mpd-support

mpdlife

the newsletter for people with MPDs

GUY'S & St THOMAS' CHARITY
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Does JAK2 status alter prognosis for those with MPDs?

Dr Claire Harrison explains the implications of JAK2 status—what we know and what we have yet to learn

Is it better to test positive or negative for the JAK2 mutation? It's a question we often hear from people with MPDs. It can be disconcerting for people with MPDs to learn the results of their tests regardless of whether they test positive or negative, because becoming aware of JAK2 status raises questions about the course and prognosis of these disorders.

We don't really know today why one patient might have the JAK2 V617F mutation and another patient might not – but in fact there is very little significant difference between positive and negative disease.

JAK2 V617F in PV About 97% of people with PV are JAK2 V617F-positive. A small minority of patients have a different mutation known as "exon 12", and these particular people tend to have more normal white cell and platelet counts and to be younger at the time of diagnosis.

JAK2 V617F in MF There is very little real difference between JAK2-positive or negative disease in patients with primary MF, although JAK2-mutated patients tend to have higher haemoglobin. Studies show different findings with regard to prognosis, suggesting that any effect is small.

JAK2 V617F in ET People with JAK2-positive ET tend to be older than the average ET patient and have higher white and red cell counts. Combined studies of over 1000 patients appear to indicate there is a small increase in risk of blood-clotting events for JAK2-positive patients. ET patients who are JAK2-positive have a slightly higher risk of miscarriage in pregnancy. This suggests that JAK2-positive patients may get diagnosed earlier, but their disease is likely to follow the same course as a JAK2-negative patient. At the present time we treat all ET patients in exactly the same way.

More information You can find more research information on our website including details about the recent discoveries of additional mutations. You'll also find information on UK drug trials and a new press release on the JAK2 inhibitor drug Incyte. ■

Next Patients' Forum

Please join us for the
MPD Patients' Forum
January 6, 2010
6 pm to 9 pm
Governors' Hall,
St Thomas' Hospital, London
Find all the details on
www.mpd-support.co.uk

How we're using our new knowledge

Faster diagnosis A JAK2 test is painless and quick, and often shortens the time it takes to make a diagnosis.

Disease monitoring We can test a person's level of JAK2 V617F as a way of monitoring minimal residual (low level) disease after treatments such as a bone marrow transplant.

Theraputic target We're using our discovery of JAK2 mutation to develop new therapies that block the effect of the mutation.

Guide to classification Our knowledge of the JAK2 mutation is guiding us in our formulation of new diagnostic criteria, and may also trigger a new classification of myeloproliferative diseases based on the molecular science.

Understanding causes Although we don't know what causes MPDs, understanding more about the JAK2 mutation is one key to of solving the mystery.

"I'm committed to the quest for a cure"

Alisia O'Sullivan spoke with Max Smith about his voyage through MF and what he sees next for research

Max Smith is a fit, physically active and vibrant man of seventy. He is also a long-term survivor of myelofibrosis (MF): Max was diagnosed nearly twenty-five years ago, back in 1985.

When I spoke with Max recently, I was immediately impressed with his positive attitude. He is a man committed to surviving, and whose steady approach to research and planning may well have extended his life over many years in the face of a complex and difficult illness.

Initial diagnosis

When Max's myelofibrosis was first diagnosed, he was given limited information – in fact, his doctors did not alert him at that time to the potential seriousness of his condition. It was only a decade later in 1996 when Max began suffering from the typical symptoms of myelofibrosis – fatigue, dizziness and an enlarged spleen – that his doctors shared the full implications of the disorder with him. They gave him a prognosis of shortened life expectancy with only a few remaining years to live. When he first heard this devastating news, Max sharpened his plan of attack for managing his condition, an approach he describes as "full-on proactive."

The hunt for trials

Beginning in 1996, Max undertook a worldwide investigation into drug trials available for myelofibrosis. He put himself forward for research trials at the Mayo Clinic in the United States, making the decision to fund several medical investigations out of his own pocket.

