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POSTER ABSTRACTS

906.OUTCOMES RESEARCH-MYELOID MALIGNANCIES

Clinical and Disease Characteristics of Patients with Myelofibrosis and Essential Thrombocythemia Who Harbor a Calreticulin (CALR) Gene Mutation: Subanalysis of the MOST Study

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Background: Calreticulin(CALR)gene mutations are the second most frequent driver of disease in myelofibrosis (MF) and essential thrombocythemia (ET). Compared with patients with *JAK2* mutations, those with *CALR* mutations are considered to have lower-risk disease; however, prospective data on clinical characteristics and disease progression for patients with *CALR* mutations are limited. This study compared the disease characteristics and treatment patterns of patients with MF or ET who had *CALR* mutations vs those who had *JAK2* mutations at enrollment in the **M**yelofibrosis and Essential Thrombocythemia **O**bservational **St**udy (MOST; NCT02953704).

Methods: Patients enrolled in MOST were aged≥18 years with clinical diagnoses of MF or ET at clinical practices within the United States. Patients with MF included those with primary or secondary MF who were low risk (or intermediate-1 by age >65 years alone) per the Dynamic International Prognostic Scoring System (Passamonti F, et al. *Blood.* 2010;115:1703-1708). Patients in the ET cohort had a clinical diagnosis of ET and were ≥60 years or had history of thromboembolic events or were receiving ET-directed therapy at enrollment. Descriptive statistics were used to summarize the data. The median (range) follow-up time for *CALR*- and *JAK2*-positive patients was 52.8 (43-68) months and 56.6 (42-70) months, respectively. ET progression was defined as transformation to MF; MF progression was defined as worsening of objective clinical and laboratory assessments of disease.

Results: A total of 881 patients (*CALR*-positive, n=137 [16%]; *JAK2*-positive, n=750 [85%]; 6 patients had both *CALR* and *JAK2* mutations) were included in this study. A summary of patient and disease characteristics are presented in Table 1 and Table 2. At enrollment, 25% and 75% of *CALR*-positive patients had a diagnosis of MF and ET, respectively, vs 16% and 84% of *JAK2*-positive patients. The majority of patients in both groups were women (*CALR*-positive, 56%; *JAK2*-positive, 65%). *CALR*-positive patients were younger at enrollment and at diagnosis compared with *JAK2*-positive patients (median age at enrollment, 63.0 [24.0-89.0] vs 70.0 [26.0-93.0] years, $P<0.001$; median age at diagnosis, 59.3 [21.0-87.0] vs 66.3 [22.0-93.0] years, $P<0.001$).

The majority of patients in this analysis (79% of *CALR*-positive, 90% of *JAK2*-positive) were receiving MPN-directed therapy at enrollment. The most common therapies in the CALR cohort were hydroxyurea (51%), interferon (12%), and anagrelide (8%); the common therapies among patients in the JAK2 cohort were hydroxyurea (66%), aspirin only (10%), and ruxolitinib (8%). Disease burden at enrollment was also assessed. The percentages of patients with white blood cell (WBC) count $>10\times10^9$/L or platelet count $>400\times10^9$/L were similar for both *CALR*- and *JAK2*-positive patients (13% vs 20% and 53% vs 51%, respectively). Percentages of patients with splenomegaly (SPM) were similar for *CALR*- vs *JAK2*-positive patients at enrollment (11.0% vs 13%). The mean MPN-SAF TSS was similar at baseline for *CALR*- and *JAK2*-positive patients (15.1 vs 16.5). The percentage of patients with MPN-SAF TSS >25 was 12% in the *CALR*-positive and 16% in *JAK2*-positive cohorts.

Disease complications and progression were also assessed. Thrombotic and hemorrhagic events during the study period were infrequent in both *CALR*- and *JAK2*-positive patients (2% vs 4% and 1% vs 3%, respectively). Rates of disease progression were similar for *CALR*- and *JAK2*-positive patients, both for MF progression (50% vs 61%) and for ET progression to MF (2% vs 5%). Leukemic transformation occurred in 6 (4%) *CALR*-positive patients and 43 (6%) *JAK2*-positive patients. Deaths due to disease progression occurred in no *CALR*-positive patients and in 18 (2%) *JAK2*-positive patients.

