ELSEVIER

Blood 142 (2023) 385–387

The 65th ASH Annual Meeting Abstracts

ORAL ABSTRACTS

906.OUTCOMES RESEARCH-MYELOID MALIGNANCIES

A Real-World Evaluation of Risk Factors for Disease Progression in Patients with Polycythemia Vera (PV) Enrolled in REVEAL

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Background: PV is a myeloproliferative neoplasm complicated by symptom burden, splenomegaly, vascular events, and disease progression to myelofibrosis (MF). Current risk models for PV include advanced age and history of thrombotic events (TEs), yet information on risk factors for PV progression is limited. In this analysis, we assessed the rate of PV progression to MF during the P **r**ospective Obs **e**rvational Study of Patients With Polycythemia **Ve**ra in US Clinic **al** Practices Trial (REVEAL) and assessed baseline demographics and disease characteristics as risk factors for PV progression.
Methods: Criteria for enrollment in REVEAL included a physician-reported PV diagnosis. PV progression was defined by meeting any of the following criteria during the study: 1) Death from MF/myelodysplastic syndrome (MDS)/acute myeloid leukemia (AML); 2) new/worsening splenomegaly, plus 2 of the following criteria: white blood cell (WBC) count $>11\times10^9$/L, platelets (PLT) $<100\times10^9$/L, hemoglobin (Hb) <10 g/dL; 3) evidence of progression to MF from bone marrow (BM) biopsy; 4) new/worsening splenomegaly, plus blasts >1%. Univariate and multivariate logistic regressions were performed to assess risk factors of PV progression.
Results: Of the 2510 patients enrolled in REVEAL, 1191 (47.5%) were reported to have a *JAK2* mutation at enrollment. To confirm PV diagnosis, digital droplet PCR for *JAK2* p.V617F was performed on all patients with the first available biospecimen from an optional biological specimen substudy; 1520/1871 (81.2%) were positive. A further 367 patients with a physician-reported *JAK2* mutation and 135 with a PV diagnosis confirmed by BM aspirate/biopsy were included; 488 patients (19.4%) who did not meet any criteria were excluded. Of the 2022 patients with confirmed diagnosis, median (range) follow-up was 44.1 (0-59.5) months; 134 (6.6%) progressed to MF (BM evidence of MF, n=69 [3.4%]; new/worsening splenomegaly, plus 2 of the following criteria WBC count $>11\times10^9$/L, PLT $<100\times10^9$/L, Hb <10 g/dL, n=44 [2.2%]; new/worsening splenomegaly, plus blasts >1%, n=37 [1.8%]; death from MF/MDS/AML, n=22 [1.1%]). A nonsignificant trend toward higher mean *JAK2* p.V617F variant allele frequency was observed in patients with vs without progression (Table 1).
Compared with patients without progression to MF, patients with progression were of similar age (69.5 vs 68.0 y) and had a longer time from PV diagnosis to enrollment (median, 7.2 vs 3.7 y; $P<0.0001$; Table 1). The percentage of patients with vs without progression enrolled via academic practices was 23.1% vs 16.9%; the percentage of patients with vs without progression who had no cytoreductive treatment prior to enrollment was 85.1% vs 91.2%. PV risk stratification (age >60 y or history of TEs) at enrollment was similar for patients with vs without progression (high risk, 61.9% vs 63.5%). However, a higher percentage of patients with vs without progression had a history of TEs at enrollment (29.9% vs 19.7%; $P=0.0050$). Univariate analysis also identified hematocrit (HCT) ≤0.45 L/L (63.9% vs 53.5%; $P=0.0288$) and WBC count $>11\times10^9$/L (50.4% vs 31.8%; $P<0.0001$) at enrollment as significantly different between patients with vs without progression, respectively (Figure 1).
In univariate analyses, time from PV diagnosis, TE history, HCT ≤0.45 L/L, WBC count $>11\times10^9$/L at enrollment were each associated with increased PV progression risk (Figure 1). These factors were retained as significant covariates in multivariate analyses with stepwise model selection (OR [90% CI]: time from PV diagnosis to enrollment, 1.030 [1.016-1.044], $P<0.0001$; history of TEs at enrollment, 1.96 [1.281-2.998], $P=0.0019$; HCT >0.45 vs ≤0.45 L/L, 0.637 [0.421-0.964], $P=0.0330$; WBC >11 vs $\leq11\times10^9$/L, 2.205 [1.477-3.292], $P<0.0001$).

Conclusions: This real-world analysis of prospective data from REVEAL found that 6.6% of patients with PV progressed to MF over the median 44.1 months of follow-up. Time from diagnosis to enrollment and history of TEs were each significantly associated with an increased risk of PV progression; the latter finding regarding TE history was unexpected and represents a potentially novel risk factor for PV progression. HCT $\leq$0.45 L/L and WBC $>11\times10^{9}$/L at enrollment were also significantly associated with an increased progression risk. Additional analysis is ongoing to better understand the causal relationships between these risk factors and PV progression.

