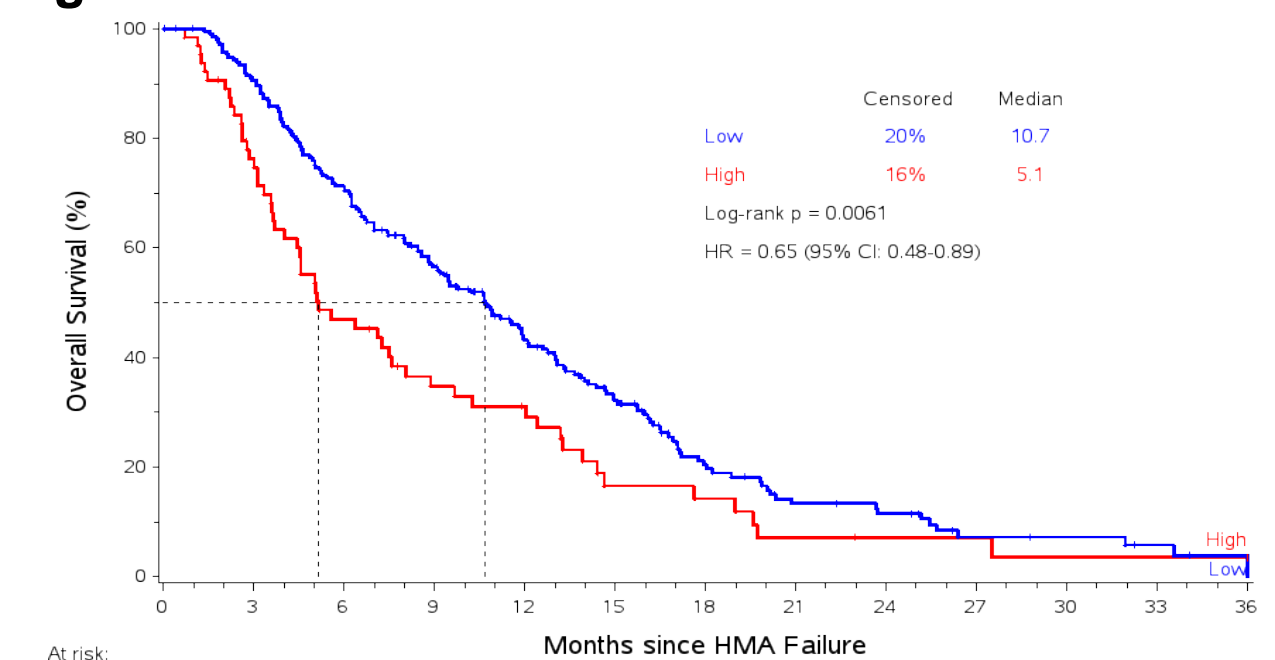
## RESULTS

**Table1: Patient Characteristics**

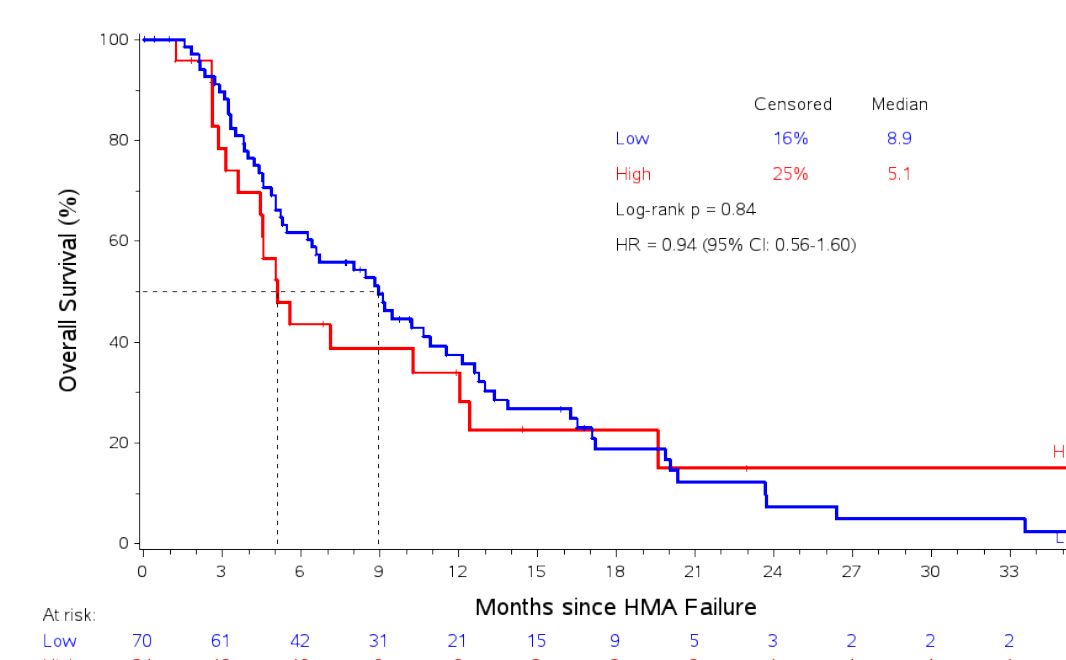
Characteristics	Rigosertib No. (%) / [Range]	BSC No. (%) / [Range]
<b>Total</b>	199	100
<b>Median Age, years</b>	74 [69–79]	74 [70–78]
<b>Gender</b>		
Female	67 (34)	34 (34)
Male	132 (66)	66 (66)
<b>Disease classification</b>		
RAEB-1	53 (27)	22 (22%)
RAEB-2	94 (47)	48 (48%)
CMML	4 (2)	7 (7%)
RAEB-t or AML	48 (24)	23 (23%)
<b>Last HMA treatment for MDS</b>		
Azacitidine	165 (83%)	84 (84%)
Decitabine	34 (17%)	15 (15%)
Unknown	0	1 (1%)
<b>MDS cytogenetic prognosis</b>		
Very good	1 (1%)	6 (6%)
Good	83 (42%)	36 (36%)
Intermediate	37 (19%)	13 (13%)
Poor	29 (15%)	11 (11%)
Very poor	26 (13%)	17 (17%)
Unknown	23 (12%)	17 (17%)
<b>IPSS-R risk</b>		
Low	1 (1%)	0
Intermediate	14 (7%)	14 (14%)
High	67 (34%)	26 (26%)
Very high	93 (47%)	41 (41%)
Unknown	24 (12%)	19 (19%)