Conclusions: The results of this real-world analysis of the MOST study demonstrate that despite nearly 80% of *CALR*-positive patients receiving MPN-directed treatment, a substantial percentage of this group did not meet treatment goals, including control of symptom burden, WBC and platelet counts, and SPM. In addition, disease progression was observed in 50% of the patients with MF in the *CALR*-positive cohort. Further analysis of the MOST study may provide insight into optimal management of patients with *CALR* mutations.

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Table 1. Clinical Characteristics of *CALR*- and *JAK2*-Positive Patients With MF or ET

Characteristic	*CALR*-Positive (n=137)	*JAK2*-Positive (n=750)	Total* (N=881)
Diagnosis, n (%)			
ET	103 (75.2)	627 (83.6)	725 (82.3)
MF	34 (24.8)	123 (16.4)	156 (17.7)
Age at enrollment, median (range), y	63.0 (24.0-89.0)	70.0 (26.0-93.0)	69.0 (24.0-93.0)
≥65, n (%)	56 (40.9)	488 (65.1)	541 (61.4)
≥60 to ≤65, n (%)	32 (23.4)	121 (16.1)	151 (17.1)
<60, n (%)	49 (35.8)	141 (18.8)	189 (21.5)
Age at diagnosis, median (range), y	59.3 (21.0-87.0)	66.3 (22.0-93.0)	65.2 (21.0-93.0)
≥65, n (%)	45 (32.8)	404 (53.9)	446 (50.6)
≥60 to ≤60, n (%)	20 (14.6)	116 (15.5)	134 (15.2)
<60, n (%)	72 (52.6)	230 (30.7)	301 (34.2)
Female, n (%)	76 (55.5)	486 (64.8)	557 (63.2)
Enrollment duration, median (range), mo	52.8 (43.0-68.0)	56.6 (42.0-70.0)	56.0 (42.0-70.0)
Time from diagnosis to enrollment, median (range), y	1.9 (0.0-38.0)	2.8 (0.0-32.0)	2.6 (0.0-38.0)
<1, n (%)	43 (31.4)	224 (29.9)	265 (30.1)
1-<5, n (%)	58 (42.3)	300 (40.0)	354 (40.2)
5-<10, n (%)	17 (12.4)	159 (21.2)	176 (20.0)
≥10, n (%)	19 (13.9)	67 (8.9)	86 (9.8)
ET/MF-directed therapy at enrollment, n (%)	108 (78.8)	676 (90.1)	778 (88.3)

*6 patients tested positive for both *CALR* and *JAK2* mutation.
ET, essential thrombocythemia; MF, myelofibrosis.

Table 2. Disease Characteristics of *CALR*- *and JAK2*-Positive Patients With MF or ET

Characteristic	*CALR*-Positive (n=137)	*JAK2*-Positive (n=750)	Total* (N=881)
MPN-SAF TSS at enrollment, mean (SD)	15.1 (14.27)	16.5 (15.15)	16.3 (15.01)
Splenomegaly at enrollment,† n/N (%)	12/109 (11.0)	75/582 (12.9)	87/691 (12.6)
WBC >10×10^9/L at enrollment , n (%)	18 (13.1)	146 (19.5)	164 (18.6)
Platelets >400×10^9/L at enrollment, n (%)	73 (53.3)	385 (51.3)	454 (51.5)
Disease progression, n (%)			
MF			
Progressed	17 (12.4)	75 (10.0)	92 (10.4)
Not progressed	17 (12.4)	48 (6.4)	64 (7.3)
ET			
Progressed	2 (1.5)	29 (3.9)	31 (3.5)
Not progressed	101 (73.7)	598 (79.7)	694 (78.8)

*6 patients tested positive for both *CALR* and *JAK2* mutation. †15 patients (2.6%) with *JAK2* mutations had indeterminate palpable spleen at enrollment.
ET, essential thrombocythemia; MF, myelofibrosis; MPN-SAF TSS, Myeloproliferative Neoplasm Symptom Assessment Form total symptom score; SD, standard deviation; WBC, white blood cell.

Figure 1

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