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CLINICO-MOLECULAR RISK STRATIFICATION IN 284 PATIENTS WITH PRE-FIBROTIC AND OVERT MYELOFIBROSIS

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INTRODUCTION

Myelofibrosis (MF) is a myeloproliferative neoplasm characterized by clonal hematopoietic cell expansion and bone marrow fibrosis. MF exhibits a variable clinical trajectory and heterogenous outcomes. Although several prognostic models have been introduced, published data concerning their applicability to the Asian population remain limited.

AIM

This study aimed to elucidate the real-world outcomes for an Asian cohort of myelofibrosis by validating various prognostic models, including IPSS, DIPSS, DIPSS Plus, MIPSS70, MIPSS70+ Version 2.0, GIPSS, and MYSEC-PM.

METHOD

- A retrospective cohort analysis of 284 patients with prefibrotic-MF and MF was conducted at the National Taiwan University Hospital.
- A total of 185 patients had adequate cryopreserved bone marrow samples for deep target gene sequencing.
- Multivariable Cox regression was performed to evaluate the prognostic value of each parameters.

RESULTS

- All prognostic scores (ex. IPSS, DIPSS, DIPSS+, MIPSS70, MIPSS70+ Version 2.0, GIPSS, and MYSEC-PM) effectively stratified the survival (p<0.001, for all except MIPSS70+ v2 p=0.002).
- High-molecular-risk (HMR) mutations, including *ASXL1, SRSF2, EZH2, U2AF1*Q157, as well as *SETBP1* and *NRAS* mutations were correlated with poorer OS (p<0.001, for all except *U2AF1*Q157 p=0.016).
- HMR mutations were associated with a poor OS in low *JAK2*V617F variant allele burden (VAF<0.75) but not in those with high VAF (mOS 4.1 vs. 19 years; p=0.006).
- Compared with those with a proliferative phenotype, patients with a cytopenic phenotype were older, had higher circulating blasts, a lower percentage of *JAK2* mutations, and a higher percentage of *ASXL1* mutations (p<0.005 for all).

Figure: Low *JAK2* VAF but not high VAF is associated poor survival in HMR mutation patients

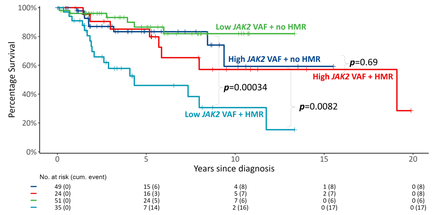


Figure: Overall survival stratified by myelofibrosis phenotype

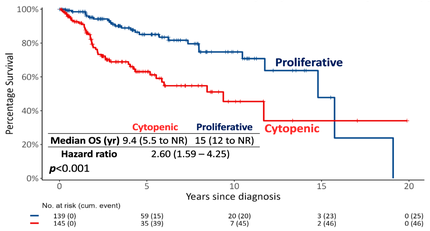
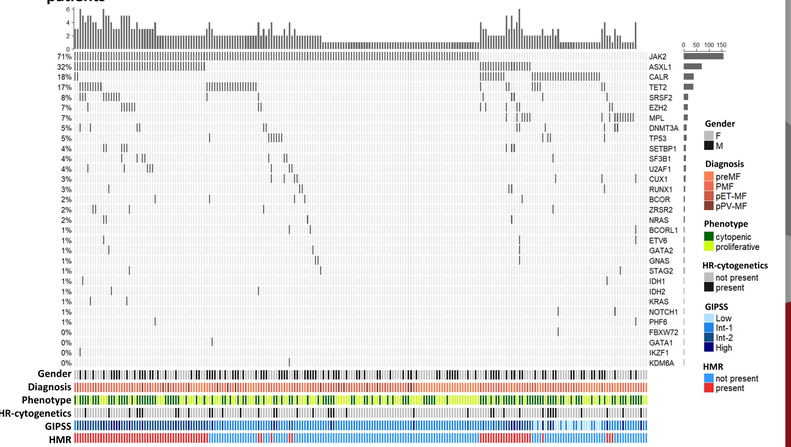


Figure: Mutation and clinical characterisitcs of 222 prefibrotic myelofibrosis and myelofibrosis patients



RESULTS

Table: Multivariable analysis for overall survival

Variables	HR	95%CI	*p* value
Age	1.03	1.00 - 1.06	**0.032**
HMR mutations	3.89	2.14 - 7.05	**<0.001**
High-risk cytogenetics	1.69	0.89 - 3.19	0.11
Cytopenic phenotype	1.87	1.02 - 3.44	**0.043**

CONCLUSIONS

This study delineates the characteristics of patients with myelofibrosis (MF) in Taiwan and validates the prognostic significance of multiple scoring systems. HMR mutations were associated with worse overall survival (OS) in patients with a lower *JAK2*V617F allele burden (VAF<0.75), but not in those with a higher allele burden (p<0.001 vs. p=0.69). Additionally, age, HMR mutations, and a cytopenic phenotype were associated with poorer outcomes.

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