

MPN RESEARCH FOUNDATION

CHANGE YOUR PROGNOSIS UPDATE



VOLUME XXI, NO. 1 SPRING 2022

NEWSLETTER FOR THE MYELOPROLIFERATIVE NEOPLASMS COMMUNITY

IMPACT@21

At 21 years, we're proud of where we are and where we're headed, and our unique global impact – on MPN research, clinical practice, drug development, and most importantly quality of life for MPN patients.

We kicked off 2022 with a reflection on how far the MPN research community has come in our 21 years, and the foundation's impact on today's deeper understanding about essential thrombocythemia, polycythemia vera, and myelofibrosis.

While history is important, we view it as a focal point to jump from – even farther and faster. It is our success that perpetuates the need for more: more questions and answers; more dollars to invest; more basic and translational research from academic and industry laboratories.

The next chapter of the foundation's story is seeded in our bold commitment to find and fund global pioneers studying innovative approaches to the biology of prevention, new therapies, disease progression, and improved daily life for people living with MPNs.

We are committed to identifying research gaps and driving collaboration, across institutions and scientific disciplines. And we are committed to bringing their investigations, successes, and redirected interests to the collective MPN table. Then we'll ask what's next and who's on board.

In this issue, read some of our research highlights. In many cases they are foundational to our current understanding of MPNs, and offer a path for continued and future investigations, including into new drug therapies.

“WE WILL CONTINUE TO CONVENE GLOBAL THOUGHT LEADERS TO HELP STEER OUR VISION FOR FUTURE PROMISE FOR PEOPLE LIVING WITH ET, PV, AND MF. WE’LL BE GUIDED BY OUR CORE PRINCIPLES FOR HIGH RISK, HIGH REWARD RESEARCH WITH NEAR-TERM OUTCOMES.”

Kapila Vigas, Chief Executive Officer

View the complete IMPACT@21 digital report on our website. And watch this space as we share research progress on disease progression from our third Progression Research Network Summit this June. ■



BUILDING ON OUR 21-YEAR IMPACT

Today, with 21 years of MPN leadership and research, our investments have paid off with extraordinary progress. As we build upon our impact, we commit ourselves to continue to drive answers to the biology, treatment, and progression of MPNs.

Continued on page 3

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).

MPNRESEARCHFOUNDATION.ORG



THE PANDEMIC'S INFLUENCE ON TELEMEDICINE AND CLINICAL TRIALS
Q&A WITH RAAJIT RAMPAL, MD, PHD

OFFICERS AND DIRECTORS OF THE MPN RESEARCH FOUNDATION

Barbara Van Husen
Chairman

David Boule
Treasurer

Ed Bartholemey

Jen Bealer

Stephen Berger

Lisa Bretones

Stephanie Cindric

Brandon Goetzman

Sam Klepper

JoAnn Mason

Pam Murphy

David Ricci

Rebecca Shapiro

Jeff Shier

Robert Rosen*
Chairman Emeritus

SCIENTIFIC ADVISORY BOARD

Andrew Schafer, MD
Weill Cornell Medicine
Co-Chair

Radek Skoda, MD, PhD
University of Basel
Co-Chair

Robert Cohen, MD
Calico Life Sciences

John Crispino, PhD
St. Jude Children's Hospital

Saar Gill, MD, PhD
University of Pennsylvania

Catriona Jamieson, MD, PhD
University of California,
San Diego

Ross Levine, MD
Memorial Sloan Kettering
Cancer Center

Ann Mullally, MD
Brigham and Women's
Hospital

Jyoti Nangalia, MBBS, PhD
Wellcome Sanger Institute

Scott Weir, PhD
University of Kansas
Medical Center

MEDICAL ADVISOR

Raajit Rampal, MD, PhD
Memorial Sloan Kettering
Cancer Center

MPN RESEARCH FOUNDATION

180 N. Michigan Avenue, Suite 1870
Chicago, IL 60601

mpnresearchfoundation.org

* DECEASED

© Copyright 2022, MPN Research Foundation

THANK YOU TO OUR SPONSOR



Amidst a global pandemic, it is compelling to search for whatever positive or hopeful effects we might find. One outcome is the increased use of telemedicine. How this might affect clinical trials in the future is something we'll be closely watching.

