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UPDATE

A PERIODIC NEWSLETTER FOR THE
MYELOPROLIFERATIVE NEOPLASMS COMMUNITY
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REMEMBERING THE PAST, LOOKING FORWARD TO THE FUTURE

By Robert Rosen

As a boy I talked frequently with my father about his experiences in the Army Air Corps in World War II. The huge piston engine planes of the era fascinated me and when I was old enough I took flying lessons, earning my pilots license over a summer vacation in the hours after my job as a camp counselor. Although I was mesmerized by the forward view provided by the seat in the cockpit, a few quirky situations in flight quickly activated my caution gene and I ultimately gave up this hobby.

Twice a year we are drawn to conferences where major advances in hematology are presented. We expect that MPN scientists like focused pilots will show the way forward. This year's ASCO (American Society of Clinical Oncology) convention in Chicago drew 40,000 participants, scientists, researchers, pharmaceutical companies and bio-techs. Entering the bustling great exhibit halls it was hard not to feel that all these resources were bound to bring dramatic resolution to our most vexing health issues.

Shortly, however, a more cautious feeling set in. The scientific process is slow to unfold, good ideas take years to explore, and all the resources in the world do not guarantee a timely outcome.

Our team met with nearly a dozen scientific firms working on new MPN drugs. The landscape was illuminated by the knowledge that the first specifically MPN drug was nearing FDA approval. Many more are working their way through the MPN drug development pipeline. Although the development

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NATIONAL CANCER INSTITUTE TO FUND MYELOPROLIFERATIVE DISORDERS RESEARCH CONSORTIUM FOR AN ADDITIONAL FIVE YEARS

As supporters of the the Myeloproliferative Disorders Research Consortium (MPD-RC) since its inception, we are thrilled to announce that the National Cancer Institute will continue to support MPD-RC for an additional five years. This positive news will lead to innovative work in the laboratory, additional clinical trials, and improved treatment for patients.

The Myeloproliferative Disorders Research Consortium, under the direction of Dr. Ronald Hoffman at the Mount Sinai School of Medicine in New York, is a multi-institutional (35 in the U.S., Canada and Europe), interactive, international group of basic scientists, biostaticians, translational researchers and clinical scientists who are expert in a variety of disciplines pertaining to the Philadelphia chromosome negative Myeloproliferative Neoplasms (MPNs) polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF).

It is estimated that together these three disorders affect at least 150,000 individuals in the United States.

Since the establishment of the MPD-RC in July of 2006, an infrastructure has been developed to allow and promote timely and efficient scientific and clinical interactions between investigators, which could lead to rapid progress in the future. The organization has created an interactive, integrated research group that has accomplished each of the objectives outlined in the original proposal.

The MPD-RC has made much progress on six projects being conducted by leading investigators at multiple institutions both in the US and overseas. They include:

1. "Genetic Basis of Polycythemia Vera" – Josef Prchal, MD - University of Utah
2. "Role of NF-E2, Jak2V617F, and PRV-1 in Polycythemia Vera" – Heike Pahl, MD – University Hospital-Freiburg
3. "Mouse Models of Polycythemia Vera" – Jerry Spivak, MD – Johns Hopkins Medical School
4. "Mouse Models of Myelofibrosis" – Anna Rita Migliaccio, MD – Mount Sinai Medical Center
5. "Mechanisms of Abnormal Stem Cell Trafficking in Myelofibrosis" – Ronald Hoffman, MD – Mount Sinai Medical Center
6. "Clinical Trials in Myeloproliferative Disorders" – Lewis Silverman, MD – Mount Sinai Medical Center

A Focus on Interferon α

Interferon α is a focal point of study for the MPD-RC in the treatment of Myeloproliferative Neoplasms. Interferon α has been used for over 20 years to treat patients with Philadelphia chromosome negative MPNs, following the seminal reports of Richard Silver and Harriet Gilbert, who both were founding members of the MPD-RC. Considerable speculation still exists as to which form of interferon α is optimal for the treatment of MPN patients.

The MPD-RC will soon be opening two clinical trials.

