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## Three new MPD treatments under trial in the UK

People with MPDs may have new treatment options. Dr Claire Harrison describes the latest research plans

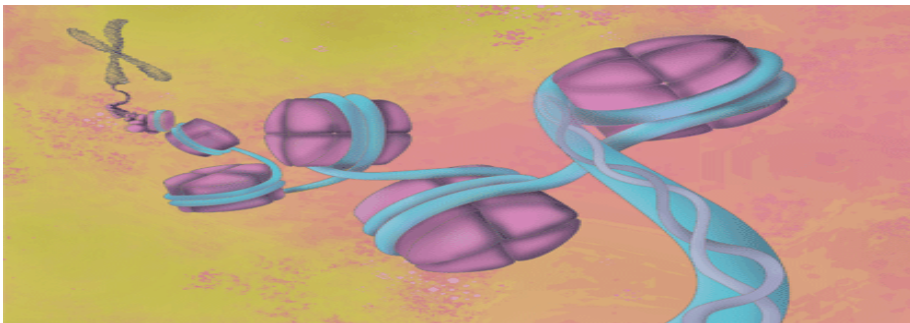
Several new drug studies will open in the UK over the next few months to test promising treatments for myeloproliferative disorders (MPDs).

**Vorinostat** A trial is opening in the UK to test the drug Vorinostat in people with polycythaemia vera (PV) and essential thrombocythemia (ET). The goal of the study is to determine whether Vorinostat reduces blood counts and thus con-

trols MPDs. This drug may offer an alternative treatment for people with MPDs whose treatment options are limited.

Vorinostat is the leading compound in a class of drugs that encourage tumour cells to cease growing and to die. This type of drug is called a histone deacetylase inhibitor.

Histones are proteins which form part of our genetic material's structure. Our DNA wraps around



DNA wrapped around histones (shown here as purple beads)

### MPD Support to fund UK drug research

- MPD Support to fund drug trials for the first time thanks to generous donations
- The charity will cover costs for a nurse coordinator in the Vorinostat study
- The trial will enrol thirty patients with PV and ET
- Six UK and several European centres to participate

histone proteins as if around a spool, which organises the DNA. Histones also regulate the activity of genes. Vorinostat acts by modifying histones chemically, inhibiting deacetylation. This action affects genetic activity, and thus suppresses cancer cells.

**JAK2 inhibitors** JAK2 inhibitor studies have already opened in the US, where the inhibitor INC18424 has been tested in over 160 patients.

A new JAK2 inhibitor study

### Walk for Cure

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[www.mpd-support.co.uk](http://www.mpd-support.co.uk)

is opening in the UK for patients with myelofibrosis (MF). COMFORT II (for Controlled MyeloFibrosis Study with ORal JAK Inhibitor Treatment) will be the first inhibitor study in Europe and will be offered in numerous locations throughout the UK.

A total of 150 patients will be entered across Europe, one hundred of whom will be randomly assigned the JAK2 inhibitor drug while the remaining fifty patients will be treated with another therapy to be chosen by their doctor.

**Interferon studies** Researchers are also testing a form of interferon called PEGASYS. PEGASYS has been shown to dramatically reduce JAK2 levels in some patients and may be an exciting new form of treatment. Patients with ET or PV may enter the study, and they will be treated with either PEGASYS or hydroxycarbamide. Patients who cannot tolerate hydroxycarbamide will also be able to participate in a second study. ■

# Cyclist's endurance race to beat polycythaemia vera

Cyclist John Taylor, age 60, continues to compete despite PV. Ann Marie Jahn learns how he fights his MPD

John Taylor has been a competitive cyclist for over forty years. He began his cycling career at age fourteen when his cousin introduced him to the sport, and two years later he embarked upon a serious racing career. He has cycled throughout the UK, France and Belgium, competing with top amateur cyclists. Today at age sixty he is lean and muscular and he continues to enjoy cycling in the Peak District.

John is married and has three grown children, all of whom are enthusiastic about sports. His eldest son is a runner and steeple chase champion, his younger son a track and road racer, and his daughter a competitive swimmer.

## Unusual cramps

As a veteran cyclist, John understands how his body reacts to physical stresses, but several years ago something in his body seemed to change. John began to experience cramps in his legs during rides.

"I've ridden at quite a high level for a long time. You get to know your body, to know what to expect. But these

cramps were somehow different from anything I'd felt before."

John was competing in a race in France when during a long uphill segment he suddenly felt cramp in both legs and

a heart attack, although doctors found nothing wrong with his heart.

