MPDlife

The newsletter for people with MPDs
November 2012

# Searching for a cure

## Ruxolitinib – a new hope for patients with myeloproliferative disorders

**Alisia O'Sullivan interviewed Professor Srdan Verstovsek, US principal investigator in one of the two studies that led to the approval of ruxolitinib**

Professor Verstovsek's interest and involvement in looking for new drugs and therapies for myeloproliferative disorder (MPD) patients started as far back as 2004, driven by his observation that for myelofibrosis (MF) patients in particular, there were no clinical studies or approved therapies. He approached his boss with a request to focus on new therapies for this group of patients and, fortunately, for MPD patients, his request was approved. Subsequently he engaged in the development of a clinical research centre for MPD, and has conducted over 40 clinical studies for MPD patients, including studies that led to the development of ruxolitinib, the first ever therapy approved for MF.

He recalls that 2005 was a significant year when the JAK2 mutation was discovered and the first patient ever treated with a JAK2 inhibitor was a patient in his clinic in 2007. That drug, used in further clinical drugs trial testing, can now be confirmed as ruxolitinib, approved November 2011 in the U.S. as the first JAK inhibitor for MF.

In the earlier trial stages, Professor Verstovsek's team observed that ruxolitinib provided a significant and longer lasting clinical benefit in managing and improving MF related symptoms such as spleen size reduction. Later trials, (called the COMFORT 1 and 2 studies), took place in Europe led by Professor Claire Harrison, and in the USA and Australia led by Professor Verstovsek. Here ruxolitinib was compared to placebo or best available therapy. Results for patients on ruxolitinib was markedly beneficial, while patients receiving placebo or best available therapy continued to see their spleen size increase and their symptoms worsen. So far, use of ruxolitinib has not been seen to eliminate bone marrow fibrosis, or the malignant cells from bone marrow or blood. Importantly however, updated analyses from

**Professor Verstovsek is based at the Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA**

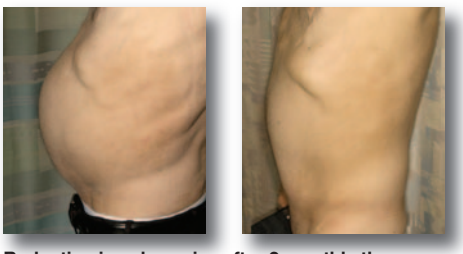
COMFORT I and Prof Verstovsek's earlier trials do indicate that ruxolitinib treatment may provide an overall survival benefit compared with placebo or best available therapy for patients with advanced MF, and as time progresses these results and observations will be updated. Further updates of both trials are expected from the American Society of Haematology meeting this December.

As with all drugs trials there are potential side effects for patients for whom the trial proved to be unsuitable and Professor Verstovsek found that anaemia and thrombocytopenia, were the most common adverse drug reactions observed. However he qualified this by saying that that these were to be expected because of the action on JAK2 inhibition and discontinuations for these reasons were very rare. In fact the discontinuation rate for any adverse event in patients receiving ruxolitinib was similar to patients receiving placebo in phase 3 randomised, blind studies.

Professor Verstovsek is hopeful that the development of JAK inhibitors as therapy for MF is the first building block towards finding a cure. He advises that efforts are now underway to combine other targeted medications, either commercial or investigational with JAK inhibitors to improve the response. In turn these may improve bone marrow fibrosis, blood cell count, and further extend good quality of life. Another exciting development is the use of ruxolitinib for a few months before bone marrow transplant to reduce the spleen and improve the body's condition.

Ruxolitinib was approved in Europe in August 2012. Until recently the drug was made available via a compassionate use scheme. Currently, for MF patients in the UK, it can be obtained either via a clinical trial, through the local cancer drug fund or via an individual treatment application.

Professor Verstovsek continues to lead research in this area and as stated above, encouraged by anecdotal evidence of some reversals of fibrosis in patients taking interferon and lenalidomide, believes that one day there could be a cure.



**Reduction in spleen size after 2 month's therapy**

### Myelofibrosis facts

- Myelofibrosis (MF), one of the myeloproliferative disorders (MPD) or neoplasms, is a rare blood disorder. It causes scar tissue or fibrosis to accumulate in the bone marrow and leads to progressive abnormalities of blood cell counts and function.
- Patients, usually over 60 years old, suffer from anaemia, often have massively enlarged spleens, and suffer debilitating symptoms including bleeding and infections. 10% may develop leukaemia.
- MF is only cured by bone marrow transplant. However, it is risky with a high failure rate (approximately 70 per cent) and is only an option for younger patients.

**Editor's note:** MPD Voice would like to thank Professor Verstovsek for his time in sharing the findings of his work with us and for his dedication to finding a cure and relief for MPD patients challenged with the effects of this condition.