MPD-RC #111 – "Single Arm Salvage Therapy With Pegylated Interferon Alfa-2a for Patients with High Risk Polycythemia Vera or High Risk Essential Thrombocythemia who are either Hydroxyurea Resistant or Intolerant or Have Had Abdominal Vein Thrombosis" is a Phase I/II trial looking to recruit 188 patients nationally and in Europe.

The second trial, MPD-RC #112 is a Phase III clinical trial entitled, "Randomized Trial of Pegylated Interferon Alfa-2a versus Hydroxyurea Therapy in the Treatment of High Risk

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Polycythemia Vera and High Risk Essential Thrombocythemia." This pivotal trial intends to recruit 612 patients nationally and in Europe.

Both trials look to answer important MPN questions that we hope will translate into key therapy options for patients.

If individuals have questions about the MPD-RC or about participating in these clinical trials please email Dr. Hoffman at **ronald.hoffman@mssm.edu** or call (212) 241-2296.

NEW PARTNERSHIP WILL EDUCATE DOCTORS ON MPNS AND MDS

It will come as no surprise to MPN patients that many doctors who treat us are not aware of the results of the latest research and treatment options for ET, PV and MF. The MPN Research Foundation is committed to providing clinicians with the information they need through our website, patient brochures, and presentations we make to cancer centers across the country.

This year we are taking that commitment to physician education one step farther. We are partnering with the Aplastic Anemia & MDS Foundation to present a series of evening programs (called the MDS/MPN Rounds) which will present scientific updates and practical case studies to MPN and MDS clinicians in Chicago.

These programs will provide an opportunity for both medical center and community physicians to meet and discuss disease diagnosis, treatment options, and anticipated developments in the science related to both MPNs and MDS.

The MDS/MPN Rounds program presents an important opportunity to clinicians who may not see enough MDS or MPN patients to have direct experience with the wide variety of symptoms and complications each of these diseases can present. It is also common for clinicians who treat MDS to treat MPNs as well, and vice versa. The MDS/MPN Rounds program fills a need for these physicians and can contribute to their Continuing Medical Education (CME) requirements, while raising their awareness of the latest diagnostic and treatment options.

An innovative, multi-institutional group of Chicago clinicians who call themselves the MPN Chicago Roundtable is planning, promoting and supporting this program. These physicians, who meet in the offices of the MPN Research Foundation, represent five large medical centers in Chicago (Rush, Northwestern, University of Chicago, Loyola and University of Illinois-Chicago.) Their determination to work across institutional boundaries for the benefit of MPN and MDS patients is, we believe, evidence of the highest commitment and dedication to their own patients and those across Chicago and potentially beyond.

We are also pleased and proud to be working with the Aplastic Anemia & MDS Foundation on this important project. Successful partnerships such as this benefit all of our patients, and working together we are able to leverage our resources to provide the largest impact for all of us.

The first MDS/MPN Rounds evening is scheduled for Tuesday, September 13, 2011, with a second event to be scheduled next February. If these events prove to be as successful and well received as we anticipate, we will implement similar programs in other cities in the next several years.

LOOKING FORWARD TO THE FUTURE *(continued from page 1)*

of JAK2 inhibitors is leading the way, there are now other mechanisms of action under intense investigation. The ASCO convention raises hopes that more discoveries will be announced six months later at the ASH (American Society of Hematology) convention, as the cycle of research, reports and hope continues.

The MPN Research Foundation has now funded more than 30 multi-year research grants to the best and the brightest in our field. Through our newsletter, symposia and email alerts and website we do our best to inform our community about new developments. Stay tuned.

WOMEN AND MPNs

By Dr. Claire Harrison
Guy's and St. Thomas' Hospital, London, UK

I was very pleased to be asked to write on this topic. Just as there are gender differences in other aspects of life; specific concerns arise for women who have MPNs. Some of my colleagues thought the idea was "sexist" or "biased" but most also felt that acknowledging and focusing on areas specific to women was both unique and important. I hope that readers of both genders benefit from the content generated.

Interestingly, recent thinking about how and why MPNs occur has highlighted again that being a woman means you are more likely to present with a diagnosis of ET than PV or MF.

