

My prog-MS ezine

For people with progressive MS and other interested people

Issue 60, May – June 2025

Hello and welcome to the 60th edition of my ezine about progressive Multiple Sclerosis and MS progression in general. My name is Ian Cook. I'm a secondary progressive MSer from Birmingham, UK. I'm 66. (EDSS 6)

The ezine is now ten years old and at last things are happening in the world of progressive MS. In issue 60 there are eight pages of prog-MS news stories and two features. One feature, on page 5, looks at at MS and anti-retroviral HIV drugs. One of these HIV drugs is being trialled in motor neurone disease and early results are impressive. Should this drug be trialled in MS? The doctor carrying out the research is interested so watch this space.

There's another feature on page 10 looking at the subject of love and MS. It's a sad fact that people with MS are more likely to be involved in relationship break-ups than those who don't have the condition. men with MS – like me – are particularly badly affected. But why is this and what, if anything, can we do about this sad situation.?

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News

Weight loss drugs may slow MS disease progression

US researchers have said they believe a class of weight loss drugs known as GLP-1 inhibitors – this includes oxempic- may slow down MS progression.

In a paper titled 'Exploring the Effect of GLP-1 Agonists on Multiple Sclerosis Disease Progression' researchers from University of California hypothesized that GLP-1 weight loss drugs could provide neuroprotective and immunomodulatory effects, potentially slowing progression in the condition.

In the paper, presented at the American Academy of Neurology, researchers looked at more than 7,000 US adults with MS receiving weight loss drugs, and comparing them to 7,046 MS patients not receiving the treatment. The researchers studied the two groups over five years, assessing neurological function based upon the Kurtzke Functional Systems Scores (FSS) and the Expanded Disability Status Scale (EDSS). It was found that MSers not treated with GLP-1 agonists demonstrated significantly more MS disease progression across all functional categories compared to those receiving the weight loss treatments.

In their conclusion the researchers say: "In this preliminary study, use of GLP-1 agonists correlated with reduced risk of MS disease progression as measured by Kurtzke Functional Systems Scores (FSS). Future research can further explore the potential role of GLP-1 agonists as a therapeutic option to delay disease progression in adults living with MS."

It has been known for some time that being overweight is associated with an increased risk of developing MS, and in individuals with MS, obesity can lead to faster disease progression, poorer health-related quality of life, and more rapid cognitive decline but the idea of using weight loss drugs to treat MS progression is a relatively new idea.

There are several theories about what explains this link between obesity and MS. Researchers have identified a handful of genes associated with obesity that are also associated with MS. This means that if you are genetically more likely to become obese, you are also more susceptible to MS. Secondly, it has been known for some time that obesity is associated with a higher relapse rate, faster disease progression and increased disability in people with MS at all ages. It is thought that fatty tissue in the body may release excess hormones that put the body into a generally inflammatory state, promoting nerve damage and interfering with repair. Excess weight can also put stress on the muscles and skeleton, and lead to the accumulation of disability beyond that caused by MS.

It has also been observed that many MS diets such as the Swank diet are low fat diets.

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Four new naSPMS patients dosed with nasal foralumab

Four more non-active secondary progressive MSers (naSPMS) have received foralumab nasal spray — Tiziana Life Sciences' therapy candidate for SPMS — via an expanded access programme, the biotechnology company has said.

The Expanded Access Programme allows patients who do not qualify for the ongoing Phase 2a clinical trial (NCT06292923) to still have access to the experimental therapy. The dosing of these patients follows a decision from the U.S. Food and Drug Administration to include 20 additional patients in the programme, based on promising data from the first 10 participants.

"We are pleased to reach this milestone of enrolling 14 patients in our na-SPMS [nonactive SPMS] expanded access program," Ivor Elrifi, PhD, Tiziana's CEO, said in a company press release. "This underscores our commitment to addressing the unmet medical needs of patients with na-SPMS, particularly those who are not eligible for our ongoing Phase 2a clinical trial."

