MPN-087

Progression to Myelofibrosis in Patients With Essential Thrombocythemia: A Real-World Analysis From the Prospective MOST Study

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Introduction

- Essential thrombocythemia (ET) is a myeloproliferative neoplasm characterized by clonal blood cell proliferation, excessive platelet production, constitutional symptoms, and increased risk of vascular complications[1]
- In some patients, disease transformation of ET into myelofibrosis (MF) can occur[2]
- Previous prognostic studies of patients with ET have largely been based on retrospective analyses, and limited prospective data exist regarding disease progression[3]
- The **M**yelofibrosis and Essential Thrombocythemia **O**bservational **St**udy (MOST) prospectively collected data from patients with ET

Objective

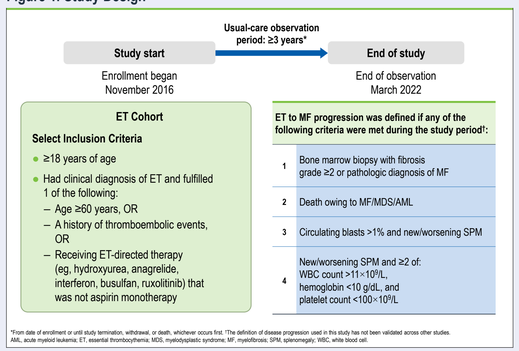
- This analysis evaluated ET to MF disease progression in patients enrolled in MOST

Methods

Study Design

- MOST (NCT02953704) is a longitudinal, noninterventional, prospective, observational study in patients with clinical diagnoses of ET or MF that enrolled patients from clinical practices throughout the United States **(Figure 1)**[3]
- Physician-reported data were collected during usual-care visits over a planned 36-month observation period as previously described[3]
- Criteria for enrollment into MOST were confirmed locally and centrally
- Progression from ET to MF for this analysis was defined as meeting any of the criteria listed in **Figure 1** during the study period. These criteria have not been validated in other studies

Figure 1. Study Design



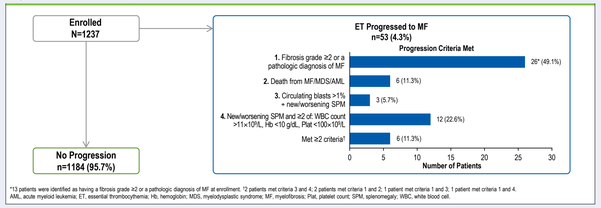
*From date of enrollment or until study termination, withdrawal, or death, whichever occurs first. †The definition of disease progression used in this study has not been validated across other studies.
AML, acute myeloid leukemia; ET, essential thrombocythemia; MDS, myelodysplastic syndrome; MF, myelofibrosis; SPM, splenomegaly; WBC, white blood cell.

Results

Patient Disposition

- All 1237 patients with ET enrolled in MOST were included in this analysis **(Figure 2)**
  - Median (range) time from ET diagnosis to enrollment was 4.2 (0-42) years
  - Median (range) duration of enrollment was 4.8 (3.5-5.8) years

Figure 2. Patient Disposition



*13 patients were identified as having a fibrosis grade ≥2 or a pathologic diagnosis of MF at enrollment. †2 patients met criteria 3 and 4; 2 patients met criteria 1 and 2; 1 patient met criteria 1 and 3; 1 patient met criteria 1 and 4.
AML, acute myeloid leukemia; ET, essential thrombocythemia; Hb, hemoglobin; MDS, myelodysplastic syndrome; MF, myelofibrosis; Plat, platelet count; SPM, splenomegaly; WBC, white blood cell.