## Foot pain

John does not smoke and drinks very little,



John racing in the Etape de Tour, a stage of the Tour de France between Pau and Bayonne in the Pyrenees, France, 2003

had to abandon the race. After this first cramping event, he experienced a series of similar attacks that struck from time to time without warning.

John experienced other inexplicable pains as well, such as sudden, severe pain that felt like

but one New Year's Eve he had a few more drinks than usual. Within an hour he developed excruciating burning and itching sensations in his feet which lasted for several hours. He took an aspirin and found that the discomfort dimin-

ished.

John's wife Sandra encouraged him to talk to his GP to rule out any serious underlying problem.

John's GP ordered a blood test, which came back showing a high red cell count. John was referred to a haematologist and diagnosed soon after with polycythaemia vera (PV). Once he was diagnosed, the reasons for many of his mysterious pains became clear.

## "It's sobering"

"My consultant gave me the right advice and put me in a positive frame of mind," says John. "He told me, 'Don't worry. It's true that there's no cure for PV – but we can keep it under control.'"

"The only time the diagnosis really hit me was when I went to venesection for the first time. My wife Sandie came with me, and the staff gave me a leaflet produced by Leukaemia Research. When you think about the connection with leukaemia and you see other patients getting chemotherapy, and then you realise you've got to take the drugs for the rest of your days...it's sobering."



John began treatment with one tablet of hydroxycarbamide daily and regular venesections. His blood counts came under control and he was able to continue his training regime.

## Beating fatigue

John has fought hard to retain his speed and endurance since his diagnosis. He sometimes feels frustrated when comparing his pace and level of fitness to that of his cycling friends.

lapse, and my wife says, 'Go out for a ride. You'll feel better.' I go a few miles and I think I'm going to fall off the bike. But within a quarter of an hour, I start to feel more energy. After an hour I come back to the house and I feel re-energised."

## Increasing fitness

At the time of his diagnosis John sometimes experienced extreme fatigue, but he has eliminated the problem with



John and his wife Sandie enjoy a holiday in Venice, Italy



John and his wife Sandie at his son Matthew's wedding

"I can ride on the flat and hold my own, but my muscles die just when I need to push hard. By the time I recover the other riders are half a mile down the road. It's a bit limiting."

John explains that athletes with PV must be patient and stubborn. "You've got to stick at it. Sometimes I feel so tired that I want to col-

apse, and my wife says, 'Go out for a ride. You'll feel better.' I go a few miles and I think I'm going to fall off the bike. But within a quarter of an hour, I start to feel more energy. After an hour I come back to the house and I feel re-energised."

## Changing priorities

John was working as an engineer with Xerox

at the time of his diagnosis, but he took early retirement with a reduced pension when he turned sixty.

"I didn't realise how tired I was getting at work until I finished. Now if I feel tired, I can rest. I made the decision to retire because I want to live well, doing the things I like," he explains.

John has decided to focus on riding with friends rather than racing. "In a race you have no choice. If the pace is high, the pace is high."

## Stable blood counts

John has been able

## Be part of John's team

Are you interested in how sports can help you stay fit and keep healthy? If you have an MPD and you'd like to connect with other sports-minded people, please contact us to join John's team.

Please email us at [info@mpd-support.co.uk](mailto:info@mpd-support.co.uk) for more information.

to reduce his treatment. He has not required venesection for two years, and working with his haematologist he has been able to halve the amount of medication he takes. He hopes to reduce the amount of medication he takes even further.

He finds that exercise helps to reduce itching and fatigue. His blood counts are stable and within normal range and he believes staying fit is helping him fight PV.

"Whatever happens, happens," says John. "I'm just grateful to be out cycling," he says. ■

## Expert Briefing

Do elevated white cell counts imply greater risks?

**Q**I have essential thrombocythaemia (ET) and I've tested positive for the JAK2 mutation. My platelets are high but so is my white blood cell (WBC) count. What could this mean for my treatment? – LS

**A**We know that white blood cells (WBCs or leukocytes) play a role in the body's defence against infection, but we've recently learned more about these cells and what they do.

New research points to a link between infection, inflammation and atherosclerosis. High WBC counts are linked to increased risk of heart attack and strokes in both healthy people and those with MPDs. The link seems to be stronger for people with ET than for those with PV. We need more research, but it appears that higher JAK2 V617F levels correlate with higher WBC levels and clotting risk. Researchers want to determine whether measuring and indeed treating high WBC counts can reduce risk.

