

SUMMER MPN RESEARCH UPDATE

By John Crispino, PhD, Scientific Advisor

As summer comes to a close, it's time to report on two important meetings where researchers presented their latest findings on MPNs: In the US, it was the American Society of Clinical Oncology (ASCO) meeting, and in Europe it was the European Hematology Association Meeting (EHA). Here's a brief summary of key findings:

PRM-151 Shows Promising Results in Phase II Myelofibrosis Study

Dr. Srdan Verstovsek presented early results for PRM-151 in treating myelofibrosis. PRM-151 is an experimental agent that mimics a normal human protein, pentraxin 2, which acts to prevent fibrosis in response to tissue damage.

The study included a total of 27 patients; seven of them showed notable responses, including five who displayed decreases in the degree of bone marrow fibrosis. PRM-151 was safe and well tolerated, with no evidence of myelosuppression. More than half of the patients remain on study beyond 24 weeks.

These early results are encouraging. Stay tuned for additional updates!

Ruxolitinib Effective for Advanced PV in Patients Resistant to Hydroxyurea

Dr. Alessandro Vannucchi presented results from the Phase III RESPONSE trial of Ruxolitinib in patients with advanced PV who were resistant or intolerant to hydroxyurea.

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\$1 MILLION IN 2014 MPN CHALLENGE GRANT AWARDS!

By Barbara Van Husen

We are proud to announce that, with the support of The Leukemia & Lymphoma Society (LLS), we are able to devote \$1 million to funding ten new research projects through our collaboration, recently renamed MPN Challenge.

The projects focus on five areas that all have one thing in common: the potential to develop new and sometimes dramatically better MPN treatments. As always, we are investing our money – and yours – where we think it can deliver the greatest benefits to MPN patients.

Here are the projects, organized by the area covered. Several of the projects overlap two or more areas, including immunology, which was the fifth proposed area of study.



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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.

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GRATEFUL PATIENTS

By Robert Rosen

Being diagnosed with an MPN wasn't a choice, but where you invest your money is.

We received a call recently from an MPN patient who wanted an opinion on whether to donate to his favorite hospital or whether to make a contribution to the MPN Research Foundation. We encounter this question frequently. Obviously we at the Foundation have our bias on this issue. But the question is worth evaluating on its own merits.

Grateful patients have options for strategic deployment of their philanthropic dollars. Hospitals and major medical centers do critical work and treat patients with many conditions.

What sets us apart is our singular focus on MPN Research grant making. We think we can fund research with the highest possibility of a meaningful outcome. Our process for selecting grantees is exhaustive and occupies much of our time during the course of the year. We solicit proposals from all over the world and we fund the ones that pass our strict standards of innovation and relevance. Our board keeps the focus on the needs and wants of the patient community, and we cap administrative costs and overhead on all grants.

Dr. Andrew Schaffer, the Chair of our Scientific Advisory Board, has written, "**The MPN Research Foundation has provided key support for virtually every major advance in the MPNs since 2000.**"

Like you, as a patient I want my contributions to have the best chance of addressing my particular health needs. When prioritizing the merits of MPN research grant applications, a difficult process because of the large number of outstanding proposals we receive every year, our Scientific Advisory Board often likes to ask which ones are most likely to provide the biggest bang for the buck for the MPN patient.

So for you, Mr. or Ms. Grateful Patient, there are choices about the best way to support the medical needs that are most important to you. Do be a grateful patient but be a smart donor.

I must say that Americans make a great deal of real sacrifices to the public welfare and I have noticed a hundred instances in which they hardly ever failed to lend a faithful support to one another.

– Alexis de Tocqueville

\$1 MILLION IN 2014 MPN CHALLENGE GRANT AWARDS!

