Anemia in MF is multi-factorial and includes disruption of the medullary erythropoietic niche due to fibrosis, anemia of inflammation, splenic sequestration, suppression of erythropoiesis by JAK-inhibitors and other factors.

The three disease hallmarks of MF are driven by three key signaling proteins:
- Janus Kinase 1 (JAK1)
- Janus Kinase 2 (JAK2)
- Activin A receptor, type I (ACVR1)

The optimal MF therapy would address all three hallmarks: constitutional symptoms, splenomegaly, and anemia.

There are currently no approved treatments that address all three dimensions of MF.

Inflammation and aberrant cytokine signaling producing debilitating constitutional symptoms.

Clonal proliferation leading to extramedullary hematopoiesis and burdensome splenomegaly.

Aberrant activation of hepcidin transcription via hyperactivated ACVR1 signaling resulting in profound functional iron deficiency and an iron restricted anemia.

Anemia of MF: Unmet Need

- A significant proportion of patients with MF develop anemia, with many becoming dependent on frequent red blood cell (RBC) transfusions.
- Intractable anemia depresses quality of life, portends poor outcomes, and can act to restrict access to currently approved JAK inhibitors in some patients.
- While progress has been made in treatment of splenomegaly and constitutional symptoms in the era of JAK inhibition, anemia remains the major untreated negative determinant of MF-related quality of life and overall survival.

Anemia in MF is multi-factorial and includes disruption of the medullary erythropoietic niche due to fibrosis, anemia of inflammation, splenic sequestration, suppression of erythropoiesis by JAK-inhibitors and other factors.

Key Manifestations of MF: Anemia, Constitutional Symptoms and Splenomegaly

Drivers of Disease in MF: Aberrant JAK1, JAK2 and ACVR1 Signaling

Extramedullary hematopoiesis & splenomegaly

Inadequate hematopoiesis & RBC sequestration

Displacement of marrow erythropoietic tissue by fibrosis

Altered bone marrow cytokine expression

Extramedullary hematopoiesis & splenomegaly

Pro-inflammatory cytokine profile

Impaired erythroid differentiation

Activated ACVR1

Elevated hepcidin

Impairment of iron metabolism

Anemia

Fibrosis & Extramedullary Hematopoiesis

Inflammation

Hepcidin

Other JAK Inhibitor Therapies

JAK inhibitor induced myelosuppression

References:

For more information, please visit www.sierraoncology.com

FOR INFORMATIONAL AND EDUCATIONAL PURPOSES ONLY; Momelotinib is an investigational agent not yet approved by the US FDA or any regulatory authority.