Abbreviations: RAEB = refractory anemia with excess blasts, CMML = chronic myelomonocytic leukemia, AML = acute myeloid leukemia, MDS, IPSS-R = Revised International Prognostic Scoring System, HMA = hypomethylating agent

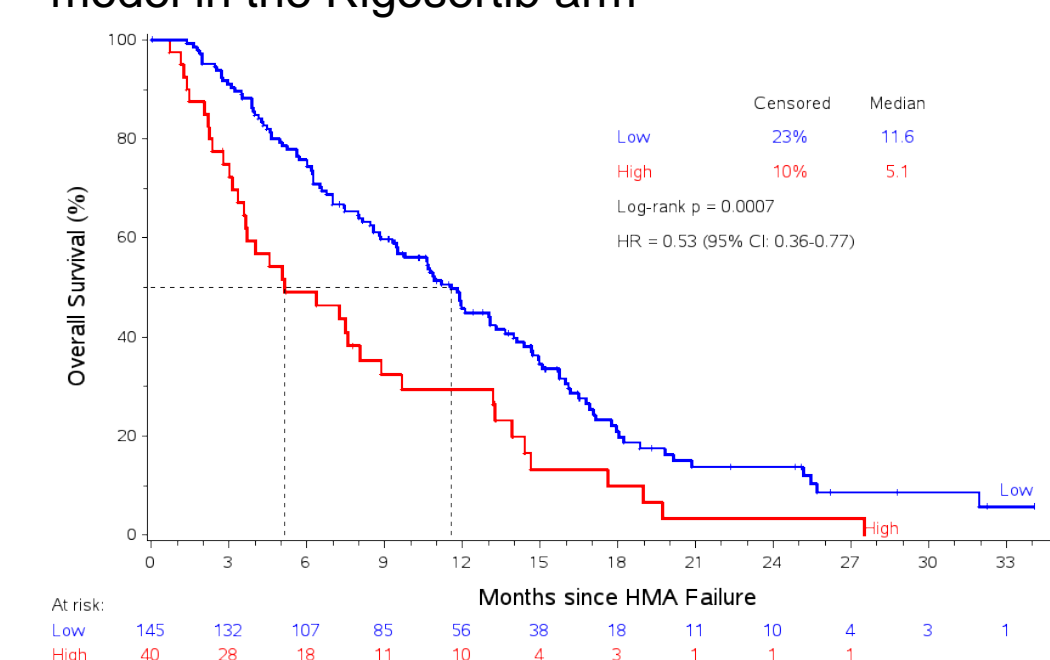
**Figure 1: Overall Survival based on Post-HMAF model**