MPD voice

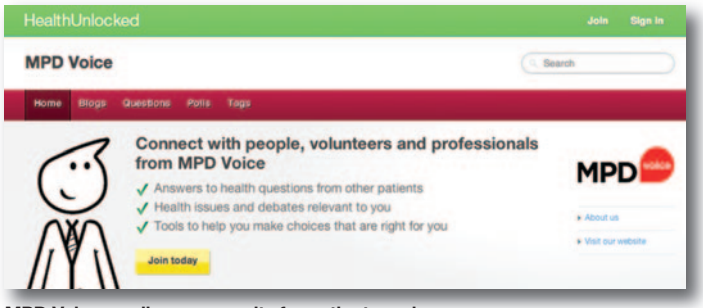
GUY'S & ST THOMAS' CHARITY

Charity number 251983

*right* Photographs courtesy of *OncoLog*, © January 2011 The University of Texas MD Anderson Cancer Center

# Health matters – fatigue

**On the recently launched MPD Voice HealthUnlocked forum, one of the most common threads of discussion is about the debilitating challenges of loss of energy experienced by patients, or as Professor Ruben Mesa titled his research, The Burden of Fatigue.**




**MPD Voice – online community for patients and carers**
**www.mpdvoice.healthunlocked.com**

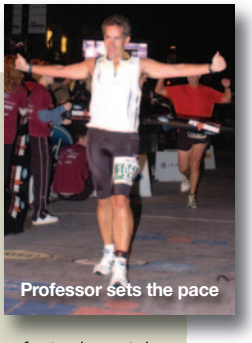
Here are some recent comments from the forum. Why not join the community and share your comments and tips for dealing with this common complaint?

*Mr Fatigue has cometh! I became ill in 2007 and before that I only needed to sleep around 7 hours per night. In 2007 the story changed. I was working but I had to stop. The tiredness is different I think, as I suddenly, and I mean suddenly within a few minutes, become so tired I cannot keep my eyes open. I feel like a zombie sometimes.'* **Swede**

*'Having suffered from fatigue for many years I can tell the difference between being tired and being fatigued. I referee football at weekends which means I get much needed exercise. During games and for a while afterwards I feel great, but when the fatigue hits I feel so weak and shake. The medication side effects also seem to be worse when fatigued.'* **Ourlife**

*'After venesection for PV my fatigue has improved a little but no doubt will soon return at full force as previously! At the moment I can last out until about 2.30 in the afternoon, then there is no energy left and I feel like a rag doll! I can sleep 10 hours per night no problem. I fall asleep when I come home from work for 2 hours and still feel fatigued – not just tired!'* **Aime**

## Professor Ruben Mesa's Top 10 Tips for Fighting Fatigue



Professor sets the pace

Fatigue is a big issue with patients who have MPDs, perhaps the worst in patients with myelofibrosis (MF), but clearly it is present in the majority of patients with essential thrombocythaemia (ET) and polycythaemia vera (PV) as well. Many things can contribute to this, including the disease, medications that an individual is on or sometimes the change in blood counts, either too high or too low. Here are some handy tips that I have found that are helpful for combating fatigue, both for MPD patients and all of us in general.

1 **Good sleep.** Making time to have adequate sleep is essential.

2 **Walking.** A good walking programme, almost despite our level of health, is vital. It always needs to be done in consultation with your doctor and appropriate for your level of fitness, but walking is key.

3 **Eat well.** Eating plans need to be individualized. Some patients may lose weight with their disease and need to eat more; others may need to decrease calories/fat in their diet and eat more vegetables and fruit. Our body responds very specifically to the fuel we put in it.

4 **Make time for reading.** Set time aside to read things that you enjoy which will decrease stress and fatigue and exercise your mind.

5 **Comfortable shoes.** Walking is part of our everyday activity and having the right shoes that fit us well and support our feet adequately is important for trying to minimize stress in our legs and help us feel well.

6 **Water activities.** Consider swimming or other activities in the water, again under the direction of your doctor. The buoyancy of water can help us stretch and exercise many muscles that we might have a harder time doing on land.

7 **Go outdoors.** Being outdoors, fresh air, sunshine with appropriate sunscreen or hats or shade are all instrumental in helping us feel better.

8 **Stretch.** Our muscles need stretching and likewise can benefit from massage.

9 **Less time on the computer.** Computers can be helpful but too much time on our electronic gadgets, computers, iPads, Blackberry and other gizmos takes valuable time away from the enjoyment of life and most likely adds to fatigue and eye strain.

10 **Work-Life balance.** If work brings you enjoyment, wonderful. However, for MPD patients, particularly the more serious the disease, the ideal is a lifestyle that is balanced, both through their energy level and their health, so that stress can be best managed.

