

# MPN RESEARCH FOUNDATION

## CHANGE YOUR PROGNOSIS UPDATE

VOLUME XXI, NO. 2 SUMMER 2022

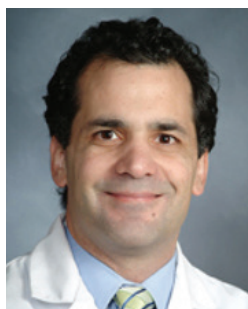
NEWSLETTER FOR THE MYELOPROLIFERATIVE NEOPLASMS COMMUNITY



### RESEARCHER PROFILE

# MPN STEM CELLS SUFFER FROM 'CORRUPTING INFLUENCE'

BY RUTH FEIN REVELL



Joseph Scandura, MD, PhD

***Interferon has been shown to be very effective in some patients with MPNs, often alleviating their fatigue, enlarged spleen, and other symptoms.***

Some patients show important additional benefits, such as molecular response, even long-term remission and the delay of disease progression. For others with essential thrombocythemia (ET), polycythemia vera (PV), or myelofibrosis (MF), interferon has no measurable effect.

As part of the MPNRF Interferon Initiative, Joe Scandura, MD, PhD, wanted to understand more about why this is the case.

A hematopoietic stem cell biologist, the question led Dr. Scandura and his research team at Weill Cornell Medicine in New York to the question of cell fitness. Why and how does an MPN mutated stem cell win when in competition with normal cells?

On any given day, a number of cells in our body are acquiring mutations. "Most of the time, they occur in a cell that doesn't really much matter," says Dr. Scandura. "But every now and then, there's a mutation that occurs in the wrong gene (in a single stem cell)."

MPNs originate in a stem cell. In fact, just a single stem cell can give rise to ET, PV or MF, because the mutated cell acquires attributes that allow it to outcompete normal cells, says Dr. Scandura. His question was how does this competition exist?

"It almost necessarily has to happen in the niche," he explains, "a unique microenvironment that provides the signals to a stem cell to allow it to exist, to do what a stem cell does. A niche isn't a static thing. It can change . . ."

It comes down to this, according to Scandura et al. "We need to understand and target the stem cells, and stem cells don't exist in a vacuum. They exist in a niche. That niche talks to the stem cell and the stem cell talks to the niche. And the mutant stem cells may be speaking in a language that's slightly different than normal stem cells and telling the niche to do things that it doesn't ordinarily do or shouldn't be doing. So it's kind of like a corrupting influence."

For that one founder mutation in a stem cell to become an MPN, "you need time and you need a fitness advantage," according to Dr. Scandura. "To me, the whole game is why do those stem cells do better than our normal stem cells? Because if you can answer that question . . . and you can prevent that mutated stem cell from taking over, you can prevent the disease. And if you already have the disease? Well, those stem cells, if they can become less comfortable, can become less fit, then the normal cells might be able to outcompete them."

"I think most people agree that the competition between normal and mutated stem cells represents the biology underlying MPNs. What we set out to do is to develop methods to make a direct biological observation that reports this competition in any person at any time.

Continued on page 2

### MISSION

THE MISSION OF THE MPN RESEARCH FOUNDATION IS TO STIMULATE ORIGINAL RESEARCH IN PURSUIT OF NEW TREATMENTS — AND EVENTUALLY A CURE — FOR MYELOPROLIFERATIVE NEOPLASMS (MPNs).

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### Corrupting Influence – Continued from page 1

We wanted to turn this method into something that can be useful clinically to help identify treatments targeting the MPN stem cells."

Specifically, the research team looked across 12 different hematopoietic lineages, including the blood stem cells, to try to understand how these mutations propagated through hematopoiesis (the formation of blood) in people with MPNs. "What we realized early on is that there are patterns," says Dr. Scandura. "And first we were associating the patterns with diseases. We would see one kind of pattern in PV; we would see one kind of pattern in myelofibrosis. But then we started finding people who weren't fitting where they should be."

When they started finding the exceptions to the patterns (i.e., ET that looked like PV or PV that looked like MF) they started investigating what was different about these patients.

