

MPN RESEARCH FOUNDATION

CHANGE YOUR PROGNOSIS

UPDATE

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PERIODIC NEWSLETTER FOR THE MYELOPROLIFERATIVE NEOPLASMS COMMUNITY

CHANGE YOUR PROGNOSIS: SHARE YOUR EXPERIENCE IN MYMPN

By Lindsey Whyte

myMPN is the first ever registry for all patients with MPNs. It will be launched in early 2017, and we hope you'll join in our effort to gather patient information about life with ET, PV and MF. The goals of myMPN are:

1. To strengthen the community of MPN patients by finding commonalities and sharing experiences.
2. To gather critical data that will drive research and improve outcomes.
3. To connect eligible patients with trials and other need-to-know information.

The common theme in all of this is empowering patients to change their prognosis. As MPN patients, many feel hopeless, powerless and alone. The registry aims to reverse that by showing patients they are NOT alone and that, by sharing their experience with their disease (their own "myMPN"), the research and pharmaceutical community will be better equipped to make decisions that will help them – thereby changing their prognosis!

MPNRF ROLE

The MPN Research Foundation's role in this is to serve as both a guide and gatekeeper. We work with the developers of the registry to make sure everything patients enter into the database is protected and is shared only with those who have valid scientific or therapy development-related reasons for wanting it – AND only with the proper consent of the patients. We work with the researchers and industry representatives to understand what information is needed to guide business and research decisions that ultimately result in better treatment and care. Finally, we talk to patients about their experience with the disease, compare those experiences with others

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MPN PROGRESSION MARKER PROJECT

By Barbara Van Husen

MPNs are blood cancers that affect over 300,000 individuals in the U.S. alone and many thousands around the world. These diseases are progressive; patients who are initially diagnosed with ET or PV often progress to MF, and a small percentage of MF patients convert to AML. Over the past 10 years, MPNs have been the subject of an increasing number of scientific studies, and treatments are currently in development based on those studies. However, to this date, none of those treatments have demonstrated the ability to change the trajectory of these diseases and significantly reduce the risk of progression.

There are tantalizing hints and varied opinions about MPN disease progression, but to date there is no generally accepted set of biomarkers that track progression. Retrospective studies have identified candidate markers, but longitudinal data to support these studies are needed.

Understanding progression may help identify additional targets and lead to new treatments for MPNs. The MPNRF is currently discussing the parameters of a Progression Marker Project to identify and track new markers of progression.

We are encouraged and enlightened by the experiences of other disease advocacy groups that have embarked on such an effort with significant success. These include the Multiple Myeloma Research Foundation's COMPASS project and the Michael J. Fox Foundation's Parkinson's Progression Markers Initiative (PPMI). We hope to use what these other organizations have learned about the challenges and opportunities of such studies as we move forward.

**JOIN THE FIGHT
AGAINST MPNs.**

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MISSION The primary mission of the MPN Research Foundation is to stimulate original research in pursuit of new treatments — and eventually a cure — for myeloproliferative neoplasms (MPNs). In addition, the MPN Research Foundation promotes collaboration in the scientific community to accelerate research and serves as a powerful patient advocacy group for patients and their families.

WWW.MPNRESEARCHFOUNDATION.ORG

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CLINICAL TRIALS, THE DOUBLE-EDGED SWORD

By Robert Rosen

Have you ever been asked to participate in a clinical trial? Have you ever been tempted to volunteer for one? Have you thought about the possibilities, the good and the bad? These can be hard questions to answer.

At MPN Research Foundation, we try to keep a close eye on clinical trials for MPN drugs. It's difficult to track the progress of MPN research in general, and we never know when a research project might pay off with an important result (like the discovery of the CALR mutation) or when a contribution will be made to the ever-increasing body of knowledge that will support future breakthroughs in patient treatment.

The number of clinical trials going on at any given time seems to us to be a meaningful indicator of forward movement. You can't have a new drug unless it passes through the clinical trial pipeline. We feel that a multitude of trials increases the probability that a compound, molecule or process will create a positive result.