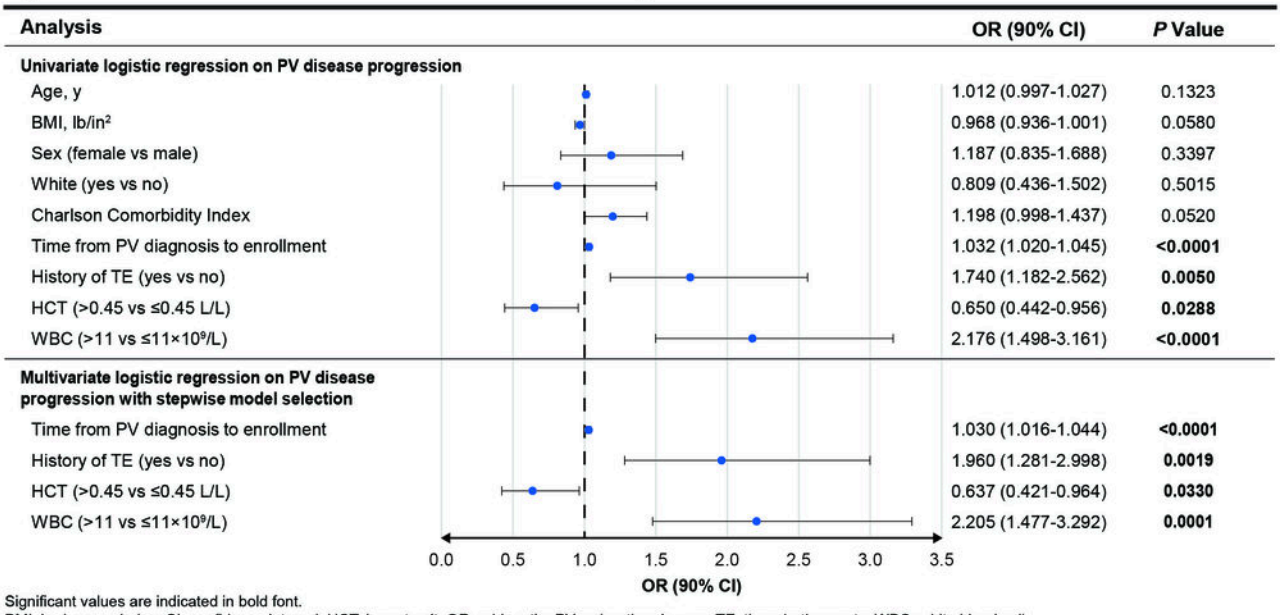
Disclosures Grunwald: *Karius, Novartis, Ono Pharmaceutical, Pfizer, Pharmacosmos, Premier, Stemline Therapeutics:* Consultancy; *Medtronic:* Current equity holder in publicly-traded company; *Incyte Corporation, Janssen:* Research Funding; *AbbVie, Agios/Servier, Amgen, Astellas Pharma, Blueprint Medicines, Bristol Myers Squibb, Cardinal Health, CTI BioPharma/Sobi, Daiichi Sankyo, Gamida Cell, Genentech, Gilead Sciences, GSK/Sierra Oncology, Incyte Corporation, Invitae, Jazz Pharmaceuticals:* Consultancy. **Zwicker:** *Incyte Corporation, Quercegen:* Research Funding; *Sanofi, CSL, Parexel:* Consultancy; *CSL Behring:* Consultancy; *Sanofi:* Consultancy; *calyx:* Consultancy; *Janssen:* Consultancy; *Pfizer/BMS, Portola, Daiichi:* Honoraria. **Gerds:** *AbbVie, Bristol Myers Squibb, Constellation Pharmaceuticals, GlaxoSmithKline, Kartos, Novartis, PharmaEssentia, Sierra Oncology:* Consultancy; *Accurate Pharmaceuticals, Constellation Pharmaceuticals, CTI BioPharma, Imago BioSciences, Incyte Corporation, Kratos Pharmaceuticals:* Research Funding. **Burke:** *Morphosys:* Research Funding; *Bayer HealthCare Pharmaceuticals:* Consultancy; *Gilead Sciences:* Consultancy; *MorphoSys AG:* Consultancy; *X4 Pharmaceuticals:* Consultancy; *Nurix:* Consultancy; *Roche/Genentech:* Consultancy; *Seagen Inc.:* Consultancy, Speakers Bureau; *Kura Oncology:* Consultancy; *Epizyme:* Consultancy; *Bristol Myers Squibb:* Consultancy; *BeiGene:* Consultancy, Speakers Bureau; *AbbVie:* Consultancy; *Adaptive Biotechnologies:* Consultancy; *AstraZeneca:* Consultancy; *Kymera:* Consultancy; *Verastem:* Consultancy. **Xue:** *Incyte Corporation:* Current Employment, Current equity holder in publicly-traded company. **Crowgey:** *Incyte Corporation:* Current Employment, Current equity holder in publicly-traded company. **Carl:** *Incyte Corporation:* Current Employment, Current equity holder in publicly-traded company. **Feldman:** *Incyte Corporation:* Current Employment, Current equity holder in publicly-traded company. **Braunstein:** *Incyte Corporation:* Current Employment, Current equity holder in private company, Current holder of *stock options* in a privately-held company. **Oh:** *Protagonist:* Membership on an entity's Board of Directors or advisory committees; *Morphic:* Membership on an entity's Board of Directors or advisory committees; *Incyte Corporation:* Membership on an entity's Board of Directors or advisory committees; *Geron:* Membership on an entity's Board of Directors or advisory committees; *CTI Biopharma:* Membership on an entity's Board of Directors or advisory committees; *Constellation/Morphosys:* Membership on an entity's Board of Directors or advisory committees; *Cogent:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Membership on an entity's Board of Directors or advisory committees; *Sierra Oncology/GSK:* Membership on an entity's Board of Directors or advisory committees.