Foralumab is an antibody-based treatment that works by blocking the CD3 receptor at the surface of immune T-cells. Such suppression simultaneously reduces the activity of inflammatory T-cells and increases the activity of regulatory T-cells that prevent excessive inflammation.

Six-month data from the program's first 10 participants demonstrated that the therapy reduced activity of microglia, the brain's resident immune cells, in 80% of them, and lessened fatigue in 70%. Also, in all patients, disability was either stabilized or reduced.

The ongoing Phase 2a trial is evaluating the safety and efficacy of foralumab nasal spray in as many as 54 patients, aged 18-75 years, with nonactive SPMS. The study may still be enrolling adults at several sites in the U.S.

The participants are being randomly assigned to receive four three-week cycles — totaling about three months — of either one of two doses of foralumab (50 or 100 mcg) or a placebo.

The trial's main goals are to assess the number of patients experiencing adverse events, changes in nasal symptoms, and changes in microglial activation in PET scans. Secondary goals include changes in validated measures of disability and fatigue. Other measures include assessing by MRI the presence of active lesions and changes in brain volume. The trial is expected to be completed by year's end.

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News

Tolebrutinib impact greater in MS patients with smouldering progression

Experimental drug tolebrutinib is more effective at reducing disability progression in people with MS who have evidence of paramagnetic rim lesions (PRL). That's according to a new analysis of three Phase 3 clinical trials.

PRLs are a type of chronic inflammatory lesions that have been associated with faster disability progression in MS. They are brain lesions characterized by an outer rim of iron-containing inflammatory immune cells and a core region with extensive demyelination — myelin loss — and nerve cell damage. They can be seen on MRI scans. PRLs are known to be associated with increased risk of disability accumulation, specifically smouldering-associated worsening, (SAW) and nearly 50% of people with MS have at least one PRL at diagnosis.

In patients with PRLs at the time treatment was started, tolebrutinib reduced progression risk by as much as 54%, the data showed. The greatest effect was seen in patients with four or more PRLs. The new information was presented at the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum 2025, held in Florida ..

Tolebrutinib is a small molecule inhibitor of the Bruton tyrosine kinase (BTK), an enzyme that's critical for the survival and activation of B-cells and microglia. These two immune cells are known to drive MS inflammation and disease progression. It is a tablet taken once daily. Tolebrutinib can cross the blood-brain barrier, a semi-permeable cellular barrier that regulates which substances can pass from the blood to the brain. A key limitation of many drugs is that they cannot cross this barrier, and are therefore not able to limit localized inflammation in the brain and spinal cord.

In terms of when tolebrutinib will be available Prof. Gavin Giovannoni wrote in his MS-Selfie Medium post: "We expect tolebrutinib to be licensed by the US FDA in the second half of this year and by the MHRA (UK) next year. After MHRA approval, there needs to be a NICE cost-effectiveness assessment and, if it gets the green light, NHS approval three months after that. So provided all the hurdles are cleared, people with smouldering or SPMS should only expect Tolebrutinib to be available in the UK in 18-24 months**"**

In a late development to the Tolebritinib story Prof. Gavin Giovannoni also wrote: "The tolebritinib data has finally been published and not only vindicates that BTK (Bruton Tyrosine Kinase) is a valid therapeutic target targeting B-cells and likely CNS macrophages and microglia but also makes the case for CNS penetrant therapies. The tolebrutinib results are a landmark in MS drug development and usher in a new phase of MS therapeutics that goes beyond targeting relapses and focal MRI activity to target smouldering MS"

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Does new research suggest HIV pills might treat MS?

Around ten years ago an Australian Professor came up with a big idea about the cause of MS and a new drug treatment that could even cure it.

The big idea was that MS is triggered by a fragment of ancient viral DNA that has been lying around for thousands of years in the human genome. In MSers this ancient viral DNA gets "re-activated" probably by an infection, setting off a cascade of auto-immunity and causing MS as the result.