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1. Reducing the MPN Allele Burden

How does Pegasys target the JAK2 mutation? Does it also target CALR positive hematopoietic stem cells? Why are some patients resistant to Pegasys? We hope these researchers will discover answers that lead to a better understanding of this important treatment option: **Jean-Luc Villeval, PhD; Sandra Pellegrini, PhD; & Stefan Constantinescu, MD, PhD**, INSERM/Institut Gustave Roussy, University Paris XI, France; Institut Pasteur Paris, France; de Duve Institute, Université Catholique de Louvain, Brussels, Belgium; Ludwig Cancer Research Institute, Brussels, Belgium.

How does the blood change *before* an MPN develops? **Leonard Zon, MD**, Boston Children's Hospital, will use unique combinations of fluorescent proteins in zebrafish to identify early changes that could lead to earlier treatment to suppress the development of fibrosis.

2. Selective JAK2 Inhibition

Current JAK2 inhibitors are not selective. They inhibit the body's ability to create needed blood cells. **Gary Reuther, PhD**, Moffit Cancer Center, proposes to investigate the role of the Pim1 oncogene in JAK2 positive MPNs, and explore the possibilities of combination JAK2/ Pim1 inhibitors, which would inhibit the over production of blood cells but allow the body to produce necessary blood cells.

3. CALR Mutation

In 2013, research partly funded by the MPN Research Foundation revealed a previously unknown mutation involved in MPNs: the Calreticulin or CALR exon 9 mutation. **Michael Deininger, MD, PhD**, Huntsman Cancer Institute / Department of Hematology and Hematologic Malignancies, University of Utah School of Medicine, will try to develop an antibody to treat CALR mutant derived MPNs.

Robert Kralovics, PhD, Center for Molecular Medicine of the Austrian Academy of Sciences, also hopes to target the CALR mutation with antibodies or develop a vaccine to use as an immunization.

4. Fibrosis and the Bone Marrow Niche

Inflammation in the bone marrow niche influences MPN disease progression, but no one knows exactly how – or, for that matter, what causes inflammation in the first place. **Nadia Carlesso, MD, PhD, and H. Schott Boswell**, Indiana University School of Medicine, hope to find some answers that could lead to new ways to counteract disease progression.

How do changes in stem cells contribute to leukemia and MPNs? **Lei Ding, PhD**, Columbia University Medical Center, will probe changes in the cells with MF and try to identify potential novel therapeutic targets for myelofibrosis.

Lymphoid cells are key inflammatory cells, but very little MPN research has focused on the lymphoid system. **Angela Fleischman, MD, PhD & Richard Van Etten, MD, PhD**, University of California, Irvine, Department of Medicine, will seek to identify the specific lymphoid cells responsible for the inflammation that causes MPNs, in the hope that this will lead to new treatment options.

Following up on her 2012 MF Challenge grant, **Ann Mullally, MD**, Harvard Medical School and The Brigham and Women's Hospital, will try to identify the role of a specific gene, CHD4, in the development of fibrosis. This could lead to a way to alter the development of fibrosis early on.

Nobody likes bone marrow biopsies. **Katya Ravid, MD, PhD**, Boston University School of Medicine, is hoping to develop a way to use CT scans and MRIs of the bone marrow, rather than bone marrow biopsies, to determine the progression of fibrosis.

We offer thanks to our Scientific Advisory Board Chair, Dr. Andrew Schafer from Weil Cornell, for leading the multi-disciplinary group that selected the award recipients from a far larger pool of excellent proposals.

As noted earlier, every one of these studies has the potential to make significant advances that will lead to new treatment options. With your help, we will continue to push the state of MPN science further until all MPN patients have the treatments they need and deserve.

NORD AWARD HONORS MPN RESEARCH FOUNDATION

By Raquel Nuñez

NORD (the National Organization for Rare Diseases) presented its 2014 Abbey S. Meyers Award to the MPN Research Foundation for demonstrating exceptional leadership in representing its members. We are honored and delighted to accept this award.

NORD is an advocate for both individual patients and organizations that address rare diseases. NORD offers networking opportunities for member organizations and patient assistance programs. It is a leader in policy initiatives related to rare diseases, and shares information to help meet the education and research goals of rare disease organizations across the United States.