ET to MF Progression

- During the study, 53 patients (4.3%) met the criteria for progression from ET to MF
  - Among these patients with progression, most had progressed due to fibrosis (30 [56.6%] met criterion 1)
  - Of all enrolled patients, only 176 (14.2%) had bone marrow data and 940 (76.0%) had spleen records available
  - Only 6 patients met >1 progression criterion

Enrollment Demographics

- Compared with patients without progression, those with progression had a significantly longer time from diagnosis to enrollment (7.9 vs 4.2 years; *P*=0.001) **(Table 1)**
- Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS) was similar at enrollment for patients with vs without progression (mean [standard deviation]: 17.2 [13.4] vs 16.9 [15.6])

Table 1. Enrollment Demographics

Characteristic	No Progression (n=1184)	ET to MF Progression (n=53)	Total (N=1237)
Age at enrollment, median (range), years	69.0 (19-95)	69.0 (30-88)	69.0 (19-95)
≥60 years, n (%)	915 (77.3)	44 (83.0)	959 (77.5)
Age at diagnosis, median (range), years	63.0 (16-93)	60.1 (20-88)	62.9 (16-93)
Male, n (%)	407 (34.4)	25 (47.2)	432 (34.9)
Race, n (%)			
White	1033 (87.2)	49 (92.5)	1082 (87.5)
Black/African American	89 (7.5)	3 (5.7)	92 (7.4)
Other*	50 (4.2)	1 (1.9)	51 (4.1)
Time from ET diagnosis to enrollment, median (range), years	4.2 (0-42)	7.9 (0-41)	4.2 (0-42)
0 to <1 year, n (%)	246 (20.8)	4 (7.5)	250 (20.2)
1 to <5 years, n (%)	412 (34.8)	15 (28.3)	427 (34.5)
5 to <10 years, n (%)	251 (21.2)	12 (22.6)	263 (21.3)
≥10 years, n (%)	275 (23.2)	22 (41.5)	297 (24.0)
Duration of disease, median (range), years	9.0 (4-47)	12.7 (5-47)	9.0 (4-47)
Enrollment duration, median (range), months	56.9 (42-70)	58.5 (45-70)	57.3 (42-70)
With family history of MF/PV/ET, n/N† (%)	42/1167 (3.6)	2/52 (3.8)	44/1219 (3.6)
Baseline MPN-SAF TSS, mean (SD)	16.9 (15.6)	17.2 (13.4)	16.9 (15.5)

Bold blue font denotes a statistically significant difference between patients with vs without progression from ET to MF (*P*<0.05).
*Other includes Asian, American Indian/Alaskan Native, and other. Race information was reported as "missing" for 12 patients in the No Progression group. †Denominator = number of patients for whom data were available.
ET, essential thrombocythemia; MF, myelofibrosis; MPN-SAF TSS, Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score; PV, polycythemia vera; SD, standard deviation.

Mutation Testing Results

- Among all enrolled patients, 950 were evaluated for ≥1 known driver mutation **(Table 2)**

Table 2. Mutation Status at Enrollment

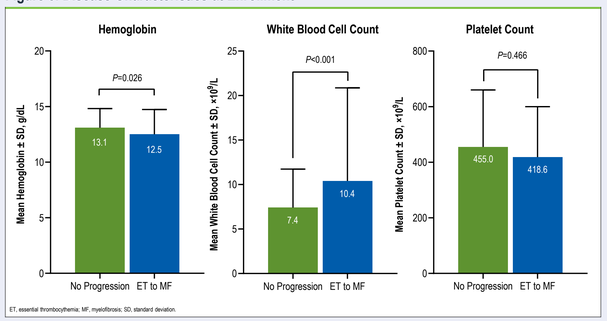
Mutation Assessments	No Progression (n=1184)	ET to MF Progression (n=53)	Total (N=1237)
Patients with ≥1 mutation test, n (%)	912 (77.0)	38 (71.7)	950 (76.8)
JAK2 positive (any *JAK2* mutations), n/N (%)*,†	598/858 (69.7)	29/36 (80.6)	627/894 (70.1)
JAK2p.V617F positive	516/727 (71.0)	28/32 (87.5)	544/759 (71.7)
CALR, n/N (%)*	101/162 (62.3)	2/6 (33.3)	103/168 (61.3)
MPL, n/N (%)*	22/124 (17.7)	2/7 (28.6)	24/131 (18.3)
JAK2p.V617F, *CALR*, *MPL* triple negative, n/N (%)*,‡	14/45 (31.1)	2/4 (50.0)	16/49 (32.7)
Unknown, n (%)§	274 (30.0)	5 (13.2)	279 (29.4)

*Numerator = patients positive for mutation; denominator = patients tested for mutation. †Some patients had >1 *JAK2* mutation test. ‡Numerator = patients negative for all 3 mutations; denominator = patients tested for all 3 mutations.
§Unknown refers to patients with ≥1 mutation test done (*JAK2*, *CALR*, or *MPL*) who did not test positive for a mutation or negative for all 3 mutations.
CALR, calreticulin; ET, essential thrombocythemia; *JAK*, Janus kinase; MF, myelofibrosis; *MPL*, myeloproliferative leukemia virus oncogene.

