Cytopenia is Associated with Real-world Disease Progression and Diminished Survival in Patients with Myelofibrosis: Analysis of a US National Administrative Claims Database

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CONCLUSIONS

- **Cytopenic myelofibrosis (MF) is associated with progression to acute myeloid leukemia (AML) and lower overall survival (OS).**
- **Cytopenia is an important factor to consider when selecting treatment options to lower risk of progression to AML and OS, as well as likelihood of receiving hematopoietic stem cell transplant (HSCT).**
- **Further studies are needed to determine whether treatment options targeting underlying anemia and/or thrombocytopenia influence risk of progression to AML and OS, as well as likelihood of receiving HSCT.**

INTRODUCTION

- Cytopenic MF is characterized by the presence of thrombocytopenia and/or anemia, which may be present at diagnosis or develop over the course of the disease.[1]
- Cytopenia is a marker of advanced disease, including higher symptom burden and increased risk of progression to leukemia and death.[1,2]
- HSCT remains the only curative option. Understanding risk factors for poor prognoses and how to appropriately tailor Janus kinase inhibitor treatment selection for patients with MF who are ineligible for transplant is clinically important.

OBJECTIVES

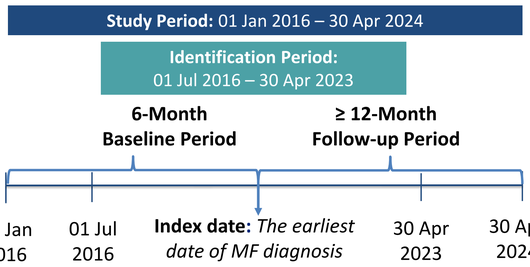
- To evaluate OS, progression to AML, and receipt of HSCT in patients with MF by cytopenic status using real-world claims data from the United States.

METHODS

Study Design

- This retrospective study included adult patients diagnosed with MF (ICD-10 codes D75.81 and D47.4) from July 2016 to April 2023 using administrative claims data from the Optum Research Database.
- Patients were required to be continuously enrolled in insurance plans for ≥6 months before diagnosis (baseline period) and ≥12 months after diagnosis, unless they died within 12 months (follow-up period) **(Figure 1)**.
- Patients were followed from MF diagnosis until the earliest date of disenrollment, death, or end of the study period (4/30/2024).

Figure 1. Study Schematic



Study Variables and Outcomes

- **Baseline Cytopenia Cohorts**: Cytopenia was defined as a diagnosis of thrombocytopenia or anemia in claims within 30 days before or after diagnosis of MF, or prior to the start of systemic anti-cancer treatment if the treatment was initiated within 30 days of MF diagnosis.
- Characteristics assessed during the baseline period included age, gender, geographic region, and Quan-Charlson comorbidity score, MF-related diagnoses, and cytoreductive treatment medications.
- Time to progression to AML, receipt of HSCT, or death were measured from MF diagnosis.

Analyses

- OS, progression to AML, and receipt of HSCT by cytopenic status were examined using Kaplan-Meier analysis, including log-rank test for difference between the cytopenic cohorts.
- Continuous variables were summarized using medians and interquartile ranges (IQR), mean with standard deviation (SD); categorical variables were presented as counts and percentages. Chi-square or t-tests were used to compare differences by cytopenic status at diagnosis. P<0.05 was significant.

Study Population

- Of 1,532 patients included, 1,074 (70%) were cytopenic at MF diagnosis.
- Overall median follow-up time was 24.7 months (IQR: 14.0- 43.2); cytopenic patients had shorter follow-up than non-cytopenic patients (median [IQR] of 21.5 [11.1-40.0] and 32.5 [20.4-51.4] months).
- Patients with cytopenia at diagnosis were older (mean±SD: 73.9 ± 10.7 years) compared to non-cytopenic patients (68.9 ± 12.0 years).
- Patients with cytopenia at diagnosis also had a higher (mean±SD) Charlson comorbidity score (2.2±2.2) than non-cytopenic patients (1.2±1.6), and lower proportion with polycythemia vera (13.3% vs. 17.7%, P=0.027) **(Table 1)**.