Jakafi endured rigorous testing before it was declared safe by the FDA. Ongoing use of this drug has allowed even longer-term evaluation. At the same time, two other drugs working with the same mechanism of action – Jak2 inhibition – have not fared as well. Fedratinib was withdrawn during phase 3 trials due to the deaths of some patients, and the jury is still out on Pacritinib (see table on page 4) due to a small percentage of serious toxicities.

We need participants to prove or disprove the value of these drugs. There is no question that many patients are reluctant to offer themselves as trial subjects. Others who feel that there are no better options, or who want to play a role in advancing the science, have been willing to try.

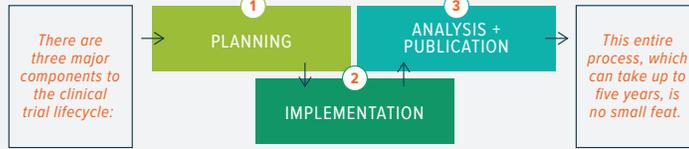
The data are variable, but it seems like less than 10 percent of new drugs make it all the way through to FDA approval. Some drugs never make it through phase 1 trials due to insufficient enrollment. The cost to a pharmaceutical company of bringing a drug through the entire clinical trial process is said to be close to a billion dollars. As such, the obstacles to this process are obvious – but the rewards to the patient community can be enormous. So tell us: How do you feel about clinical trials?

WE CAN'T DO IT WITHOUT YOU

Like it or not, MPNs are rare diseases, and they don't attract widespread publicity. So it's up to us in the MPN community – patients, family, friends and caregivers – to do everything possible to help develop new treatments and, one day, a cure. And we can do it – if we do it together. Please be generous.

MPNRESEARCHFOUNDATION.ORG

THE LIFE CYCLE OF A CLINICAL TRIAL



1

PLANNING

During this phase, researchers draft the roadmap + protocol of the study.



THEY DETERMINE:

 <small>THE REASON FOR THE TRIAL</small>	 <small>WHO IS ELIGIBLE TO JOIN</small>	 <small>HOW MANY PARTICIPANTS ARE NEEDED</small>
 <small>WHAT INFO WILL BE COLLECTED</small>	 <small>WHAT DRUGS WILL BE TESTED</small>	 <small>WHAT MEDICAL TESTS WILL BE CONDUCTED</small>

Next, the entire protocol must be approved by the Institutional Review Board (IRB) and filed with the FDA.



The final step in the planning process is to establish a Data Monitoring Committee (DMC), and then the trial can officially begin.



2

IMPLEMENTATION

After the planning steps are completed, the study begins with enrolling participants and distributing the drugs that are to be tested.



RESEARCHERS COLLECT AND INPUT ALL PARTICIPANT DATA.



3

ANALYSIS + PUBLICATION

During the final phase, all data is analyzed for primary efficacy and safety.



FINALLY, THE RESEARCHERS CAN SUBMIT THE MANUSCRIPT FOR PUBLICATION IN A SCIENTIFIC JOURNAL + PREPARE FOR FDA SUBMISSION.



Topline results can now be released to the public + a clinical report is prepared, while the abstract is submitted to a scientific meeting.



Finally, the researchers can submit the manuscript for publication in a scientific journal + prepare for FDA submission.



WOODY WOODRUFF, IN MEMORIAM

By Robert Rosen

I knew Woody only through email correspondence when he joined our small group of founding members of the MPD Research Foundation. When we agreed to meet sometime in 2000 at a hamburger joint in New York City, I wasn't sure what to expect from this Yale graduate and professional copywriter at an NY advertising firm. Then a tall, lanky guy wearing jeans and cowboy boots showed up at the table. We talked a little. Woody was a laconic type but a wordsmith at the computer. He cared deeply about helping the MPN community and he became an important board member.

After that first meeting Woody served as a key member of the MPN Research Foundation for the rest of his life – first as a board member and always as the editor of this newsletter. He never let us down; when we needed an opinion, he served it up straight. And when it was time to develop the newsletters, he was there shaping and twisting and rewriting to make it all fit while also making it as polished as possible.