Although it sounded a rather far-fetched idea, several academic papers were published showing that fragments of this ancient DNA, called Human Endogenous Retroviruses (HERVs) really do exist. They make up about 8% of human DNA, and there is evidence of HERV activity in MS. One particular fragment of interest to MSers is a human endogenous retrovirus called HERV-W.

In research which began in 2012 the Australian Professor, Julian Gold, whose specialism is HIV/AIDS, became aware that people with MS diagnosed with HIV sometimes see their MS symptoms improve and even disappear when they start taking anti-retroviral HIV drugs. It was possible, he thought, that some sort of virus, possibly a HERV, was involved in MS and that the anti-retroviral HIV drugs these patients were taking was treating the HERV as well as their HIV. There was a strong scientific basis for looking further.

This is exactly what Professor Gold did. In 2018, Gold was able to get one small and short Phase II clinical trial underway in the UK, using a HIV drug called Raltegravir in a small group of 20 MSers. Sadly, the short, small, and arguably underfunded trial did not provide positive results although it did find 'interesting correlations' between HERV-W and new MRI lesions in MSers. That was the last the MS world heard of Prof. Gold. He didn't abandon the HERV idea but the pandemic came along, he returned to Australia and took his big idea to a more sympathetic community.

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Continued from page 5 Fast forward six years and Professor Gold is currently carrying out a major Phase III trial into the use of another anti-HIV drug targeting another HERV. This one is not HERV-W but HERV-K and the disease is not MS but another neurodegenerative condition, motor neurone disease (MND).

Professor Gold is currently lead investigator of a clinical trial investigating the HIV drug Triumeq in people with MND. The trial is called "Lighthouse III" and an earlier Phase II clinical trial (Lighthouse II) found a statistically significant reduction in MND disease progression after 24 weeks' treatment with Triumeq. The neurological decline of MND patients slowed from 1.12 points per month during the initial observation period to 0.76 points per month whilst on the treatment. Breathing was also shown to stabilise after 18 weeks treatment, indicating another positive change. In most trial participants levels of HERV-K were reduced, suggesting that the treatment was working as it should. However, it took around 24-weeks for levels of HERV-K to significantly reduce.

As the Phase II trial was only 24-weeks long, the full potential clinical benefits of Triumeq may not have been observed. However, the trial provided 'proof-of-concept' for Triumeq as a potential treatment for MND and has led the MND community to fund the development of the larger, and longer, phase III trial (Lighthouse III) which is currently taking place.

The Phase III trial has enrolled 390 participants who will take Triumeq or a placebo for a maximum of two years. Measurements of disease progression and reaction to the drug will be recorded every three months. Throughout the 24-months there will be two interim analyses where data collected from the trial will be independently reviewed by people not involved in it. The study is due to report final results next year, in 2026.

The relevance of this MND trial to people with MS is huge. If successful, Lighthouse III will show that HERVs do contribute or even cause a serious neurodegenerative condition like MND. It will also beg questions like: "If a HIV anti-retroviral drug works in MND, could it work too in MS?" Interestingly, Prof. Gold once described antiretrovirals as "the penicillins of the 21st century" suggesting these drugs may have a huge role in treating a wide variety of other diseases as well as HIV. Could this include MS?

Photo (p1 and 5) by Christina Victoria Craft on Unsplash

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News

Eating more fish linked to slower MS disability progression

People with MS who eat more fish are significantly less likely to see confirmed disability progression and the greater the intake, the lower the progression risk, a study in Sweden finds.

The dietary habits of patients were assessed at the time of their diagnosis and disability progression was tracked for up to 15 years. While greater benefits were observed in those who regularly ate fish since their diagnosis, patients who increased their fish intake in the years after being diagnosed also saw reductions in the risk of disability progression over those who continued to eat little or no fish.

The findings suggest "diet, particularly fish consumption, as a modifiable factor that could complement existing therapeutic strategies for MS," the study's researchers wrote in "Impact of fish consumption on disability progression in multiple sclerosis," which was published in the Journal of Neurology, Neurosurgery and Psychiatry.

