THE BURDEN OF Polycthemia Vera

What Is PV?
Polycthemia vera (PV) is a myeloproliferative neoplasm characterized by the overproduction of red blood cells, white blood cells and platelets that leads to an increased risk of thrombosis and substantial symptom burden. Erythrocytosis (elevated red blood cell mass) is the most prominent clinical manifestation of PV and causes some most serious complications of the disease. PV is also characterized by dysregulated pathway signaling, driven by the Janus-associated kinase 2 (JAK2) V617F or JAK2V617F, mutation. The mutation is an important characteristic and diagnostic indicator in PV, and it is present in >95% of patients.

The Course of PV
PV may develop slowly and may not be recognized for years. PV can occur at any age but often presents later in life, with a median age at diagnosis of 60 years. Approximately 100,000 patients in the United States are living with PV.

Elevated Hematocrit Level and Cardiovascular Events in PV
Elevated hematocrit levels may contribute to worse outcomes in PV. Consistent control of hematocrit at levels <45% is an important therapeutic target recently confirmed in a large, randomized, controlled clinical trial. Data from this trial show that the rate of death from cardiovascular events or major thrombosis was 4 times higher in patients with elevated hematocrit levels of 45% to 50% compared with those who maintained a target hematocrit level of <45%.

Thrombosis and Splenomegaly in PV
Patients with elevated hematocrit levels are at increased risk for thrombosis, splenomegaly and worsening symptoms. Thrombosis is the leading cause of morbidity and mortality in PV, and splenomegaly is present in 20% to 40% of patients.

Symptom Burden of PV
Data also show that PV causes a significant and clinically meaningful erosion of quality of life. The majority of patients experience PV-related symptoms, including fatigue, pruritus, night sweats, bone pain, fever and weight loss (Table 1).

Prognosis of PV
PV leads to substantial morbidity and mortality. In a large population-based study of >4,300 patients with PV, life expectancy was 36% lower than that expected in the general population. Malignancies and cardiovascular mortality account for a large proportion of deaths in PV. Hematologic transformation may occur in some patients; PV may progress to myelofibrosis or acute myelogenous leukemia, further complicating the prognosis.

Unmet Medical Need in Uncontrolled PV
No drug treatments for PV have been approved by the US Food and Drug Administration. The current treatment approach focuses on avoiding and controlling thrombotic and bleeding events and complications, controlling hematocrit levels and other blood counts, managing disease-related symptoms and lowering the risk of thrombotic events, without increasing the risk of progression to myelofibrosis or of leukemic transformation. Yet based on results of a study assessing outcomes in >1,600 patients with PV, despite treatment with phlebotomy, hydroxyurea and antiplatelet drugs and routine follow-up yearly for 5 years, fewer than half of patients achieved the target hematocrit level of <45% at every time point.

Even with standard treatment, as many as 1 in 4 patients with PV may have elevated hematocrit levels and uncontrolled disease.

References