

My prog-MS ezine

For people with progressive Multiple Sclerosis

Issue number 19, May/ June 2018

Welcome to issue 19 of my ezine about progressive Multiple Sclerosis and progression. My name is Ian Cook. I have secondary progressive Multiple Sclerosis, and live in the UK.

In this issue are seven pages of news plus two features about issues that matter to people with progressive MS . In news there's a story about an early stage Australian drug which has shown "striking improvements" in those who took it for those with progressive MS and some impressive results from a trial looking at the role an inherited retrovirus plays in MS and its progression.

There are two features. One on pages 4-5 looks at a subject that is probably rarely discussed by your consultant, family doctor or MS nurse – assisted dying The other feature on pages 8 and 9 is more upbeat looking at robotic legs which are now on sale in Canada.

Finally, if there is any story you would like me to follow then I'm at iancookjournalist@yahoo.co.uk

IN THIS ISSUE



Feature

Robotic legs are on their way for MSers

Pages 7-8

'Striking improvements' with new prog-MS drug, p2

The solution to MS problems no-one wants to discuss – p4

New drug shows 'striking improvements' in prog-MS symptoms – better walking, no spasms

Researchers at The University of Queensland in Brisbane, Australia have reported that half of the progressive MS patients in a study of a new treatment called ATA188 had a reversal of several symptoms.

Although only six patients were studied and the study was Phase I, designed only to evaluate the safety of the treatment and identify possible side effects, it was found that MS symptoms improved for three of the six participants, starting only two to eight weeks after the first infusion of the drug.

"One person with secondary progressive MS showed striking improvement," said report author, Michael Pender, MD, PhD, in a press release. "This participant had a significant increase in ambulation from 100 yards with a walker at the start of the study, and over the previous five years, to three quarters of a mile, and was now also able to walk shorter distances with only one-sided assistance. Lower leg spasms that had persisted for 20 years resolved," he said.

The treatment being studied seems, in some ways, similar to the way Lemtrada and Ocrevus attempt to treat MS — by attacking specific cells in the body's immune system. (B cells and T cells).

In the study researchers removed the participants' own T-cells and then stimulated them to boost their ability to recognize and destroy cells infected with the Epstein-Barr virus. The researchers then injected participants with infusions of their modified T-cells every two weeks for six weeks. The patients were then followed for the next 26 weeks. The researchers hope that by eliminating the EBV-infected B-cells they may be able to reduce the destruction of myelin that occurs in MS.

"The best responses were seen in the two people who received T-cells with the highest amount of reactivity to the Epstein-Barr virus," Pender said. "The results add to the mounting evidence for a role of the Epstein-Barr virus infection in MS and set the stage for further clinical trials."

Details of all stories on p13

Retrovirus drug may provide new treatment option for neuro-degeneration in progressive MS

Results from the CHANGE-MS phase 2b study of an experimental drug GNbAC1 have shown it has a significant, consistent positive impact on key neuroprotective markers known to be linked to MS disease progression.

GNbAC1 is a monoclonal antibody designed to neutralise a pathogenic protein encoded by a member of the Human endogenous retroviruses (HERV-W) family. HERVs are ancestral, retroviral DNA insertions in the human genome, thought to account for up to 8% of the total DNA. The HERV-W protein is thought to be a factor in the development of multiple sclerosis (MS), as well as Type 1 diabetes and Chronic inflammatory demyelinating polyneuropathy.

270 patients took part in the study, which was conducted in 12 European countries. MRI scans showed a coherent neuroprotective benefit on brain shrinkage. Benefits were seen in shrinkage of the cortical and thalamic areas of the brain, with relative volume loss reductions of 31% and 72% respectively between the highest dose of 18 mg/kg and the control group, demonstrating a statistically significant dose-relationship ie: the higher the dose the less brain shrinkage.

This is the first time that the benefits of a treatment targeting endogenous (inherited) retrovirus protein has been shown in a clinical trial and is a real step forward for this theory about the cause of MS.

Prof Hans-Peter Hartung, chairman of the Department of Neurology of the University Hospital Düsseldorf and Lead Investigator of the study said: “What is impressive is the consistency of the effect already observed at one year across all these key markers of neurodegeneration, and that this effect appears to be independent from an anti-inflammatory action.”

“These positive effects are very promising and may open new doors towards addressing the key unmet medical need of disease progression in MS,” he added.

Achieving these positive Phase 2b results through the neutralisation of pathogenic HERV-W protein supports its causal role in the neurodegenerative mechanisms of MS. GNbAC1 may provide a safe treatment option against neurodegeneration unrelated to inflammation in all forms of the disease, a major objective that is not addressed by currently available MS treatments. **For further details of all news stories go to page 13**



The “solution” to MS problems none of us wants to talk about

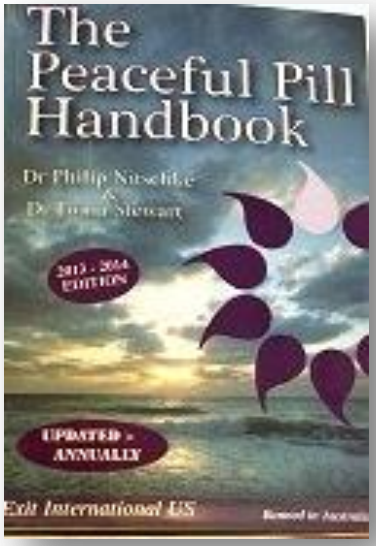
It is probably one of the most difficult problems people with progressive MS face. The problem can be summed up in two words - “the end” or “assisted suicide” to use the technical term, and the difficulty lies in the fact there are huge political and practical issues to consider.

