CMPD EDUCATION FOUNDATION

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MPD VOICE

Voice of the Myeloproliferative Disorders Community

MPD Progress Report

MF ISSUE

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President's Note

Joyce Niblack

These are exiting times for MPD patients. Much has happened in the world of research since the stunning news last year of the finding of the JAK2 V617F mutation which has precipitated a great deal of activity and funding. Collaborations among leading MPD investigators have been formed. Patient cooperation and support is an integral part of everyone working together.

Bob and I will be meeting with Bob Rosen and some of his Board in Chicago in June to explore how the CMPD Education Foundation can best work with and support the efforts of the MPD Foundation and the newly formed MPD Alliance which is being funded by Bob's group.

Tests to identify mpd patients who express the JAK2 mutation have been available for some months. A number of us have been tested and found to be positive for this mutation. Some have tested negative and are concerned that this means improved therapies are not in their future. Not so. Ongoing research is focused on learning more about how the JAK2 mutation affects errant blood cell production as well as finding targeted therapies as CML patients have in Gleevec and the second generation bcr-abl tyrosine kinase inhibitors currently in clinical trial and awaiting FDA approval. But efforts are also being made to find better therapies whether one is JAK2 mutation positive or not. There is hope for all mpd patients for a brighter future. This newsletter focuses on the highlights of developments since the JAK2 mutation news broke last spring.

International Working Group (IWG) on Myelofibrosis

John Camoriano, MD
Mayo Clinic Scottsdale

On March 4th, 2006, at MD Anderson in Houston Texas several world experts on the myeloproliferative disorders gathered for 8 hours to hammer out their final draft of an agreement defining the criteria for response of myelofibrosis to therapy. This landmark meeting, chaired by Dr Tefferi of Mayo Rochester represents the first of what is hoped to be many more productive meetings by the IWG (International Working Group) on myelofibrosis. The motivation for this meeting was the recognition that several potentially active drugs for myelofibrosis are in the development pipeline and slated to be available for therapeutic trials in the next 6 to 18 months. Myelofibrosis, unlike other blood disorders like myeloma or leukemia, has no one specific marker to measure response to treatment. Several other proposed response criteria have been suggested but none are designed to adequately capture the differences between partially effective therapy and therapy with a curative potential. Many of the members of the IWG were key persons in similar efforts such as the European Myelofibrosis Response Criteria published just this decade. The members representing countries including the UK, Spain, Italy, France and the US were able to create a document that will likely be published soon and will help investigators around the world to agree in a uniform manner to the criteria necessary to define if a drug is working or not. These criteria

(continued next page)

1. Mayo Clinic, Scottsdale, Arizona
2. Fred Hutchinson Cancer Research Center, Seattle, Washington
3. Harvard Institutes of Medicine, Boston, Massachusetts
4. Mayo Clinic, Rochester, Minnesota
5. Mayo Clinic, Rochester, Minnesota
6. MD Anderson Cancer Center, Houston, Texas

were also designed to be similar to the criteria used in a similar stem-cell disease of the bone marrow, myelodysplasia. The new criteria will help researcher avoid pitfalls unique and peculiar to the natural history of myelofibrosis. For example, many drugs that are effective in myelofibrosis or myelodysplasia may temporarily result in a worsening of the blood counts such as the white cells, platelets and red cells. Many potentially successful drugs could be missed if this fact is not taken into account. Accordingly, the IWG response criteria do not mandate improvements in all of these cells lines in order to define a benefit. Another recommendation in the paper is that treatment be continued for a minimum of 3 months even if, initally, benefit is not seen so that there is adequate time for the new drug to do the presumably hard work of reversing years of fibrosis. There will be three categories of response; Complete Response, Partial Response and Clinical Improvement. For the first time, Complete response as a category will exist and will mandate the disappearance of bone marrow evidence of fibrosis. Now that the JAK-2 and other molecular correlates are being teased out of the various patients with myelofibrosis there is reason to hope that molecularly targeted therapy may be effective enough in the near future to result in some patients with complete responses. More details on this new criteria will be forth-coming in this newsletter after the publication of the IWG criteria occurs. Members of the IWG who participated in the discussions on this criteria are as follows; Ayalew Tefferi, Giovanni Barosi, Ruben A. Mesa, Francisco Cervantes, H. Joachim Deeg, John T. Reilly, Srdan Verstovsek, Brigitte Dupriez, Richard T. Silver, Olatoyosi Odenike, Jorge Cortes, Martha Wadleigh, Lawrence A. Solberg, Jr., John K. Camoriano, Heinz Gisslinger, Pierre Noel, Jurgen Thiele, James W. Vardiman, Ronald Hoffman, Nicholas C.P. Cross, D. Gary Gilliland, Hagop Kantarjian