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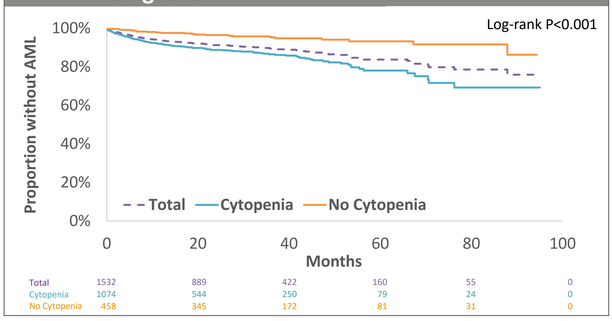
RESULTS

Time to AML

- The 5-year probability of progression to AML was 16.3% overall and tripled in patients with cytopenia at diagnosis (22.0%) compared to those who did not have cytopenia at diagnosis (6.9%); log-rank P<0.001. Median time to AML was not reached over the study period. **(Figure 2)**.

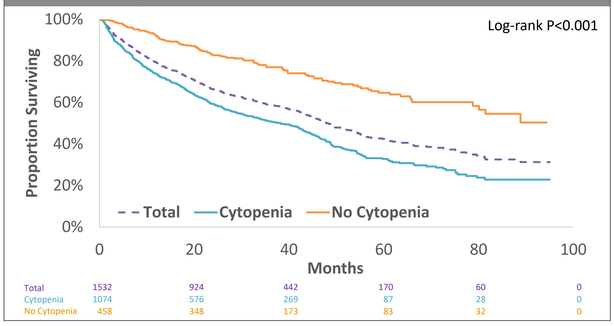
Figure 2. Progression to AML by Cytopenic Status at MF Diagnosis



Overall Survival

- The 5-year OS probability from MF diagnosis was 42.4% overall and was doubled in those without cytopenia (64.6%) vs those with cytopenia (32.8%); log-rank P<0.001 **(Figure 3)**.
- Median survival time for patients with cytopenia was 38 months (95% confidence interval: [32, 42]), and median survival not reached in patients without cytopenia; P<0.001.

Figure 3. Overall Survival by Cytopenic Status at MF Diagnosis



Time to HSCT

- Overall, 69 patients (4.5%) received HSCT with similar patterns among those with (4.8%) and without (3.9%) cytopenia at MF diagnosis; log-rank P=0.094. Among those received HSCT, the median time to HSCT was 8 and 11 months in cytopenic and non-cytopenic patients, respectively.

Table 1: Baseline Demographic and Clinical Characteristics

	Total (N=1,532)	Cytopenia (N=1,074)	No Cytopenia (N=458)	P value**
Age, mean (SD)	72.4 (11.4)	73.9 (10.7)	68.9 (12.0)	<0.001
Age group, n (%)				<0.001
18-44	43 (2.8)	22 (2.1)	21 (4.6)	
45-64	248 (16.2)	135 (12.6)	113 (24.7)	
65+	1,241 (81.0)	917 (85.4)	324 (70.7)	
Gender, n (%)				0.121
Female	713 (46.5)	486 (45.3)	227 (49.6)	
Male	819 (53.5)	588 (54.8)	231 (50.4)	
Region, n (%)				0.570
Northeast	281 (18.3)	196 (18.3)	85 (18.6)	
Midwest	384 (25.1)	266 (24.8)	118 (25.8)	
South	661 (43.2)	475 (44.2)	186 (40.6)	
West*	206 (13.5)	137 (12.8)	69 (15.1)	
Insurance type, n (%)				<0.001
Commercial	308 (20.1)	170 (15.9)	138 (30.1)	
Medicare Advantage	1,224 (80.0)	904 (84.2)	320 (69.9)	
Quan-Charlson comorbidity score, mean (SD)	1.9 (2.1)	2.2 (2.2)	1.2 (1.6)	<0.001
MF-related diagnoses, n (%)				
Polycythemia vera	224 (14.6)	143 (13.3)	81 (17.7)	0.027
Essential thrombocythemia	465 (30.4)	320 (29.8)	145 (31.7)	0.468
Cytoreductive treatment, n (%)				
Hydroxyurea	321 (21.0)	192 (17.9)	129 (28.2)	<0.001
Ruxolitinib	185 (12.1)	128 (11.9)	57 (12.5)	0.772

*Includes n<5 patients with *Other* geographic region. **Comparing cytopenia vs. no cytopenia cohorts; P-values from chi-square tests for categorical variables and independent t-tests for continuous variables.

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