Over the past two years, we have witnessed the benefits of telemedicine play out in situations when the advantages outweigh the risks of travel and in-person clinic visits. For example, there has been more flexibility in protocols for patients in current clinical trials. Televisits have been allowed to take the place of some in-person appointments, when a procedure isn't necessary and a person's healthcare is not expected to be compromised.

Certainly the prospect of fewer in-person visits – often coupled with related travel expenses to a major academic medical center – could positively impact the successful recruitment of participants into clinical trials. This in turn might increase the diversity of the patient pool, an ongoing challenge for researchers. We recently spoke to Raajit Rampal, MD, PhD, about his thoughts on this. He is clinical director of Leukemia Service at Memorial Sloan Kettering Cancer Center and serves as MPNRF Medical Advisor.

What is your experience with these or other benefits of telemedicine since the pandemic began?

Dr. Rampal: Telemedicine has enormous benefits in terms of patient accessibility and flexibility. Broadly speaking, I think we can broaden the reach of expert care. There are challenges and limitations, however. Some challenges are currently inherent (lack of ability to do an exam). Others have to do with patients' access to high-speed internet and their relative technological acumen. These last two points are important as we want to strive to bring this technology to the largest number of patients possible, particularly across educational and socio-economic status.

Do you believe our pandemic era telemedicine experience will make it easier to attract clinical trial participants in the future? What evidence have you begun to see?

Dr. Rampal: I do. Many trials are allowing us to substitute virtual visits for some in-person visits, as a result of the pandemic. This has made participating in trials less burdensome for some of our patients. Indeed, at MSK this has made a major difference, as we have a variety of regional sites within New York and New Jersey where patients can also get lab work and other tests, and thus, in conjunction with telemed visits, the number of trips to NYC for many patients has been reduced.

What are your thoughts about making some of these pandemic-induced changes permanent?

Dr. Rampal: I think we have learned a lot about utilizing telemedicine in the last two years. It is clear to me that telemedicine will be an important part of the future of medicine, without a doubt. However, we need to think about in which situations and for which patients it is best utilized. It will not take the place of in-person visits, but will become a component of our care delivery models.

Continued on page 5

RESEARCH HIGHLIGHTS

Progression Projects

Funding six current pilot projects directed at assessing new therapeutic targets and risk biomarkers for disease progression – 2020 MPN Progression grants.

Genomic testing impact on post-stem cell transplant outcomes for MF patients

Contributed to development and funding of ongoing multi-institutional retrospective study to understand impact of genomic testing on post-stem cell transplant outcomes for MF patients, led by Memorial Sloan Kettering – 2020 Emerging Trends research. Also supported development of Stem Cell Transplant Spectrum Timing Tool to guide patients and physicians around transplant timing.

Driver mutations often acquired decades before diagnosis

Funded early groundbreaking research showing MPN driver mutations were often acquired decades before diagnosis, suggesting possible opportunities to detect early changes and potentially intervene to prevent or slow MPN development. 2019 MPN Challenge grant – Jyoti Nangalia, MBBS, PhD, Wellcome Sanger Institute and University of Cambridge.

Impaired iron metabolism's role in PV

Funded research on pivotal role of dysregulated iron metabolism in patients with PV. Research outcomes provide premise for ongoing clinical trial of PTG-300. 2019 MPN Challenge grant – Yelena Ginzburg, MD, Icahn School of Medicine at Mount Sinai.

3-year MPNRF Interferon Initiative offers important insights

Gained insight into understanding why and how interferon works and sometimes doesn't work in MPN patients through three-year global MPNRF Interferon Initiative. Results released November 2021.

Molecular studies explore intracellular tool to eliminate JAK2 mutated cells while sparing others

Funded molecular target studies presenting strategy to selectively eliminate JAK2 mutated cells, using their own intracellular degradation machinery and sparing non-mutated JAK2. 2017 and 2021 MPN Challenge grants – James Griffin, MD, and Sara Buhrlage, PhD, Dana Farber Cancer Institute.

Role of inflammation, inflammatory mediators, and bone marrow environment

Multiple research projects funded to understand role of inflammation, inflammatory mediators, and bone marrow microenvironment in pathogenesis and progression of MPNs, laying groundwork for clinical trials targeting inflammatory pathways in MPNs. 2014 and 2017 MPN Challenge grants – Angela Fleischman, MD, UC, Irvine; Stephen Oh, MD, PhD, Washington University School of Medicine at St. Louis. Clinical Trials: An Optimal Dose Finding Study of N-Acetylcysteine in Patients With Myeloproliferative Neoplasms and Pevonedistat in Combination With Ruxolitinib for Treatment of Patients With Myelofibrosis.