Growing evidence touts the benefits of a healthy diet in slowing disease progression. For example, a Mediterranean diet, rich in fish and other healthy foods like vegetables, is linked to less disability, with older patients also reporting better quality of life.

Researchers at the Karolinska Institute in Sweden drew on data from 2,719 patients in a Swedish MS registry to explore whether eating more fish could slow disability progression. The registry included patients diagnosed between 2005 and 2015 who responded at enrolment to a questionnaire about environmental exposures and lifestyle habits. The patients were followed for up to 15 years.

The amount of fish they consumed had no impact on their disability levels, as assessed with the Expanded Disability Status Scale (EDSS), at the time of enrolment. However, those who reported eating fish weekly had a significantly lower risk of confirmed disability progression throughout the follow-up.

Specifically, eating lean fish each week such as cod, haddock, and whiting was linked to a 16% lower risk of confirmed disability worsening compared with seldom eating lean fish. Eating oily fish — herring, mackerel, tuna, salmon, and trout — each week was linked to a 19% lower risk. **For further details of all news and features go to page 14**

News

Cognitive impairment more common in untreated prog-MS

Cognitive impairment is relatively common in MSers who have not been treated with disease modifying drugs. It affects about 1 in 4 patients, and rates are particularly higher in those with secondary progressive MS (SPMS), a new study says.

The new study demonstrates that a significant portion of MS patients who are drug-naïve (never teared with disease modifying drugs) have cognitive impairment, the researchers wrote, noting their goal was "to estimate the frequency and contributing factors for developing" problems with cognition."

The study, done by the researchers, from Egypt, published in the Journal of Neuroimmunology.

While MS is primarily marked by muscle weakness and walking difficulties, cognitive dysfunction is known to be a common symptom of the neurodegenerative disease, affecting as many as 90% of patients in some studies. Individuals with MS can experience a range of problems, including issues with memory and learning, as well as trouble with attention and information processing.

Building on the hypothesis that neurodegeneration may play a major role in MS-related cognitive impairment, the team of researchers studied 140 adults with MS who had never received treatment, known as drug-naïve.

According to the researchers, the "acquired knowledge" from this study "may help manage cognitive decline as the disease progresses and aid in the early diagnosis of CI in MS."

The team noted that "there are few previous studies of Cognitive Impairment in drug naïve MS patients." As such, these findings may provide insights to cognitive decline as seen in the natural disease course, the researchers noted.

"By focusing exclusively on drug-naïve patients, our study provides insights into the relationship between CI without the confounding effects of disease-modifying therapies," the team wrote.

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Inflammation is potential cause of progression

Australian researchers have identified that inflammation appears to cause increased mutations linked to MS progression.

The researchers, from Melbourne Univrsity, studied MS brain lesions, visible as spots on MRI scans, which are areas of past or ongoing brain inflammation. They found neurons located in MS brain lesions have a mutation rate that is two-and-a-half times faster than in normal neurons.

Associate Professor Justin Rubio, Head of The Florey and Melbourne University's Neurogenetics Group, led the research published in Nature Neuroscience. Associate Professor Rubio said: "Our research suggests that inflammation in the brain of people with MS causes mutations in neurons, which may contribute to progression."

The team from The Florey and University of Melbourne focused on 'somatic mutations', which are not inherited but occur over time in cells during ageing. These mutations can disrupt a cell's normal function or survival.

The researchers compared mutations in neurons from the brains of 10 people with MS and 16 people without MS. They found that neurons in non-lesion areas and the brains of people without MS accumulated 17.7 mutations per year, while neurons in MS lesions accumulated 43.9 mutations per year. "This means that by age 70, neurons in MS lesions have around 1,300 more mutations than normal neurons," Associate Professor Rubio said.

Bioinformatician and first author on the paper, Dr Allan Motyer, was involved in the research during his time at the University's Melbourne Integrative Genomics and School of Mathematics and Statistics.