Robert Rosen, Chairman, MPN Research Foundation, and Annette De Bow, who was recognized by NORD as a Portrait of Courage for her patient advocacy work. Annette led the 2013 Trek For A Cure that raised over \$30,000 to support the MPN Research Foundation.

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Ruxolitinib was superior to best available therapy, with the majority of patients showing a reduction in spleen size and a significant decrease in symptoms. Ruxolitinib was well tolerated, and the majority of patients showed a durable response. These results suggest that Ruxolitinib may be a viable therapy for individuals with advanced PV.

Equally important, continuing studies could lead to FDA approval of Ruxolitinib for PV – which, in turn, means the cost could be covered by insurance.

Exciting New Study on the Stem Cell Niche and Its Relationship to the MPNs

This is painfully technical, but bear with me. You all know about JAK2 inhibitors; this is something totally different that could lead to a whole new way to treat MPNs.

Dr. Simón Méndez-Ferrer demonstrated that sympathetic nerve fibers are consistently reduced in the bone marrow of MPN patients. Enhancement of these cells restored normal sympathetic regulation and blocked MPN progression in a mouse model.

Next step: Find out what happens in humans. Dr. Méndez-Ferrer and colleagues are planning a Phase II study in Europe to test the effects of beta-3-sympathomimetic agonists on the disease course and mutant allele burden in MPN patients.

That's the technical part – but it could lead to extremely good news.

Looking Forward – Eagerly

There's a lot happening in MPN research – probably more than at any time in the past. I look forward to reporting significant advances on a regular basis.

Look for my next update after the American Society of Hematology Meeting (ASH) in December.

NEW PARTNERS TO HELP FOCUS RESEARCH: THE MPNRF INDUSTRY ADVISORY BOARD

In November 2013, MPNRF convened a forum to bring together scientists from both academia and industry to discuss the state of MPN science and to identify unmet needs toward which the Foundation could direct its grant programs.

The meeting was more successful than we could have imagined. There was lively dialog across academic/industry lines, and all participants contributed to the list of needs around which our 2014 grant programs have been based. Without violating anyone's proprietary information, both academic and industry participants were able to identify opportunities for partnership that may help bridge the gap between basic science and its translation to patient use.

More Collaboration, Faster Progress

This experience convinced us that further collaboration across academic and industry lines would be beneficial to the direction and speed of MPN research. Therefore, the MPN Research Foundation is proud to announce the formation of a new Industry Advisory Board (IAB). Members of this Board will include scientific representatives of companies with interest and expertise in the MPNs, and academic scientists who are or have been our grantees and in whom we place much trust. This group will meet annually in November at the annual MPN Roundtable, and will communicate with the Foundation online during the rest of the year.

The annual Roundtable meeting will be different from the many meetings that all these scientists attend frequently, in part because it bridges the academic/industry divide. In addition, we will attempt to keep the meeting relatively small to promote collegiality and conversation. And finally, members of the Foundation family will attend as observers (and occasional contributors) to bring a patient perspective to these discussions.

The Foundation is very excited about this new Advisory Board. Please join us in welcoming these new partners to our research process.

STUDY HINTS AT POTENTIAL OF COMBINATION THERAPY FOR POLYCYTHEMIA VERA

We have been interested in the potential of combination therapy for treatment of MPNs and are pleased to see some initial findings released.

In an article published by Hans Hasselbach et al in *Leukemia Research Reports*, Interferon (Pegasys) in combination with Ruxolitinib (Jakafi) was found to have a profound effect in the case of a woman with advanced Polycythemia Vera.

The woman had had post-ET PV for 12 years. Her spleen was enlarged, and caused significant abdominal discomfort. She suffered from fatigue as well as night sweats and persistent itching. She couldn't take hydroxyurea (HU) because it caused fever and a widespread rash. Pegylated interferon-alpha2b (PEG-Intron) also gave her a rash.

The doctors began treating the patient with Ruxolitinib, and soon added a low dose of Pegylated Interferon every second week.