In 1997, Max was assessed at the Mayo Clinic (US) in preparation for enrollment in the medical centre's myelofibrosis drug trials. Since that time Max has taken part in a total of seven research trials.

Although he is enrolled in trials in the US, he has continued to work closely with his local haematologist as well, with two goals in mind: to extend his life expectancy and to improve his quality of life.

"I understand that the NHS in the UK is not in a position to assist in experimental trials overseas," Max explains. "I am fortunate in that I have been financially secure enough to fund this care personally." Max has incurred many costs including flights back and forth to the US and hotel accommodation while he undergoes medical assessments prior to, during and post-trial – costs that have quickly mounted and are on-going. Max also made the financial commitment to self-fund the medical tests that he requires every twelve weeks, including bone marrow biopsies (BMBs), full blood counts, electrocardiograms (EKGs) and more.

NHS collaboration

Max's haematologist in the UK has been his consultant and mentor for the last thirteen years, and although he was initially unsure about the benefits of Max's participation in US-based research, he has subsequently proven very supportive, even encouraged by some of the research and the results. Max speaks highly of the way in which shared-care support between his UK haematologist and the Mayo Clinic has worked in his case. He stresses that, "Support from the Blackpool Victoria Hospital's Department of Haematology and Oncology led by Dr Paul Kelsey has been wonderful."

In November 2007 Max enrolled in Phase 1 of the JAK-2 inhibitor trials at the Mayo Clinic in Rochester, Minnesota, then under the study leadership of Dr Ruben Mesa. The goal in the first phase of any drug trial is to ensure the drug is safe and to check the effectiveness of the drug, initially in a very small group of patients. A group of about twenty patients were enrolled in Phase 1 of the Mayo Clinic's JAK2 inhibitor trial, including Max.

Extensive testing

At the start of the study, Max underwent an extensive physical examination involving an electrocardiogram, a bone marrow biopsy and blood work analysis. He was then given approval to enter the trial and he began taking the

MPD medications free of charge

People with MPDs in the UK are now entitled to receive their MPD medications free of charge under the NHS. Ask your haematologist for details

full dose of the JAK-2 inhibitor drug, an oral drug taken twice a day. Max's responses to the drug were and continue to be monitored on a twelve-week cycle in Minnesota. Max also makes a fortnightly visit to his haematology department in the UK for a full blood chemistry check, results of which are forwarded to the US.

The trial expands

The Mayo Clinic's inhibitor drug has initially proven safe and has shown signs of effectiveness. The trial has thus moved into Phase 2 allowing more patients to enrol, and it is now under the leadership of Dr A Tefferi.

Max was able to continue into Phase 2 of the study, and he remains committed to frequent visits to Minnesota for continued testing. He explains that he is in a unique position: "As far as I'm aware I'm the only patient to remain on the maximum daily dose of the drug. The other patients in the trial are now now taking a lower daily dose."

Excellent results

"Out of all of the trials I've undertaken, this is the first time that I have ever reached Phase 2 of a trial," says Max. And so far, this trial has provided the most satisfactory results and relief for his symptoms.

Max recalls, "I did suffer some minor stomach upset and disorientation in the early days, but these problems have now passed. Since I began taking the drug my spleen has much reduced and my haemoglobin, white cell counts and platelets levels have all stabilised to within almost normal range," he says, and all this without any current discernible side effects.

Max feels that the drug is helping to slow the progress of his disease. He also believes that the experimental medicines he took during previous trials – drugs geared to slowing down the progress of MF – must have played some part in extending his life expectancy beyond the original two to fifteen years predicted at the outset of his disease in 1985.

However, Max is keen to stress that because he is probably the only patient to remain on the high dose JAK-2 inhibitor he is obviously an atypical patient. He knows that the results for other participants in the trial have been mixed, although he also adds that he is not aware of any patients in whom there has been a seriously adverse consequence. The only non-beneficial outcome has been that in some cases the drug has not relieved existing symptoms of MF.