Woody had PV for at least 25 years. It progressed to MF some years ago, and it took his life in July of this year. This is the first newsletter without Woody's imprint. He will be missed.



CLINICAL TRIAL UPDATE ^{*} † ‡

COMPANY	COMPOUND	MECH OF ACTION	Phase 1	Phase 2	Phase 3
CTI Biopharma	Pacritinib	JAK2/FLT3	PV/MF	On hold	
Galena Biopharma	Gale-401	cr anagrelide	MF		
Gilead	Momelotinib	JAK2 inhib	MF		
Incyte	Ruxolitinib / Jakafi	JAK2 inhib	PV/MF	FDA approved	
Janssen	Imetelstat	telomerase inhib	MF		
Kalobios	KB004	ephrin inhib	MF		
Pfizer	B1371013	hedgehog inhib	MF		
NS Pharma	NS-018	JAK2 inhib	MF		
BMS / Promedior	PRM-151	anti-fibrotic	PV/MF	Fast tracked	
AOP/Pharmessentia	P1101	interferon	PV/MF		

* This table does not include investigator initiated trials. An investigator initiated table will follow in the next newsletter.

† We made an attempt to be inclusive. If we missed a trial, please email rnunez@mpnresearchfoundation.org.

‡ The clinical phase may have changed since this graph was created.

NOVEL THERAPIES: CLOSE BUT NOT CLOSE ENOUGH

By MPNRF Scientific Advisor John Crispino, PhD; Rober I Lurie, MD;
Lora S. Lurie, Professor, Northwestern University

One question that always comes up when Bob and I talk is this: "Why don't we have new drugs for the MPNs?" It is a difficult question for me to answer. Is it for lack of trying? No, I'm sure that's not it. Basic and clinical researchers are working harder than ever to identify new targets and develop new therapies. Is it that the best researchers are working on other diseases? Certainly not. No, I think it is the usual challenge of translating discoveries into therapies that work not just in animal models, but also in humans. Let's consider the mainstay of therapy, JAK inhibitors. We are fortunate to have ruxolitinib available for PV and PMF patients. Despite its shortcomings, which include myelosuppression at higher doses and limited activity in some individuals, it has helped so many people. Why don't we have a second JAK inhibitor in our arsenal to treat those who are intolerant or resistant to ruxolitinib? There are a few reasons, such as the challenge of accruing large numbers of patients to studies and severe side effects in a small percentage of patients. With respect to the latter, it isn't for me to say whether the benefits outweigh the risks, but it's a critical issue for patients and their advocates to consider.

Where is the field headed? Perhaps the therapy with the most potential is a JAK2V617F selective inhibitor. This would be a drug that inhibits the mutant kinase while leaving the normal (or wild-type) protein alone. Although such a drug would be effective in only the 50 percent of PMF patients with the V617F driver mutation, it would be applicable for nearly all patients with PV who need therapy. It is likely that this drug would be more active in patients than ruxolitinib, as the doses could be increased with less toxicity than drugs that inhibit both the mutant and wild-type versions. JAK2V617F selective inhibitors are not in the clinic, but it is likely that companies and academics are aggressively searching for these. If they aren't, they should be. Finally, type II JAK inhibitors, which target the kinase in a slightly different way from ruxolitinib, are under investigation. I expect that we will see one or more of these novel JAK inhibitors in patients in the future.

There are a number of other targets that are being investigated in clinical studies. These include inhibitors of aurora kinase, a protein that regulates the cell cycle; histone deacetylases, factors that regulate gene expression through modifications of DNA associated proteins; and heat shock proteins, factors that regulate the stability of other proteins. I'm, of course, most excited about the aurora kinase inhibitor, which my laboratory has shown leads to maturation of abnormal megakaryocytes in pre-clinical models of PMF.

