MPD FOUNDATION®
UPDATE

A PERIODIC NEWSLETTER FOR
THE MYELOPROLIFERATIVE DISORDERS COMMUNITY

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# SPEED OF LIGHT

*by Robert Rosen*

In my college physics course, one of the experiments that gave me trouble involved the use of small spinning mirrors to measure the speed of light. It all seemed quite overwhelming and I was unable to produce the desired result. I do remember the effort however very clearly.

I was reminded of this because of a comment that Dr. Gary Gilliland made in our last meeting between the Research Alliance researchers and our Scientific Advisory Board. The process of drug development in America is often thought to be frustratingly slow. The painstaking process of genetic discovery, the development of appropriate molecular compounds, preclinical in vitro testing, mouse model testing, human testing, and FDA approvals can test the patience of our best patients.

So when Dr. Gilliland surprised us with his observation that we have seen new candidate drugs brought to human clinical trials at the relative speed of light, we took notice. And we were proud that our focused approach has contributed mightily to these results.

## Clinical Trials

In the relatively short time (less than three years) since the remarkable discovery of JAK2V617F we have witnessed a flurry of highly focused drug development activity among biotechs and academic labs, much of which we directly funded. This exploration has produced a surprising number of candidate drugs that work on one primary principal: If we can inhibit the activity of the JAK2 gene, we will be able to treat

*(continued on page 8)*

## NOT SO RARE

### New Epidemiology Study Pegs the Number of PV and ET Patients in the U.S. at 136,000

Until recently there has been little understanding, aside from a few small-scale research projects, of how many people have MPDs and how many new cases are diagnosed each year. This began to change in 2001when the incidence (new cases per year) of MPDs became reportable to SEER, the National Cancer Institute Registry. At that time, based on the available data, the Philadelphia chromosome negative MPDs (Polycythemia Vera, Essential Thrombocythemia, and Primary Myelofibrosis) were considered rare orphan diseases with an incidence estimated at 1 or 2 per 100,000 per year.

In December 2005, the MPD Foundation, along with the Leukemia and Lymphoma Society, awarded a grant to the Yale Medical School to conduct more extensive research on the epidemiology of MPDs. The objective of the study was to estimate the prevalence (total population of patients) and incidence of the Philadelphia chromosome negative MPDs. This is significant for the MPD community as we believe that establishing a more accurate view of MPD diagnosis in the U.S. population can have an impact on public policy.

The report, by Xiaomei Ma, Brenda Cartmel and Yun Wang of the Yale University School of Medicine, New Haven, Connecticut; Gary Vanasse of Brigham and Women's Hospital, Boston, Massachusetts; and H. Andrew Selinger of Prohealth Physicians Inc, Bristol, Connecticut appeared in the *American Journal of Hematology*.

They utilized health claims data from major commercial insurance payers in Connecticut and the Center for Medicare and Medicaid Services to estimate the prevalence of PV and ET in Connecticut. They found that as of 2003, the age-standardized prevalence for PV was 22 per 100,000 and for ET, 24 per 100,000.

Then they extrapolated the data to the entire U.S. population and came up with an estimated total of 65,243 patients with PV and 71,078 patients with ET in the United States in 2003. If we add in an estimate of 30,000 MF patients (from other studies), there seem to be about 166,000 MPD patients in the U.S.

The researchers pointed out that this was the first study to assess the prevalence of PV and ET in a large US population. They concluded that it is imperative to conduct more systematic research into the etiology and treatment of PV and ET, given the larger-than-expected number of patients and the fact that an aging population will further increase the burden of these diseases.

## MPD FOUNDATION CO-SPONSORS NEW YORK PATIENT SYMPOSIUM

Over 210 MPD patients and family members attended a daylong patient symposium in New York City in November 2007. The MPD Foundation and the Cancer Research and Treatment Fund co-sponsored this event in midtown Manhattan. Patients came from as far away as Ghana, India and London, as well as the west coast and southern United States.

Leading MPD researchers presented the latest data on the state of research and updates on clinical trials. The MPD Foundation's Research Alliance investigators, Drs. Hoffman, Tefferi and Gilliland, shared updates on the research funded by the Foundation.

Patients broke into groups based on their specific disease and were able to discuss challenges and share information with physicians and other patients. Many newly diagnosed patients were particularly pleased to be able to talk openly about their disease and learn from experts in the field.

Programs like these prove to be a great venue for patients and researchers alike. Researchers hear firsthand from patients what they endure with each disease, and patients are given an opportunity to not only share information with one another, but to speak to the experts, sometimes one-on-one, to get answers to puzzling questions about their disease.

