The Hanns A. Pielenz Clinical Research Center for Myeloproliferative Neoplasm Newsletter

MPNFocus

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Making Cancer History®

WINTER 2022-23

Patient Spotlight: Scott Rauch

Q: When were you first diagnosed with a hematological malignancy and which one? Did you have any symptoms that led to its diagnosis?

A: In January 2017, I noticed a bump on my cheekbone near my ear. The doctor gave me antibiotics for 3 weeks. However, in 2 weeks, I noticed that the lymph nodes in my groin were swollen on both sides. The swelling persisted after treatment with antibiotics and I had abdominal pain, so I went to an urgent care center. After the doctor examined me, he admitted me to the hospital. The PET scan that was performed revealed extensive adenopathy from the upper neck to the groin, consistent with T-cell lymphoblastic lymphoma, and splenomegaly. The blood work showed eosinophilia (high number of eosinophils), and very high counts of white blood cells. These results together with the findings of the bone marrow biopsy were consistent with diagnosis of a rare hematological malignancy named myeloid/lymphoid neoplasm with eosinophilia and *FGFR1* rearrangement (MLN^{FGFR1}).

Q: When did you have the first bone marrow biopsy? Which techniques were used to verify diagnosis of MLN^{FGFR1}? What were the results of your first biopsy?

A: My first bone marrow biopsy was performed in February 2017. I had another confirmatory bone marrow biopsy a month later when I first came to MD Anderson. Both biopsies showed the same findings, which were consistent with diagnosis of myeloid/lymphoid neoplasm with *FGFR1*.

"My experience has been truly amazing! I feel great because I have been a critical part of this clinical trial that developed a life-changing medication, which transformed a deadly disease to a treatable one, and saves lives!" *– Scott Rauch*

A (continued): The techniques were chromosomal analysis (karyotyping or cytogenetic testing) and f*luorescence in situ hybridization* (FISH) of the cells obtained from my bone marrow. FISH is a technique that is applied to verify the chromosomal abnormality in chromosome 8p11. In 2017, both tests showed that I had the characteristic chromosomal abnormality of this disease (MLN^{FGFR1}) in chromosome 8 (specifically 8p11).

Q: Did your local oncologist give you any treatment? When and how were you referred to the Clinical Center for MPNs?

A: Initially, I was treated with 2 cycles of chemotherapy (CHOP) for the lymphoma. However, when my bone marrow tests were completed, my local oncologist diagnosed MLN^{FGFR1}; the primary clinical presentation of MLN^{FGFR1} was lymphoma in my case. At that point, instead of continuing with a third cycle of CHOP, to his credit, my local oncologist immediately referred me to Dr. Verstovsek. My oncologist made the appointment and gave me the date to come to MD Anderson (March 2017). My local oncologist knew that Dr. Verstovsek was an expert in the field and was aware of a clinical trial that Dr. Verstovsek was going to lead for an investigational medication named pemigatinib to treat my disease at MD Anderson. I am very grateful to my local oncologist for having the knowledge and nobleness to refer me to Dr. Verstovsek because thanks to both doctors, I am alive today!

Q: How did your physician treat your disease at MD Anderson? Were you enrolled in a clinical trial? Which medication did you receive?

A: In our first discussions, Dr. Verstovsek didn't give me a time frame (life expectancy). Instead, he informed me about the pioneering clinical trial that he was leading to evaluate pemigatinib as a novel treatment for patients with MLN^{FGFR1}. Dr. Verstovsek was very confident that my disease would respond to the treatment in a few months. After confirming that I was eligible to participate, I was enrolled in this clinical trial.

Letter from the Director

Greetings to All!

As we approach the end of 2022 and the beginning of the new year, we have seminal advancements to celebrate in the treatment of MPNs. In particular, in 2022, two medications, **pemigatinib** and **pacritinib**, which we led in clinical development, received regulatory approval.

On August 26, 2022, the Federal Drug Administration (FDA) approved **pemigatinib** as a treatment for patients with relapsed or refractory myeloid/lymphoid neoplasm (MLN) with rearrangement of the gene Fibroblast Growth Factor Receptor 1 (*FGFR1*) or MLN^{FGFR1}. MLN^{FGFR1} is a rare yet aggressive hematological malignancy with very poor prognosis (survival 12-18 months). Pemigatinib demonstrated very high rates of complete response in the phase 2 FIGHT-203 clinical trial (NCT03011372), which I led as the Principal Investigator. Regulatory approval of pemigatinib has a dramatic impact in patients with MLN^{FGFR1} because it transformed a fatal disease into a treatable one and significantly extended survival.

"It is a very exciting time in the field of MPNs in light of the recent approvals of two MPN medications and the array of other medications in advanced clinical development. We are very optimistic that these novel treatments will substantially improve the quality of life and the outcomes of MPN patients and transform the field of MPNs in the near future!"

— Srdan Verstovsek, MD, PhD, Professor of Medicine and Director of the MPN Clinical Research Center

Last February, the FDA also approved **pacritinib** as a treatment for patients who have primary or secondary myelofibrosis and severe thrombocytopenia (platelet counts below $50x10^9$/L). Regulatory approval of pacritinib was an important advancement because there was a critical unmet need for thrombocytopenic patients with myelofibrosis prior to approval of pacritinib. Thrombocytopenic patients had poor prognosis and cannot be treated with the other approved JAK2 inhibitors (ruxolitinib and fedratinib) because these medications can further exacerbate low platelet counts.

In 2023, we look forward to another important advancement, namely regulatory approval of momelotinib. **Momelotinib** is unique among JAK1/2 inhibitors because it provides significant anemia benefits besides improving splenomegaly and symptoms. In light of the remarkable progress that has been made in the field of MPNs, we aspire to further improve the lives and outcomes of our patients substantially in the near future! •

Blessed and Happy Holidays and New Year!

Spotlight: Scott Rauch

[continued from page 1]

Q: What was the prognosis and life expectancy that your community oncologist gave you?

A: According to my community oncologist, my prognosis was very poor, and my life expectancy was about 12-18 months. Remarkably, because of being treated with pemigatinib, in March 2023, it will be 6 years that I have been alive since my diagnosis!

Q: How soon after you were enrolled in the trial of pemigatinib did your chromosome analysis become normal? How often do you have a bone marrow biopsy? Do the analyses continue to be normal?