Other promising "out of the box" therapies include imetelstat and PRM-151, which target telomerase or cells that contribute to fibrosis, respectively. Both of these drugs have shown promise in clinical trials and are enrolling patients in phase 2 studies. Finally, new therapeutic agents under investigation include PARP and BET inhibitors, which alter DNA damage and epigenetic factors, respectively.

Why don't we have new drugs for the MPNs? Bob, with more research and your support, we will.

SHARE YOUR EXPERIENCE: CHANGE YOUR PROGNOSIS IN MYMPN

(CONTINUED FROM PAGE 1)

and show them that they are NOT alone.

There are many questions we hope to be able to answer reliably once we have consistent participation in the registry. For example, are patients with the Jak2 mutation more likely to experience certain symptoms? Is there some commonality in the timing of those symptoms from one Jak2 (or non-Jak2) patient to the next?

We would also like to understand if some of the medicines patients take work better than others, according to patient reporting. The timing of the medicine is helpful to understand here. Did patients who began taking a certain medication early in their diagnosis experience fewer or different side effects? Did their platelet counts return to normal after taking the medication, or did the medicine just stabilize the elevation?

Finally, we would like to understand how patient experiences change over longer periods of time (often referred to as "longitudinal studies"). For example, what is the typical frequency and duration of episodes of extreme fatigue for patients over the course of several years? Can we link those symptoms with any outside factors such as diet, exercise, environment, etc.?

The answers to these questions are helpful if collected from one or two ET patients, for example. This is often the information that a hematologist in a local medical center may have access to. What if that same doctor had access to data collected from a much larger number of patients? With the data that is provided through myMPN, we will have more compelling statistics from which conclusions can be drawn about the validity of treatments, what patients can expect, and how pharmaceutical companies should plan their research and development dollars.

MAKING myMPN A SUCCESS

The key to the success of myMPN is the participation of the patients. There is power in numbers. The more patients who share their experience, the better equipped the MPNRF is to make a case to the pharmaceutical industry and research community for therapies and research needed to change your prognosis.

NEXT STEPS

If you have questions or concerns, please do not be shy! Contact Lindsey Whyte at myMPN@MPNResearchFoundation.org. We want to have an open dialogue with patients, your families, doctors and other individuals, because the more people who understand what we're aiming to achieve and why it is so important, the better our chance at success!

Our registry is in the beta testing process now, but we will be launching it to the MPN community for full participation in early 2017. Look out for an announcement of the full launch on our website, Facebook page and other outlets, register yourself or your loved one and SPREAD THE WORD!

PARTNER'S CORNER: CANCER SUPPORT COMMUNITY

EXCERPTS FROM AN INTERVIEW WITH SARA GOLDBERGER, SENIOR DIRECTOR, PROGRAM, CANCER SUPPORT COMMUNITY

Tell me how you first got involved in with CSC.

My initial involvement was with Gilda's Club Westchester in New York. I had always known about the organization and referred people to the one in New York City, but I read in the local paper that a new site was opening up in my community. I offered to volunteer, and at the time, they needed help with stuffing envelopes. Who knew that would lead to an offer to be the first program director there? After several years I moved to the headquarters (Gilda's Club Worldwide) and then through the merger to the newly combined organization, Cancer Support Community.

What was your first impression of CSC?

My first impression of the organization was that they have an amazingly talented team who are incredibly passionate about their work. The mission is at the forefront of everything we do.

What is CSC?

CSC is the largest professionally led nonprofit network of cancer support worldwide. We provide psychosocial support and education to anyone whose life has been affected by any kind of cancer at any stage, including bereavement, for men, women and children. We offer the same services to family and friends as we do for those with a diagnosis of cancer. All services are provided at no cost.

Who started it, and when?

The Cancer Support Community was founded in 2009 from the merging of two organizations, The Wellness Community and Gilda's Club Worldwide. The Wellness Community was founded in 1982 by Harold and Harriet Benjamin, and Gilda's Club was founded in 1995 by the family of Gilda Radner, a former comedian on "Saturday Night Live" and an ovarian cancer patient, in honor of Gilda's memory.

Both of these organizations were formed with the goal of providing social and emotional support to cancer patients and their families, friends and caregivers.