## MPD FOUNDATION PATIENT RECEPTION AND LIVING WITH A BLOOD CANCER SYMPOSIUM — CHICAGO, MAY 2-4, 2008

Dr. Ruben Mesa, of the Mayo Clinic, will be hosting a patient symposium in Chicago, May 2nd through the 4th, *Living with a Blood Cancer: A Comprehensive Patient Centered Symposium* is for patients and family members who are currently fighting a cancer of the blood or who have been cured.

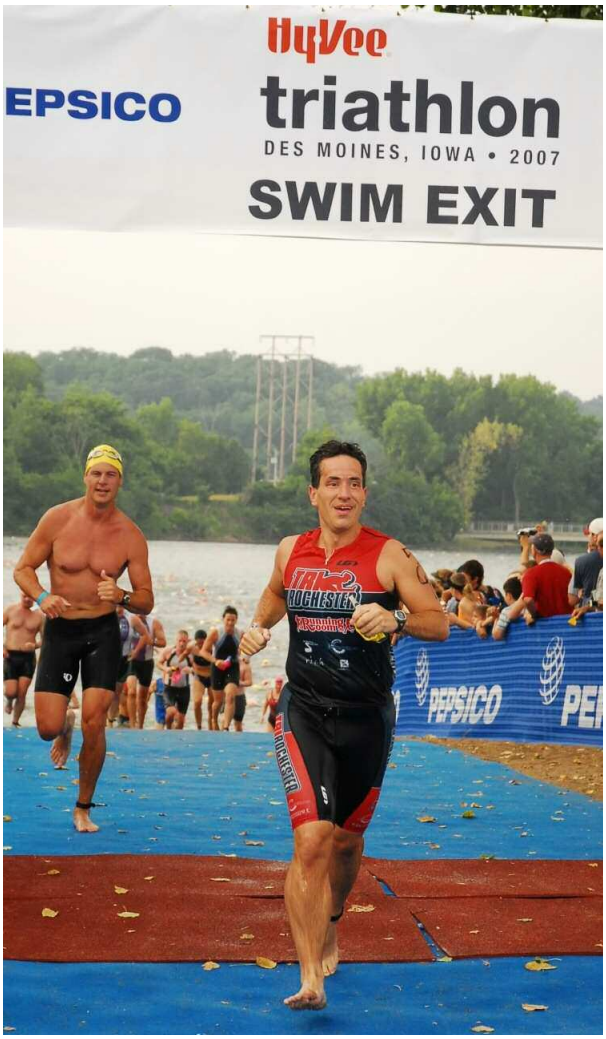
An internationally renowned group of speakers will offer a comprehensive, patient friendly program on the diagnosis and treatment of the blood cancers. Breakout sessions will include one on Myeloproliferative Disorders.

In conjunction with the symposium, the MPD Foundation will be hosting an MPD Patient Reception immediately following registration from 6 to 8 p.m., Friday, May 2, 2008 at the Sheraton Chicago Hotel & Towers.

If you receive this in time, and are in Chicago, please join us to mingle with fellow patients and meet leading MPD researchers in an informal setting.

To register for the symposium, please visit www.mayo.edu/cme/bloodpatientmeeting.






*Dr. Ruben Mesa of the Mayo Clinic, Rochester, MN, gives his all to support MPD patients – and not only in his clinic.*

## TRI-ING FOR AN MPD CURE

Dr. Ruben Mesa – host of the Living with a Blood Cancer symposium covered nearby – has worked with MPD patients for over 17 years. And he keeps on going long after office hours are over. Here he is at the HyVee Triathlon in Des Moines.

On September 7, 2008, Dr. Mesa will race in the ultimate amateur endurance challenge, the Ironman Wisconsin Triathlon (2.4 miles swimming, 112 miles cycling, 26.2 miles running) with a goal of raising $100,000 for MPD research and education, and to raise awareness of MPDs.

Please sign up to support Dr. Mesa's run at www.mpdfoundation.org.

# YEAR 2 OF MPD RESEARCH ALLIANCE CLOSES WITH STRONG PROGRESS, BIG PLANS

*by Barbara Van Husen*

On February 4, 2008, The Scientific Advisory Board of the MPD Research Alliance met in Chicago to review the accomplishments of Year 2 of the MPD Research Alliance and to plan for an equally successful Year 3. Our collaborative and innovative program has paid off with the accelerated development of JAK2 inhibiting drugs. Our goal is to continue on this productive track, expanding the scope of research as the scientific landscape provides more feedback from the current drug trials.