"Not only did we find there are more mutations in MS lesions, but they are also of different types to those seen in normal ageing, indicating a distinct molecular process causes mutations in MS," Dr Motyer said.

Associate Professor Rubio and team are working to build on this important finding and investigate new treatment avenues for progressive MS.

Co-author on the paper, University of Melbourne Honorary and practising neurologist Professor Trevor Kilpatrick, said: "This research is significant because it's the first to show that inflammation could be connected to the death of neurons in MS via accelerated mutation of the genetic code.

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Love, life and MS

With Spring very much in the air, it seems like a good time to look at love, life and MS.

Anyone who has read the statistics will know that MS can be a huge burden on a relationship. Just in case you aren't familiar with the figures they read like this - men with MS have a 21% higher risk of divorce then men without the condition. Paradoxically there is little difference for women with MS. That's according to a Swedish study carried out in 2018.

So, it's a man thing. And as a man who recently separated from his partner of three years, I have undergone a lot of soul searching trying to work out why relationship breakdowns have happened repeatedly to me, a male prog-MSer. It would be easy to go down the role of sexual stereotyping, but diving into easy explanations, or excuses, is sexual stereotyping, and involves an element of blaming the other, so it would be more productive for me to ask what role, either direct or indirect, my illness and how I handle it has played in my relationship break-ups.

It's sadly true that one of the aspects of MS that I have too often been reluctant to explore is the effect it has on mental health. In a provocatively titled 2017 paper 'Should we rebrand multiple sclerosis a dementia?' author Prof. Gavin Giovannoni looked at the mental health effects of what is, after all, a disease affecting the brain.

He said: "Compared to patients with other chronic diseases, such as cancer, patients with MS (pwMS) are twice as likely to be abandoned by their partners. Anxiety and depression are common in pwMS, and personality changes are well described.

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Continued from p10 "These psychiatric manifestations of the disease may explain why MS has a more significant impact on interpersonal relationships than other disabling diseases that don't primarily involve the brain, for example, rheumatoid arthritis and cancer."

Perhaps what Prof. Giovannoni is saying is that MS is always going to be a great challenge to any relationship. My most recent partner used to contribute poems to local magazines and during our relationship many of these poems were about me and my MS, so are quite illustrative.

One poem I have in front of me is titled "Love and MS". In this poem there are frequent references to "a cloud" being present in our relationship". To quote the poem directly: "The cloud defines our lives in everywhere we go. It has a life of its own, MS is its name." And to emphasise the negative influence of MS the poem goes on: "Alone I will face the storm, but you won't be there, tears and rain, like love and pain will be the ones I feel".

One of the paradoxes of progressive MS is that you live with a condition that impacts greatly on your life but because it is always there you don't really notice it on a day to day basis, unless it changes or advances unexpectedly quickly. For a partner of someone who has MS I guess things are quite different. MS is there all the time, like my former partner said, it can be a "cloud" hanging over the relationship.

Last week I caught a glimpse of my reflection in a shop window as I limped through a shopping centre and I was shocked to see how bad my walking has become. Seeing the "real me" was helpful nevertheless because it forced me to accept what my MS really looks like and is like to others close to me. For much of my MS I have subconsciously denied my MS. Basically I have lived a lie.

To live a lie is a psychological strategy fraught with problems for the self- deceiver, but it makes life even more difficult for their partner. The partner can see the struggles that life presents for the person with progressive MS and are doubtless aware of their partner's futile denial strategy. The greatest problem for the partner of the self-deceiving MSer is that they have to live that lie too although they can see through the lie with greater clarity than the self-deceiver.

To quote the poem once again: "The cloud defines our lives in everywhere we go. It has a life of its own, MS is its name". That cloud is the sad reality of my relationship failures. Yes, as my former partner said "MS is its name".

Photo page 10 Aaron Burden on Unsplash

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News

Phase 2 trial of obexelimab recruiting adults with SPMS

A Phase 2 clinical trial is currently recruiting adults with active secondary progressive and relapsing MS to investigate Zenas Biopharma's experimental therapy obexelimab as a weekly under-the-skin injection, the company has announced.