1st CALR vaccine-based MPN clinical trial in US

Initial laboratory work funded by MPNRF made possible the first CALR vaccine-based MPN clinical trial in the US – an investment driven by understanding the potential impact such work will have when translated to the clinic. 2015 MPN Challenge grant – Camelia Iancu-Rubin, PhD, Icahn School of Medicine at Mount Sinai.

Discovery of CALR mutations leads to immunotherapeutic approaches

Funded one of two teams that discovered mutations in CALR gene, found in the great majority of JAK2 and MPL negative MPN patients, leading to better understanding of why large subset of patients with ET and MF have the disease. The team continues to use these findings to develop CALR-based immunotherapeutic approaches. 2011 and 2014 MPN Challenge grants – Robert Kralovics, PhD research team, Austria.

Barcoding to understand control of mutated cells taking over bone marrow

Pioneering work funded on use of barcoding to study clonal hematopoiesis in zebrafish. This system provides a more rapid approach to understanding why and how to control mutated stem cells from taking over bone marrow. 2014 MPN Challenge grant – Len Zon, MD, Harvard Medical School.

TGF-beta and PIM kinase as therapeutic targets for MF

Translational research funded into roles of TGF-beta and PIM kinase as therapeutic targets for myelofibrosis, supporting preclinical proof of concept for clinical trials now using this approach. 2012 and 2014 MPN Challenge grants – Amit Verma, MD, Albert Einstein School of Medicine and Gary Reuther, PhD, Moffit Cancer Center, respectively. Clinical Trials: MPN-RC 118 AVID200 in Myelofibrosis and A Study of Oral TP-3654 in Patients With Myelofibrosis.

Therapeutic targets and risk biomarkers for fibrotic transformation

Funded numerous grants to better understand and establish therapeutic targets and risk biomarkers for fibrotic transformation of chronic MPNs, including fibrotic transformation targets such as thrombopoietin, SHP-2, HMGA2, CXCL4 and PDGF-R, TNF-alpha, IL-1beta, and NFkB. 2012, 2014 and 2017 MPN Challenge grants.

MPD Research Alliance and rapid testing of new JAK2 inhibiting drugs

Funded multi-year, multi-institutional MPD Research Alliance, enabling preclinical studies of JAK inhibitors in MPN animal models, MPN stem cell characterizations, and development of large-scale tissue bank and associated data bank, leading to rapid testing of new JAK2 inhibiting drugs. 2006 and 2009 MPD Research Alliance grants. ■

STUDYING MPNS IN THE LAB AND IN SPACE

BY RUTH FEIN REVELL



Catriona Jamieson, MD, PhD,
University of California, San Diego

Why is it that not everyone with polycythemia vera or essential thrombocythemia progresses to myelofibrosis? And why is it that only some people with myelofibrosis progress to AML (acute myeloid leukemia)?

When Catriona Jamieson, MD, PhD, and her colleagues at University of California, San Diego began to ask these questions around 2008, they knew the

most important answers would explain the differences between these groups – those who progress and those who don't. They wanted to identify and understand the factors that fuel progression in established MPN. Their work was funded in part by the MPN Research Foundation.

"We were able to ask patients at different stages of their MPN to see if they would donate saliva and also blood or bone marrow, so we could purify the stem cells from their blood or bone marrow to see if mutations (at the time just JAK2) actually were there at the level of the stem cell," explains Dr. Jamieson. "And did they become more numerous or did they change in the stem cell compartment during disease progression?" The stem cell compartment of a tissue is the fundamental source of cells for turnover and regenerative processes.

Enter Craig Venter (The Institute for Genomic Research), who was the first to sequence the human genome. "Craig met one of my patients who at the time was in her late thirties," says Dr. Jamieson. "She said, 'I can't predict whether my myelofibrosis is going to progress to AML. I don't have anything that allows me to decide whether I should get married, have a family.' All these major life decisions are things she'd been putting off."

Craig offered to have his company, Human Longevity, sequence the first 50 patients for free. And of those 50 patients, 38 samples provided sufficient information to offer value about changes in mutation profiles.