We don't know yet, but in the meantime we strongly advise all people with MPDs to reduce risks overall. Maintain a healthy weight and of course don't smoke. – Dr Claire Harrison ■

*You can find more information on treatments at [www.mpd-support.co.uk](http://www.mpd-support.co.uk). 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.*

## Understanding drug trial lingo

Haematology research nurse Dominic Conroy explains trial phases

Three new MPD drug trials are opening in the UK and many people are following the trial news closely. The specialist terminology associated with clinical trials can be confusing, and whether you're reading the news or hoping to enrol in a trial, it helps to understand the concepts. Here's a primer:

**Phase 1-3 trials** Many drug studies are divided into three distinct stages of clinical investigation. This type of study is called a "Phase 1-3 trial".

**Safe dose range** When researchers evaluate new treatments, their first aim is to explore the safe dose range of the drug, and this is the principal aim in Phase 1. These studies usually recruit patients in very small numbers and the data collection process tends to be more intensive than for later-stage trials.

People receiving new treatments in a Phase 1 clinical trial may be required to spend several days either in inpatient or outpatient hospital settings to allow staff to monitor them closely for their ongoing response to treatment. The staff also collects blood samples frequently, both to ensure patients' safety and to determine how the treatment is working.

**Tests in larger populations** New treatments demonstrating a certain degree of safety and reliability are considered safe to test in a larger group of people, and the trial can move to Phase 2. In this phase researchers recruit greater numbers of participants, normally

about one hundred individuals in total.

**Comparing old to new** Treatments move to Phase 3 once researchers have acquired a reasonable level of safety data and determined that the drugs have demonstrated a certain degree of effectiveness. The main aim of Phase 3 studies is to explore the effects of standard versus new treatments in larger populations than in earlier phase studies.

Thousands of patients can be recruited to Phase 3 studies, which often take place internationally across many centres.

Confusingly, data from ongoing Phase 2 studies can continue to inform successive Phase 3 studies, and there may be some relay of information between clinical studies at different stages of investigation.

**Demands on patients** Clinical trials can vary greatly in terms of the demands they place on patients' time, though study visits for most Phase 2/3 trials are often not significantly more involved than regular clinic visits. If you are thinking of enrolling in a study, it's important to discuss just what participation will involve with your haematologist or trials nurse.

**Risks and benefits** Trials involve risks, but they have tremendous benefits for patients. It's an opportunity to join the search for better treatments, and perhaps one day a cure. ■

# Options when pregnancy ends in miscarriage

Alisia O'Sullivan talks about issues, options and solutions for people with MPDs wishing to start a family

The pain and loss caused by miscarriage is often underestimated by family, friends and health professionals. The euphoria and excitement of planning for a family can turn to sadness, anxiety, feelings of failure and sometimes depression for couples who suffer one or recurrent miscarriages.

Research studies conducted at numerous centres have shown that MPDs are associated with pregnancy complications. The research indicates that there is a 65% success rate for live births for women with MPDs. The risk of miscarriage or foetal growth problems can thus be a real concern. Couples affected by MPDs often need to consider what is best for them. While these challenges are often distressing, many options and potential solutions exist for creating families.

**Coping with miscarriage** The

Miscarriage Association is a UK charity offering support and information to anyone grieving the loss of a pregnancy – please see box for more information.

**Surrogacy** If a couple affected by an MPD has decided to consider an alternative route to having a family, surrogacy may be an option. In surrogacy, a woman's eggs are collected and combined with her partner's sperm. The fertilised eggs are transferred to a surrogate mother, often a sister or cousin, who carries the baby to term. The numbers of surrogacy births are relatively small in the UK (approximately 700 since 1985) but surrogacy can be an option if adoption and natural child birth are not suitable or possible.

**Adoption** Adoption may also be an option for some MPD couples for whom a full-term pregnancy is not a viable option. The first step in adoption is to contact your local adoption agency to make an initial inquiry. After this, your adoption agency may ask you to a meeting where you can meet and chat with social workers and adoptive parents. The process can take some time but if successful can provide an equally fulfilling route to parenting – read more at right.

As with any consideration for pursuing parenthood, anyone considering adoption or surrogacy is urged to consider their own long term health issues and ability to be there for children as they grow. ■

## Adoption experience

Cathy and Tony wanted to start a family, but after suffering several miscarriages they decided to adopt. Although Cathy suffers from ET, her MPD was not identified at the time she was tested for potential causes of miscarriage, and she only recently learned that she has an MPD.

Cathy and Tony briefly considered IVF, but Cathy felt that the emotional roller coaster of trying to become pregnant, hoping for a more successful outcome and then the pain of possibly losing another 'baby' would be too great a strain on their marriage.