"These were our patients. So we knew about them and had a vested interest in their outcomes," says Dr. Scandura. In some cases, he did bone marrow biopsies on people with PV, "because, for instance, they had some clinical findings associated with fibrosis and a fitness measure that looked like MF. But the marrow pathology still showed PV. Then later, we saw they progressed to fibrosis. We realized that we actually were predicting things that were happening down the line a year, two years, three years later, and explaining things that we didn't initially have an explanation for." In essence, their biological experiment turned into an informal clinical experiment.

In their studies, they take the individual cells that are floating around in the blood and separate them. They then analyze how many mutant cells are within each of those populations and turn that back into one composite measure they call MPN fitness. "When we talk about fitness, it's really that composite of how much that mutated stem cell contributes to mutated blood cell production."

Today, there are MPN scoring systems used as prognostic indicators (clinical or molecular features such as age or symptoms) to gauge how groups of similar patients tend to behave clinically. But these prognostic systems are not as good at anticipating how one individual patient is likely to do – because every rule has many exceptions.

"What we need is a monitoring biomarker, says Dr. Scandura, "something that we can measure over time knowing that changes predict an outcome. If you have a measure that tells you that a drug is doing something that's moving in the right direction, and you can back that up with data . . . then we can use these for clinical decision making. Then, all of a sudden, we're attaching an immediately realizable measure to a predicted outcome and a treatment effect. And so that's really what we we're trying to accomplish."

This work was published in *Blood Advances* late in July 2022. ■

### NEW PERSONALIZED CLINICAL TRIAL FINDER

Launched in May 2022, the MPN Research Foundation clinical trial finder –



powered by Trialjectory – easily and quickly matches an MPN patient's diagnosis and medical history. By filling out a short profile, a list is generated that a patient can share with a doctor who manages their MPN. And live support is available in multiple languages. Get started today at [www.mpnresearchfoundation.org/mpn-clinical-trials](http://www.mpnresearchfoundation.org/mpn-clinical-trials). ■

# MPN CHALLENGE AWARDS: SCIENTIFIC REPORT ON FINDINGS

**MPN Challenge is our open solicitation research initiative that allows us to fund the most pressing MPN science. Focus areas change each round as we learn more about unmet needs in MPN research.**

Research projects funded in the 2019-2021 MPN Challenge help us better understand MPNs, including genetic risks for inheriting an MPN, driver mutations, and progression. Following is a brief summary of each project. Though the pandemic caused significant delays for some projects as noted, the outcomes are meaningful.

## MPN DRIVER MUTATION IDENTIFIED AS EARLY AS IN-UTERO

**Origins of MPN: Understanding the Timing of Acquisition of Driver Mutations and Dynamics of Clonal Expansion**

*Jyoti Nangalia, et al, Wellcome Sanger Institute, Cambridge, UK*



Central to understanding long-term disease progression are the factors driving initial disease acquisition and evolution. This project utilized whole genome

sequencing and computational biology to trace the life history of individual tumors from 12 patients with MPNs.

Mutations from more than 1,000 clonal hematopoietic colonies were used to reconstruct their organic evolution and determine the clonal histories for each patient. The results showed that the MPN driver mutations that cause these diseases can occur early in life, even during the in-utero period, and are present often many years before an MPN is diagnosed. Some clones acquire additional mutations over life and can often evolve before the disease diagnosis. The mean latency between

JAK2V617F acquisition and diagnosis was approximately 30 years.

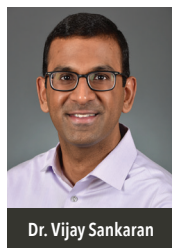
► Overall, this study suggests that the early acquisition of an MPN driver mutation, and its growth and evolution over time, likely underlie adult MPNs. This raises opportunities for early detection and preventative strategies, as well as early identification of those on a path to future high-risk disease.

This work was cited as a 2020 Best of ASH (American Society of Hematology) abstract and was published in *Nature*.

## EXAMINING THE INHERITABILITY OF MPNS

**Germline Genetic Risk for Myeloproliferative Neoplasms**

*Vijay Sankaran, et al, Boston Children's Hospital, Boston, MA*



Epidemiological studies indicate a substantial inherited component of MPNs. Yet to date, only a few genetic risk indicators have been identified. Studies like this are needed to understand the biological

mechanisms that underlie these germline genetic variants that increase risk of acquisition of MPNs.