## Research update
## Epidemiology study – MOSAICC

This pilot study, now known as MOSAICC (MyelOproliferative neoplasmS: An In-depth Case-Control) has now started with the recruitment of PHD student Mr Glen Titmarsh who will lead patient recruitment. Glen has already started a review of the scientific literature to investigate the numbers of MPD patients and is designing the study questionnaire.

Glen Titmarsh

**International collaborators: Dr Frank De Vocht (left), Dr Lesley Anderson (centre) and Professor Lin Fritschi (right)**

As reported in the May issue of MPDLife, this is part of a long term investigation into whether causative factors can be identified in MPDs. MPD Voice is funding this initial research and will be launching a fundraising campaign to reach a target of £100,000.

Patient recruitment will begin in January 2013 and the study involves a multinational team of leading expert collaborators.

# Keep on going

patient story

**Mark Hill, 54, married and currently working as a consultant, shares his recent experience on the UK MAJIC drug trial**


'**IN 2004** after a lingering chest infection and blood tests, my GP called to advise that the high level of red blood cells results were indicative of an MPD, subsequently confirmed as Polycythaemia Vera (PV). The disease was initially controlled with venesections on an ongoing need basis, daily aspirin and regular monitoring.

For 2–3 years I continued with this regime and usually had a venesection depending on haematocrit levels. Then I developed unpleasant itching on my legs every time I came into contact with water and was given a drug to counter this but unfortunately this didn't really work. Rosacea (red face) developed and I started to experience fatigue during the day.

By 2010 my disease had advanced and due to the deterioration in my condition I was asked to consider a new trial of Vorinostat. The trial started off well and brought the itching under control and my spleen shrunk considerably but it made me more fatigued than ever. My hair thinned and started to fall out, I lost weight and began to dread every dose. Concerned, and in discussion with the lead consultant, I decided to discontinue the trial.

I was then prescribed Hydroxycarbomide which seemed okay but did not have the desired impact. My blood levels were difficult to control, I still had itching, fibre in my marrow, rosacea and an enlarged spleen. I had regular venesections and worst of all my fatigue made it difficult to work. On top of the experience with Vorinostat this was becoming increasingly difficult to manage.

Early this year the MAJIC trial was being launched which I discussed with my consultants. The opportunity to join the randomized trial came up and in August I was successfully randomized to ruxolitinib. The doctors were supportive and took me through the pros and cons and I started the trial, feeling the impact almost immediately. It has been quite a dramatic improvement. My symptoms have all now gone. I am delighted by the progress to date and hopeful that it will continue to give me respite from the symptoms of the disease which were becoming a cause of great worry to me and my family and impacting on my career.

Emotionally I am fine. I feel much more confident that the disease is coming under control. I am so happy that I have energy back, I am working at full speed again and I am less grumpy. The doctors have been terrific, closely monitoring my progress and sharing information about the trial, their observations and including me all the way with their reasoning and concerns whilst also including my wife with information to address her concerns. On the trial I have met a couple of other people at the clinics and I find this contact very useful and it seems that both men are similarly experiencing dramatic results with MAJIC.

MAJIC TAP From Leukaemia & Lymphoma Research

**MAJIC is a double first trial. It is the first JAK inhibitor study run by academics not a pharmacuetical company and the first TAP trial. TAP or therapy acceleration programme aims to get clinical trials open in an accelerated manner.**

In terms of advice to other MPD sufferers I would say that you should push to keep taking opportunities to try new treatments until you find the one that suits you. This is not easy as there are difficulties in getting onto the trials and then keeping up the regular visits to the hospital etc. I would learn as much as you can about the disease and listen to the experience of others. The feeling of not being alone with the disease has helped me immeasurably. My current experience is good but it has been really bad in the recent past. Keep on going until something works.'

Mark Hill was the first patient on the MAJIC trial. More information about this trial and recruitment centres can be found on the MPD Voice website.

## Trials and drug development

### Different stages of trials

All clinical trials of new medicines go through a series of phases to test whether the medicines are safe or work. Medicines will usually be tested against another treatment, (a control) which will either be a substance containing no medication (a placebo) or a standard treatment already in use. Early research may involve volunteers (who may or may not have a health problem) attending a clinic to assess the effects and safety of a new treatment.

From these beginnings, clinical trials become larger and more complicated as the tests of safety and effectiveness become more strictly regulated. Most drug trials go 2 or 3 phases before a licence is granted.

**Phase one trials** test the safety of a new medicine. Involve a small number of people including healthy volunteers. Researchers test for side effects and calculate what the right dose might be to use in treatment.