Yet Cathy felt unfulfilled at not being able to be a mother, so they began to investigate adoption. They attended an open evening and then applied to adopt. In November 2004 Cathy and Tony completed their adoption 'journey' and were able to take home two sisters aged two and ten months.

Speaking about the experience Cathy says, 'It wasn't easy, but it wasn't as hard as losing several babies! My girls are great and we have been really blessed, so for us it's been absolutely the right thing to do.'

"I'd definitely encourage anyone who can't have children naturally to explore adoption as an option. Don't be put off by the media's negative press. The process is not complex for most applicants and it is well worth the effort in the end." ■

## Resources

**Miscarriage** For practical information and support visit:  
[www.miscarriageassociation.org.uk](http://www.miscarriageassociation.org.uk)

**Surrogacy**  
The Surrogacy Charity  
Tel 0560 1491284  
[surrogacy.org.uk](http://surrogacy.org.uk)

**Adoption information**  
Adoption UK  
[www.adoptionuk.org](http://www.adoptionuk.org)

Can I adopt?  
[www.adoption.org.uk](http://www.adoption.org.uk)

British Association for Adoption and Fostering  
[www.baaf.org.uk](http://www.baaf.org.uk)



# Why your “active” Vitamin B12 may be low

Dr Glenn Tisman talks with Ann Marie Jahn about Vitamin B12 and why it's important for people with MPDs

In the last issue of *MPD Life* US haematologist and oncologist Dr Glenn Tisman spoke with us about his research on vitamin deficiencies in cancer patients. In addition to studying the role of Vitamin D (covered in our December 2008 issue), Dr Tisman is looking at Vitamin B12.

According to data from Oregon State University (US), Vitamin B12 deficiency may lead to an elevated rate of DNA damage, an important risk factor for cancer.

“We find in our practice here in Los Angeles that thirty per cent of cancer patients are deficient in active B12, so this vitamin appears to be quite significant,” explains Dr Tisman.

**AMJ** *What is the role of Vitamin B12 in our bodies?*

**DrT** Vitamin B12 allows our brains and nervous systems to function normally, and it is important for the formation of blood.

**AMJ** *Which foods contain B12?*

**DrT** Our main sources of B12 are animal-based foods, such as meat and milk; B12 is often added as a supplement to cereals and breads as well. The vitamin must be absorbed in our digestive tract in the presence of digestive acids in order for it to enter our bloodstream. In some cases people consume plenty of the vitamin, but they cannot absorb it.

**AMJ:** *How can people with myeloproliferative disorders (MPDs) know if they need more?*

**DrT** You can ask your doctor to test your Vitamin B12 level. Your results may show that your level is elevated. However, keep in mind that people with MPDs can appear to have too much of the vitamin while in fact they may be deficient in true, “active” B12. This is because people with MPDs can have an abnormal amount of the white blood cells called granulocytes. Vitamin B12 can bind to protein in these cells, which can cause the B12 level to read high, even though “active” B12 levels may be low.

**AMJ** *Just what is “active” B12?*

**DrT** “Active” B12 or holotranscobalamin is only 20% of the total measured B12, but it is the most important component to measure for anyone with a diagnosis of MPD. It is a measure of how much Vitamin B12 is actually absorbed and available for your cells to use.

**AMJ** *Why might someone be deficient in Vitamin B12?*

**DrT** Many people experience gastritis as they age, which is an inflammation of the stomach lining. Gastritis prevents B12 absorption in approximately one third of patients over fifty years old. People with gastritis are able to absorb the synthetic vitamin B12 added to fortified foods and dietary supplements, so this may be the best source of vitamin B12 for adults older than fifty.

**AMJ** *Do some medications decrease absorption of B12?*

**DrT** Hydroxycarbamide is a drug often used to treat people with MPD. It can cause drops in holotranscobalamin. Some common over-the-counter and prescription medications for indigestion and diabetes can also suppress stomach acid, leading to poor absorption of B12 in the digestive system.

**AMJ** *And now the question that all people with MPDs want to ask: Can any foods or supplements reduce fatigue?*

**DrT** I suspect that fatigue in people with MPDs has more to do with overproduction of cytokines (the signalling molecules used in cell communication) than anything to do with nutrition. I say this because JAK2 inhibitors often reverse tiredness, though they may not decrease marrow fibrosis. I do not think that nutrition will change this to a major degree. However, a healthy diet and reasonable exercise programme are important for everyone, whether or not they have an MPD. ■

## More on Vitamin D

“We find Vitamin D deficiency to be extremely prevalent. Seventy per cent of people in our care suffer from this deficiency, which may play a role in up to 28 different cancers. I strongly recommend to all my patients that they take a supplement of at least 2000 IU (international units) of D3,” says Dr Tisman.