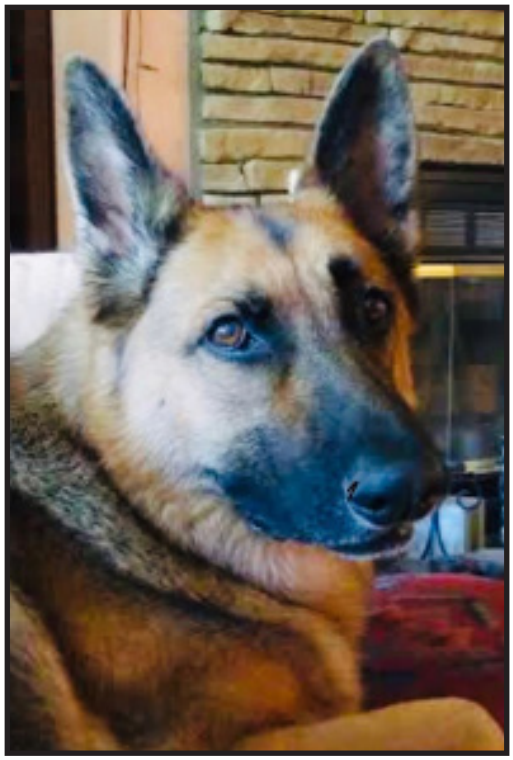
A: The analyses of my chromosomes were normalized in about 5 months (August 2017) after I started treatment with pemigatinib. Also, the PET scan that was performed showed elimination of the lymphadenopathy and splenomegaly I had. These results indicated that I had a complete response to pemigatinib, and therefore, the disease had been eliminated. At first, I had a bone marrow biopsy every few months for 3 years; then, I had a bone marrow biopsy every 6 months. For the last 2 years, I have had one bone marrow biopsy annually. Since August 2017, the analyses of my chromosomes continue to be normal, which indicates that the disease has been eliminated.

"When I had no hope, Dr. Verstovsek gave it to me and saved my life!"

– Scott Rauch

Q: How do you feel as the first patient enrolling in a clinical trial of a medication that received regulatory approval as the first treatment for MLN^{FGFR1}?

A: I am very proud and pleased to be the first patient on this clinical trial and experience the remarkable benefits from treatment with pemigatinib! My experience has been truly amazing!



Quinn, Scott's loyal dog and best friend

Q: Do you remain optimistic about your health? Are you considering allogeneic stem cell transplant?

A: Despite enrolling in the clinical trial on pemigatinib and the positive prognosis that Dr. Verstovsek gave me, at first, I was skeptical and hesitant about my outcome until I reached the benchmark of 1 1/2 years. After that point, I started thinking that I may actually make it! As long as pemigatinib keeps my disease in remission, I will continue this course of treatment and prefer not to undergo allogeneic stem cell transplant.

Q: Given your remarkable outcome from treatment with pemigatinib, what are your thoughts about the importance of clinical studies?

A: Clinical studies are vital in order to test medications and determine their efficacy. Without conducting clinical trials, we would never be able to make advancements in treating cancer. When the team did the first bone marrow biopsy, they asked me if they could aspirate more bone marrow for research studies. I readily agreed because these studies would not only benefit me but could help others with MLN^{FGFR1}. We had everything to gain and nothing to lose by my participation. I feel great to be a critical part of this study that developed a life-changing medication, which transformed a deadly disease to a treatable one, and saves lives!

Q: What have been the positive aspects of your journey?

A: I have been able to live more in the moment and not take anything for granted. I also feel extremely fortunate that Dr. Verstovsek had the extensive expertise to treat me with this medication! When I had no hope, Dr. Verstovsek gave it to me and saved my life!

Q: Have you had any symptoms since your diagnosis and enrollment in the clinical trial?

A: Pemigatinib improved my life and saved it! I have had mild fatigue, arthralgias and myalgias, excessive sweating, severe hair loss, digestive problems, and massive headaches, which recently improved. I also had brittle nails, onycholysis (nails separating from the nail beds), and mild dryness of the skin. By lowering the dose of pemigatinib in the last 6 months, I had 25-35% improvement in the skin symptoms. I visit the ophthalmologist every 3 months to have my eyes checked. Overall, my symptoms have been manageable and very minor compared to the extraordinary benefits of pemigatinib.

Q: What have been your sources of support since you were diagnosed with MLN^{FGFR1}?

A: Dr. Verstovsek and his team (physician assistant and research nurses) have been fantastic! They have been taking great care of me for nearly 6 years! My wife has been by my side from the beginning of my journey. I have also been fortunate to have "my family at work" and my neighbors. "It takes a village to save a life!" My co-workers (I have ~250 of whom I know 150), the owner and the general manager of the large resort where I have been working for 12 years have been extremely supportive. My manager readily gives me time off when I come to MD Anderson. I also have 4 wonderful neighbors who have helped me a lot through the years. I own 4 acres of land and have animals (a horse, a dog, a cat, and chickens). My neighbors have keys to my gate, and they take care of the property and our animals when my wife and I come to MD Anderson. Last but not least, I would like to mention my most loyal dog Quinn (in the picture). When I was in bed for 3 months in 2017, Quinn never left my side! Quinn was with me the entire time and thereafter. Quinn was the best friend I ever had! •

Myeloid/Lymphoid Neoplasms (MLN) with *FGFR1* Rearrangement

On August 26, 2022, the FDA approved pemigatinib as a treatment for patients with relapsed or refractory myeloid/lymphoid neoplasms (MLN) with rearrangement of the gene Fibroblast Growth Factor Receptor 1 (*FGFR1*) or MLN^{FGFR1}. MLN^{FGFR1} is a rare yet aggressive hematological malignancy involving myeloid and/or lymphoid cell proliferation that results from proliferation of the FGFR1 protein (this is an enzyme called tyrosine kinase). Many patients may have marked eosinophilia (abnormal number of eosinophils). Eosinophils (Figure 2) are a type of disease-fighting white blood cells with granules (small particles) containing enzymes that are released during infections, allergic reactions, and asthma.

In MLN^{FGFR1}, abnormal cell growth can involve the myeloid type of cells (for example, neutrophils, myelocytes, blasts) resulting in a myeloproliferative neoplasm (MPN) or acute myeloid leukemia. Other times, it may involve the lymphoid type of cells (for example, lymphocytes, lymphoblasts) resulting in acute lymphoblastic leukemia or lymphoma. A number of patients have a mixture of both. These are all possible presentations of this disease. MLN^{FGFR1} is suspected when analysis of the chromosomes (karyotype or cytogenetic testing) in cells obtained from the bone marrow shows chromosomal translocation (exchange of genetic material between two chromosomes) involving chromosome 8 (specifically at the 8p11 locus). This chromosomal abnormality involving 8p11 activates the *FGFR1* gene, which is located at that specific region. Activation of the gene results in production of the protein tyrosine kinase FGFR1 at high levels. Overproduction of protein FGFR1 drives the disease. In simple terms, abnormality in gene *FGFR1* is implied by the chromosome analysis, which identifies the 8p11 chromosomal abnormality. Figure 1A depicts the abnormal chromosomes 8 and 13, where they exchanged material (parts of chromosomes). The abnormality is verified by using a sensitive technique named *fluorescence in situ hybridization* (FISH) (Figure 1B; please review legend below). Translocation involving chromosome 8p11 is a hallmark of the disease and supports diagnosis of MLN^{FGFR1}. Patients with MLN^{FGFR1} had very poor prognosis and short life expectancy until pemigatinib was developed– the average survival was 12-18 months even after intensive chemotherapy and allogeneic stem cell transplant– and effective treatments were lacking until pemigatinib was approved.