"This is a very expensive study; this is why we had so many people that came together to do this most important work," says Dr. Jamieson, "including the California Institute for Regenerative Medicine, NCI (National Cancer Institute), NIH (National Institutes of Health), the MPN Research Foundation, the Leukemia & Lymphoma Society, NASA and private foundations, including the Moores Family Foundation and the Koman Family Foundation."

What they found was that people who progressed and had high-risk disease, particularly those who progressed to myelofibrosis, had activated one protein coding gene called APOBEC3C.

"We saw mutations induced by this enzymatic mutator," she explains. "And it was not radiation. It was not a chemical exposure. It was an antiviral gene that got turned on. We didn't expect that."

This begged the next question. Is there a viral exposure in MPN? "We couldn't find an obvious virus, so we started to look for our endogenous retroviruses. Our genome has viruses in it. And we have been asking are these endogenous retroviruses activated in this disease. And we're still doing that research."

What is very clear is that APOBEC3C was massively upregulated as people started to transition from intermediate to high-risk myelofibrosis, and ultimately to AML.

"This is an enzyme that's part of our innate antiviral immune response that becomes a sushi chef for retroviruses, but if not properly regulated will chop up or introduce mutations into DNA in the genome. This anti-retroviral system is basically hijacked in patients with MPN, who overexpress the anti-viral APOBEC3C enzyme. Although APOBEC3C forms part of an antiviral response, it can be activated just from massive inflammatory growth factor up regulation," Dr. Jamieson and team found.

They then discovered that most people have a natural turnoff switch for APOBEC3C, called ADAR1. "So ADAR is on our radar because that's kind of the dimmer switch for APOBEC3C," she explains. "So we don't mutate our genome like crazy while we're trying to shut off these endogenous retroviruses from proliferating in our cells, and specifically in our blood stem cells. What we found was if people had very high APOBEC3C expression, they upregulated ADAR1. But unlike a normal stem cell, they couldn't shut it off."

"IF YOU HAVE EVER WATCHED A SPACE LAUNCH, THE FINAL THING THEY DO JUST BEFORE THE LAUNCH IS THEY ADD LIQUID OXYGEN TO THE ROCKETS. THAT LIQUID OXYGEN GIVES IT THAT EXTRA THRUST SO THAT IT CAN GET OUT OF THE EARTH'S ATMOSPHERE. SO ADAR IS THE LIQUID OXYGEN FOR CANCER, AND IT ALLOWS IT TO REALLY BLAST OFF.

"IN THE MPN STEM CELLS, DNA IS NOW BEING CORRUPTED. RNA IS BEING CORRUPTED, AND NOW THAT CELL IS CLONING ITSELF AND IT CAN'T SHUT THIS CLONING PROCESS OFF. SO YOU'VE GOT THIS LIQUID OXYGEN FUELED ROCKET ALLOWING MPNS TO TAKE OFF."

Catriona Jamieson, MD, PhD

Now the questions move on to why. Are people with MPNs activating antiviral enzymes or do they have chronic inflammatory growth factor driven events? Or is it that some people have adaptive immune systems that are too tolerant, so they need to activate these innate immune responses mediated by APOBEC3C and ADAR1? In the second case, the antiviral response could be a backup pathway to fight infections.

"The good news is that we found that we can dial down the activity of ADAR1 with JAK2 inhibitors, (i.e., ruxolitinib)," explains Dr. Jamieson. "And now we've found a much more potent inhibitor we're calling Rebecsinib. What the MPN Research Foundation has helped us do is understand how it's working . . . a disruption of splicing . . . and the biomarkers that we'll need to get into clinical trials."

Her earlier space analogy doesn't go unnoticed. When Dr. Jamieson and team saw these inflammatory growth factor receptors being upregulated in people that had progressed to myelofibrosis, all had increased viral signaling pathway activation. "We thought, that's weird. These are growth factors that get upregulated when you have a virus or chronic inflammation."

They turned to the NASA twin study for some potential answers. That study showed that Scott Kelly came back two inches taller than his twin brother, Mark Kelly. "He spent almost a year in space and he comes back taller, looking like superman, but his blood did not look like superman's blood." And those changes reported in his blood caused Dr. Jamieson et al concern.