The three current MPDRA researchers (Dr. Gary Gilliland, Dr. Ayalew Tefferi, and Dr. Ron Hoffman) met with SAB members and presented results and conclusions from the previous year's work. Highlights included:

- The astonishing number of MPD clinical trials both underway and imminent: at least four trials currently underway and others coming soon. Many of these trials relied on analysis, insight, and preclinical testing platforms from members of the MPD Research Alliance working closely with the biotech and pharmaceutical industry.

*Left to Right: MPD Research Alliance investigators Dr. Ron Hoffman, Dr. Ayalew Tefferi and Dr. Gary Gilliland.*

- The proliferation of research results published by members of the MPD Research Alliance and their collaborators. At least 20 articles have been published as a result of our funding in the last two years.

All three researchers made strong proposals for building on the progress of MPD drug development and clinical trial activities. Highlights for their Year 3 efforts include the following initiatives:

- Focusing on understanding both positive and negative results exhibited in current clinical trials as a way of guiding further discovery of candidate compounds.
- Redoubling efforts to identify candidate drugs not currently being considered by commercial bio/pharma activities.
- Continuing and expanding support for the testing of JAK2 inhibitor-based compounds. Comprehensive preclinical testing can make a difference.
- Identifying mutations beyond JAK2 that contribute to JAK2-negative MPDs and to inherited forms of MPDs.
- Continuing to search for the true origin of the MPDs by looking earlier in the blood cell hierarchy for the originating (probably stem cell) cause for these disorders.

Based on these presentations, the SAB recommended that the MPD Foundation continue to support Drs. Gilliland, Tefferi and Hoffman at the same grant level for a third year, beginning April 1, 2008.

In addition, the SAB looked beyond Year 3, and recommended that the MPD Foundation begin to plan for the expansion of the Research Alliance. The current explosion of interest in the MPDs worldwide makes such an expansion both timely and potentially of great benefit. To that end, the SAB recommended that Year 4 of the MPDRA be opened to additional competitive proposals, with the anticipation that in early 2009, one or more additional researchers will be brought into this effort.

Detailed plans for Year 4 of the MPD Research Alliance will be made available as they are developed at www.mpdfoundation.org.

# CLINICAL TRIALS IN BRIEF

*by Ann Brazeau*

## What Is a Clinical Trial?

A clinical trial is defined as a comparison test of a medication or other medical treatment (such as a medical device), versus a placebo (inactive look-alike), other medications or devices, or the gold standard current medical treatment for a patient's condition.

## The Four Phases of Clinical Trials

Clinical trials are conducted in phases, with each phase designed to help scientists answer different questions:

In Phase I trials, researchers test an experimental drug for the first time in humans – usually a small group of from 20 to 80 – to evaluate its safety, determine a dosage range, and identify side effects.

In Phase II trials, the experimental study drug is given to a larger group of people (100-300) to see if it is effective and to further evaluate its safety.

In Phase III trials, the experimental drug is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow it to be used safely.

In Phase IV trials, which occur after the drug has been approved by regulators, scientists collect additional "real world" information about the drug's risks, benefits, and optimal use.

## Clinical Trials Are Designed to:

- Assess the safety and effectiveness of a new medication or device on a specific patient.
- Assess the safety and effectiveness of a different dose of medication than is commonly used.
- Assess whether the new medication or device is more effective for the patient's condition than the gold standard medication or device.
- Compare the effectiveness in patients with a specific disease of two or more already approved or common interventions for that disease.

## Why Participate in a Clinical Trial?

Participants in clinical trails can play a more active role in their own health care, gain access to new research treatments before they are widely available, and help others by contributing to medical research.

## What You Should Know About Participating in a Clinical Trial

Patients should meet with their hematologist to decide whether a trial exists that is appropriate for their stage of disease and whether the logistics of participation in that specific trial work for them.

All clinical trials have guidelines about who can participate. These criteria are based on factors such as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. Before joining a clinical trial, a participant must qualify for the study.

Patients should know as much as possible about the clinical trial before agreeing to participate. The following questions may be useful when considering involvement in a clinical trial.

- What is the purpose of the study?
- Who is going to be in the study?
- Why do researchers believe the experimental treatment being tested may be effective? Has it been tested before?
- What kinds of tests and experimental treatments are involved?
- How do the possible risks, side effects, and benefits in the study compare with my current treatment?
- How might this trial affect my daily life?
- How long will the trial last?
- Will hospitalization be required?
- Who will pay for the experimental treatment?
- Will I be reimbursed for other expenses?
- What type of long-term follow-up care is part of this study?
- How will I know that the experimental treatment is working? Will results of the trials be provided to me?