Within three days, the woman's physical symptoms were dramatically alleviated. She achieved complete hematological remission within four weeks, and within 10 months her JAK2V617F-allele burden was reduced from 90% to 28%. In addition, the woman could tolerate Pegasys.

The case qualifies as a Proof of Concept that combination therapy is significantly more effective than conventional regimens of either Ruxolitinib or Interferon alone.

But this is a single case and because the researchers aren't sure why this transformation occurred, more research is needed.

In our upcoming assembly of industry and academia (the MPN Roundtable) we will be addressing what we and others in the MPN field can do to better understand this case and what the potential is for combination therapy. We will report back on the discussion in our Spring 2015 newsletter.

ONE (MORE) VOICE AGAINST CANCER

By Lina

On Monday July 8th, I found myself in Washington D.C. to participate on behalf of the MPN Research Foundation in the One Voice Against Cancer Lobby Day. OVAC is a group of cancer-focused patient groups that MPNRF is a part of, and their message is simple: Congress should support an increase in funding for programs that help cancer patients around the country.

There is something oddly uniting about cancer; we all know someone who has been touched by it in some way, but despite our varied experiences, we truly were speaking against cancer with One Voice.

Monday started with registration, and for me, an awkward wandering around the lobby until a few of us got talking. After getting to know one another we began our training. There were 88 participants from 30 states. During training we were given three goals, or “asks.”

- 1) \$5.26 billion for the National Cancer Institute (NCI)
- 2) A proportional increase to NCI funding when there is an increase in NIH funding
- 3) \$510 million to be budgeted for the CDC Division of Cancer Prevention and Control

These are pretty big things to be asking for, and it’s pretty intimidating to be asking political leaders for them. But who better to speak to than the people with the power to help make the changes we are asking for? To speak to the decision makers, to tell them what their constituents want, and need; that is why we were there.

I was in a very small delegation from my state (Missouri). We started the day on the Senate side of the Capitol, where we met with staffers from Senators McCaskill’s and Blunt’s offices. After those were a lunch break; then we headed over to the House side, where we had meetings with Ann Wagner and a staffer from Sam Graves’ office.

For my part of each presentation, and knowing my tendency to be nervous, I decided to focus on my story: when I was diagnosed, what my disease is, treatment options available, and the cost of said treatments.

I would start by pulling out the box of meds that I brought (Pegasys), place it on the table, and explain, “This drug is not yet FDA approved for MPN patients. I have been denied three times by my insurance company on the grounds that my purposes are ‘off label.’ This box costs \$2000. It contains ONE dose of medicine. I take this once a week. That’s \$104,000 a year for however many years I’m lucky enough to live.” That tended to leave a strong impression on our listeners. Then we worked in the “asks.”

While I believe I was alone representing MPNs, I’d like to think that my presentations were memorable, both to the elected officials and to fellow participants, as few had heard of MPNs before.

As always, we are our own best advocates. If we do not take care of ourselves, who will?

<http://linampn.com/>

**The MPN Research Foundation
has provided key support for
virtually every major advance in
MPN research since 2000.**

– Andrew Schafer, MD, Director of the
Richard T. Silver, MD Myeloproliferative
Neoplasm Center at Weill Cornell and
Chairman, MPN Research Foundation
Scientific Advisory Board.

TEACHING OLD DRUGS NEW TRICKS

"The most fruitful basis for the discovery of a new drug is to start with an old drug."

~ Sir James Black, Nobel Laureate

We agree with that. So the MPN Research Foundation just entered into a collaboration with an organization called Cures Within Reach. They have been helping patients since 2005 by repurposing drugs to quickly deliver safe and affordable treatments and cures for rare disorders that currently do not have effective treatments.

That makes sense, because developing new drugs is a risky business. Only one in 10,000 new chemical entities makes it to market. The average time for development of a new drug is 14 years, and the average cost is \$3 billion. A repurposed drug can be approved for off-label use in three years or less at a cost around \$250,000.