What are some examples of things CSC has done in the MPN community?

We have expanded our direct services by relaunching our Cancer Support Helpline at (888)793-9355. Our Cancer Experience Registry helps to elevate the voice of patients and their loved ones. We have also launched the Cancer Policy Institute and have presented our work at national and international conferences.

Specific to the MPN population:

- Frankly Speaking About Cancer Educational Series:
 - Spotlight on MF
 - Fact sheet on MPN
 - Fact sheet on PV



CANCER SUPPORT COMMUNITY®

A Global Network of Education and Hope

- "10 Tips to Living Well With MPN" print and video series
- Participated in the MPN Coalition work, including hosting MPN Awareness Days at our local sites
- Host MPN networking groups at various Cancer Support Community/ Gilda's Club Sites

The interest in MPNs seems to be growing. Why do you think that is?

I think the work of the MPN advocacy organizations has helped to spread the word. New discoveries for management and treatment have given hope to many.

What's the best thing to happen since you started working with CSC?

Working with a wonderful team to improve the lives of people impacted by cancer is so great. They keep me motivated. I am personally very proud of the work I have done in the MPN space. Being honored by Cure Media as an MPN Hero was a very proud moment for me.

What would you tell someone who is thinking about volunteering?

Providing support to individuals impacted by cancer is at the core of the CSC mission and everything we do, and achieving this goal would not be possible without the help of volunteers. There are a variety of volunteer opportunities available at our local centers located throughout North America and our headquarters office located in Washington, DC. For more information contact help@cancersupportcommunity.org

What might someone be surprised to know about CSC?

That we serve anyone whose life is touched by cancer and that all our services are offered at no charge to our participants.

To contact Cancer Support Community or volunteer visit: www.cancersupportcommunity.org/myeloproliferative-neoplasms.

SOMEONE TO TALK TO

Living with PV,ET or MF can be frustrating and confusing, largely because these conditions are so misunderstood. But you can talk to someone who understands, either online or in person.

For a list of support groups and patient resources please go to www.mpnresearchfoundation.org/Find-Support or email rnunez@mpnresearchfoundation.org

TEAM MPN HIGHLIGHT



My name is Nisha Patel and I am a Chicagoan, mother of three, wife, physician and an MPN patient. For the past two months, I have been training for a half marathon (13.1 mile run) in support of MPNRF, the Myeloproliferative Neoplasm Research Foundation.

I am a former marathon runner and completed six distance runs in the past (three full marathons and three half-marathons). This will be my first distance run in six years!

This process has helped me appreciate life and be grateful for all my blessings in spite of this health speed bump. I will continue to ...

- be the best mom I can be to my Max, Luke and Arya;
- be a good wife to my rock of a husband, Vikas;
- be a dedicated physician to my patients whom I adore;
- and to run my heart out like I always have!

If my story has inspired you, join me and team MPN:

<http://www.mpnresearchfoundation.org/Team-MPN-to-Fund-Research>

WHERE THERE'S A WILL, THERE'S A WAY... ALMOST ALWAYS

It's almost impossible to overstate the importance of estate planning, regardless of the size of your estate or the stage of life you are in. A close second to planning your estate is getting it done right. You probably think that the rich and famous are way ahead of the curve when it comes to estate planning. After all, they presumably have access to accountants and lawyers. But here are a few examples of celebrities who failed to plan or plan correctly.

Supreme Court Chief Justice Warren E. Burger

You've seen the ads for the do-it-yourself legal documents, including wills and trusts. The law does not require that an attorney prepare your will. The high-ranking justice prepared his own will (consisting of only 176 words), which contained several typographical errors. More importantly, he neglected to address several issues that cost his estate over \$450,000 in taxes.

Florence Griffith-Joyner

When the Olympic medalist Florence Griffith-Joyner died, her husband Al claimed he could not locate her will. This led to a dispute between Al and Florence's mother, who claimed the right to live in the Joyner house for the rest of her life.

