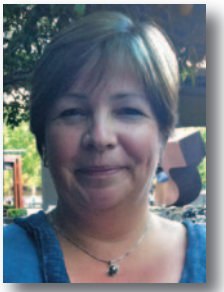
MPDlife

The newsletter for people with MPNs
November 2014

Rapid changes in MPN research and treatment options

Professor Claire Harrison reports


Professor Claire Harrison

During October I attended the European School of Haematology MPN meeting in Estoril, Portugal. This meeting is essentially 'a workshop with an audience' as Professor Tony Green likes to say. It's an opportunity for MPN professionals to share data which often might not yet be in the public domain and discuss it with each other. The result is a highly successful and stimulating blend of science and clinical data! Since the last biannual meeting, such a lot has changed with the approval of Ruxolitinib for myelofibrosis (MF), the withdrawal of Fedratinib and the start of many trials with novel agents*. We have also seen the completion of the first randomised trials with Ruxolitinib in polycythaemia vera (PV) and finally, we are starting the long awaited and much needed first line studies** comparing Pegasys with Hydroxycarbamide.

New scientific developments

We are finally beginning to understand a little more about how the different genetic mutations we find in MPN might work together and how the order in which they appear influences whether the disease looks more like an example of JAK positive essential thrombocythaemia (ET) with high platelets or PV with high red cells, white cells and platelets. Some really interesting data on how the environment interacts with stem cells has come from a group in Madrid. This shows how the nerve supply to the cells surrounding the stem cells and a substance called Nestin are vitally important for human JAK2 V617F positive stem cells to grow and for an MPN to develop in a mouse model.

This introduces ideas about how, for example, we could influence the environment the stem cells are in within the bone marrow and then which may have an effect upon whether or not a disease develops. The same group has gone on to examine the effect of several drugs upon the stem cell environment. Equally interesting regarding the stem cell environment is information about drugs affecting the environment. One such drug is PRM-151 which is an analogue of pentraxin a natural protein which interacts with DAMP proteins and can reduce fibrosis. It's been tested in patients suffering with lung fibrosis and is being tested in America in patients with MF where it has been shown to reduce spleen size. Early data suggests it also reduces fibrosis in the bone marrow.

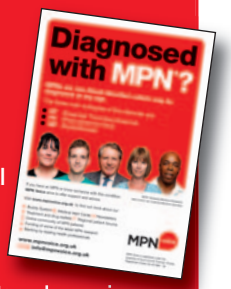
New trials and treatment updates

We have recruited all the patients with ET we needed into the MAJIC study which is testing Ruxolitinib and we have about 50% of the patients with PV that were needed. We expect the first results for the ET patients in about 15 months. For all those PV patients whose counts aren't quite well enough controlled or still have symptoms or side effects on Hydroxycarbamide, do think about giving this study a whirl! Drug companies Novartis and Incyte have just announced that Ruxolitinib was good at reducing spleen size and controlling haematocrit (blood thickness) in patients with PV who had big spleens and needed venesection even whilst taking Hydroxycarbamide. We now need to ask the wider question about this drug in the more general PV patient population. NICE (National Institute for Health and Care Excellence) is starting a review of Ruxolitinib in PV so it will be important to have data about UK patients. Another key update for NICE is that they are reopening their assessment of Ruxolitinib in MF.

* *Novel agents* refers to new drugs which may be completely new or even old drugs that haven't been used for that condition before.
** *First line studies* test the first treatment for disease.

Promote MPN Voice

Help us to raise awareness about our MPN patient support. Posters are available to display in your haematology or hospital department.
Either visit our website to download or email info@mpnvoice.org.uk to order copies.



MPN Voice

Readers will notice that we are now referring to our charity as MPN Voice rather than MPD Voice. This change brings us in line with the WHO classification of MPDs as myeloproliferative neoplasms.

We are also in the process of finalising the changes needed to improve the current website which will introduce some new sections and update the current content, making it even more accessible and useful for new and returning visitors.

Please do send us feedback on areas that you would like to see in the future. Email **info@mpnvoice.org.uk**

MPN voice

GUY'S & ST THOMAS' CHARITY

Charity number 251983

Bone marrow transplant – two patient experiences

patient stories

Emily's story

Emily now aged 47 was diagnosed at 33 with myelofibrosis (MF), shortly after the birth of her first child when a lump in her stomach prompted tests including scans and a bone marrow biopsy.