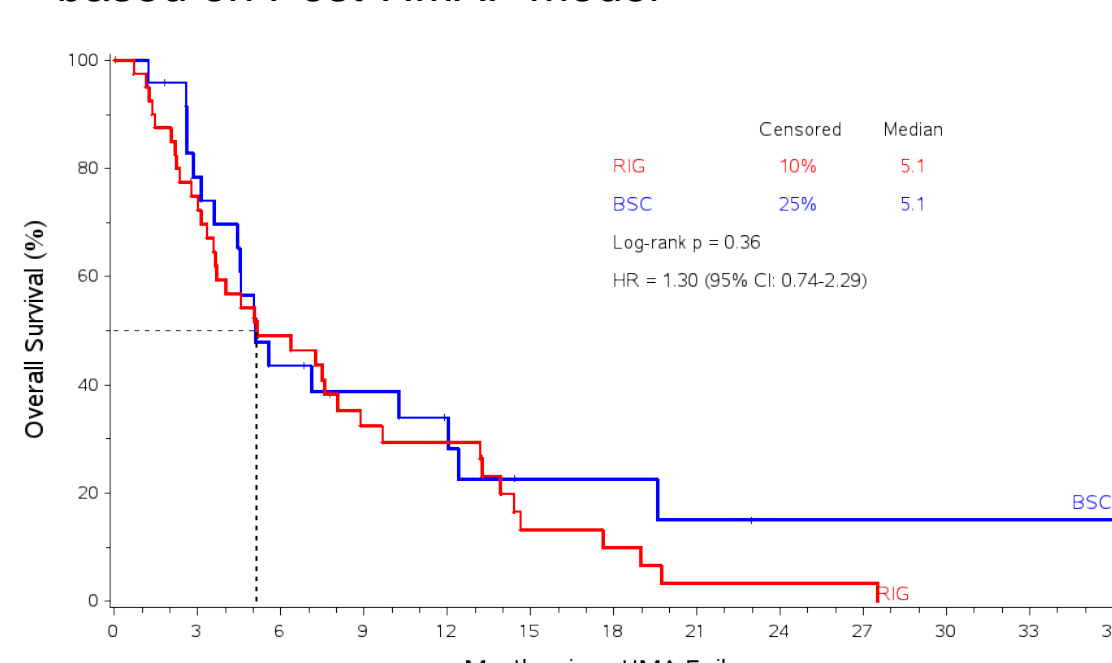
**Figure 2: Overall Survival based on Post-HMAF model in the BSC arm**



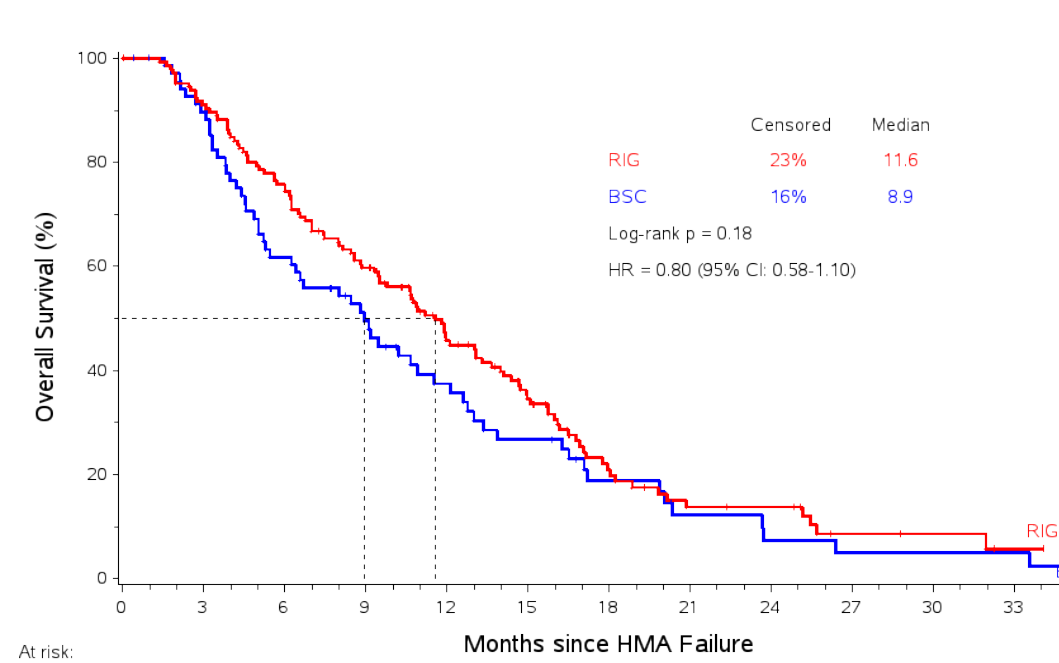
**Figure 3: Overall Survival based on Post-HMAF model in the Rigosertib arm**



**Figure 4: Overall Survival in Higher-Risk disease based on Post-HMAF model**



**Figure 5: Overall Survival in Lower-Risk disease based on Post-HMAF model**



## CONCLUSIONS

- The post-HMA failure model separated lower- from higher-risk MDS patients treated homogeneously in a prospective randomized clinical trial.
- The model was also validated in an independent cohort from the GFM database.
- This model can be incorporated into clinical trial eligibility criteria at the time of HMAF.

## REFERENCES

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- Prebet T, Fenau P, Vey N. Predicting outcome of patients with myelodysplastic syndromes after failure of azacitidine: validation of the North American MDS consortium scoring system. *Haematologica* 2016; **101**(10): e427-e8.
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