Pemigatinib is a highly selective inhibitor of protein FGFR1. Pemigatinib demonstrated high rates of complete responses and complete cytogenetic responses (normalization of chromosomes in nearly 80% of the patients) as well as durability of responses (several years so far) in the open-label phase 2 FIGHT-203 clinical trial (NCT03011372). The impressive findings noted in the FIGHT-203 trial supported regulatory approval of pemigatinib. Regulatory approval of pemigatinib constitutes a remarkable advancement with extraordinary transformative impact for patients diagnosed with MLN^{FGFR1} because this fatal neoplasm became treatable and possibly curable with pemigatinib. •

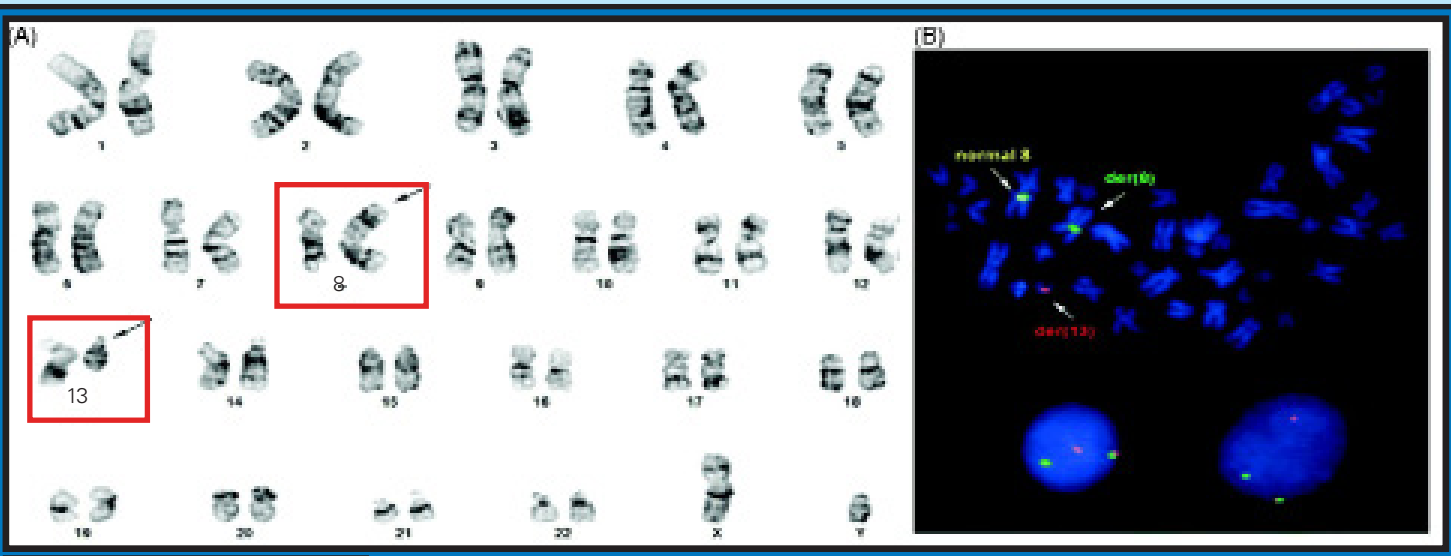


Figure 1 (please review upper figure). **Panel A.** Chromosome (karyotyping) analysis of the bone marrow from a patient with an abnormality in chromosome 8 (specifically 8p11) and chromosome 13 (marked with red boxes). **Panel B.** Confirmatory analysis of the *FGFR1* gene rearrangement by the technique *fluorescence in situ hybridization* (FISH). In FISH, two-color breakapart fluorescent dyes are used as probes to demonstrate the *FGFR1* gene rearrangement. In Figure 1B, the normal chromosome 8 is stained yellow. In the same figure, the deleted region of the *FGFR1* gene in the abnormal chromosome 8 is stained green (centromere, center of gene during cell division), and the fusion partner (different gene) of *FGFR1* in chromosome 13 is stained red (telomer, end of gene). Figure 1: Strati P. et al. *Leukemia & Lymphoma* 2018;59(7):1672.

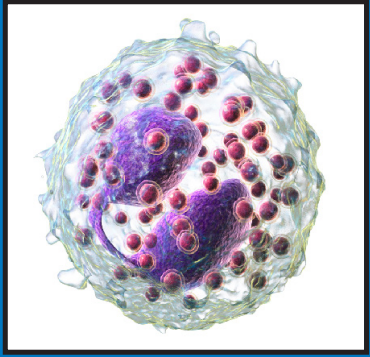


Figure 2. Eosinophil

MPN Clinical Trials

Listed below are clinical trials enrolling patients with MPNs at The University of Texas MD Anderson Cancer Center. For more information on these clinical trials, please call the information line toll-free at 1-800-392-1611 or visit: https://www.mdanderson.org/research/departments-labs-institutes/departments-divisions/leukemia/clinical-trials.html and review the MPN section. To find other clinical trials for MPN, please go to clinicaltrials.gov. To schedule an appointment with a doctor in the Leukemia Department at the MD Anderson Cancer Center, please call 713-563-2000 (new patient line).

Phase 3 Study (VERIFY) of the Hepcidin Mimetic Rusfertide (PTG-300) in Patients with Phlebotomy-Requiring Polycythemia Vera (PV)

Protocol # 2022-0005
clinicaltrials.gov NCT No: 05210790
Principal Investigator:
Srdan Verstovsek, MD, PhD

Study Description: The objective of this study is to evaluate the safety and efficacy of rusfertide compared to placebo in patients diagnosed with PV who required phlebotomies to maintain the hematocrit < 45% (with or without concurrent cytoreductive therapy). Rusfertide is a mimetic of hepcidin, which is a short peptide synthesized by hepatocytes (liver cells). Rusfertide is a key regulator of iron levels in the body, and therefore, it affects the production of red blood cells. In the phase 2 trial, patients required ≥3 phlebotomies before rusfertide treatment; rusfertide treatment essentially eliminated phlebotomies in all the patients. Rusfertide is injected under the skin.

Phase 1, Open-label Study of INCB057643 in Participants with Myelofibrosis and Other Advanced Myeloid Neoplasms (LIMBER)

Protocol # 2021-1092

clinicaltrials.gov NCT No: 04279847

Principal Investigator:

Prithviraj Bose, MD

Study Description: The goal of this open-label, two-part phase 1 study is to further evaluate the safety and tolerability as well as the anemia response of INCB057643 (alone or in combination with ruxolitinib) in patients with myelofibrosis (relapsed/refractory primary and secondary MF) and MPN in the accelerated phase (blasts are ≥10-19% in the peripheral blood or bone marrow). INCB057643 is an investigational agent that inhibits the activity of bromodomain and extra-terminal domain (BET) proteins, which have a wide range of cell functions. INCB057643 is administered by mouth. The study is open and enrolling patients.