Happy to be back in her studio

Emily recalls the devastation and worry of being advised of the potential need for a bone marrow transplant and the difficulty with the open-ended timescale of the illness saying, 'The diagnosis hung over the family like a dark cloud'. However, with lots of medical support, Emily went on to successfully have a second child and managed to juggle work, bringing up children and remain relatively well until her blood counts began to trend downwards and she was affected by an ever enlargening spleen.

Emily was advised to have a review of the condition and after a new bone marrow biopsy and other tests, was advised that the disease was now showing signs of becoming aggressive and it was time to seriously consider a bone marrow transplant. She recalls that this was a 'huge blow and very daunting as to deciding when this should be, wanting to play for time. Not so soon as to be putting myself in harms way, but not too late so that I should become very ill'.

Her local haematology consultant worked with the Guy's Hospital haematology team to apply for funding for Emily to take the trial drug Ruxolitinib to help shrink her enlarged spleen and give her more time to prepare for the transplant. Fortunately the application was successful and Emily responded well to the drug which she took for a year, during which time Emily reports two side effects; one being weight gain and secondly, an unexpected but welcome end to monthly hormonal migraines.

In May 2014 Emily started treatment for the bone marrow transplant and at the time of writing is now +160 days post transplant. Obviously there is a way to go to full recovery but Emily reports having recovered sufficiently to have started mosaicing again, saying, 'It's very exciting to feel well enough to be in my studio again. Even though it is a long road ahead, I am getting there'.

Sally's story

Unique combination of disease leads to transplant


Chemotherapy 'conditioning' side effects

Sally's bone marrow transplant journey began in April 2012 following a GP referral to her local hospital haematology department, several tests and bone marrow biopsies and an eventual diagnosis of MF. She was then referred to the Guy's Hospital haematology team where further tests revealed her condition was more complex than at first diagnosis. Examination of her bone marrow biopsy slides revealed a second and rarely talked about MPN known as systemic mastocytosis. The World Health Organisation (WHO), have classified this as an MPN in which excess mast cells are produced in the blood and invade any and all organs of the body. Sally was put on medication to suppress mast cell production and the MF was kept on a watch and wait brief. A further biopsy revealed a third element of myelodysplasia and the combination made her somewhat unique. Sally says, 'Give me boring and common any day! Unique can feel a lonely place. Having an MPN can make us all feel pretty alone as even your GP, never mind your friends, may not have heard of them'.

Sally started on Imatinib to control the MF symptoms which were becoming more bothersome but this proved ineffective in her case and the consultant applied and was given permission to prescribe Ruxolitinib. This had a much better effect and her fatigue levels lessened considerably whilst her spleen size also reduced by a small amount.

However, her body's idiosyncratic decision to combine three relatively rare conditions meant that even Ruxolitinib wasn't considered a viable treatment long-term and after being the subject of some multi-disciplinary discussions the idea of a stem cell transplant was mooted. Sally's initial reaction was 'No way,' particularly as she felt better than she had in a long time, but she agreed to meet with a specialist for transplant patients.

Sally shares, 'His understanding but honest appraisal of my options and prognosis without the transplant and continued support from Guy's made me re-evaluate the situation. Sharing that particular set of facts and figures with my family was particularly tough especially as we were newly bereaved of my much loved mum and still grieving at her loss. However, to coin a phrase from the younger generation it was a "no brainer" as without the transplant my prognosis was two and a half years so long as none of the three conditions transformed to acute leukaemia during that period. No crystal ball, but that transformation was a "when" not "if"'.

As no family match could be established, through the Anthony Nolan Trust Sally was matched with a 10 out of 10 donor on the international database and started her transplant journey process in January 2014.

Sally continues, 'For the first 4 months all went well with my transplant and at one stage I had achieved a 99% chimerism, (carrying two types of genetically different cells), in my blood and bone marrow with my myelodysplasia already in remission. It was predicted the MPN components would take longer to disappear. However, a bone marrow biopsy in August showed my chimerism had dropped considerably and it was decided in September that I required a further course of chemotherapy followed by a donor lymphocyte infusion. I have now received the chemotherapy and am awaiting my recovery before the infusion. Yet again my wonderful donor has stepped up to the mark and donated these specialist white blood cells ready for my use.