They have since received a grant from NASA to send hematopoietic stem cells, and their daughter cells called progenitor cells, into space to study the effects, sparing a human host. They are developing a dedicated stem cell research lab within the International Space Station.

With the first launch of stem cells aboard SpaceX 24 this past December, the team is looking at accelerated aging of human stem of brain organoids (mini brain organs). Are they damaged in space flight? And if so, is that induced by microgravity or radiation?

"WHAT WE FOUND WAS IN SPACE COMPARED TO THE NANO BIO REACTION THAT WE HAD ON THE GROUND. THE STEM CELLS WENT NUTS. IT LOOKS LIKE THEY JUST WENT. OH NO, WE PARTIED TOO HARD. NOW, WE CAN'T GET BACK INTO THE SLEEP ZONE."

Catriona Jamieson, MD, PhD

"Our blood stem cells should be asleep 80% of the time. They should make red cells, white cells and platelets. What we're finding so far . . . it looks like they're losing their capacity to make red blood cells as well as to self-renew or in other words clone themselves," according to Dr. Jamieson.

And the relationship to MPNs and the MPNRF? The space studies aim to inform how aging, degenerative diseases, cancers and other conditions, including MPNs, develop in a setting with increased exposure to ionizing radiation and induced pro-inflammatory factor conditions. The findings may help us understand more about what activates (or over activates) MPN cells to mutate and proliferate.

Ongoing projects funded by the foundation have examined the role of inflammation in MPNs, and our current MPN Progression Network initiative will continue to shed light on disease progression. ■



STAY INFORMED!

To receive our monthly digest, *Under the Microscope*, and other timely communications about what's happening in the MPN community, visit us on the web at mpnresearchfoundation.org

MPN RESEARCH FOUNDATION

CONNECT WITH US ONLINE



THE PANDEMIC'S INFLUENCE ON TELEMEDICINE AND CLINICAL TRIALS

Continued from page 2

Others weighing in on this topic agree with the need for caution and continued discussion in the MPN medical and research community, without "slipping back" to limited pre-pandemic use of telemedicine.

"We can't telemed our way out of MPNs," said one MPN specialist. She was referring to the vital need for regular in-person visits, which can be an important factor in earlier diagnosis and treatment, and in some cases more proactive management of potential complications and disease progression.

According to a June 2021 article in the journal *Nature*, studies to assess the impact of the pandemic on the quality of trial data are underway.

In the meantime, a number of states (35 at last count) have formally joined the Interstate Medical Licensure Compact, an agreement among participating U.S. states to work together to significantly streamline the licensing process for physicians who want to practice in multiple states. It offers an expedited pathway for physicians who qualify, and aims to extend the reach of physicians, improve access to medical specialists, and leverage the use of new medical technologies, such as telemedicine. ■

VOICE OF THE PATIENT

An important initial step in MPN drug development is to ensure that the outcomes being measured are those most meaningful to patients. This data can then inform future endpoints in the advancement of new treatments.

Our December 2021 Voice of the Patient report offered deep insights into the experiences, concerns, and priorities shared by people living with essential thrombocythemia, polycythemia vera, and myelofibrosis, as compiled from an externally-led Patient-Focused Drug Development (EL-PFDD) meeting in September of 2019.

These patient perspectives are now available as a unique resource for FDA staff, the biopharma industry, and MPN researchers. Their comprehensive voice will be invaluable in the design of new clinical trials, assessing treatment benefits, and the approval process for new drug therapies.