Many aspects of disease management are identical for both women and men but it is important to recognise that MPN may come to light in different ways. For example, a woman may suffer multiple miscarriages or particularly heavy periods due to an underlying MPN. Another interesting observation from some of my own patients has been that their platelet counts tend to be higher during menstruation and some tolerate venesections very poorly at this time. Heavy menstruation needs to be assessed by a gynaecologist but can be managed by reducing aspirin dose, low doses of clot stabilising drugs or a hormone coated device such as the mirena coil.

The use of combined oral contraceptive either as contraception or to control excessive menstrual loss is not appropriate due to risks of venous thrombosis. Other forms of contraception such as the progesterone-only pill are acceptable. My advice regarding hormone replacement therapy is to use the lowest dose of oestrogen and to avoid it where there has already been a thrombosis.

Can I Get Pregnant and What Are the Risks?

We can answer most confidently that the chance of a successful pregnancy with ET is about 60-70%; slightly lower than for women with PV or PMF. The development of the placenta, much like the growth of the baby, can be monitored in pregnancy by use of ultrasound scanning to examine blood flow in the placental blood vessels. We recommend these at least once in pregnancy. The risks to the mother are of thrombosis and the risks here are largest in the first 6 weeks after the baby is born so extra precautions with heparin are usually advised at this time.

As with all pregnancies, the healthier the mother in general the more successful the pregnancy; and so it is important to maximise your health when planning to get pregnant. I would also add that planning to have your family when young where possible is best for a healthy pregnancy as all risks not only that of Down's syndrome increase with age.

If pregnancy happens whilst taking hydrea or xagrid, get in touch with your haematologist and stop the drug as soon as safely possible, switching to interferon.

After pregnancy, blood counts return quite rapidly to their previous levels; sometimes they can overshoot. This overshoot may be risky and so remember to keep an eye on the blood count and how you are feeling. Remember also this is the time when blood clots happen even to women without MPN so we use heparin for the first 6 weeks and continue other treatments such as aspirin and interferon.

The aim of this article was to discuss issues specific to women who have MPNs. There are many inspiring stories about successful pregnancies with women who have MPN. One such story is included in this newsletter.

ON BEGINNINGS

By Sarah Dreller

Four years ago I wrote an essay for this newsletter in which I talked about how I was coping with my PV diagnosis, symptoms, and complications, but didn't share how I came to be diagnosed in the first place. During an annual physical in 2003 I mentioned my husband and I wanted to start a family, and in response my doctor ordered a simple blood test to make sure I wasn't going to begin a pregnancy already anemic. Of course, because of my as-yet-undiagnosed PV the counts came back completely the opposite of what was expected, and I then entered the cycle of tests and specialist appointments familiar to other MPN patients. Our doctors urged us to put our baby plans on hold until my health stabilized. I was 31 years old.

Over the next few years a key element of my PV treatment was avoiding anything that might impede my ability to become pregnant later. This mostly meant enduring serious doses of Interferon-alpha rather than the more-easily tolerated hydroxyurea, since that drug was known to negatively effect the reproductive system. But when, at the age of 35, my doctors finally cleared to me to return to our plan to start a family, nothing happened. And so, my husband and I eventually submitted ourselves to tests and treatment for infertility.

For this, the point was to try to become pregnant while avoiding anything that might increase my bone marrow's hyperactivity and the severity of my associated symptoms. When it appeared In-Vitro Fertilization was our last option, our doctor carefully planned the procedure to give us as much possibility of success with as little medication as possible. It worked on the first attempt, I'm happy to report in retrospect. But the joy we felt on hearing the positive news will never entirely erase our memory of profound confusion and fear during the moments before the first injection, wondering what we were about to do to my body and our future together.

The pregnancy progressed reasonably well. I took blood thinners to counteract any potential hormone-induced clotting problems, and all the good reports we were getting about our baby's development helped us cope with the fact that blood thinners could also put me at real risk of massive bleeding during the delivery. Finally, now 38 years old, I went into labor. Our son was born perfectly healthy and was placed immediately into my arms. Naturally, my husband and I were completely infatuated – so much so, in fact, that we didn't really notice the turmoil around us. An hour later, when I couldn't get out of bed without fainting, we learned I had hemorrhaged. Even after I was home and able to walk without help, it was several frustrating weeks before I was physically strong enough to carry my son, change his diaper, or care for him in any way other than nursing.