Phase 1/2 Study of INCB000928 as a Monotherapy in Participants with Anemia due to Myeloproliferative Disorders

Protocol # 2020-0409

clinicaltrials.gov NCT No: 04455841

Principal Investigator:

Srdan Verstovsek, MD, PhD

Study Description: In this study, the safety and tolerability of INCB000928 will be assessed in participants with myelofibrosis (post-polycythemia vera MF and post-essential thrombocythemia MF) who are transfusion-dependent or present with symptomatic anemia (hemoglobin <10 g/dL). The main goals of the study are to assess the efficacy of INCB000928 in improving anemia, the duration of anemia response, and the rate of transfusion-independence in MF patients with anemia. INCB000928 will be administered as monotherapy. INCB000928 is administered by mouth.

Phase 3 Randomized, Double-Blind Active-Control Study of CPI-0610 (Pelabresib) and Ruxolitinib vs. Placebo and Ruxolitinib in JAK-Inhibitor Treatment-Naïve MF Patients (MANIFEST-2 trial)

Protocol #2020-0739
clinicaltrials.gov NCT No: 04603495

Principal Investigator:
Srdan Verstovsek, MD, PhD

Study Description: Pelabresib (formerly CPI-0610) is an oral epigenetic modifier that interferes with the activity BET proteins, which have a wide range of cell functions. Inhibition of BET proteins reduces the levels of many other proteins that are important for survival and multiplication of cells, including drivers of bone marrow fibrosis. In this phase 3 study, pelabresib is administered in combination with ruxolitinib to MF patients not previously treated with JAK inhibitors. In the MANIFEST trial, pelabresib alone or in combination with ruxolitinib showed significant improvements in spleen volume reduction, hemoglobin levels, red blood cell transfusion burden, and bone marrow fibrosis and symptoms. Treatment with pelabresib may have disease-modifying potential in MF.

Phase Open-Label, Multicenter, Phase 1b/2 Study of the Safety and Efficacy of TL-895 Combined with Ruxolitinib in Patients with MF

Protocol # 2022-0183
clinicaltrials.gov NCT No: 05280509

Principal Investigator:

Prithviraj Bose, MD

Study Description: TL-895 is a selective inhibitor of Bruton's tyrosine kinase (BTK), which mediates myeloid extramedullary hematopoiesis and proinflammatory cytokine production. TL-895 may benefit MF patients by blocking activation of NF-κB. NF-κB is a protein that controls DNA transcription, cytokine production, and cell survival. BTK activity is important for the growth of cancer cells; malignant cells die when they are treated with TL-895. In this study, patients with myelofibrosis who have a suboptimal response to ruxolitinib will be treated with the combination of TL-895 and ruxolitinib. TL-895 has a novel mechanism of action and is administered by mouth.

Phase 2 Study of Bezuclastinib Safety and Efficacy in Patients with Indolent or Smoldering Systemic Mastocytosis (SUMMIT trial)

Protocol # 2021-0880
clinicaltrials.gov NCT No: 05186753

Principal Investigator:
Prithviraj Bose, MD

Study Description: In mastocytosis, the body makes too many mast cells. Mast cells respond to allergic and immune reactions. Non-advanced systemic mastocytosis (SM) includes the indolent (namely, benign) and smoldering subtypes. No mast cell-related organ damage occurs in non-advanced SM, which is much more common. In this phase 2 study, the safety and efficacy of bezuclastinib vs. placebo is evaluated in patients with non-advanced SM. Bezuclastinib (formerly CGT9486) is an oral small-molecule tyrosine kinase inhibitor with unique selectivity for mutation *KIT* D816V, which drives growth of mast cells. Bezuclastinib minimally penetrates the blood-brain barrier and is administered by mouth.

Phase 3 Study of Luspatercept (ACE-536) versus Placebo in Subjects with Myeloproliferative Neoplasm-Associated Myelofibrosis on Concomitant JAK2 Inhibitor Therapy and Who Require Red Blood Cell Transfusions (INDEPENDENCE trial)

Protocol # 2020-1010
clinicaltrials.gov NCT No: 04717414

Principal Investigator:
Srdan Verstovsek, MD, PhD

Study Description: The goal of this pivotal phase 3 clinical study is to evaluate the efficacy of luspatercept (formerly ACE-536) versus placebo in patients with MF-associated anemia who are receiving concomitant JAK2 inhibitors and require red blood cell (RBC) transfusions. The study will assess the drug's potential to increase hemoglobin and eliminate the necessity for red blood cell transfusions. Anemia is a critical challenge in MF patients. Luspatercept increases RBC production Adding luspatercept to the treatment of MF patients with anemia can eliminate the need for RBC transfusions when symptoms are responding to JAK2 inhibitors. Luspatercept is administered as an injection under the skin.

A Randomized Double-Blind Placebo-Controlled Phase 2/3 Study of BLU-263 in Indolent Systemic Mastocytosis (HARBOR trial)

Protocol # 2022-0072
clinicaltrials.gov NCT No: 04910685

Principal Investigator:
Prithviraj Bose, MD

Study Description: The body makes too many mast cells in mastocytosis. Indolent (namely, benign) systemic mastocytosis is much more common; it does not affect organ function, but it may cause many symptoms and poor quality of life. In this phase 2/3 study, the safety and efficacy of BLU-263 compared to placebo is evaluated in patients with indolent systemic mastocytosis whose symptoms are not adequately controlled with best supportive care. BLU-263 is a novel investigational tyrosine kinase inhibitor with high selectivity and potency for KIT D816V, which drives the growth of mast cells. BLU-263 showed limited penetration of the central nervous system and is administered by mouth.

An Open-Label, Phase 2a/2b Study of KRT-232 (Navtemadlin) in Patients with Primary MF, Post-PV MF or Post-ET MF Who Have Failed Prior Treatment with a JAK Inhibitor (BOREAS trial)

Protocol # 2018-0906
clinicaltrials.gov NCT No: 03662126

Principal Investigator: Prithvi Bose, MD

Study Description: The goal of this study is to evaluate the safety and efficacy of navtemadlin (formerly KRT-232) in patients diagnosed with MF. Navtemadlin is an inhibitor of protein human double minute 2 (HDM2). HDM2 inhibits the function of p53, an important protein that plays a critical role in cell survival and death (tumor suppressor). The phase 2 part of the study, evaluating navtemadlin in MF patients who relapsed or were refractory to ruxolitinib, was completed, and the optimal daily dose was determined. The phase 2 study was amended to the phase 3 study in which navtemadlin will be compared to best available therapy (excluding JAK inhibitors) in MF patients who are refractory/resistant to JAK inhibitors. The phase 3 part of the study (BOREAS) is accruing patients. Navtemadlin is administered by mouth.

Phase 2 Open-label Clinical Study of the Safety and Efficacy of Bezuclastinib (CGT9486) in Patients with Advanced Systemic Mastocytosis (APEX trial)

Protocol # 2021-0587

clinicaltrials.gov NCT No: 04996875

Principal Investigator:

Prithviraj Bose, MD

Study Description: In mastocytosis, the body makes too many mast cells. In this multicenter, open-label phase 2 study, the safety and efficacy of bezuclastinib will be evaluated in patients with advanced systemic mastocytosis. Bezuclastinib is an oral small-molecule tyrosine kinase inhibitor and has unique selectivity for the mutation *KIT* D816V, which drives growth of mast cells. Early results showed that bezuclastinib is well tolerated and clinically active. Bezuclastinib minimally penetrates the blood-brain barrier and is administered by mouth.