► The main focus of this project was to utilize large population-based studies to distinguish common and rare genetic variants that predispose individuals to MPNs.

The investigators also looked to characterize the gene regulatory effects of MPN risk variants in human hematopoietic stem cells (HSCs) and progenitor cells (HSPCs) with an emphasis on human hematopoietic stem cell self-renewal.

Initially, a large-scale genome-wide association study was conducted and 17 risk loci were identified, where a specific gene is located on a chromosome. Results show a shared genetic architecture between MPN risk and several hematopoietic traits from distinct lineages. Further gene mapping studies were used to identify additional modulators of HSC biology linked to MPN risk.

These results indicate that mechanisms that alter hematopoietic stem cell function may be more important in understanding inherited MPN risk.

Published in *Nature*, these studies have now been expanded through collaborations with the BioVU cohort from Vanderbilt University, an MPN cohort from the UK/Cambridge University, an expansion of the UK Biobank, and the AllofUs cohort from the US. This work on germline genetic risk was further expanded to include a focus on disease progression and is supported by an MPNRF Progression grant.

Continued on page 4

## LOOKING AT BIOMARKERS FOR MYELOFIBROSIS PROGRESSION TO AML

### Detection and Inhibition of Malignant RNA Processing Dysregulation in Myelofibrosis

Catriona Jamieson, et al, University of California, San Diego



The main objective of this research was to uncover RNA processing mechanisms that govern myelofibrosis (MF) progenitor cell

transformation into leukemia stem cells (LSCs), with the overall goal of establishing RNA processing dysregulation as a biomarker of disease progression from MF to secondary acute myeloid leukemia (sAML).

Results from this highly collaborative project showed that MF progenitor cells overexpress inflammatory cytokine-induced ADAR1p150 (an RNA editing enzyme) during progression to high-risk MF and transformation to sAML. The resulting biological effects that follow suggest a possible malignant feedback loop as pre-leukemia stem cells in MPNs transform to leukemia cells in AML.

Importantly, studies show that fedratinib and a selective RNA splicing modulator (17S-FD-895) can inhibit transcriptional activation of ADAR1p150.

► The team's research continues to determine if the levels of enzymes and other physiological mechanisms they are studying can serve as biomarkers for the generation of leukemic stem cells, and a path toward developing new treatments for high-risk MF and secondary AML.

Some of the supportive work appears in the publication *Cell*. In addition, Dr. Jamieson received follow-up funding connected to this research from NASA (featured in the Spring 2022 MPNRF Update).

## WHEN RED BLOOD CELL FORMATION IS HIGH DESPITE IRON DEFICIENCY

### Dysregulated Iron Metabolism Plays a Pivotal Role in Polycythemia Vera

Yelena Ginzburg, et al, Icahn School of Medicine at Mount Sinai



Dr. Yelena Ginzburg

Dr. Ginzburg's research focuses on how iron metabolism is regulated differently in polycythemia vera (PV).

► Specifically, these investigators look at how red blood cell formation remains high, despite iron deficiency, and how iron metabolism is altered in JAK2 mutated erythroblasts, the bone marrow precursors to circulating red blood cells.

Overall, their results demonstrated that PV leads to persistent erythrocytosis – a phenomenon they newly referred to as iron-hypersensitive erythropoiesis.

Because iron availability is critically important for erythropoiesis, and the transferrin receptor 2 (TFR2) coordinates iron availability with erythropoietin responsiveness, the researchers hypothesize that TFR2 may be a key factor that enables the iron-hypersensitive erythropoiesis in PV. TFR2 is normally decreased during iron deficiency, whereas in PV, they demonstrated persistent TFR2 expression in spite of iron deficiency, which may enable erythropoiesis in the presence of a limited iron supply.

They also showed that hepcidin levels are low in PV mice even in the presence of increased inflammation-mediated STAT3 signaling in hepatocytes. This work helped to support a Phase II trial using the hepcidin-mimetic PTG-300 (rusfertide) in PV patients, in which preliminary results demonstrate that in addition to stabilizing hematocrit <45% without phlebotomy, iron deficiency is also reversed. (See ASCO

highlights on page 6 of this issue.)