While this collaboration with Cures Within Reach is just beginning, the MPN Research Foundation has already funded a project that is repurposing an existing drug to develop a new treatment for PV.

Dr. Shaoguang Li from the University of Massachusetts is researching the use in MPNs of Zileuton, a common asthma drug sold in your local pharmacy as Zyflo. Dr. Li's research with laboratory mice showed that the drug weakens PV.

This research is funded with money raised by one of our board members, JoAnn Mason. As a parent of an MPN patient, JoAnn felt it was important to support the MPN Research Foundation's efforts to raise funds and facilitate earlier access to affordable, effective therapies.

DON'T WORRY. YOU DON'T NEED A WILL.

By Bill Crowley

Hey, who needs a Will? Sure, the government – not your family – decides what happens to your estate if you die without one. But you trust the government to do the right thing. Of course you do. After all, governments always make amazing decisions about other people's money.

Here are few more excuses for not having a Will.

- **Attorney fees** – Why should you pay to have a will? All the attorney will do is type your will instead of writing out how you want your assets divided. Save a few hundred bucks and type it yourself. The rumor that lawyers make more money representing families who battle in court when there's no Will is simply hearsay.
- **You enjoy paying taxes** – You feel contributing 50% of your estate to the government is a good use of funds.
- **You will live forever** – You may be the first to live forever.

All right, maybe you should have a Will. And including the MPN Research Foundation is a wonderful way to help find a cure for MPNs and make a significant impact.

We can provide bequest language to include the Foundation in your Will, or to talk with you or your financial advisor about a wide variety of planned giving options.

To establish your legacy, please contact Bill Crowley at 312 683-7226 or wcrowley@mpnresearchfoundation.org.



THE IMPORTANCE OF CLINICAL TRIALS

By Diana Huizar, MPNRF Intern, Summer 2014

Clinical trials give you a chance to try new medical treatments not yet available in the marketplace. They are also required by regulators, to demonstrate that new drugs or medical devices are both safe and effective. During the course of a trial, data is collected recording all observations related to lab results, the patient's progress (or lack thereof), effectiveness, and side effects of the treatment. Clinical trials are conducted at many types of sites, but usually by investigators at specialty clinics or teaching hospitals.

Data from the U.S. National Institutes of Health shows that clinical trials testing treatments for MPNs have increased significantly since the Foundation began funding research. While fewer than 20 clinical trials for MPN treatments were conducted from 1999-2005, there have since been over 750 trials in MPNs.

Although the Foundation does not fund clinical trials directly, we have helped put a spotlight on the need for an increased focus on ET, PV and MF research. Our funding focuses on preclinical trials and basic science that can lead the way to new treatment options. By bridging the gap between academic researchers and industry, the Foundation seeks to encourage the development of better treatments and, one day, a cure.

MPN Research Foundation Update is 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.

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BEYOND RESEARCH: OTHER INITIATIVES AT MPNRF

By Michelle Woehrle

The Foundation sees itself as a driver of innovative and (hopefully) game-changing MPN research. But that's only part of the story.

We also keep patients informed about community and science updates related to MPNs. That includes informing patients about (though not endorsing) clinical trials. Therefore we maintain a list of all PV, ET, and MF clinical trials at www.mpnresearchfoundation.org/Clinical-Trials and periodically send updates about trial recruitment.

MPNRF Goes to Washington

We know that the system by which medicines are approved isn't perfect. So we have increased our involvement with advocacy at the federal level. We are learning more about how to navigate FDA and NIH to promote the best interests of MPN patients.

Simultaneously we're helping to repurpose already approved drugs for MPNs. Pegasys is the most prominent example. Another example is Zileuton, approved for use in asthma, but recently tested by Shaoguang Li, with our support, for use in PV.

Our friends at the MPN Forum are also taking action. They are recruiting patient advocates to assist the FDA with monitoring clinical trials. They're even taking volunteers. To get involved contact ourmpnforum@gmail.com.

Whatever it takes, we're helping to usher in a new day in MPN treatments. We welcome your suggestions.