Phase 1/2a Study to Evaluate Safety, Pharmacokinetic and Pharmacodynamic Dose Escalation and Expansion Study of PXS-5505 in Patients with Primary, Post-Polycythemia Vera or Post-Essential Thrombocythemia Myelofibrosis

Protocol #2021-0753

clinicaltrials.gov NCT No: 04676529

Principal Investigator:

Lucia Masarova, MD

Study Description: This is an open-label phase 1/2a clinical trial evaluating the safety and tolerability of PXS-5505 in patients with myelofibrosis. PXS-5505 is a small molecule pan-lysyl oxidase (LOX) inhibitor. The enzyme lysyl oxidase promotes formation of a network of collagen fibers and is elevated in the bone marrow of MF patients, thereby promoting fibrosis (scarring). Enrolled patients should not be eligible to receive ruxolitinib or fedratinib. Also, eligible patients developed severe thrombocytopenia (platelet counts below $50x10^9$/L) or red blood cell transfusion dependence while treated with JAK2 inhibitors or were refractory/relapsed after at least 3 months of treatment with JAK2 inhibitors. PXS-5505 is administered by mouth as a capsule.

Phase 2 Study to Evaluate Sapablursen (formerly IONIS TMPRSS6-LRx, ISIS 702843) in Patients with Polycythemia Vera

Protocol #2021-0897

clinicaltrials.gov NCT No: 05143957

Principal Investigator:

Prithviraj Bose, MD

Study Description: Sapablursen (formerly IONIS-TMPRSS6-LRx, ISIS 702843) is a type of oligonucleotide (DNA) that increases secretion of hepcidin from liver cells. Hepcidin is a master regulator of iron metabolism in the body; a high quantity of hepcidin results in production of fewer red blood cells in the body. In patients with polycythemia vera (PV), the goal is to maintain the hematocrit below 45% in order to decrease or eliminate thrombotic events. In this phase 2 study, the efficacy, safety and tolerability of sapablursen will be evaluated in phlebotomy-dependent (requiring bloodletting) patients with PV. Sapablursen is administered subcutaneously (by injection under the skin) every 4 weeks. The study is open and enrolling patients.

An Open-label, Phase 2a Study of the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of GB2064 (LOXL2 Inhibitor) in Participants with Myelofibrosis

Protocol # 2020-1217

clinicaltrials.gov NCT No: 04679870

Principal Investigator:

Srdan Verstovsek, MD, PhD

Study Description: In this study, the safety and efficacy of GB2064 will be evaluated in patients with myelofibrosis (intermediate- or high-risk) who are not currently taking a JAK inhibitor (e.g., ruxolitinib or fedratinib) and are refractory, intolerant or ineligible. It has been shown that the enzyme lysyl oxidase (LOX) promotes formation of a network of collagen fibers and is elevated in the bone marrow of mice and MF patients, thereby promoting fibrosis (scarring). In preclinical studies, small-molecule inhibitors of LOX showed promising results in slowing down the progression of myelofibrosis. GB2064 is administered by mouth.

Phase 3 Clinical Study Evaluating Imetelstat vs. BAT in Adult Patients with Intermediate-2 or High-Risk Myelofibrosis (MF), Refractory to Janus Kinase (JAK) Inhibitors (IMpactMF)

Protocol # 2020-1141

clinicaltrials.gov NCT No: 04576156

Principal Investigator:

Srdan Verstovsek, MD, PhD

Study Description: Imetelstat is a potent inhibitor of telomerase. Telomerase is an enzyme that maintains the structural integrity of chromosomes in normal and cancer cells. Chromosomes are finger-like structures in the nuclei of cells that carry genes. The clinical efficacy of imetelstat and the possible benefit in prolonging the survival of patients with myelofibrosis who relapsed/were refractory to ruxolitinib (JAK inhibitor, standard first-line therapy for most MF patients) was evaluated in the phase 2 trial IMbark. In the phase 2 study, the higher dose of imetelstat was possibly associated with prolonged survival compared to what one would expect; this higher dose of imetelstat will be administered intravenously (under the skin) every 21 days to MF patients in the pivotal phase 3 trial (IMpactMF). In the IMpactMF trial, imetelstat will be compared to best available therapy (BAT), excluding JAK inhibitors in intermediate-2 and high-risk MF patients who relapsed/were refractory to JAK inhibitors. Imetelstat is the first medication to be evaluated in clinical trials for patients with MF regarding its ability to prolong survival.

Phase 3 (SURPASS ET), Open-label, Multicenter, Randomized, Active-Controlled Study to Assess Pharmacokinetics and Compare the Efficacy, Safety, and Tolerability of Ropeginterferon alpha-2b (P1101) versus Anagrelide as Second-Line Therapy for Essential Thrombocythemia (ET)

Protocol # 2020-0108
clinicaltrials.gov NCT No: 04285086

Principal Investigator:
Srdan Verstovsek, MD, PhD

Study Description: Ropeginterferon alpha -2b is a novel, long-acting interferon formulation that can be administered by injection, bi-monthly instead of weekly. Ropeginterferon alpha-2b was approved as a treatment for PV patients who require phlebotomies in the European Union in February 2019 and was approved in the US in November 2021. This phase 3 study (SURPASS ET) will assess the efficacy (platelet and white blood cell counts, disease symptoms, hemorrhagic/thrombotic events), safety and tolerability of ropeginterferon alpha-2b compared to anagrelide (a medicine that reduces platelets), after 12 months of treatment, as a therapy for high-risk ET patients with resistance or intolance to hydroxyurea (standard first line therapy). A white blood cell count $\geq 10x10^9$/L is required at screening to be enrolled in the study.

Phase 1 Study of Elotuzumab in the Treatment of *JAK2*-Mutated Primary Myelofibrosis, Post-PV MF, or Post-ET MF

Protocol # 2020-0522
clinicaltrials.gov NCT No: 04517851

Principal Investigator:
Prithviraj Bose, MD

Study Description: The goal of this pilot study is to assess the efficacy (improvements in blood cell counts and bone marrow fibrosis grade, splenomegaly, and disease-related symptoms), safety and tolerability of elotuzumab in patients with MF who are not candidates for JAK inhibitors or have failed JAK inhibitors. Elotuzumab is an anti-SLAMF7 monoclonal antibody that has the potential to improve or reverse bone marrow fibrosis. Elotuzumab is administered by injection.