Results from this project have been presented at multiple annual meetings over the past two years. A manuscript is being finalized: *Aberrant Responsiveness of Erythropoiesis to Iron Deficiency in Polycythemia Vera* (in preparation).

## REDUCING THROMBOPOIETIN COULD BE A THERAPEUTIC STRATEGY

### Targeting Thrombopoietin Signaling in the MPNs

Alison Moliterno, et al, Johns Hopkins University School of Medicine



Dr. Alison Moliterno

MPN driver mutations ultimately activate the hormone thrombopoietin's signaling pathway, which drives excess megakaryocyte

proliferation – cells in the bone marrow responsible for making platelets. This in turn increases platelet production, thrombosis risk, and bone marrow fibrosis.

Individuals with MPN do not metabolize thrombopoietin, due to an inability to clear this hormone, and due to the effects of inflammation increasing its production by the liver. This leads to a chronic increase in plasma thrombopoietin levels and continuous hyper-signaling in MPN mutant stem cells.

► Dr. Moliterno's group has studied the effects of the hormone thrombopoietin in mouse models of the MPN mutation JAK2V617F. Using genetic approaches where the thrombopoietin or *HMGAI* genes were deleted in the JAK2V617F mouse, the group showed an impact on key features of MPN progression, including marked reductions in bone marrow fibrosis and spleen enlargement.

The investigators are looking at two therapeutics that can effectively silence the thrombopoietin gene and lower thrombopoietin levels in the blood. In recently completed normal mouse studies, these agents reduced thrombopoietin levels, platelet counts, and bone marrow megakaryocytes, and were well tolerated.

The goal now is to test these agents alone and in combination with ruxolitinib in the JAK2 mutant mice. Studies to see if this approach of silencing thrombopoietin will impact myelofibrosis and myeloproliferation should be completed by the end of the year. A publication highlighting the role of thrombopoietin in the JAK2 mutant mouse model was published in the journal *PLOS One*.

## PATIENT CHOSEN THERAPY AS STUDY OPTION FOR MF

### *Feasibility of a Patient Preferences-Controlled Study of Allogeneic Hematopoietic Cell Transplantation Versus Best Available Non-Transplant Therapies (BAT) in Patients with Myelofibrosis (ALLO-BAT Study)*

Vikas Gupta et al, Princess Margaret Cancer Center, University Health



Dr. Vikas Gupta

High-risk myelofibrosis patients appear to have better survival with hematopoietic cell transplantation (HCT). Retrospective studies using molecular

integrated scoring systems indicate better outcomes of patients treated with HCT versus best available non-transplant therapies (BAT). However, the efficacy of HCT versus BAT has never been prospectively evaluated in MF.

A randomized study would be logistically difficult due to disease rarity, and strong patient and/or physician preferences. This

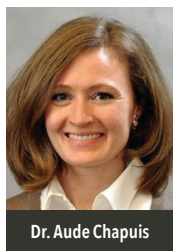
project was designed to test the feasibility of a patient-preferences controlled, multicenter prospective study to compare the efficacy of HCT vs. BAT in high-risk MF using molecular integrated risk scores.

- ▶ Participants will choose the MF treatment they prefer to receive (HCT or BAT), then the outcomes will be compared. The authors expect that within the next year, they will be able to address the feasibility of this approach. Then they will compare the quality of life over time and survival of patients undergoing hematopoietic cell transplant as compared to those who chose best available non-transplant treatment.

The goal is to recruit and study 72 patients. COVID-19 restrictions dramatically impacted the expected progress, which now has a target completion date of April 2023. The study has been expanded to six other clinical trial sites throughout Canada and potentially in Australia.

## THE ANTICANCER POTENTIAL OF T CELL RECEPTOR-ENGINEERED T CELLS

Aude Chapuis et al, Fred Hutchinson Cancer Research Center



Dr. Aude Chapuis

The original goal of this project was to specifically target the MPN-inducing single-point JAK2 V617F mutation that remains present in patients treated with

JAK2 inhibitors. T cell receptors (TCRs) were developed that specifically recognized the JAK2V617F peptide, but not its wild-type counterpart.

Further work demonstrated that the JAK2V617F peptide is not processed to a level required to trigger a T cell receptor

response, and would not likely result in a therapeutic treatment. Therefore, a new set of project aims was developed that shifted to identify other novel TCR targets in MPN.