JAK2 inhibitor trial participant Max Smith

Uncertain future

With only one month to go before the end of Year 2 of the study, Max explains that "the overall feedback on the drug appears to show mixed results. This creates a certain level of uncertainty and anxiety about what may happen next, especially for me as I myself have responded so well to the drug." At this moment Max does not know if the study will continue. And even if it does, there is no guarantee that he will be allowed to continue in the trials.

Max is quite phlegmatic about the risks involved in any research trial and the uncertainty of the outcomes, but he does express some concerns. "If the trial did not continue it would be a great disappointment to me personally. I hope and believe that at some point there will be a cure for this disease. I have an on-going commitment to be part of this quest in whatever way possible." ■

Author's note: Having interviewed Max, I would like to add a postscript and offer a big thank-you to Max for being willing to share his experience of this particular trial, but also for his obvious willingness to take a risk as a 'research guinea-pig'. Without people like Max as a fellow MPD sufferer I believe we would be a long way from finding any new drugs.

Therefore I do hope that Max will continue to be allowed access to a drug that appears to work, as well as enjoying many many more active and happy years with his wife, children, grandchildren and great-grandchildren.

Expert Briefing

Why have the myeloproliferative disorders been renamed?

Q I recently read that the MPDs have a new name and are now called "myeloproliferative neoplasms." Why the change? – PJ

A The MPDs were first recognised in 1951 by researcher William Dameshek. The diseases PV and ET had been described decades earlier, but Dameshek was the first researcher to observe parallels between the disorders both in clinical observations and in the laboratory. Dameshek grouped PV and ET together with chronic myeloid leukaemia and named this new category "myeloproliferative disorders" or MPDs.

The World Health Organization (WHO) has now renamed these disorders "myeloprolifeative neoplasms" or MPNs. The term neoplasm means "a new growth" from the Greek "neo" or new and "plasma" or growth. The discovery of the JAK2 mutation has shown that these diseases are likely caused by a mutated blood cell. For many this implies "cancer" – but MPNs are usually benign forms of blood cancer, and for this reason the WHO has chosen the word "neoplasm". Good news for patients in the UK: you can now obtain your MPN treatments at no charge – ask your haematologist for details. – Dr Claire Harrison ■

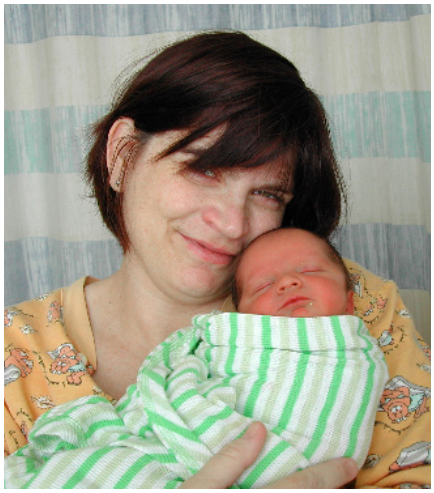
Please note that nothing contained in this newsletter is intended to constitute professional advice for medical diagnosis or treatment. You should always seek the advice of your physician or other qualified health provider prior to starting any new treatment or consult them on any questions you may have regarding a medical condition.

Survey of pregnancy in MPDs

A UK-wide survey of MPDs in pregnancy will open in 2010. Haematologist Dr Susan Robinson explains what we hope to learn

Many women with myeloproliferative disorders are young adults in their child-bearing years. These women face unique challenges as they start families – risks to their own health as well as that of their unborn children. Unfortunately, very little is known about the best way for haematologists and obstetricians to treat young women in pregnancy.

At St Thomas' Hospital we are very pleased to be opening the first UK-wide study of pregnancy in essential thrombocythaemia (ET), polycythaemia vera (PV) and myelofibrosis (MF). The study opens in 2010 and will track the outcome of pregnancies in women with these MPDs.



Newborn Arthur's mum has ET. He was born in St Thomas' Hospital

The St Thomas' Haematology Department is a tertiary referral centre for the management of women with a diagnosis of a myeloproliferative disorder in pregnancy, and as such is an ideal centre for this type of research.