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## MPD PATIENT SUPPORT GROUPS UPDATE

We now know of over 25 support groups, and new ones are starting on an average of one every 3 months. The MPD Foundation remains actively involved assisting group coordinators and facilitating periodic conference call meetings. All group coordinators will be meeting in person in Chicago in 2008. If you are interested in starting an MPD Patient Support Group in your area, please contact Ann Brazeau at abrazeau@mpdfoundation.org, or by phone at 312-683-7226.

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## A READER WRITES

*From: Dean Finch*
*Sent: Tuesday, February 26, 2008*
*To: rrosen@mpdfoundation.org*
*Subject: Clinical Trials*

Good morning, Bob!

I wanted to let you know that Breaking News & Clinical Trial information on the MPD Foundation website is very good. I also wanted to let you know that as a result of the symposium in NYC last November for both patients & subsequently doctors, I seriously researched and discussed open clinical trials with my hematologist and we found a trial that opened in December 07 at Weill Cornell Medical in New York City.

Last Friday I had my physical and signed all the necessary paper work and yesterday began the meds. The drug is CEP-701 produced by Cephalon. This is very exciting, but I'm not so sure I would have been as receptive unless I'd attended the symposium and had the opportunity to speak with other MPD patients and hear from some of the major researchers in the field.

It was still a difficult decision that my wife and I had to make and we performed a thorough risk analysis, discussed the pros & cons extensively and as a result are very positive about the decision.

I am very hopeful that this will prove effective for myself and ultimately for the larger population of MPD patients; but, even if it doesn't, the information provided by the research team will certainly have a positive benefit to future research and that is of prime importance.

I want to thank you and the entire organization for the excellent work that you do.

Have a great day and God Bless!!!!

***Dean***

Deacon Dean Finch
Diocese of Bridgeport
Norwalk, Connecticut

## CLINICAL TRIALS *(continued from page 5)*

- Who will be in charge of my care?
- Will my current physicians (hematologist/primary care) be made aware of the results?
- Can a participant leave a clinical trial after it has begun?

Some of this information was taken from www.clinicaltrails.gov.

Specific information on clinical trials for PV, ET and MF patients can be found at:

1. The CMPD Foundation maintains a list of current clinical trials for PMF, PV and ET. Enrollment eligibility and contact information is provided. The list can be found at:
www.mpdinfo.org/clinicaltrials.html.

2. The National Institutes of Health (NIH) provide regularly updated information about federally and privately supported clinical research in human volunteers. www.clinicaltrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details.

3. The National Cancer Institute (NCI) maintains a comprehensive cancer database which includes information on open and closed clinical trials for all cancers from around the world. This information can be found at
www.cancer.gov/clinicaltrials/search.

MPD patients at a new level of effectiveness. There is even proof of principle that patients who do not exhibit the JAK 2 mutation will benefit.

At this writing I am vary happy to report that there are at least 4 JAK2 drugs currently in small scale human clinical trials at MPD clinics around the USA. We know of two more that are scheduled to start momentarily, and several others that are getting close. All trials underway are initially targeting MF patients, with clinical trials for PV and ET patients planned to begin later in 2008 or next year. Companies like Incyte, Targegen, Exelexis and Cephalon have developed JAK2 inhibitors and others are not far behind.

While waiting for additional publications to assess the effectiveness of these new candidate drugs, it is clear that at least some of them show positive activity in the MF patients participating in these trials. Additionally, observations of where and how these drugs are effective is already directing new research into areas not previously explored. By the time we write our next newsletter, more information will be available. We are optimistic.

### Beyond JAK2

Many of the researchers we talk to do not think that the JAK2 mutation is the initiating event in the MPDs. In the upcoming years the researchers in the Research Alliance will be looking beyond JAK2, analyzing data from the early clinical trials, with an eye to determining where to look next for an even more thorough and complete understanding of the origins and the progression of these diseases.

### New Grant Programs

We will soon be entering the third year of funding the MPD Research Alliance and couldn't be more pleased by the critical role the scientists have played in the drug development process. We are now committed to expanding the RA with the addition of new scientists working collaboratively towards drug development. A more formal plan will be forthcoming this year.

Additionally, we will be initiating a New Investigator grant program, aimed at attracting junior faculty members who are already focused on MPD research or established investigators in other fields who are interested in refocusing on the MPDs. Our objective is to expand the breadth of MPD research being conducted in academic institutions by encouraging and supporting new researchers.

### Website Revisions

Finally, we are in the process of some minor revisions to the website. Be sure to check it out for the latest news on clinical trials, press releases from biotech and pharma companies, and hard news on new discoveries. You'll find it at www.mpdfoundation.org.

**MPD Foundation Update** is a periodic newsletter published by the MPD Foundation to provide members of the MPD community with information on current research and the Foundation's activities.

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