I can't pretend this hasn't been a setback. We all want things to go smoothly but it is a

setback and the clinical expertise and emotional care I have continued to receive from the transplant team, plus the ongoing interest taken in my case by my consultant at Guy's, gives me great faith that I could not be in better hands'.

Although at the time of writing, Sally still has a challenging time ahead she shares a personal side of dealing with the time in hospital saying, 'Finally and most frivolously I make up pictures. I put it down to a lifetime of being an infant teacher. My mast cells are mischievous imps with horns on their heads and pins in their hands rushing around my body going "Aha another organ to invade!" My donor is Danish and when I was experiencing Graft versus Host disease of the skin I envisaged an army of Viking warrior cells hunting down and killing off my last Anglo-Saxon cells. I even have a wonderful cartoon to that effect drawn by an artist friend of mine and I smile whenever I look at it'.

Editor's note: On behalf of *MPD Life* we wish Sally a full and healthy recovery and look forward to sharing an update on her progress via the real life stories section on our website.

Bone marrow transplants for MPN patients

For some myelofibrosis (MF) patients whose disease symptoms and quality of life deteriorate, even with the current range of drug therapies and treatments available, a stem cell or bone marrow transplant (BMT) may be considered.

BMT for MF involves using blood stem cells from a family member, unrelated donor or umbilical cord blood unit. An autologous BMT, where the patients own cells are used, is not an option.

Every patient's circumstances will be unique to them and the haematologist and transplant team will need to consider numerous factors including:

The International Prognostic Scoring System (IPSS) for MF. This is a risk stratification system which uses five variables of anaemia, age, leukocytosis, (high white blood cell count), peripheral blasts (immature cells) and constitutional symptoms such as weight loss, drenching sweats and fever. Consideration of these variables provide clinicians with four levels of risk factor from low risk, (no risk factors), through to high risk, (three of more risk factors). Using these variables plus additional factors such as low platelets, chromosomal changes or abnormalities and being dependent on blood transfusions, a patients risk and prognosis can then be categorised at any stage in the disease.

In general, clinicians do not routinely transplant patients who have an IPSS of low or intermediate risk 1 of the disease and await a 'trigger' to move forward to transplant. However it is not wise to leave a transplant until MF is high risk or progressing to leukaemia as the success of transplant is then less.

The general health of the patient is also important in assessing the possibilities of transplant. By the nature of the median age of onset of MF, many patients referred for consideration of transplant are of a more advanced age. Many transplant centres will consider patients aged up to 70–75 years of age. However, with advancing years, other medical problems may make transplant more complicated or risky and therefore will be taken into account for assessment of suitability for transplant.

Stem cell transplant: simplified facts

Haematopoietic stem cells (HSC) – immature bone marrow cells which mature into red or white cells or platelets. In a stem cell transplant these cells are 'harvested' from a donor and transplanted to the recipient.

Donors may be found from family members, but siblings only offer a one in four chance of being a 'tissue-type' match. Many BMTs involve unrelated donors from large international Stem Cell Transplant registries. Sometimes it can be difficult to find a suitable donor and this may mean that a transplant is not possible.

Conditioning prior to the transplant refers to the preparation of the patient's bone marrow to receive the donor cells. Usually 7–10 days of high dose chemotherapy +/- radiotherapy which helps to destroy diseased cells in the patients system but also weakens or dampens the immune system.

Transplant day: Day zero This is not surgery but where the patient receives healthy donated stem cells via a central infusion line via blood bags similar to ones used for blood transfusions.The transfused cells will find their way to the patient's bone marrow where they will eventually start to divide and make healthy new blood cells. This is known as engraftment and typically will take two to three weeks for the neutrophil levels to rise over 0.5. Engraftment of red cells and platelets take longer.

Graft-Versus-Host Disease (GVHD)
A common complication of BMT. There are two types, acute and chronic ranging from mild to severe. GVHD occurs because of the differences between the patient and donor cells so that the new immune system from the donor may see the recipient's cells as different and attack them. Depending on the type of GVHD, the treatment options and risk of having GVHD will be different.

Other considerations

A BMT is a serious undertaking and a wide range of complications can occur. Infectious complications occur frequently as well as common side effects like 'musositis', a painful mouth making eating temporarily difficult.

Post transplant management and outcomes

Every patient's outcomes and recovery times will vary enormously but regular monitoring will be part of the post transplant regime. In the early stages, hospital visits will be more often and it can be common to be re-admitted to hospital for a period of time depending on the individual patient needs.