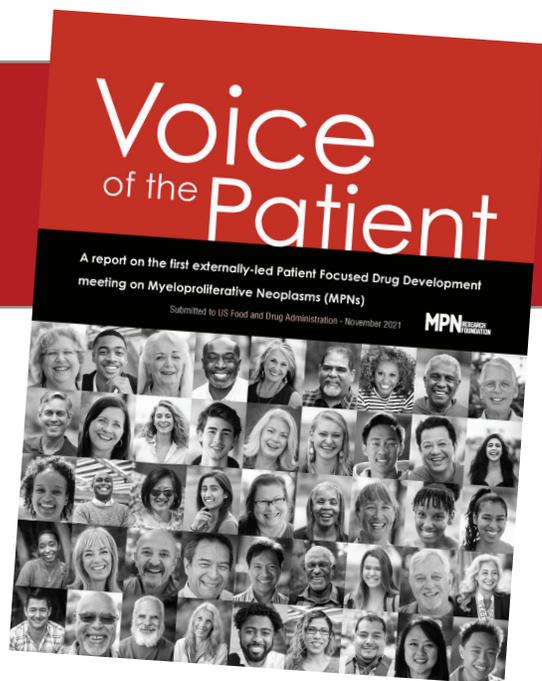
HIGHLIGHTS FROM VOICE OF THE PATIENT

Among the many valuable takeaways from the voices of some 300 MPN patient participants is that each person has his or her own journey. While the severity of many symptoms is not always easily measured, the symptoms are troublesome and sometimes debilitating. And they may not be apparent to people around the person experiencing them – including caregivers, family, friends, and employers.

These factors, in addition to the uncertainty of this group of chronic cancers and the fear of progression, adds a level of frustration and stress to what can already be a difficult to manage condition.

Through in-person patient panels and discussion, real time live polling, and an advance survey, continued unmet medical needs were spotlighted. A number of common misbeliefs were also dispelled.

- #1** The needs of MPN patients can be considered under one umbrella. In fact, the experience of MPN patients is broad.
- #2** Watching and waiting is a sufficient strategy to monitor for progression because MPNs are chronic conditions. In fact, research is helping practitioners sort patients into more accurate groups based on predictors of low- and high-risk complications and disease progression.
- #3** MPNs are exclusively diseases of the elderly. In fact, patients can be in their prime years, including women of child-bearing age.



A BROAD RANGE OF SYMPTOMS

"On a daily basis I struggle the most with tingling, and numbness, and burning sensations. It's very disconcerting and hard to be out in the world or at work when this is happening."
– Bridget, ET patient (age 49)

Overall, 51 symptoms were identified throughout the meeting, including several that patients had not formerly attributed to their MPNs, a number of which were described as "daily" and "debilitating." The most common included:

- + Fatigue and breathing symptoms including decreased endurance and shortness of breath.
- + Clinical symptoms including spleen enlargement and blood clotting.
- + Pain-related symptoms including bone pain.
- + Gastrointestinal symptoms including irritable bowel syndrome and weight loss.
- + Neurological and migraine-related symptoms including severe head pain, visual disturbances and dizziness.
- + Emotional/psychological impacts including worry about disease progression.
- + Cognitive impacts including difficulty with focus and "brain fog."

"For as long as I remember I had 'unexplained' bone pain, migraine headaches with neurological symptoms, and irritable bowel syndrome, which mysteriously went away once my blood counts were normalized decades later."
– Ruth, MF patient (age 62)

IMPACTS ON ACTIVITIES OF DAILY LIVING

"Having an MPN affects every area of your life and those close to you. People don't know how to react to you having a cancer that is chronic . . . Because the symptoms can't be seen, you often encounter ignorance and find yourself having to explain what it is you have exactly."

– Morgan, MF patient (age 52)

The most commonly mentioned impacts on daily life were: emotional/psychological impacts (including worry about disease progression); general worry about the disease; fear of the future and unknown; cognitive impacts, including memory and distraction; physical activity and exercise limitations; completing work-related tasks; and performing household activities.

In addition, several participants shared that living with an MPN has resulted in financial burden, indicating that treatment costs impact their financial security and that they worry about both treatment costs and insurance coverage.

"Don't let anybody tell you that pruritis is only itching and only after a shower. It was nearly body-wide pain . . . Due to fear, I dared not go out in the rain . . . or even sleep under covers."

– David, PV patient (age 64)

PANEL AND AUDIENCE PERSPECTIVES ON CURRENT TREATMENTS

A theme among all meeting participants was the importance of drug treatments to improve quality of life for people living with MPNs. Participants were resolute on their desire for therapies that positively impact progression-free survival, with side effect burdens that they could live with long term. The ideal treatment, it was said, would address the underlying cause(s), not only the symptoms.

Forty percent of live polling respondents indicated that they do not have confidence in the availability of additional drug treatments if their current treatment stops working for them.

"In my view, there's simply no good choices when it comes to medication. I feel like I'm faced with choosing the lesser of two or three evils. I'd say my biggest wish other than a cure is that the treatment I ultimately end up with to manage my disease also reduces the symptom burden without the risk of additional side effects."

