Facts about Polycythemia Vera (PV)

- *Rare, chronic, progressive blood cancer with no FDA-approved treatments*
- *Phlebotomy, aspirin and chemotherapy are currently used to try to control the disease*
- *One in four patients is unable to achieve disease control despite existing treatments*
- *Uncontrolled PV can lead to four times the risk of major thrombosis or death due to cardiovascular events*
- *PV is associated with disease transformation to myelofibrosis or acute myeloid leukemia*
- *Clear unmet need for new therapies able to provide more effective disease control*

Overview

PV is a myeloproliferative neoplasm (MPN) and is typically characterized by elevated hematocrit, the volume percentage of red blood cells in whole blood, which can lead to a thickening of the blood and an increased risk of blood clots, as well as an elevated white blood cell and platelet count[1]. PV may occur at any age but often presents later in life, with a median age at diagnosis of 60 years[1,2]. Approximately 100,000 patients in the U.S. are living with PV[3].

Treatment Options

Current standard treatment for PV is phlebotomy (the removal of blood from the body) plus aspirin. When phlebotomy can no longer control PV, chemotherapy such as hydroxyurea, or interferon, is utilized[4,5]. Approximately one in four (~25,000) patients with PV are considered uncontrolled[6,7] because they have an inadequate response to or are intolerant of hydroxyurea, the most commonly used chemotherapeutic agent for the treatment of PV.

Patients with PV who fail to consistently maintain appropriate blood count levels, including appropriate hematocrit levels, have an approximately four times higher risk of major thrombosis (blood clots) or cardiovascular death[8].

Prognosis/Life Expectancy

In a large population-based study in more than 4,000 patients with PV, the 10-year life expectancy was 36% lower than that of the general population[9]. Proper monitoring and treatment are important to prevent cardiovascular complications and/or disease transformation to myelofibrosis or acute myeloid leukemia[,10,11]. A proportion of patients with PV have an inadequate response to, or become intolerant of, commonly used therapies and are therefore unable to effectively control their disease, which is associated with an increased risk of progression or death[7].

Symptoms

Patients with PV can also suffer from an enlarged spleen and a significant symptom burden which may be attributed to thickening of the blood and lack of oxygen to parts of the body[12]. These symptoms commonly include:

- fatigue
- itching
- night sweats
- bone pain
- fever
- weight loss[5]

Prevalence

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What Causes Polycythemia Vera?

While the exact cause of PV is unknown, researchers believe that the condition results from overactive cell signaling of a pathway called the JAK (Janus kinase) pathway. The JAK pathway involves a number of JAK proteins: JAK1, JAK2, JAK3 and tyrosine kinase 2. These proteins are key players in many important biological processes, including the regulation of cytokines and the formation and development of blood cells[13,14].

Normally, the JAK pathway is tightly controlled to ensure normal blood cell production and cytokine signaling. However, in patients with PV, the JAK pathway is overactive. Generally, blood cell growth factors work through JAK2, and pro-inflammatory cytokines work though JAK1[15]. Since overactive JAK signaling can affect both JAK1 and JAK2, it is associated with both overproduction of blood cells and inflammation.

The overactivity of this pathway may be caused by a number of genetic mutations, such as the *JAK2*V617F, *MPL* and *LNK* mutations[16]. The *JAK2*V617F mutation is present in more than 95 percent of patients with PV[14]. These changes may cause the bone marrow to make the wrong number of blood cells. This imbalance of blood cells may cause some of the symptoms of PV.

Additional Resources on Polycythemia Vera

MPN Research Foundation	www.mpnresearchfoundation.org
MPN Advocacy & International	www.mpnadvocacy.com

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References

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