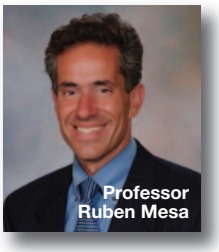
It is possible to have a short recovery but for some patients recovery can last for many years. Don't forget, MPN Voice offers patients the opportunity for buddy support in all aspects of living with MPNs so if you are considering a transplant or have undergone one, and would like support, please do contact us at **buddies@mpnvoice.org.uk**

Editor's note: BMT and Stem cell Transplant are interchangeable names/terms.

The MPN Fatigue Project

A step towards comprehensively understanding MPN-related fatigue

Professor Ruben Mesa, Mayo Clinic Arizona USA writes


Professor Ruben Mesa

Patients with MPNs suffer from severe and debilitating fatigue that greatly impairs their overall quality of life. In order to better understand MPN-related fatigue, our collaborative team of investigators has embarked on the second part of a three-part project to better understand fatigue. The first phase of this project evaluated the severity of fatigue as well as what strategies patients used to alleviate fatigue. This phase of our project aims to better comprehend the many contributing medical and psychological causes of fatigue as well as the individual impact of fatigue on daily functioning. In order to do this, our team of MPN investigators and patient advocates created a 70-item internet-based survey which included an assessment of fatigue and related psychological and medical co-morbidities.

Overall 1788 MPN patients participated in the month-long survey. Fatigue was prevalent and severe among survey respondents. Patients most often noticed their fatigue in the evening or afternoon and fatigue lasted at least a few hours or through most of the day. Fatigue triggers included physical work, stress, exercise, medications, intellectual work, eating, and sexual activity. Numerous strategies were implemented in order to combat fatigue, including setting priorities, postponing essential activities, exercise and naps. Of these interventions, patients most often felt that scheduling activities during peak energy times, pacing activities, labour-saving devices, and setting priorities were most effective in reducing fatigue.

Many patients endorsed having co-existing medical or psychological diseases that could also contribute to overall fatigue. There were many patients who suffered from co-existing depression and depressed individuals were significantly more likely to have higher fatigue and MPN-related symptom burden. Overall 20.2% of patients endorsed having low thyroid function, which is higher than in the general population. Twenty three percent endorsed having a new sleep disturbance in the last six months. Many patients also experienced a high rate of unintended weight loss. Low blood counts were also very common. Current use of alcohol and tobacco were also significantly associated with greater burden of fatigue.

Overall, fatigue contributes greatly to the impaired quality of life experienced by MPN patients. In the third phase of this project, we will plan to implement the data we have gathered on successful MPN-related fatigue strategies to initiate a home-based, online intervention to alleviate fatigue. We would like to thank all of the MPN patients who partnered with us to further our knowledge of MPN fatigue and would ask that you consider being involved in the final, interventional stage of this project.

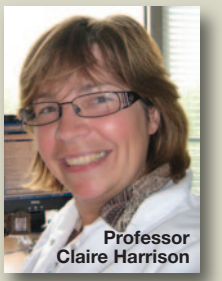
Details will be promoted via the MPN Voice website when available.

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

MPN voice

Trials

Professor Claire Harrison comments on the latest MPN research and trials


Professor Claire Harrison

At the moment, for patients interested in trials there are many available with Ruxolitinib; these are mainly in combination with other drugs to try to achieve better control of symptoms in MF.

New JAK inhibitors

There are two other JAK inhibitors being tested at the moment. Professor Ruben Mesa from the Mayo Clinic, Arizona and myself are globally heading up a study of pacritinib in MF patients. This study is called PERSIST-1 and we expect results early 2015. A second study PERSIST-2 is open for patients with platelet counts less than 100.

Patients can enter this study even if they have been treated with Ruxolitinib or Fedratinib in the past. Pacritinib appears to have less of a platelet or red cell lowering effect than Ruxolitinib. For patients with anaemia, Momelotinib may be of interest. Results show that over 60% of patients in earlier studies had important increases in haemoglobin with this drug. We are about to start studies comparing Ruxolitinib with Momelotinib and to use this drug for patients who became more anaemic on Ruxolitinib. These two drugs could provide important treatments for MF patients with large spleens, poor quality of life symptoms and low blood counts. Lastly there is increasing interest in drugs which can inhibit the smoothened pathway* and some of its components particularly, believe it or not, sonic hedgehog**. One of these compounds is made by drug company Novartis the other by a company called Pfizer; both want to make these trials available for UK patients. These agents and studies are really interesting and offer us major hope of a significant breakthrough in treating MF.