An Open-label, Multicenter, Phase 1b/2 Study of the Safety and Efficacy of KRT-232 Combined with Ruxolitinib in Patients with PMF, Post-PV MF, or Post-ET MF Who Have a Suboptimal Response to Ruxolitinib

Protocol # 2020-0279
clinicaltrials.gov NCT No: 04485260

Principal Investigator:
Prithviraj Bose, MD

Study Description: This clinical research study will evaluate the safety and efficacy of ruxolitinib and navtemadlin (formerly KRT-232), an orally administered inhibitor of the human double minute 2 (HDM2) protein, in patients with myelofibrosis. HDM2 inhibits the function of a very important protein (p53), which plays a critical role in cell survival and death. Navtemadlin in combination with ruxolitinib may show synergistic efficacy and disease modification through a complementary mechanism promoting death of malignant cells. Patients participating in this clinical trial should be on a stable dose of ruxolitinib and have suboptimal response to it. Navtemadlin is administered by mouth as a pill.

Phase 2b, Open-label, Randomized Study to Assess the Efficacy and Safety of NS-018 (Ilginatinib) versus BAT in Patients with Primary Myelofibrosis, Post Polycythemia Vera MF, or Post-Essential Thrombocythemia MF and Severe Thrombocytopenia

Protocol # 2021-0348
clinicaltrials.gov NCT No: 04854096

Principal Investigator:
Lucia Masarova, MD

Study Description: Ilginatinib (formerly NS-018) is a selective, small molecule inhibitor of JAK2 that is more selective for $JAK2^{V617F}$ and less myelosuppressive. In previous clinical trials, ilginatinib improved splenomegaly and constitutional symptoms in patients with myelofibrosis and was generally well tolerated. In this randomized phase 2 study, ilginatinib will be evaluated in comparison to best available therapy (BAT) in patients who have myelofibrosis and severe thrombocytopenia (platelet counts below $50x10^9$/L). Ilginatinib is administered by mouth.

Phase 2 Open-label, Multicenter Study of TL-895 in Patients with Relapsed/Refractory Myelofibrosis, Janus Kinase Inhibitor-Intolerant Myelofibrosis and Janus Kinase Inhibitor Treatment-Ineligible Myelofibrosis

Protocol # 2020-0738
clinicaltrials.gov NCT No: 04655118

Principal Investigator:
Srdan Verstovsek, MD, PhD

Study Description: This study aims to evaluate the efficacy of TL-895 in myelofibrosis patients who do not respond to ruxolitinib. Ruxolitinib (JAK1/2 inhibitor) is the standard first-line therapy for the majority of myelofibrosis patients. Patients who relapse or are not eligible to be treated with JAK inhibitors can also be enrolled in this study. TL-895 is a selective inhibitor of Bruton's tyrosine kinase (BTK). TL-895 may benefit MF patients by blocking activation of NF-κB. NF-κB is a protein that controls DNA transcription, cytokine production, and cell survival. BTK activity is important for the growth of cancer cells; malignant cells die when they are treated with TL-895. TL-895 has a novel mode of action and is administered by mouth.

Phase Ib, Open-label Study of CK0804 as an Add-on Therapy in Participants with Myelofibrosis and Suboptimal Response to Ruxolitinib (LIMBER-TREG108)

Protocol # 2021-0341
clinicaltrials.gov NCT No: 05423691

Principal Investigator:
Lucia Masarova, MD

Study Description: This study will assess the safety and tolerability of CK0804 in patients with myelofibrosis who have suboptimal response to ruxolitinib. CK0804 is a novel therapeutic derived from allogeneic umbilical cord blood-derived T-regulatory cells (T-reg). CK0804 is prepared in a way to target the bone marrow. T-cells are white blood cells that are important for the immune system. The T-regulatory cells used to make CK0804 will come from a donor who is not related to the patient. CK0804 will be combined with ruxolitinib and will be evaluated with respect to improvement in anemia and splenomegaly. CK0804 can be infused intravenously in the outpatient setting. •

Highlights of MPN Clinical Trials

Presentations from the 64th Annual Meeting American Society of Hematology

DECEMBER 10-13, 2022 • NEW ORLEANS, LA

Pelabresib (CPI-0610) Combined with Ruxolitinib for JAK Inhibitor Treatment-Naïve Patients with Myelofibrosis: Durability of Response and Safety beyond Wk 24

Presenter: John Mascarenhas, MD

Pelabresib (formerly CPI-0610) is a selective and potent small-molecule inhibitor of bromodomain and extra-terminal (BET) proteins, which have a wide range of cell functions. Inhibition of BET proteins reduces the levels of many other proteins that are important for survival and multiplication of cells, including drivers of bone marrow fibrosis, splenomegaly, and cytopenias.

In Arm 3 of the multicenter MANIFEST phase 2 trial, pelabresib is evaluated in combination with ruxolitinib in JAK-inhibitor naïve patients with myelofibrosis (MF). Interim data from the trial showed significant reduction in spleen volume. At 24 weeks, 68% of the patients had 35% or more reduction in spleen volume (median decrease –50%) and 56% of the patients had 50% or more improvement in the total symptom score (median decrease –59%). Significant improvements were observed in bone marrow fibrosis (1 grade or more) in nearly 30% of the patients, and the treatment was well tolerated; the most common adverse event was thrombocytopenia. The phase 3 clinical trial MANIFEST-2, evaluating pelabresib in combination with ruxolitinib in JAK-inhibitor naïve patients, is open at the Clinical Research Center for MPNs (protocol # 2020-0739).

Updated Results from the MOMENTUM Phase 3 Study of Momelotinib (MMB) versus Danazol (DAN) in Symptomatic and Anemic Myelofibrosis (MF) Patients, Previously Treated with a JAK Inhibitor

Presenter: Aaron Gerds, MD

Momelotinib is a JAK1/2 inhibitor that significantly improved anemia besides splenomegaly and disease-related symptoms in patients with myelofibrosis (MF) in previous trials. Momelotinib increased hemoglobin and reduced the need for red blood cell transfusions. Momelotinib mproves anemia because it decreases production of hepcidin in the liver; hepcidin is the master regulator of iron metabolism in the body. In the pivotal phase 3 MOMENTUM trial, momelotinib demonstrated significantly superior efficacy compared to danazol with respect to improving total symptom scores, transfusion-independence and spleen responses in anemic and symptomatic MF patients at 24 weeks. Momelotinib was effective in patients with low platelet counts, including patients with platelets $<50x10^9$/L. After 24 weeks, patients receiving danazol could be treated with momelotinib. Significant benefits in overall survival and leukemia-free survival were noted in patients with platelet counts $<50x10^9$/L who were treated with momelotinib vs. danazol. In August 2022, the FDA accepted a new drug application for momelotinib as a treatment for MF.

Ropeginterferon alfa-2b versus Standard Therapy for Low-Risk Patients with PV. Final Results of Low-PV Randomized Phase 2 Trial

Presenter: Tiziano Barbui, MD

Ropeginterferon alfa-2b is a novel, long-acting interferon formulation that can be administered by injection once every 2 weeks or less frequently. Ropeginterferon alpha-2b was approved in the US for treatment of PV patients who need phlebotomies in late 2021; it was also approved in the European Union in February 2019.