– Diane, PV patient (unknown age)

CONCLUSION

Considering the heterogeneity of the MPN patient experience, the need for relief from symptoms not addressed by current approved therapies, and the urgency felt by many patients, heightened by the uncertainty of progression, the Voice of the Patient report suggests that regulatory authorities consider a broad review of endpoints in the evaluation of potential new treatments.

The complete Voice of the Patient report is available on our website. ■

MPN CLINICAL TRIAL DEVELOPMENT

A potential new drug is first identified as an agent with a particular biological action that may have therapeutic benefits. This will be extensively validated in the laboratory. For every one drug candidate that enters the drug discovery and pre-clinical investigation phases, there are thousands that do not move forward.

CLINICAL RESEARCH

Drug developers or sponsors first submit an Investigational New Drug (IND) application to the FDA. The IND application must include:

- Animal study data and toxicity data
- Manufacturing information
- Clinical protocols including study plans
- Data from any prior human research
- Information about the investigator



PHASE 1 SAFETY & DOSAGE

Closely monitored studies gather information from 20-100 individuals about how a drug interacts with the human body, including safe dosage, acute side effects, and benefits.



PHASE 2 EFFICACY & SIDE EFFECTS

Larger group of MPN participants provide additional efficacy and safety data. These data are used to refine research questions, develop research methods, and design new Phase 3 research protocols.



PHASE 3 EFFICACY & MONITORING OF ADVERSE REACTIONS

Examining treatment benefits for a specific MPN patient population, these pivotal studies involve 300 to 3,000 participants and are from 1-4 years. Results are more likely to show long-term benefits or rare side effects.



PHASE 4 POST MARKET

Once drug is FDA approved, several thousand MPN patient volunteers participate in post-market safety monitoring.

180 N. Michigan Avenue | Suite 1870
Chicago, Illinois 60601

MAXIMIZE THE IMPACT OF YOUR DONATION

Make your donation go further by going paperless. Donating online means less administrative costs and more funding for MPN research. If you do donate by check, please provide your email address. You'll receive quicker confirmation, and we will save on costly processing and postage fees. **Thank you!**

**SUPPORT MPN
RESEARCH FOUNDATION!**
Visit mpnresearchfoundation.org/donate
or scan the QR Code:



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. Data collected in clinical trials are necessary for the Food and Drug Administration (FDA) to review prior to approving any new therapy or a new use of a therapy previously approved to treat a different disease. The decision to participate in a clinical trial is one to consider carefully and discuss with your physician.



Manifest 2 (Phase 3)

Sponsor: Constellation Pharmaceuticals
Diagnosis: MF
More Info: www.manifestclinicaltrials.com
Notes: For patients without prior experience with a JAK inhibitor this is a trial of pelabresib, a BET inhibitor, and ruxitinib.

Navtemadlin plus TL-895 (Phase 1/2)

Sponsor: Kartos/Telios
Diagnosis: MF
More Info: www.clinicaltrials.gov/ct2/show/NCT04640532
Notes: For patients who cannot tolerate a JAK inhibitor this is a trial of an MDM2 inhibitor in combination with a tyrosine kinase inhibitor.

Surpass ET (Phase 3)

Sponsor: PharmaEssentia
Diagnosis: ET
More Info: www.surpasset.com
Notes: For patients who have had a suboptimal response or did not benefit from hydroxyurea. Response of patients on this interferon formulation (ropeg interferon alfa-2b-njft), which was approved by the FDA for PV patients, is compared to response of patients on anagrelide.

Independence (Phase 3)

Sponsor: BMS
Diagnosis: MF
More Info: www.clinicaltrials.gov/ct2/show/NCT04717414
Notes: Trial for patients on a JAK2 inhibitor who require transfusions. Luspatercept was previously approved by the FDA for another blood cancer.

TP-3654 (Phase 1)

Sponsor: SDP Oncology
Diagnosis: MF
More Info: www.clinicaltrials.gov/ct2/show/NCT04176198
Notes: For higher risk patients who were ineligible for or did not previously benefit from a JAK inhibitor. TP-3654 focuses on fibrosis reduction.

INCB057643 (Phase 1)

Sponsor: Incyte
Diagnosis: MF
More Info: www.clinicaltrials.gov/ct2/show/NCT04279847
Notes: For patients who did not respond to prior treatment or relapsed. This is a study of a BET inhibitor alone and in combination with ruxotinib. ■