Get involved

How about if you want to take part in research but not by taking a new drug? You can do this in several ways: One option is that we have a large sample bank in the UK which several hospitals send samples to. In addition we hope to open the MOSAICC epidemiology study on a much bigger scale and opened the MEASURES study to assess symptoms and quality of life affecting MPN patients in October 2014 at Guy's with plans for more centres to be added soon.

You can hear more about these trials and meet other patients at the many forums we have running in the next few months and I am particularly please to let you know we will be running another all day "Living with MPN" event in 2015 so mark you diaries now for November 2015.

* *Smoothened pathway* A pathway important in cell survival and multiplication.

** *Sonic hedgehog* A component of the smoothened pathway.

FUNDRAISING update

Marilyn Webster fundraising co-ordinator writes

We would like to thank all our wonderful supporters for their fantastic fundraising during 2014. MPN Voice fundraisers have had various coffee and cake mornings, garden parties, craft and retro bling fayres, treasure hunts and spa days as well as personal challenges including abseils, half marathons, a triathalon, the Great North Run, and many more.

With all these events and generous donations we have raised almost **£90,000** this year to date. Most importantly through our enthusiastic fundraisers, wearing their MPN Voice T-shirts, waving their flags, rattling collection boxes, putting up posters and talking to sponsors, we have also raised awareness of our rare blood cancers and the need for support and research. So if you are planning your own event, please contact us at **fundraising@mpnvoice.org.uk**. We can supply you with all the support materials you might need and we will advertise your event to the wider MPN Voice community in our monthly online fundraising update.

Exciting plans for 2015

MPN Voice has teamed up with Charity Challenge, who have a fantastic calendar of events for 2015. Katie has already signed up for her Great Wall of China Discovery Challenge commencing 9th May 2015. Have a look on their website at **www.charitychallenge.com**.

We are delighted that MPN Voice has secured guaranteed places in some iconic running events for 2015. These include The Virgin Money London Marathon, BUPA London 10K and Adidas Silverstone Half Marathon. Our MPN Voice running team members have already started their training and fundraising. We do still have a few spaces left for the BUPA 10K and Adidas Silverstone Half marathon. For more information please contact us at **fundraising@mpnvoice.org.uk**

2014 has been an amazing year for MPN Voice fundraising. Let's make 2015 even better!

Thank You

UPCOMING EVENTS

- **March 2015** **The Adidas Silverstone Half Marathon**
- **April 2015** **The Virgin Money London Marathon**
- **May 2015** **The BUPA London 10K**
- **September 2015** **Blood Cancer Awareness Month** Join MPN Voice and Host a Coffee Morning to raise awareness.

Fundraising heroes

John Messenger

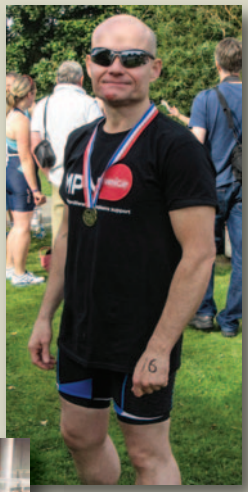
Raised £550 by running the St Albans Half Marathon in June 2014 and has set himself a target to raise a minimum of £2,500 from the London Marathon next year. Diagnosed with ET, John says that being back to his active self has lifted his spirits and feels it's important to spread the word that being diagnosed with MPN doesn't necessarily stop you doing the activities you enjoy.

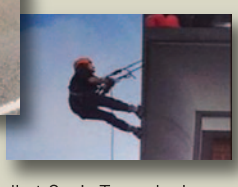
Claire Piggott

Raised £712 running The Royal Parks half marathon in October. Claire is the friend of Pamela Cromie, who's husband has PV. The final total raised was doubled by her company charity matching her achievement bringing the final total to £1,424.

Andy Manning

Raised £602 after completing the Tunbridge Wells Sprint Triathalon in August. Andy was running on behalf of his wife who was diagnosed with ET in 2013.





Mary Green

Took part in the abseil at Guy's Tower in June and raised over £170. The summer abseils raised over £2000 from our amazing and brave supporters!