In patients who have PV, it is critical to keep the hematocrit ≤45% to reduce the risk of thrombosis. In this phase 2 low-PV study, the effect of ropeginterferon alfa-2b administered with standard therapy vs. phlebotomy only was assessed in low-risk PV patients after follow-up at 1 year. The hematocrit remained below 45% in the majority of the patients who were treated with ropeginterferon alfa-2b compared to the patients who received cytoreductive therapy only. No disease progression was noted in the patients treated with ropeginterferon alfa-2b. Conversely, disease progression was seen in a proportion of the patients who did not receive ropeginterferon alfa-2b.

The final results of the study demonstrated that ropeginterferon alpha-2b is superior to cytoreductive therapy alone in order to keep the hematocrit ≤45% and limit disease progression in low-risk PV patients.

Highlights of MPN Clinical Trials (continued)

Presentations from the 64th Annual Meeting of ASH

A Phase 2 Study of the LSD1 Inhibitor Bomedemstat (IMG-7289) for the Treatment of Essential Thrombocythemia (ET)

Presenter: Harinder Gill, MD

This global phase 2 study is evaluating bomedemstat (formerly IMG-7289) in patients with essential thrombocythemia (ET) who are resistant or intolerant to at least one standard-of-care treatment. Bomedemstat is an oral inhibitor of lysine-specific histone demethylase 1 (LSD1), a regulator protein that is critical in differentiation of progenitors into megakaryocytes, which produce platelets and are important in ET pathogenesis. The enrolled patients are required to have platelet counts >450x10^9/L, history of thrombosis or age >60 years. The vast majority of the patients (94%) achieved platelet counts below 400x10^9/L, without thromboembolic events and the white blood cell counts decreased below 10x10^9/L in all the patients who had higher counts. Based on these promising results, a phase 3 trial of bomedemstat in ET patients is planned.

Preliminary Safety and Efficacy from APEX, a Phase2 Study of Bezuclastinib (CGT9486), a Novel, Highly Selective, Potent *KIT*D816V Tyrosine Kinase Inhibitor, in Adults with AdvSM

Pres.: Daniel J. DeAngelo, MD, PhD

Advanced systemic mastocytosis is a rare, aggressive cancer of mast cells, which are a type of white blood cell found in connective tissues and the bone marrow. Bezuclastinib is an oral small-molecule inhibitor of the tyrosine kinase KIT and has unique selectivity for mutation *KIT* D816V, which drives the growth of mast cells. Bezuclastinib is currently studied in patients with advanced systemic mastocytosis and minimally penetrates the blood-brain barrier. The majority of patients who were treated with bezuclastinib had >50% reduction in mast cells, tryptase levels, and *KIT* D816V mutation burden. No cognitive issues or intracranial bleeding was observed. The trial on bezuclastinib in patients with AdvSM is open at our MPN Clinical Center (protocol #2021-0587).

Avapritinib as First-Line Therapy in Patients with Advanced Systemic Mastocytosis: Efficacy and Safety from the PATHFINDER Study

Presenter: Deepti Radia, MBBS

Avapritinib is a potent and highly selective inhibitor of the mutant tyrosine kinase protein KIT (mutation *KIT*D816V). Mutation *KIT* D816V produces an abnormal protein and is the key driver of the disease in 90-95% of the cases. Avapritinib showed high efficacy in the phase 1 EXPLORER and the phase 2 PATHFINDER studies, regardless of disease subtypes. In the PATHFINDER study, avapritinib elicited profound, rapid and durable responses; and the medication was generally well tolerated. The overall response rate was 84%, and the overall survival rate was 88% at 2 years. Bone marrow mast cells, tryptase levels and the *KIT* D816V burden decreased in nearly all the patients. The FDA approved avapritinib for treatment of patients with advanced systemic mastocytosis in June 2021. Avapritinib is not recommended for patients with platelet counts below 50x10^9/L.

Efficacy and Safety of Ropeginterferon alfa-2b for Pre-Fibrotic Primary Myelofibrosis and DIPSS Low/Intermediate-1 Risk Myelofibrosis

Presenter: Harinder Gill, MD

Ropeginterferon alfa-2b is a novel, long-acting interferon formulation that is administered by injection. Ropeginterferon alfa-2b was approved in the US for treatment of PV patients who need phlebotomies in late 2021. In this phase 2 study, patients with prefibrotic MF, and primary or secondary MF who needed cytoreduction were enrolled. After 24 and 48 weeks of treatment with ropeginterferon alfa-2b, 74% and 67% of the patients achieved complete response (did not need cytoreduction), respectively, and the *JAK2*V617F burden decreased in the majority of the patients. Ropeginterferon alfa-2b was well tolerated.

Combination of Navitoclax and Ruxolitinib in JAK Inhibitor-Naïve Patients with Myelofibrosis Mediates Responses Suggestive of Disease Modification

Pres.: Francesco Passamonti, MD

Navitoclax is a novel small molecule that inhibits the B-cell lymphoma 2 (Bcl-2) family of proteins (primarily Bcl-xL), which are overexpressed in many types of cancer and prevent cancer cells from dying. Preclinical studies demonstrated that inhibition of both Bcl-1/Bcl-xL and JAK2 has the potential to enhance the death of malignant cells. In this phase 2 study (REFINE trial, cohort 3), the efficacy of navitoclax combined with ruxolitinib was evaluated in patients with myelofibrosis who had not been previously treated with a JAK inhibitor. The goals of the study were to measure the percentage of patients who achieved spleen volume reduction 35% or more (SVR35) at 24 weeks, improvement in bone marrow (BM) fibrosis and % decrease in driver gene burden (*JAK2*V617F, *MPL*, *CALR*). SVR35 and one or more grades of BM fibrosis improvement were noted in all subgroups of patients, including high-risk. Also, the % *JAK2* V617F burden decreased by 20% or more in 50% of the patients. These findings are very encouraging and may suggest disease modification by navitoclax.

Highlights of MPN Clinical Trials (continued)

Presentations from the 64th Annual Meeting of ASH

Siremadlin, a Human Double Minute-2 Inhibitor, Added to Ruxolitinib after Suboptimal Response in Patients with Myelofibrosis: Results from Part 1 of the Phase 1/2 ADORE Study

Presenter: Florian Heidel, MD

Siremadlin is a potent and selective inhibitor of the human double minute 2 (HDM2) protein. HDM2 inhibits the function of a very important protein (p53), which plays a critical role in cell survival and death. Siremadlin restores p53-mediated apoptosis (cell death), which may promote spleen volume reduction in MF patients. In this phase 1/2 study (ADORE), the combination of siremadlin with ruxolitinib is studied in MF patients who have suboptimal response to ruxolitinib alone. The study established the recommended dose of siremadlin and showed that the medication was well tolerated. At 24 weeks, robust spleen responses were recorded in the patients who were treated with the combination of siremadlin with ruxolitinib.