# Twelve friends climb three Peaks, raising £15k

Rachel and Paul Bridgman and their team scaled three peaks in 24 hours with one goal: funding research

Rachel Bridgman learned she has essential thrombocythaemia (ET) just three years ago at age 37. She has taken a positive approach to her diagnosis. "I decided very quickly that I did not want to



Rachel feeling the heat halfway up Ben Nevis

forces with ten friends to enter the "Three Peaks Challenge" this May, climbing 40km in a 24 hour period – with no sleep. The team scaled Ben Nevis, Scafell Pike and Snowdon in often difficult conditions. The event raised £30k for two charities, with MPD Support to receive half.

Rachel was motivated by her own experiences. At the time she learned she had ET, she felt she received little if any emotional support. "My consultant just gave me my diagnosis and handed me a brochure on leukaemia, and that was it. It took me a year to find the MPD Support group, but after that my world changed immediately. Being part of a group, finding the website and making contact with other people who are in the same boat – all this gave

me a sense of belonging. It meant a lot to me."

Rachel decided to mark her fortieth birthday by organising a fundraising event for MPD Support: "I decided to support the group that's done so much to support me. I want MPD Support to have funds to invest in research."

Rachel now plans to organise an event every year. "I'm already planning the challenge for 2010, I think it'll be a good one! The Three Peaks has given me a real boost of energy and positive mind-set. It was something new for me to focus and challenge myself. It has made me realise that I don't have to think of myself as ill. I can get out there and go for it. With positive thinking, teamwork and a very supportive husband I made it happen!" ■

think of myself as ill," she says.

Rachel's platelet count is around 1300; she takes aspirin only. "My consultant suggested I start drug treatment but I don't feel ready to do so yet. I have realised that a large part of my accepting that I have ET is being able to have some say in what I do and when," she says.

Rachel leads a very busy life as mum to three children (Laura 13, Jemima 11 and George 9) and part-time doula. "We have a fairly busy home with dogs, chickens and sometimes pigs!" she explains.

Now Rachel has a new role as one of MPD Support's most successful fundraisers. Rachel and her husband Paul combined



The Three Peaks Team atop Ben Nevis



# A courageous battle against MF

Lianne Kolirin remembers her father Haim, who died this year of myelofibrosis: "He never shied away from fighting his corner"

Haim Kolirin was born in Jerusalem in 1947. He first came to Britain in the early seventies, after meeting his British girlfriend while travelling. The couple married in 1972 and Haim officially moved to London with his wife Pamela the following year.

He started off working for the family clothing business, but moved into the financial services sector in the mid-eighties. He swiftly rose through the ranks and went on to develop a highly successful business as an Independent Financial Advisor (IFA). He had a fantastic sense of humour and was a real people person.

Haim could certainly be prickly on the outside, but deep down he was the sweetest man whose family meant everything to him. He was a courageous man and a hero to those closest to him.

He first fell ill with myelofibrosis (MF) in the early 1990s, but was relatively free of symptoms until about five years ago. Sadly, the real problems started soon after his first grandson was born. He was so happy to finally become a grandfather, but so very sad that he didn't have the strength – or the time – to spend with his grandchildren. Despite all the physical pain and discomfort that he experienced over the last year, the thing that hurt him most was that he would never again see any of his family.

He never shied away from fighting his corner. He would go to the ends of the earth to defend his principles. Yet however hard he tried, his greatest battle to stay alive eventually got the better of him. We were repeatedly told over the last two years to say



Haim with his young grandson

good-bye as the doctors told us that dad's struggle against myelofibrosis had reached the end of the road. But he defied us all – family, friends and doctors – as he refused to give in and continued to fight. He lived to see the birth of his two youngest grandsons, something no one would have ever expected. We all held on to the smallest ray of hope for as long as we could, but ultimately his suffering became too much. Haim was taken before his time at 61 years old.

His death has left a gaping wide hole in our family and we all miss him terribly. ■

*Lianne's husband Simon recently climbed Mt Kilimanjaro to raise money for MPD Support's programmes. Read the full story of his adventures on our website at [www.mpd-support.co.uk](http://www.mpd-support.co.uk)*

*MPD Support wishes to thank the Kolirin family for sharing their personal story.*

## Your gift helps our work

Learn more at MPD Support  
[www.mpd-support.co.uk/giving](http://www.mpd-support.co.uk/giving)

## Our next issue

- Diagnosed at age 12: what it's like to be young with polycythaemia vera
- Inside the JAK2 inhibitor trials
- The MPD in pregnancy trial: what we hope to learn, how you can participate

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