Disease Characteristics at Enrollment

- Among patients with vs without progression, at enrollment **(Figure 3)**:
  - Mean hemoglobin was significantly lower
  - Mean white blood cell count was significantly higher
  - Mean platelet count was not significantly different
  - Mean MPN-SAF TSS did not differ between the 2 groups throughout the study period (results not shown)

Figure 3. Disease Characteristics at Enrollment

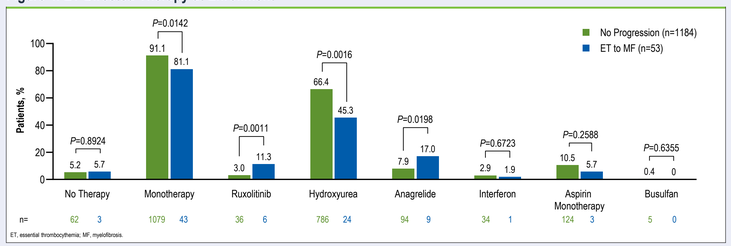


ET, essential thrombocythemia; MF, myelofibrosis; SD, standard deviation.

ET-Directed Therapy at Enrollment

- Although the percentages of patients receiving any ET-directed therapy were similar for those with vs without progression (94.8% vs 94.3%), more patients without progression were receiving ET monotherapy **(Figure 4)**:
  - More patients with vs without progression were receiving ruxolitinib, whereas fewer were receiving hydroxyurea
- Disease duration at enrollment was significantly longer in patients receiving ruxolitinib compared with those receiving hydroxyurea (13.2 [4-41] years vs 8.7 [4-47] years; *P*<0.001)

Figure 4. ET-Directed Therapy at Enrollment



ET, essential thrombocythemia; MF, myelofibrosis.

Thrombotic and Hemorrhagic Events During Study Period

- Both thrombotic and hemorrhagic events were infrequent; however, hemorrhagic events were relatively increased in patients with progression **(Table 3)**

Table 3. Thrombotic and Hemorrhagic Events During Study Period

	Number of Patients, n (%)			Number of Events, n		
Adverse Events	No Progression (n=1184)	ET to MF Progression (n=53)	Total (N=1237)	No Progression (n=1184)	ET to MF Progression (n=53)	Total (N=1237)
Thrombotic events	44 (3.7)	1 (1.9)	45 (3.6)	59	2	61
Arterial	29 (2.4)	0	29 (2.3)	40	0	40
Venous	15 (1.3)	1 (1.9)	16 (1.3)	19	2	21
Hemorrhagic events	15 (1.3)	4 (7.5)	19 (1.5)	16	5	21
Death from thrombotic or hemorrhagic events	4 (0.3)	0	4 (0.3)	4	0	4

ET, essential thrombocythemia; MF, myelofibrosis.

Conclusions

- **This prospective analysis of patients enrolled in MOST evaluated disease progression from ET to MF**
- **Of the 1237 patients with ET, 53 (4.3%) progressed to MF during the study period**
- **Compared with patients without progression, those with progression had longer duration of disease, higher white blood cell counts, and lower hemoglobin at enrollment; symptom burden at enrollment was similar between the 2 groups**
- **One limitation of this study is the lack of bone marrow data for the majority of patients, which likely contributed to an underestimation of the rate of progression to MF**
- **These findings and further analyses of MOST data will add insight into disease progression in patients with ET and facilitate clinical management of this patient population**

Disclosures

Yacoub: Speaker's bureau — *Incyte Corporation*.

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