Final Efficacy and Safety of Add-on Parsaclisib to Ruxolitinib Therapy in Myelofibrosis Patients with Suboptimal Response to Ruxolitinib: Final Results from a Phase 2 Study

Pres.: Abdulraheem Yacoub, MD

Parsaclisib is a highly selective and potent oral inhibitor of the delta isoform of phosphatidylinositol-3-kinase (PI3K). PI3K is an enzyme primarily expressed in hematopoietic cells and plays a key role in cell signaling and growth, survival, and multiplication of cancer cells. Persistent activation of the PI3K-AKT pathway, due to JAK2 activation, may cause suboptimal response of myelofibrosis patients to ruxolitinib treatment. In this phase 2 trial, patients who had primary or secondary MF and received ruxolitinib for more than 6 months (stable dose for >8 weeks) were treated with parsaclisib in combination with ruxolitinib. The final results of the study were reported. The combination of ruxolitinib and parsaclisib was efficacious, primarily in the subgroup that was treated with daily regimens of parsaclisib; this cohort experienced considerable changes in palpable spleen length and reduction of symptoms at 12 and 24 weeks. Parsaclisib had an acceptable safety profile.

Final Results of RUXOPEG, a Phase 1/2 Adaptive Randomized Trial of Ruxolitinib (Rux) and Pegylated Interferon alpha (IFNa) 2a in Patients with Myelofibrosis

Presenter: J-J. Kiladjian, MD, PhD

The multicenter phase 1/2 RUXOPEG trial evaluated the efficacy of different doses of ruxolitinib combined with pegylated interferon alpha in patients with myelofibrosis who had not been previously treated with either one of the medications. The spleen length was reduced by 50% or more in 70% of the patients at 24 weeks, and splenomegaly was fully resolved in 38% of the patients. The final results of the RUXOPEG study, which is the first trial that assessed the safety and efficacy of the combined regimen, demonstrated that the combination of ruxolitinib with pegylated interferon provided high rates of spleen and molecular responses (lowered the *JAK2* V617F burden) due to selectively targeting mutated progenitors.

JAK2 V617F Molecular Response to Ruxolitinib in Patients with PV and ET Is Associated with Lower Risk of Progression to Secondary Myelofibrosis

Presenter: P. Guglielmelli MD, PhD

In 2014, ruxolitinib was approved as a treatment for patients with polycythemia vera (PV) who are refractory or intolerant to hydroxyurea.

In this study, 65 patients with PV and 12 with essential thrombocythemia (ET) were treated with ruxolitinib, and the molecular responses were assessed after long term treatment.

The groups of patients who had molecular responses to ruxolitinib were the following: 1. complete molecular response (undetectable *JAK2* V617F); 2. deep molecular response (*JAK2* V617F≤2%; and 3. partial molecular response (*JAK2* V617F ≥50%). The mean decrease of *JAK2* V617F burden was 65%. Overall, the PV and ET patients who achieved complete and deep molecular responses over long term treatment with ruxolitinib had significantly lower risk to progress to secondary MF compared to patients who did not have changes in the burden (%) of *JAK2* V617F. Patients who had a partial molecular response showed lower probability to progress to MF. These findings indicate that attainment of a molecular response may indicate disease modification in patients with PV and ET. •

The Hanns A. Pielenz Clinical Research Center for Myeloproliferative Neoplasm Newsletter

MPN Focus

MPN Focus is a periodic newsletter published by The Hanns A. Pielenz Clinical Research Center for Myeloproliferative Neoplasm at MD Anderson Cancer Center. MPN Focus provides the members of the MPN community with information on current research and treatments.

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Resources for Physicians & Patients

MPN ADVOCACY & EDUCATION INTERNATIONAL

Founded by Ann Brazeau, former vice president of development at **MPN Research Foundation, MPN Advocacy & Education International** provides educational programs, materials, and resources for patients, caregivers, physicians, and entire healthcare teams to improve their understanding of MF, PV, and ET. Information on 2019 Patient Education Symposia, hosted by MPN Advocacy & Education International, can be found at http://mpnadvocacy.com/events/. For more information, visit mpnadvocacy.com or contact Ann Brazeau at 517-889-6889 or abrazeau@mpnadvocacy.com.

MPNforum – the MPN community's publication – is a non-profit online magazine, founded by Zhenya Senyak (MPN patient). MPNforum (mpnforum.com) publishes articles and stories focused on patients diagnosed with an MPN. Founded in 1994 by patient advocate, Robert Tollen, the MPDSupport.org website and email list offers interesting information on MPNs. All are welcome to subscribe, and all archives are available. Robert, who was diagnosed with PV in 1990, has created a closed Facebook group with more than 1500 members. For more information or to join the listserve, please go to mpnsupport.org or email listserv@listserv.icors.org with "subscribe mpdsupport" in the email.

MPN EDUCATION FOUNDATION

Formed in 2004, the **MPN Education Foundation** aims to bring information and support to MPN patients and their loved ones all over the world via the website mpninfo.org, by convening a conference every 2 years and via the email-based group MPN-NET.

MPN-NET is an email-based support group that was formed in 1994 by patient Joyce Niblack. In May 1996, the group became a member of the Association of Cancer Online Resources, distributing email via a listserv platform. Although MPN-NET remains a US-centered organization, the group has nearly 2,900 members across the globe. All discussions are archived and available to all members since its inception (May 1996). You can subscribe to MPN-NET on the Foundation's homepage at mpninfo.org.

The Patient Story

The Patient Story was initiated by Stephanie Chuan to help cancer patients. Stories of cancer patients and expert interviews are posted. For MPNs, please visit: https://www.thepatientstory.com/medical-experts/oncologist/srdan-verstovsek/

Apfed
American Partnership for Eosinophilic Disorders

APFED is a non-profit patient advocacy organization established to assist and support patients and their families coping with eosinophilic disorders, including eosinophil-associated gastrointestinal disorders, hypereosinophilic syndrome, and Churg-Strauss Syndrome. For more information, visit Apfed.org.

MPN Cancer CONNECTION

MPN Cancer Connection, also founded by David Wallace, is a non-profit "patient-focused" organization that helps educate and empower MPN patients by providing the necessary resources and funding for PV Reporter. For more information or to subscribe to their newsletter, please visit mpncancerconnection.org.

The Mastocytosis Society, Inc. Mastocytosis • Mast Cell Activation Disorders

The Mastocytosis Society, Inc. is a non-profit organization dedicated to supporting patients with mastocytosis and mast cell activation disorders, as well as their families, caregivers and physicians through research, education and advocacy. Please visit tmsforacure.org.

PV Reporter

PV Reporter.com is a comprehensive, easy-to-navigate, patient-focused website for MPNs developed by David Wallace, "an aspiring web designer, publisher, writer, patient advocate," who was diagnosed with polycythemia vera in 2009. PV Reporter.com was created to provide "easy access" to pertinent information on PV, ET, and MF. For more information, please visit pvreporter.com.

MPN RESEARCH FOUNDATION
CHANGE YOUR PROGNOSIS

Founded by patients for patients, the **MPN Research Foundation** is a catalyst for research funding, in pursuit of new treatments – and eventually a cure – for MPNs. The Foundation has funded numerous laboratory and clinical projects related to MPN research to date. The Foundation is also dedicated to helping patients change their prognosis by serving as a valuable source of education and resources in the MPN community. For more information, please visit mpnresearchfoundation.org.