The study, called MoonStone (NCT06564311), is open to adults ages 18 to 60 with active secondary progressive or relapsing remitting MS. Enrolment is ongoing at more than 40 sites across the U.S., Europe, and China, and results are expected later this year.

In MS, inflammation in the brain and spinal cord causes damage to nerve cells, causing problems with normal nerve signalling that ultimately give rise to symptoms of MS. One type of immune cell with a central role in MS inflammation are B-cells. Several approved MS treatments, such as Ocrevus (ocrelizumab), Briumvi (ublituximab), and Kesimpta (ofatumumab), work by depleting B-cells by targeting a protein called CD20.

Obexelimab is designed to reduce the activity of B-cells without depleting them. The therapy specifically targets two B-cell proteins called CD19 and FcgammaRIIb. According to Zenas, the therapy is expected to reduce the activity of a broader range of B-cells than available treatments that target CD20.

"This unique mechanism of action and self-administered, subcutaneous once-weekly injection regimen may broadly and effectively address the [disease-driving] role of B cell lineage in chronic autoimmune disease," the company stated.

About 93 participants will be randomly assigned to receive 250 mg obexelimab or a placebo, given by subcutaneous injections once weekly for 12 weeks (about three months).

After completing the placebo-controlled part of the study, participants will have the option to enter an open-label period where all will receive obexelimab for at least three months. This will be followed by another open-label extension lasting one year.

The trial's main goal is to test whether obexelimab is better than a placebo at reducing the number of new actively inflamed lesions visible on MRI scans. The treatment's effects on other MRI outcomes and markers of nerve damage will also be assessed.

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News

Sacral neuromodulation seen to ease MS bladder problems

Sacral neuromodulation (SNM), in which an implanted device delivers mild electrical pulses to the nerves that control the bladder, led to sustained improvements in urinary function in half of people with MS who underwent surgery to have the device put into place, according to a review of medical records.

Overall, SNM was found to have "sustained efficacy" in easing bladder dysfunction in 51% of the MS patients in the study, with "just over half continuing] to perceive benefit from their therapy over an average follow-up duration of just over 6 years," the researchers wrote. The study, "Sacral neuromodulation outcomes in the management of lower urinary tract symptoms in multiple sclerosis patients," was published in the journal Continence.

SNM, also called sacral nerve stimulation, is a minimally invasive surgical procedure in which a device implanted in the body delivers mild electrical pulses to the sacral nerves. These nerves extend from the base of the spinal cord through the sacrum, the triangular bone at the base of the spine, and then the bladder and bowels. In many patients, SNM has been shown to be effective in managing bowel incontinence.

Little has been detailed, however, about the success of SNM in managing bladder dysfunction in people with MS. To learn more, a team led by U.S. researchers reviewed the medical records of 58 MS patients who sought to undergo the procedure between 2013 and 2022. In total, 49 of the 58 patients (85%) progressed from the preliminary testing phase to IPG implantation, which occurred at a higher rate among those with urinary urgency and frequency than urinary retention (95% vs. 61%). The implantation rate was 56% for patients with detrusor underactivity and 100% for detrusor sphincter dysynergia, but it was similar regardless of preliminary testing methods.

Of the 49 patients who received the IPG implant, SNM continued to be effective in easing bladder dysfunction in half (51%), while the other half reported decreased efficacy over time, the data showed. Still, no factors were found to predict sustained efficacy.

Overall, the team concluded that "SNM is an effective treatment option for LUTS (Lower Urinary Tract Symptoms) associated with MS," though they noted that "many patients will experience declining efficacy as time progresses regardless of indication for implantation."
For details of all news stories see page 14

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Pages 5-6 Could anti-retrovirals treat MS

Details of the Lighthouse trial into MND can be found at https://www.mndassociation.org/research/clinical-trials/treatment-trials/triumeq

Page 7 High fish consumption linked to lower progression

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