The aim of this study is to learn more about pregnancy in MPDs in order to develop a more evidence-based management strategy.

The survey will capture anonymous data on pregnancy in MPD patients through UK haematologists, midwives and obstetricians and will be run in conjunction with the UK-wide Obstetric Surveillance Survey (UKOSS).

St Thomas' will share the findings of this research with all those who have an interest in treating women with MPDs. We will make any potential management strategies available worldwide in an effort to increase awareness of these issues across the globe. Our ultimate objective is to improve pregnancy outcomes for both mother and child. We are extremely grateful to the Guy's and St Thomas' Charity for providing a grant to fund this research.

You will find further information on the MPD Support website in the New Year. Please visit us at www.mpd-support.co.uk

You can also learn more about UKOSS on their website: www.npeu.ox.ac.uk/ukoss ■

Would you like to fund research?

If you would like advice or want to know more about making a gift or leaving a legacy, we can help. Please contact Ruth Bishop on 020 7188 1204 or by email at ruth.bishop@gsttcharity.org.uk

Supporting cancer patients at the end of life

Oncology nurse Brenda Keenan describes a half century of caring for cancer patients and their families

I have been a registered nurse for fifty-two years, and in these many years of patient care I have discovered that the relationship between nurse and patient is not a simple matter of medical care. Nurses, patients and their families are bound together emotionally, sometimes at the very edge of survival.

In my work as oncology nurse I have treated many patients with cancer as they went through the lengthy and complicated process of diagnosis and treatment. Patients often stayed in hospital for long periods undergoing treatments in an acute care setting, and the nurses and doctors came to know the patients and their families well.

Partnering for support

Our hospital advocated a team approach including physicians, pharmacists, dietitians and nurses. The result was a strong partnership of professionals who took an effective, efficient and caring approach to patient care. As nurses treating patients with cancer, we also met as a group with a psychologist once every week to discuss issues that affected us as medical professionals: death, dying, feelings of anger and of acceptance. We were trained to communicate and to grapple with our own feelings.

Gifts of tenderness

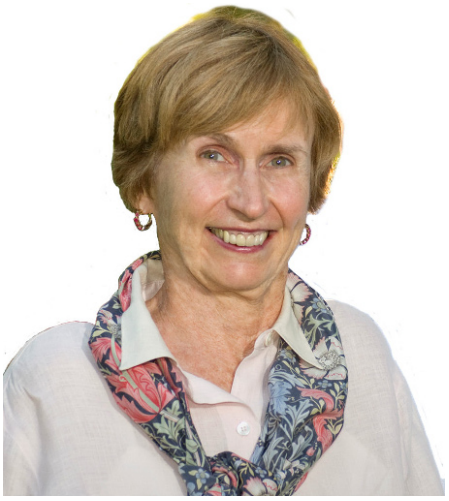
Some particular cases have never left my memory. I remember a beautiful, middle-aged woman who was dying and whose husband helped with her care. When he prepared to go home every evening he would place rose petals on his wife's hospital blanket. I have never forgotten this gesture of love and tenderness, this gift for his dying wife.

Picking up the pieces

I also treated a patient who was divorced. Although he had remarried, he returned to his first wife when he became ill – she became his caregiver. His second wife may have been unprepared or somehow unable to act as family caregiver. His first wife picked up the pieces. Unexpected things can happen when people are ill, and people with cancer can find support in ways that they could not have predicted or planned.

Patients' beliefs

Many members of the clergy were available for patients to speak with at our hospital. Belief is very individual, but seemed to me that many people turned to religious belief at the end of their lives regardless of their denomination. You could say that some of my patients turned to God.



Oncology nurse Brenda Keenan

A challenge of my own

I am now retired from nursing and facing a new and personal challenge in my life. I have become the caregiver to my own husband, who has been diagnosed with cancer. I have begun to realise that if my husband dies before I do, I will need to face losing a man who I love and upon whom I depend. I attend a patient support group and I try to make the best of every day – to enjoy all the time my husband and I have left together.