If you don't have an estate plan, you need one, regardless of the size of your estate. If you do have an estate plan, did a lawyer review the plan? When did you review it last? Do people know where to find your plan?

Tomorrow's results are created by today's dreamers. Many people dream of a way to help find a cure for MPNs. Some have found that a good way to accomplish this dream is to designate the MPN Research Foundation as the beneficiary of part of their estate. Learn more about this support option by calling **Bill Crowley at (312) 683-7226**.



**FUND RESEARCH. FIGHT MPNs.
CREATE SUCCESS STORIES.**

PATIENT STORY



WIM LOUAGE - PATIENT WITH A CALR (TYPE 2 - INSERTION) MUTATION

Hello, my name is Wim Louage. I turned 44 years old in October, and I am Belgian but have lived in France since 2012. Together my partner and I are running a B&B in the French Southern Alps – an awesome activity that allows me to meet people from all over the world.

I guess my disease started when I was +/- 18 years old, because I already suffered with lightheadedness in my 12th grade at high school. I had a busy career in finance & human resources in the oil industry that brought about frequent stress. I was never really sick, seldom stayed at home and worked as much as possible, even when I felt especially horrible and weak. All the time doctors told me I had health problems caused by workload and stress but that nothing was wrong with my body. After we moved to France, I went back to Belgium to visit my father in November after losing my lovely mother in 2006. One night I really felt bad and had heavy tremors all over my body, which I could not control. After a stay in the ER in a hospital in the city where I was born, they sent me home again after sharing the same reaction as usual: You are stressed and need to take a break. The next three years in France were great, but they also included dizzy spells and weird pains all over my body, which I tried to accept.

WE'RE NOT ALONE. AND TOGETHER WE CAN CHANGE OUR PROGNOSSES.

Please be generous. And don't be shy about asking your friends to help out, too.

In September 2015 I began to experience a pulsatile tinnitus (heartbeat in my left ear) together with pain in my legs when I woke up in bed. After a visit to an ear specialist, who did not find anything unusual, I asked my GP in October for a complete blood count. This was the moment when we began to get closer to a diagnosis. My GP called me as soon as the results came in. My platelet count was 1,260,000, and she wanted me to immediately take an aspirin. She organized an appointment with my hematologist in November, a bone marrow biopsy was done, and in January 2016 I received the complete results: I had ET, CALR mutation, type 2 (insertion) with reticulin fibres (grade 1 MF).

I tried to obtain all my previous blood counts from the past years, which were done in Belgium, and the oldest one from 2004 showed that my platelets were at 640,000 already in those days. I still do not understand why my previous doctors did not warn me about it, especially the hospital in 2012. I could not believe it when I saw the result from my visit to the ER; my platelets were at 1,207,000 and they sent me home without any warning.

In January 2017 I will go to Paris to meet the MPN expert Dr Kiladjian for a second opinion regarding my treatment. For the moment I am just on aspirin (only since October 2015), but I would like to start a treatment with pegylated interferon because I am not happy with my grade 1 of fibrosis in my marrow. The CALR mutation brings higher platelet counts but also a lower risk for thrombosis. My tinnitus and lightheadedness is much better since taking aspirin, but I still have pains in my feet, hands and hips. My spleen is not enlarged, but sometimes I have pain in that area.

My advice is to learn as much as possible about MPNs, try to get a second opinion from a true MPN expert, and enjoy life as much as possible.

I started a support group on Facebook for people with ET and MF with CALR. We are a small family with a special disease and mutation in common: <https://www.facebook.com/groups/188986661472055/>

MPN RESEARCH FOUNDATION UPDATE

A periodic newsletter published by the MPN Research Foundation to provide members of the MPN community with information on current research and the Foundation's activities.

MPN RESEARCH FOUNDATION

180 N. Michigan Avenue, Suite 1870
Chicago, IL 60601
Tel (312) 683-7249 | Fax: (312) 332-0840
mpnresearchfoundation.org

UPDATE EDITORIAL STAFF

Raquel Nuñez, Editor
Susan E Rinehart, Layout Editor