**Phase two trials** test the new medicine on a larger group of people who are ill, to get a better idea of whether it works and how well it works in the short-term.

**Phase three trials** are only for medicines that have already passed phases one and two. They test medicines in larger groups of people who are ill, and compare a new medicine against an existing treatment or a placebo to see if it works better in practice and if it has important side effects.

**Phase four trials** take place once new medicines have passed all the previous stages and have been given marketing licences. A marketing licence means the medicine can be made available on prescription. The safety, side effects and effectiveness of the medicine continue to be studied while it is being used in practice. Phase four trials are not required for every medicine.

## Congratulations to Professor Claire Harrison!

MPD Voice would like to congratulate Dr Harrison who has achieved the title and position of Professor. As a patient run group we are enormously grateful for Claire's dedication, interest, time and commitment to the group. WELL DONE and thank you for all you do. ☺

# Fundraising
## Thanks to all our supporters in 2012

### 10k success

Eileen Maclennan, whose uncle has MF, took part in a 10k race in Glasgow in summer 2012. She says 'It was a fantastic event, which I really enjoyed taking part in, and I'm very pleased to say that I have managed to raise £1,240!'

Eileen Maclennan supports MPD Voice

### Trish does it again!

Trish Sweeting featured in our last issue after she raised £2,705 from her year as Lady Captain at her Golf Club. Since then Trish amazingly took part in the abseil at Kings College Hospital in July which she described as 'terrifying' AND persuaded her friends to donate money in lieu of presents for her 70th birthday. The result is another £1,085 donated to MPD Voice.
Trish has MF and suffers side effects from the disorder and medication. Despite this she said 'I am trying to do my bit for the charity. I think it helps me to have something to focus on and keep going as best I can.'


Twish Sweeting abseiling at Kings College Hospital

Thanks to Eileen and Trish and to other generous supporters who fundraised and donated money through the year. If you want to raise funds for us please obtain details from Rachel Bridgman who co-ordinates all our fundraising. Email her on fundraising@mpdvoice.org.uk or visit our webpage 'How you can help'.

### The Samuel Sebba Charitable Trust

Our continued thanks to The Samuel Sebba Charitable Trust for their generous financial support, which enabled us to increase the distribution of our newsletter and number of regional patient forums in 2012.

## *Feedback*

Please do contact us with any ideas for other regional forums/fundraising events etc, or if you know a Trust or Foundation that may be sympathetic to supporting our work, please let us know on info@mpdvoice.org.uk.

## Forums **Listen… chat… be informed… get support…**

Our forums are a great way to hear about the latest research, meet other patients and their families and generally feel part of a community. Here's a selection of comments from a recent regional forum in Cardiff:

*'The MPD Voice patients' doctors were excellent, their experience and support and time given is really great – a big thank you.'*

*'I had high expectations and was not disappointed.'*

*'My first visit to a MPD forum, very interesting.'*

*'Great to hear about new drugs, tests and results etc.'*

*'Very informative and helpful in raising awareness and providing support and alleviating fear.'*

*'Have met lots of lovely people been good to listen to the speakers, more info to take home.'*

### Forthcoming forums 2013

**Cambridge** Feb 2013
**London** May 2013
**Patient day – London** 16th Nov 2013

For upcoming and additional 2013 dates please keep an eye on the website www.mpdvoice.org.uk

Visit our **News and Events blog**: www.mpdvoice.org.uk/news-events or visit our Facebook and Twitter pages

## *Save the date*

- **4th July 2013** Fundraising concert MPD organized by Rachel Bridgman at the Savile Club London
- **May 2013** Charity Ball May 2013, Manchester to be hosted by Jennie Barnes. Profits to be split between CLICSargent, (cancer and leukaemia in childhood) and MPD Voice

Further details and links for both these events will be posted on the MPDVoice website in 2013.

## *Ideas*

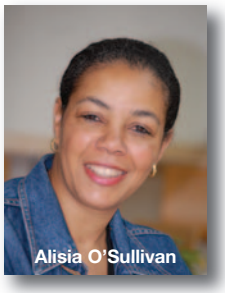
You don't have to super fit or super-organized – there are 100's of ways to raise money for us. Why not try… a raffle … dress down day … car wash … bring and buy … pamper night … cake sale … clothes swap … sponsored event … auction of promises … swear box … tug of war … treasure hunt … lucky dip … bad hair day … phone recycling … sponsored cycle … charity football tournament … skydiving … online donation … tea morning … karaoke night … **WHAT WILL YOU DO?**

Visit the website for an update of fundraising events throughout 2013 www.mpdvoice.org.uk

## MPDlife

- Want to be featured in our patient story?
- Do you have tips to share with readers on managing MPDs?

If so, please email the editor at the address below.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