Memories of patients and their families have become an integral part of my life, and I believe that I became a better person having had the opportunity not only to serve these patients but also to have been part of their lives. ■

A nurse's perspective

- Support from a reliable caregiver is crucial to any patient's physical and emotional well-being
- People can discover positive new paths in their lives and relationships as they approach the end of their lives
- The experience of loss is individual - you may find that you cannot anticipate what you may feel when a family member dies
- Try to make the most of each and every day

Why do I feel so tired? Fatigue and MPDs

BY DR RUBEN MESA

A woman in our care suffering from polycythaemia vera (PV) has a problem that's very typical for people with MPDs – she feels fatigued. Her daughter has observed this problem first-hand, and recently wrote to us with a question. She asked:

"Why is my mum so fatigued? She was diagnosed last year with PV. Now she feels chronically tired and is not eating. My mum was an active professional and she walked many miles each day until recently. Now she will not go on a day outing with her friends because she feels she is holding them back. Quite honestly she feels as if her life is over. What can I do to help?"

People in our care with MPDs face problems like these every day – problems of fatigue that range from the mild to the severe and even debilitating.

Jus what is fatigue?

"Fatigue" is when we feel more tired than we feel we should, either at rest or after some episode of activity or physical exertion. Similarly, you may find yourself feeling fatigued compared to how you felt before your MPD was diagnosed.

Who experiences fatigue?

The Mayo Clinic (US) performed an internet-based survey several years ago, which was published in 2006 in *Cancer*, a publication of the American Cancer Society. This study showed that people with MPDs frequently complain of fatigue. In fact, over seventy per cent of people with PV, essential thrombocythaemia (ET) and virtually everyone surveyed who had myelofibrosis (MF) felt fatigue.

Why so tired?

There are multiple causes of fatigue in people with MPDs. First are the effects of the disease itself – possible anaemia, enlarged spleen, perhaps prior blood clots and effects on heart or lungs.

Second is stress – both of having an illness and being uncertain what the future holds.

Third, researchers have found that the bone marrow itself makes a series of proteins called "cytokines". These proteins are released into the blood and can physically make you feel more tired – even without the addition of anaemia or other features of myeloproliferative illnesses.

Practical steps

The woman with PV mentioned at the beginning of our story is in a difficult situation, but is fortunate in having a caring family member looking after her. When someone begins to feel fatigued, it can be quite easy to fall into a downward cycle, but this cycle can be reversed.

A first step is to review this patient's medical treatment, to ensure she has the medications that she needs and to rule out any additional medical problems.

The next step is improve overall health. This woman's family can help to ensure that she is eating a nutritious and balanced diet, especially if she is too fatigued to go to the shops or to prepare meals herself.

Her family can also help her to gradually gain strength by walking a few steps every day. As her diet and circulation improve, she may begin to feel stronger and can build on this. It's important to take a steady, consistent and conservative approach to exercise.

Staying involved can help alleviate the social isolation that can result from long-term fatigue. Perhaps this patient's daughter can plan easy outings so that her mum has a chance to socialise.

As we work to help patients like this, new treatments for MPDs are on the horizon. These drugs are still under evaluation, but hopefully better days are ahead for everyone with an MPD. ■

Reducing fatigue

There is no magic bullet for eliminating fatigue in MPDs, but these suggestions can help:

- **Exercise** (as you have seen in July's *mpdLife*) can help to lessen or overcome fatigue. Be sure to only start an exercise plan with your physician's involvement.
- Get as much **education** as you can about your disease. This gives you the tools and knowledge to fight back.
- **New treatments** such as JAK2 inhibitors – while still experimental – appear to reduce fatigue by blocking and reducing cytokines.

Inspired fundraisers cirle around their friend

Jenny Charles and her husband Charlie were stunned by his diagnosis. Then Jenny found she could make a difference

When my husband Charlie was first diagnosed with essential thrombocythaemia (ET), he and I were terrified: everything we read pointed to cancer and leukaemia. I tried to find out as much as I could, but the information available to us was quite limited. Then I discovered the MPD Support website and the patients' forum, which have proved invaluable.