Editor's Note. *Myelofibrosis is the most serious of the Philadelphia Chromsome Negative myeloproliferative disorders. The establishment of the International Working Group on Myelofibrosis will have profound effects on the future treatment of this variant, whether primary or secondary to essential thrombocythemia and polycythemia vera. We all owe a huge debt of gratitude to Dr. Ayalew Tefferi of Mayo Rochester for organizing and chairing this important initiative.*

MPD Research Alliance

The MPD Foundation has awarded the newly formed MPD Research Alliance a $750,000 grant for the first year. The lead investigators of the MPD Alliance are Ayalew Tefferi, MD, Mayo Clinic Rochester; Gary Gilliland, PhD, MD, Harvard Medical School and Ronald Hoffman, MD, University of Illinois at Chicago.The primary goal of the MPD Alliance is to accelerate development of targeted therapies for all Philadelphia chromosome negative myeloproliferative disorder patients (essential thrombocythemia, myelofibrosis and polycythemia vera).

For additional information about this initiative, see **www.mpdfoundation.org**

The CMPD Education Foundation is committed to serve in any capacity the MPD Foundation and lead investigators ask of us in furtherance of our common goal of providing improved therapies for all mpd patients.

MPD Epidemiology Study

Myeloproliferative disorders are thought to be rare (orphan) diseases, but are they? The answer to that question is important for all of us. In an effort to determine whether the figures in the literature are accurate, the MPD Foundation and co-sponsor Leukemia and Lymphoma Society have awarded a one year grant to Xiaomei Ma, PhD, Assistant Professor in the Department of Epidemeology and Public Health at Yale University School of Medicine.

This study will evaluate the incidence and prevalence of myeloproliferative disorders in the United States and analyze data for potential age and gender differences.

MPD Consortium wins $26.5 Million Dollar NCI Grant

The JAK2 mutation finding gave impetus to the MPD Consortium's attempts to gain National Cancer Institution Funding for MPD Research. The Consortium has been awarded a $26.5 million dollar grant to conduct a wide range of studies for MPD patients. Research will involve an international collaboration of MPD scientists and physicians.

December 2005 Ash Highlights

Myeloproliferative disorders received a great deal of attention at the December 2005 meeting of the American Society of Hematology, in large measure because of the stunning discovery of the JAK2 mutation found in many mpd patients that will make targeted therapies possible and lead to an upsurge in mpd research.

- As expected, a number of abstracts focused on the JAK2 V617F Mutation (Nos. 253, 254, 255, 256, 257, 374, 376, 1206, 2575, 2578, 2580, 2581, 2586, etc.)
- Tefferi et al reported on Lenalidomide (cc-5013, Revlamid) for the treatment of anemia associated with myelofibrosis with myeloid Metaplasia (Abstract 2583) This study was monotherapy with Lenalidomide alone. The coming study will combine Revlamid with a steroid since that was found to be more effective in the case of Thalidomide. In

this study, Revlamid improved anemia in at least 20% of patients with MMM. Some of the responses were "spectacular. The documentation of a positive effect on LDH, constitutional symptoms and Splenomegaly in patients not showing early response in anemia suggests the possibility of an even higher response with a longer treatment schedule.

- Mesa et al reported on the results of the International QOL survey run on MPD-NET. At the time of the deadline, there were 830 participants. I believe the final number was around 1200. The abstract (2577) is titled Fatigue, the Un-addressed Curse of Myeloproliferative Diseases: Results of an International Internet Based QOL Survey of 830 MPD patients. Of the participating patients, 87% had undergone treatment for their mpd (drugs 84.6%, phlebotomy 49.5%, other 16%).