A new reporter system was developed to match MPN patient-specific T cell receptors to their cognate antigens (specific antigens to which the TCRs bind). The plan is to utilize it to identify new peptide targets for the MPN-associated proteins calreticulin del52 and ins5, JAK2V617F and MPLW515L.

- ▶ Driving toward more personalized treatments, the immunotherapy that could be developed from this work would be directed specifically to a patient's identified MPN tumor antigen, a tumor marker that triggers an anti-cancer immune response.

The complex system utilizes patient-specific mutation encoding genes and HLA alleles co-transduced in a reporter cell line. This enables an immunogenic peptide to be processed and presented on the reporter T cell's surface to nearby TCRs, to activate both the TCR reporter and target reporter.

At this time, the system is being further validated. The plan is to utilize it for the remainder of this year to identify new peptide targets and the cognate TCRs from the tumor microenvironment. A poster on this work was presented at the Keystone Symposium on Emerging Cellular Therapies 2022. A review was published in *Trends in Cancer*. ■

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# MPN HIGHLIGHTS FROM 2022 ASCO

**ASCO**  
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

*A number of important findings regarding MPNs were featured at the American Society of Clinical Oncology 2022 Annual Meeting in Chicago. A few key highlights follow, presented by MPN leaders previously funded by the MPN Research Foundation.*



Dr. Ruben Mesa

## MOMENTUM STUDY PHASE 3 PROMISING FOR MYELOFIBROSIS

In this widely reported study, momelotinib proved to be a significantly better option than danazol for myelofibrosis (MF) patients with a combination of splenomegaly (enlarged spleen), anemia, and other symptoms, and also for

patients with thrombocytopenia.

"This study was designed specifically to highlight a select group of individuals for whom there is a significant unmet need," according to Ruben Mesa, MD, executive director of the Mays Cancer Center, UT Health San Antonio MD Anderson.

Dr. Mesa presented an update on the phase 3 randomized study of momelotinib versus danazol. Specifically, the trial looked at symptomatic and anemic MF patients previously treated with a JAK inhibitor.

"It was superior to arguably our best alternative therapy for these patients (danazol)," he said. "Momelotinib was superior in terms of improvement in symptoms, and superior in terms of being transfusion free."

The primary end point of the trial was a 50 percent or greater improvement in Total Symptom Score after 24 weeks. Secondary end points were transfusion independence and a reduction of the spleen by at least 35 percent. A number of patients crossed over to the momelotinib arm at the end of 24 weeks on danazol.

Findings from the study of 195 patients across 21 countries suggest that momelotinib represents a promising treatment approach to MF with anemia, or for patients with MF who may progress to symptomatic anemia.



Dr. Ronald Hoffman

## RUSFERTIDE SHOWN TO REDUCE PHLEBOTOMY

Most patients with polycythemia vera (PV) are severely iron deficient, either due to their underlying disease or repeated phlebotomies.

"The target in treating patients with PV is to chronically maintain adequate hematocrit levels

below 45 percent, which reduces the risk of thrombosis," explains Ronald Hoffman, MD, of Tisch Cancer Institute, Mount Sinai.

Phlebotomy – the periodic "letting" of blood to reduce red cell volume – is often the only means to that end.

Dr. Hoffman, who presented on two phase 2 studies of rusfertide treatment in phlebotomy-dependent PV, reports that rusfertide was shown to maintain target hematocrit levels, essentially reducing or eliminating the need for phlebotomy, typically associated with varying hematocrit levels and contributing to anemia.

Patients showed normalization of iron deficiency, serum ferritin, and mean corpuscular volume (MCV), a value associated with the size of red blood cells. "There was also improvement in systemic symptoms," according to Dr. Hoffman, "specifically in the impairment of intellectual capacity, so called brain fog."

With side effects primarily limited to the local injection site, Dr. Hoffman and colleagues are more than hopeful about the potential therapeutic reach of rusfertide in PV.

"I think it would make an important contribution, essentially freeing these people up from the burdens of coming to the office frequently, getting phlebotomy . . . while hopefully continuing to improve their systemic symptoms. And I would anticipate that they would not require as close follow up to make sure they meet their target and management levels." The phase 3 rusfertide trial is currently recruiting.