Diane Hashimi

Sister of MPN patient Anita, raised £533 in the 5K Race for Life earlier this year. Anita wants to thank her sister and knows how proud Diane was to raise the money on behalf of MPN Voice.

Diane Carter

Raised £300 at a church fete, selling jewellery and scarves on behalf of MPN Voice. Diane's daughter Alex has MF.

Scott Davey

Raised £986 for MPN Voice in his first cycling challenge, Tour de Tendring in April 2014. Since that event Scott has ridden in even more challenging events including Annecy in France cycling up mountains totalling 10,000 ft in 3 days and next year he plans to ride London to Paris in aid of MPN Voice. Since his diagnosis in 2011, Scott has found cycling offers a great way to raise awareness and money for MPN Voice and that the exercise helps offset the chronic fatigue and helps him feel relaxed.

Thanks to all our featured fundraisers and those who send financial support on a regular basis. We really appreciate all contributions whatever the amount. If you are planning an event, please let us know so that we can include your achievements in future issues.

MOSAICC

The MOSAICC Pilot Study to look at the epidemiology of MPNs has now closed the recruitment phase of the study, finishing with 233 participants. A fantastic achievement.

The study team would like to thank everyone who took part, and particularly appreciate the patient participation.

Glen Titmarsh

Over the next few months, PhD student Glen Titmarsh will be conducting statistical analysis and writing his thesis based on the study findings. Once analysis is complete, results will be made available via the study website (http://mosaicc.qub.ac.uk).

Glen recently attended the European School of Haematology 6th international conference on myeloproliferative neoplasms (MPN) where he presented 4 posters. In December, the MOSAICC study team will be meeting in Belfast to discuss the results of the MOSAICC pilot study and plan a strategy to take a much larger study forward.

Advocacy update

patient power

Jon Mathias, chair for MPN Voice reports


Jon Mathias

Newly diagnosed MPN patient, Caroline Thomas, has volunteered to contribute to the advocacy work that we've started via MPN Voice. Caroline read the piece on the subject in the recent newsletter and kindly offered her time to become involved. Caroline also happens to work in the same building where The National Institute for Health and Care Excellence (NICE), has its offices, which should help us establish contacts there. NICE is the primary decision-making body in the UK for determining whether new treatments should be made available on the NHS and we're keen to make sure that MPN patients are as effectively represented as possible in those discussions.

Related to this, we have been active in establishing an international network of MPN patient groups, with the objective of sharing knowledge and best practice around patient support, whilst also having a louder collective voice in the growing debate around drug access, pricing and participation in clinical trials. International collaboration is not easy and it's taken a while to get the network to the point where we can start approaching potential sponsors for funding. One of our main concerns has been that we should not need to draw on MPN Voice funds to support the network. We are now legally established as a non-profit organisation under Swiss law and planning to host a meeting of European MPN advocates in early 2015.

Forums

New locations added...

2014 has been a busy year with over 400 MPN patients, family members and friends attending MPN Voice forums around the country. New locations were added for 2014: Southampton, Manchester and Colchester, alongside a return to Belfast, and a joint forum for Newcastle and Edinburgh. MPN Voice would like to thank the consultants and volunteers who made these events possible in 2014.

Forums are a great way to keep up to date with the latest on MPNs, treatment and research as well as to meet other patients and families living with the disease. These forums are informal, relaxed and designed for you, so do come along.


Informal and fun!

Next year we will be holding a forum in Cardiff in May and the dates for other locations will be publicised on the website as soon as they are confirmed.

You can also organise your own informal get-togethers for MPN patients as Violet Slade did on two occasions this year in Cambridge. Violet describes the get-together as fun with MPN patients, family and friends meeting for a coffee, cake and a chat and plans to host further informal catch ups. One attendee, Lesley writes, 'We came away having spent a very enjoyable day, well worth the trip from Aylesbury, Bucks, and look forward to the next get-together'. All you need is a venue and time.

Our continued thanks to Samuel Sebba Charitable Trust whose generous financial donations continue to support MPN Voice in it's expansion of regional forums.

STOP PRESS! Diary date

Living with MPN's Day confirmed for London, 14th November 2015.

MPDlife

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

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


Alisia O'Sullivan

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Medical Advisor Professor Claire Harrison

Contributors Professor Claire Harrison, Jon Mathias, Professor Ruben Mesa, Glen Titmarsh, Marilyn Webster

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