Why I started hemorrhaging is a mystery. It could have been the blood thinners or even the PV itself for some reason—or perhaps it might have happened anyway and those other things just made it worse. Why we had problems conceiving is also an unanswered question. Maybe we would have discovered our infertility when I was 31, or maybe the fact that my poor health forced us to wait put us in a situation we would not have experienced otherwise. What I can say with absolute certainty, though, is that despite everything my body actually did a pretty good job of nurturing a strong new life into existence. And for that beginning, my husband and I will feel eternally lucky.

Photo caption: Sarah Dreller shares a moment with her happy, healthy new baby.

THE PEGASYS DIALOGUE

By Felisse Sigurdson

How One Patient Persuaded Her Insurance Company to Cover the Cost of Pegasys

Like many MPN patients, I decided to try Pegasys when myelosuppressive therapy was recommended to control my PV. The good news is that a very low dose of the drug has been nothing short of remarkable in controlling and reversing the progression of the disease.

However, like many MPN patients, I had to appeal to my insurance company in order to receive coverage for the off-label use of the drug. Thankfully, the appeal was successful. I am sharing my story to offer some guidance and encouragement to patients who need to pursue an appeal.

Not all insurance companies deny Pegasys even though it is prescribed off-label for PV. For the first 18 months, my insurance company covered Pegasys without any additional information other than the doctor's prescription. Then my insurance company was acquired by another company, and when the Pegasys script needed to be renewed, I received a denial letter for coverage on the grounds that it was not FDA approved for PV.

The denial letter from the new insurance company stated they cover medications for 'off-label' indications when the drug is approved by the FDA and proven safe and effective for treatment of the specific medical condition as evidenced by supporting documentation in the standard compendia OR as evidenced by supporting documentation in the form of results of controlled clinical studies published in at least two peer-reviewed English language, biomedical journals.

I called the medical director who sent me the letter and explained that while Pegasys is not listed in any of the compendia for Polycythemia Vera, there are many published articles discussing the safety and effectiveness of Pegasys for PV. He told me that my case would be stronger to the extent I provided published research of clinical trials conducted with a good number of patients rather than small studies with less than 10 patients or secondary reports.

I sent the insurance company three things:

1. A summary of my personal experience pre- and post- Pegasys, including the efficacy of Pegasys in terms of hematological and clinical response. I provided a chart that compared HCT, WBC, Platelets, CD34, LDH, Spleen Size and JAK2 % pre-Pegasys, 6 months later, 12 months, 20 and 27 months later. The chart showed all blood counts under control and signs of disease progression reversed.

2. A letter from my hematologist.

3. Seven published articles from peer reviewed scientific journals. The first three were the important clinical studies from France and MD Anderson. The other articles were published by leading researchers in the field discussing the safety and efficacy of Pegasys in treating PV patients. The MPNRF website contains the complete list of articles to consider using for a Pegasys appeal. This list is updated as new articles are published.

As a result of this initial submission, I received notification that my reconsideration was approved for 6 months. At the end of 6 months, the insurance company requested clinical data from my hematologist showing continued stability on the drug. They renewed the prescription for another year.

In addition to the process I just completed, I am currently in discussion with the insurance company to update its coverage policy for Pegasys for all MPN patients.

I realize that the process is not the same for all insurance companies, but perhaps sharing my story can reduce the stress of the appeals process and improve the outcome for some patients.

SUPPORTING SUPPORT GROUPS

By Ann Brazeau, Vice President of Development

Services That Help MPN Patients Worldwide

No one understands what you're going through, as an MPN patient, as well as other MPN patients. If you want to learn more about your disease, clinical trials and meet with other patients who offer compassion and insight on polycythemia vera, myelofibrosis and essential thrombocythemia, you may want to visit one of the many support groups associated with the MPN Research Foundation.

The number of support groups is growing so rapidly that we have room here only to mention the many cities or states in which they are active. For more information, visit **mpnresearchfoundation.org**, click on MPN Patient Resources in the left column and then click on MPN Support Group Directory.