Dr. Raajit Rampal

## NAVTEMADLIN FOR MPN PROGRESSION TO AML

A poster session led by Raajit Rampal, MD, PhD, Memorial Sloan Kettering Cancer Center, presented findings of an open-label, multicenter, phase 1b/2 study of navtemadlin (KRT-232) for patients with relapsed/refractory acute myeloid leukemia

(AML) secondary to MPN.

This patient group has limited treatment options, resulting in poor prognosis. Although conventional AML therapy can induce responses in a subset of patients, it does not prolong survival in AML secondary to MPN, according to the authors. They suggest that these studies provide biological and clinical support for evaluating navtemadlin in this patient population. This trial is ongoing and will enroll patients at 65 global sites.

*Dr. Rampal is medical advisor for the MPN Research Foundation. ■*

# TODAY'S PLANS SUPPORT TOMORROW'S ANSWERS



***Have you ever envisioned what the future of MPNs might look like? Where will the research be directing us three or four years from now? What advances in medicine will we make in the next 15-25 years?***

At the MPN Research Foundation, we dare to dream about the future for

those living with an MPN. We think about the community of patients every day as we consider the best way to invest our valuable resources into new ideas, the continuation of promising research, and filling research gaps. We boldly look to fund projects which may be seen as risky, yet they have the potential to transform how MPN patients feel, live, and dream.

We invite you to be a part of the next stages of MPN research with a planned future gift.

Research takes time – often years – before what happens in the lab is translated into more available treatment options. Along the way, there are inevitably side effects which require continued monitoring, studying, then improving upon the original breakthroughs. Research is not quick or easy, particularly considering the complexities of blood cancers.

Until MPNs can be easily managed or even cured, we must increase the level of investment in MPN research, in order to have earlier, meaningful impact on a patient's disease and quality of life.

As you consider what is important to you, we encourage you to think beyond today's research needs, about how you can make an impact on our future understanding and treatment of MPNs.

By making a planned gift to MPN Research Foundation through your estate, you can stamp your legacy on the future of MPN research *and* impact the lives of MPN patients for generations to come. This is an open invitation.

To learn more about making a gift for the future, explore our website at [www.plannedgiving.mpnresearchfoundation.org](http://www.plannedgiving.mpnresearchfoundation.org). To speak with someone directly, contact our Development Office at (312) 683-7249 or email [giving@mpnrf.org](mailto:giving@mpnrf.org). ■

## ADVANCES OF NOTE FROM EHA2022



The European Hematology Association's EHA2022 Congress in Vienna brought together global research leaders, practitioners, and other participants in June to share the latest advances in hematology. Read highlights of MPN research presented at EHA on our website at [mpnresearchfoundation.org/mpn-news](http://mpnresearchfoundation.org/mpn-news). ■

## NEW FUNDING OPPORTUNITY: 2022 THRIVE INITIATIVE



***Through the 2022 Thrive Initiative, MPNRF seeks to address research funding gaps, some of which are likely due to the impact of the pandemic on the research community.***

The overall goal is to advance scientific understanding of MPNs, to drive better outcomes and eventual cures for MPN patients.

The Leukemia & Lymphoma Society, in its continued support of MPNRF, is contributing funds for this initiative over the next three years, enabling funding of more projects and expanding our reach into the research community.

This initiative has four unique funding mechanisms:

- + Advance existing MPN research projects the applicant is engaged in currently.
- + Foster growth and development of early career MPN researchers.
- + Attract established researchers in other fields to apply new ideas to MPN research.
- + Encourage collaborative translational projects with near-term clinical impact.