  Frequent symptoms reported fatigue (90%), pruritis (57%), night sweats (54%), bone pain (48%), undesired weight loss (15%) and/or fevers (15%). 41% felt restricted in their activities and 11% were medically disabled secondary to their MPD. Additionally 69% curtail social activities because of fatigue and 41% need some degree of assistance with daily living.

- Several abstracts reported on Gleevec treatment in PV (2589, 2601, 373, 4951, etc. According to one abstract, Gleevec has been demonstrated to be effective in the treatment of PV with initial responses up to 80%. Reported side effects included diarrhea, periorbital edema, reflux, dry mouth, fatigue, pruritis, headache, nausea, arthrlagias, insomnia, weight gain, etc.

- Abstract 4937 discusses Essential thrombocytosis risk factors for thrombotic events in a series of 306 patients.

  To search the ASH 2005 Abstracts online and read those of interest, go to **http://www.abstracts2view.com/hem_ash05atlanta/**

- There were a number of educational sessions on myeloproliferative disorders. One focused on management of polycythemia vera and essential thrombocythemia by Peter J Campbell and Anthony Green. Professors Campbell and Green also propose new diagnostic criteria. You can read the full text of this article at **http://www.asheducationbook.org/cgi/content/full/2005/1/201**

  You should also review the 2005 Ash Education book online for other articles of interest.

Caregiver Resources

We often overlook MPD patient caregivers. While most of us who have gained good control of our diseases can enjoy an essentially normal life, many are more deeply affected by their MPD. Whether we are relatively healthy or not, stress is a daily fact of life for our family members or significant others. Patients aren't the only one's who at least in the back of one's mind, are waiting for the other shoe to drop. And for those with advanced disease, caregiving often takes a great deal of effort, time and work. Studies show it is important for caregivers to look out for their own health and wellbeing in order to be effective helpers/supporters to their loved ones.

There are a number of caregiver resources.

- Acor Caregivers List- To join, go to **http://listserv.acor.org/archives/caregivers.html**
- The National Family Caregivers Association
  Phone: 1-800-896-3650
  www.nfcacares.org
- The National Family Caregiver Support Program
  Phone: 1-202-619-0724
  www.aoa.gov/prof/aoaprog/caregiver/caregiver.asp
- Caregiver.com
  The website of Caregiver Magazine has a chat room, discussion forum, articles from the magazine, a care directory and other helpful links
- The Caregiver's Handbook
  This handbook is available on the internet through San Diego Mental Health Services. **www.acsu.buffalo.edu/ndrstall/hndbk0.html**
- Well Spouse Association
  This non-profit membership organization is part of the Association of Spousal Caregivers, offering support groups, a newsletter, letter-writing round robins, along with books on caregiving. **www.wellspounse.org**

2007 Mayo Clinic/CMPD Education Foundation MPD Conference

Dr. Camoriano is checking on availability dates for the Ashton Tate Auditorium and fountain area for the 2007 MPD conference. We are targeting late Feb-early March. We hope to announce firm dates for your planning in the next MPD Voice Newsletter.

Membership Application

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❑ Patient ❑ Family member of Patient ❑ Friend of Patient

❑ Physician ❑ Other healthcare professional _____

❑ Agnogenic Myeloid Metaplasia (AMM aka MF, IMF, MMM)

❑ Essential thrombocythemia (ET)

❑ Polycythemia Vera (PV) ❑ MF Secondary to ET or PV

❑ Chronic Myelogenous Leukemia (CML)

❑ Mastocytosis

❑ Eosinophilic Syndrome/leukemia

❑ Chronic monomyelocytic leukemia (CMML)

❑ Myelodysplastic Syndrome (MDS)

Donation Included (make checks out to cMPD Education Foundation)

❑ $25 ❑ $50* ❑ $100* ❑ $150* ❑ $200* ❑ $500* ❑ $1000* ❑ Other

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❑ for JAK2 research

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