Table 1. Patient Characteristics by PV Progression Status

Characteristic	PV Progression (n=134)	No PV Progression (n=1888)	Total (n=2022)
Age at enrollment, median (range), y	69.5 (42-92)	68.0 (22-95)	68.0 (22-95)
Male, n (%)	74 (55.2)	962 (51.0)	1036 (51.2)
Race, n (%)			
White	113 (84.3)	1688 (89.4)	1801 (89.1)
Other*	12 (9.0)	145 (7.7)	157 (7.8)
Time from PV diagnosis to enrollment, median (range), y	7.2 (0-34.1)	3.7 (0-38.5)	3.8 (0-38.5)
<5 years, n (%)	51 (38.1)	1141 (60.4)	1192 (59.0)
≥5 years, n (%)	83 (61.9)	742 (39.3)	825 (40.8)
PV risk, n (%)			
Low risk at diagnosis	51 (38.1)	685 (36.3)	736 (36.4)
High risk at diagnosis	83 (61.9)	1198 (63.5)	1281 (63.4)
Clinical practice setting, n (%)			
Academic	31 (23.1)	320 (16.9)	351 (17.4)
Community	103 (76.9)	1568 (83.1)	1671 (82.6)
PV treatment prior to enrollment, n (%)			
Hydroxyurea	15 (11.2)	143 (7.6)	158 (7.8)
Other	5 (3.7)	23 (1.2)	28 (1.4)
No treatment	114 (85.1)	1722 (91.2)	1836 (90.8)
History of TE at enrollment, n (%)	40 (29.9)	371 (19.7)	411 (20.3)
Baseline hematocrit level, n (%)			
≤0.45 L/L	76 (63.9)	932 (53.5)	1008 (54.1)
>0.45 L/L	43 (36.1)	811 (46.5)	854 (45.9)
Baseline WBC count, n (%)			
≤11×10⁹/L	59 (49.6)	1179 (68.2)	1238 (67.0)
>11×10⁹/L	60 (50.4)	551 (31.8)	611 (33.0)
Number of TE, n (%)			
0	122 (91.0)	1790 (94.8)	1912 (94.6)
≥1	12 (9.0)	98 (5.2)	110 (5.4)
Number of venous TE, n (%)			
0	123 (91.8)	1820 (96.4)	1943 (96.1)
≥1	11 (8.2)	68 (3.6)	79 (3.9)
Number of arterial TE, n (%)			
0	133 (99.3)	1858 (98.4)	1991 (98.5)
≥1	1 (0.7)	30 (1.6)	31 (1.5)
JAK2 p.V617F variant allele frequency, mean (SD)	61.6 (30.7)	46.0 (29.1)	47.1 (29.5)

*Other includes Asian, American Indian/Alaskan Native, Black or African American, Native Hawaiian or Other Pacific Islander, and other.
PV, polycythemia vera; SD, standard deviation; TE, thrombotic events; WBC, white blood cell.

Figure 1. Associations Between Patient Characteristics and PV Progression



Significant values are indicated in bold font.
BMI, body mass index; CI, confidence interval; HCT, hematocrit; OR, odds ratio; PV, polycythemia vera; TE, thrombotic events; WBC, white blood cell.

Figure 1

https://doi.org/10.1182/blood-2023-180215