As the partner of someone with ET, I wanted to do more. I remembered what it was like for us when we first heard Charlie's diagnosis and I realised that what helped us the most was having organisations like MPD Support to which we could turn. I realised that I could do something important and useful by increasing public awareness of MPDs and by raising funds, funds that would enable our organisation to continue its work of supporting people.

A friend of ours works for Transport for London, and together we came up with the idea of an event sponsored by the Circle Line. I asked all my friends if anyone would help me to raise some money. Imagine my surprise and delight when seventeen of my friends said they would join me and Charlie. None of our friends have an MPD and they only became aware of this illness when my husband was diagnosed.

Fundraisers Jenny and Charlie

Jenny, Charlie (bottom left) and friends set off to fundraise on the Circle Line

On the day of the event, my husband and I met our friends at our local pub, where I split the group into three. I gave each team a list of ten clues to train stations on the Circle Line. Each team also had to be at Gloucester Road station to stand with collection boxes at various times throughout the afternoon. As the Circle Line went round, we bumped into each other several times, and this caused great amusement amongst passengers when they saw all of us together. Several tourists asked to take our photograph and we agreed in return for a donation. We had hoped for more donations that we received and we all vowed that in future if we saw a collector we would put something in, even if it were only loose change. Our final total, with sponsorship, and donations looks set to reach £2,500.

Everyone has said what a great day out it was and how rare it is for all of us to get together, so not only were we able to raise money but also catch up with old friends.

When one person in a family has an illness it has an impact on the whole family but often, other than to be supportive, I often feel I don't have a useful role to play. Actively organising and taking part in this event has left me with a feeling of usefulness. It has reinforced the bond between me and my husband, as it is not his illness but ours.

Charlie has said how positive and empowered he feels that so many people have supported us. He feels truly valued. And besides raising money, we hope that we have also raised awareness of MPDs. ■

Want to support Jenny and Charlie? You can make a pledge on their page at www.justgiving.com (search Jenny-Charles). You can also read more about Charlie's battle with ET in an upcoming edition of mpdLife.

Newly diagnosed and want to talk?

MPD Support's "buddy programme" can help. Tamara Kosta explains

The mission of MPD Support's Buddy Programme is to help patients cope with the common and emotional side-effects of an MPD diagnosis. These often include feelings of fear, confusion, isolation and other difficult emotions. Often the best person to speak to is not a relative, partner or friend – as often they are as confused as we are – but instead to someone who also has an MPD, a "buddy" or peer group supporter.

Your buddy can give you support either via e-mail or the telephone during this often difficult time. They will empathise and answer questions you might have about everything that comes with having an MPD, as they themselves have already experienced it. The relationship helps

Tamara Kosta organises Peer Support

both the person offering support and the recipient. If you would like to offer support to a newly-diagnosed person, do not need any particular skills to become a buddy. It's enough that you are able to cope with your MPD and that you feel you could help others. If you would like to have a buddy or indeed to be a buddy yourself, then please contact us. You can reach us by email at info@mpd-support.co.uk ■

MPD Support honoured with industry award

BY JON MATHIAS

MPD Support is honoured to have been awarded first prize in the 2009 Innovation Awards given by the industry journal *Myeloproliferative Disorders in Practice*. Representatives of the group were given a cheque for £5000 from the award's sponsor, Shire Pharmaceuticals, at the Royal Society of Medicine on 30th October. The award is made to recognise innovative practice in the MPD field. The other nominees came from all over the UK; the variety of nominations showed that there are many opportunities to improve patient care in the UK. What's more, the energy and enthusiasm of the people involved is making a difference on a day-to-day basis.

Dr Harrison and Dr Anne Mwigri display the award cheque

As well as being a great endorsement of the efforts that have led to the establishment of MPD Support, the prize money will be very useful to the group, as we look to improve the website and to reach out to more MPD patients around the country. ■

Our next issue

- The sometimes complicated path to diagnosis
- Financial concerns
- Manage your cholesterol to reduce risks of heart attack and stroke

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GUY'S & St THOMAS' CHARITY

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