Proposals are due August 15th, 2022, with scientific peer review beginning in October. For more information and to apply, visit [www.mpnresearchfoundation.org](http://www.mpnresearchfoundation.org). ■

**"WE ARE PROUD OF OUR LONG-STANDING RELATIONSHIP WITH THE MPN RESEARCH FOUNDATION TO FUND RESEARCH TOWARDS MORE EFFECTIVE AND SAFER TREATMENTS FOR MPN. OUR ORGANIZATIONS ARE DRIVING THE GROUNDBREAKING RESEARCH THAT IS HELPING PEOPLE WITH MPN LIVE A BETTER QUALITY OF LIFE."**

*Lee Greenberger, Chief Scientific Officer  
Leukemia & Lymphoma Society*

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## CLINICAL TRIAL HIGHLIGHTS

*With the help of patients who choose to participate, clinical trials determine whether a therapy is safe and effective in treating a particular disease.*

Trials are designed to test a medication or other medical treatment against a placebo (inactive look-a-like), other medication, or the standard medical treatment for a patient's condition, in order to truly understand its effect. Data collected in clinical trials are necessary for review prior to approval of a new therapy or new use of a therapy previously approved to treat a different disease. The decision to participate in a clinical trial is one a patient should consider carefully and discuss with their physician.

#### **DISC-0974 (Phase 1/2)**

**Sponsor:** DISC Medicine, Inc.

**Diagnosis:** MF

**More Info:** [www.clinicaltrials.gov/ct2/show/study/NCT05320198](http://www.clinicaltrials.gov/ct2/show/study/NCT05320198)

**Notes:** Study of a monoclonal antibody developed

to target hepcidin, a key regulator of hepcidin and iron homeostasis, to increase circulating iron availability in patients with anemia.

#### **Rusfertide/VERIFY (Phase 3)**

**Sponsor:** Protagonist

**Diagnosis:** PV

**More Info:** [www.clinicaltrials.gov/ct2/show/NCT05210790](http://www.clinicaltrials.gov/ct2/show/NCT05210790)

**Notes:** For patients requiring phlebotomy, rusfertide is a hepcidin mimetic which regulates blood iron levels. The goal is to maintain target hematocrit levels and improve symptoms.

#### **Parsaclisib/LIMBER 313 (Phase 3)**

**Sponsor:** Incyte

**Diagnosis:** MF

**More Info:** [www.incyteclinicaltrials.com/limber/](http://www.incyteclinicaltrials.com/limber/)  
**Notes:** Study of parsaclisib, a PI3 kinase inhibitor, for patients who have not previously used a JAK inhibitor or PI3 kinase inhibitor. One group will receive ruxolitinib and parsaclisib and a second group will receive ruxolitinib and a placebo.

#### **Navitoclax/TRANSFORM 2 (Phase 3)**

**Sponsor:** AbbVie

**Diagnosis:** MF

**More Info:** [www.abbvieclinicaltrials.com/study/?id=M20-178](http://www.abbvieclinicaltrials.com/study/?id=M20-178)

**Notes:** For patients who did not benefit from

ruxolitinib previously or for whom it stopped working, navitoclax focuses on cell death pathway in combination with ruxolitinib versus best available therapy.

#### **Fedratinib Plus Ivosidenib or Enasidenib (Phase 1)**

**Sponsor:** University of Chicago

**Diagnosis:** MF, PV or ET

**More Info:** [www.clinicaltrials.gov/ct2/show/NCT04955938](http://www.clinicaltrials.gov/ct2/show/NCT04955938)

**Notes:** This study has two arms for advanced phase patients with an IDH mutation. Enasidenib and ivosidenib were previously approved by the FDA for other indications. Ivosidenib will be given initially to IDH1 participants followed by a combination of ivosidenib with fedratinib. For IDH2 patients enasidenib monotherapy will be followed by combination with fedratinib.

#### **Tagraxofusp (Phase 2)**

**Sponsor:** Stemline Therapeutics, Inc.

**Diagnosis:** MF or CMML

**More Info:** [www.clinicaltrials.gov/ct2/show/study/NCT02268253](http://www.clinicaltrials.gov/ct2/show/study/NCT02268253)

**Notes:** For higher risk patients for whom a previous therapy was unsuccessful. Tagraxofusp was previously approved by the FDA for a different rare blood cancer. ■

**FOR A PERSONALIZED LIST OF TRIALS THAT MATCH YOUR DIAGNOSIS AND HISTORY USE THE MPN CLINICAL TRIAL FINDER ON OUR WEBSITE. VISIT: [MPNRESEARCHFOUNDATION.ORG/MPN-CLINICAL-TRIALS](http://MPNRESEARCHFOUNDATION.ORG/MPN-CLINICAL-TRIALS)**