U.S. Groups That Have Regular Meetings

24 groups offer support across the U.S., in

Akron/Cleveland, Ohio
Albuquerque, New Mexico
Atlanta, Georgia
Chicago, Illinois
Cincinnati, Ohio
NE Kentucky & SE Indiana
Denver, Colorado
Lansing, Michigan
Los Angeles, California
Maryland
Massachusetts and greater New England
Naples, Florida
New Brunswick, New Jersey
New York, New York
North Carolina
Philadelphia, Pennsylvania
Phoenix, Arizona
Racine, Wisconsin
San Diego, California
San Francisco Bay Area, California
San Juan, Puerto Rico
Seattle, Washington
South Carolina
Texas
Washington, D.C..

Groups Outside the U.S.

Australia
Germany
Japan
London, United Kingdom
Netherlands
Saskatoon, Saskatchewan, Canada
Scotland
Toronto, Ontario, Canada
Vancouver, BC, Canada

Online MPN Patient Support Groups

There are also a number of online support groups accessible to just about everyone, regardless of location: MPD Chat, MPDInfo, Facebook Myelofibrosis Support, and Myeloproliferative Disease Support and Free Daily Email Digest. You'll find more information on all of them on our web site.

How We Support Support Groups

The MPN Research Foundation assists support group coordinators by reaching out to patients and hematologists in our database in the city and surrounding areas to generate interest. We send brochures to the coordinator to distribute to doctor's offices and cancer centers with a label attached with their contact information. We send a starter packet with a support group coordinator's guide and CDs with information about MPNs that will be useful to the patients and caregivers. We assist with procuring speakers either in person or through conference calls. We provide updated meeting information on our web site. We send Constant Contacts to patients in your area to remind them of meetings. And we provide general assistance in starting, organizing and maintaining the group.

If you need help joining or organizing a support group, contact Ann Brazeau at 312-683-7226 or abrazeau@MPNResearchFoundation.org.

UPDATES

By Ann Brazeau

New Myelofibrosis Drug Nears FDA Approval

Ruxolitinib, Incyte Corporation's myelofibrosis drug is getting close to FDA approval. The drug dramatically reduces spleen size while improving other constitutional symptoms, and was found to improve quality of life issues suffered by MF patients. Although there is no evidence of halting disease progression, the symptomatic improvement is a major step forward.

Ruxolitinib is the lead JAK1 and JAK2 inhibitor and is now being investigated in other hematology conditions. It is the first JAK inhibitor to be submitted to the FDA for the treatment of myelofibrosis and could be approved by the end of this year.

For MPN patients who have waited for treatments targeted to their disease, this is very good news. Ruxolitinib was granted Fast Track designation by the FDA in October 2009. The Fast Track program is intended to facilitate the development and expedite the review of drug candidates that demonstrate the potential to address unmet medical needs.

The JAK2 gene mutation was discovered only six years ago. The MPN Research Foundation immediately responded to this news, and we believe our research initiatives and patient education programs have had a direct impact on the course of new drug development. The MPN Research Foundation supported the discovery work for JAK2 and is encouraged by the rapid progress and growing interest in this underserved therapeutic area.

UPCOMING EVENTS

6th International MPN Patient Symposium, New York City, November 2, 2011

On November 2nd, the MPN Research Foundation and the Cancer Research and Treatment Fund will co-host the 6th International MPN Patient Symposium in New York City. This daylong event will bring the experts to the patients and caregivers and give them an opportunity to ask questions, share stories and learn cutting edge information about current research, promising drugs in clinical trials, the pros and cons of available treatments and how to cope with the day-to-day issues facing MPN patients and caregivers. This year's speakers include Drs. Richard Silver, Jerry Spivak, Babette Weksler, Ross Levine, Srdan Verstovsek, Sergio Giralt, Ruben Mesa, Tiziano Barbui, and Ronald Hoffman.

To register and for more information visit our website at www.mpnresearchfoundation.org

Coming in 2012

MPN Research Foundation Patient Symposium, Palm Beach, Florida, January 12th

MPN Research Foundation Patient Symposium, San Mateo, California, May 17th

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