From personal experience I know that as MS progresses you become less mobile and prone to more MS related problems. Your life inevitably becomes less enjoyable and on occasions you ask yourself – is it worth it? Even if your life is OK you ask yourself: “ will there come a point when it isn’t OK?” I am 60 next year and ten years ago I could do far more than I can do now, so what will things be like in ten years’ time when I am 70? Will there be a point where I can do so little that I want to end it all?

The subject of assisted suicide is one that has vexed not just individuals like me but also courts and parliamentarians. Parliament has considered various attempts to change the law but successive bills have failed to make it on to the statute book. The courts have considered whether assisted suicide should be allowed under human rights legislation. In law, suicide is legal, but it is illegal to assist someone to commit suicide.

It has been argued this creates an injustice because severely disabled people need assistance to do virtually anything, even get out of bed. It follows therefore they need assistance to commit suicide and it has been argued denying them this assistance is denying them the same human rights as able bodied people. This argument has never been accepted by courts.

In spite of this, the subject refuses to go away. Various cases have been heard arguing that UK laws banning assisted dying are incompatible with the European Convention on Human Rights, which guarantees a right to respect for private life and personal autonomy. And while UK legislators routinely vote down private members’ bills on the subject a growing number of other countries most notably Switzerland take a very different view **Continued on page 5**



Continued from page 4.

As well as having a political and international dimension assisted suicide has a personal dimension for me. A few years ago a friend who had been diagnosed with MS at the same time as me started to go downhill alarmingly quickly. He was suddenly in a nursing home and then one day, in a dreadful state, he asked me if I would kill him.

He pointed to a plastic bag at the end of his bed and asked me to asphyxiate him. I was utterly shocked, and upset and I said I wouldn't do it. Six months later his rapidly advancing MS took his life. But looking back I wonder if my refusal merely prolonged the misery of a wretched existence.

Knowing that death comes to us all and that as MSers it tends to come earlier than for others I thought I would do a little research on how as a disabled person you can end your life in way that is quick, effective and as free from pain as possible. I stress this is just academic research. I just want to know what my options are so I decided to look at the group EXIT.

The group's website revealed that annual membership was $100 Aus (£60) but when I phoned a man on the helpline he advised me a cheaper option was to buy a second hand copy of an EXIT handbook on ebay called the "Peaceful Pill handbook" (pictured above) for about £10 and it would tell me all I needed to know.

And that is exactly what I did. I now have "The Peaceful Pill Handbook" published by EXIT which goes through a variety of suicide options from the peaceful or suicide pill to carbon monoxide, and various gases such as nitrogen and helium. Combinations of methods are explored and each method is rated for its ease of use, reliability, speed, availability and various other criteria.

I would stress I am not planning to depart in a hurry but I want to be sure I have considered all the options when my MS progresses further and those options include that of taking my own life if it becomes no longer worth living. This may sound morbid but in reality it isn't.

Paradoxically I believe my newly acquired knowledge of how to end my own life means I'm less likely to end it because it puts me back in control. In one area of my life I now have all the answers, and I find that a comforting thought. If only everything in MS was so simple.

For more details of all news and features go to page 13

Further proof of asthma drug Ibudilast's role in slowing brain shrink in progressive MS

New evidence from a Phase 2b trial of a licensed asthma drug ibudilast in treating progressive MS shows the drug leads to an even more significant reduction of brain atrophy in progressive MS than previously thought.

Results of the trial shared at the 2018 Annual Meeting of the American Academy of Neurology, in a presentation titled "A Phase II Trial of Ibudilast in Progressive Multiple Sclerosis", showed that treatment with ibudilast was associated with a reduction in the speed of brain atrophy progression by 48 percent as measured by the "brain parenchymal fraction".

The brain's "parenchyma" refers to brain tissue made up of the two types of cells - neurons and glial cells so this measure is probably of more value in MS research than measuring whole brain volume which is more commonly used in trials.

The Phase 2 SPRINT-MS trial (NCT01982942), looked at the effectiveness, of ibudilast in progressive MS patients. Conducted at 28 centres across the U.S., the trial randomized 255 patients with primary or secondary progressive MS, with evidence of disability progression in the two years prior to enrollment, and starting treatment with ibudilast or a placebo.

Ibudilast was delivered in daily doses up to 100 mg for 96 weeks . Clinical and imaging outcomes were assessed every 24 weeks (5.5 months).The study's primary objective was to evaluate changes in brain shrinkage over the treatment period, using parenchymal fraction.

Results showed that treatment with ibudilast was associated with a significant reduction in the rate of brain atrophy progression — by 48 percent — as measured by the brain parenchymal fraction.

These results support further investigation of ibudilast as a potential treatment for progressive MS, the team concluded.

More details of all news stories on page 13

Siponimod may delay progression in SPMS – but effects may only be small

A study of Siponimod, a new drug to treat progressive multiple sclerosis, suggests it may be possible to delay progression of the disease in the short term, although the effects may only be small.

In a trial of 1,327 people, published in The Lancet, 26% saw their disability worsen after three months taking siponimod compared with 32% taking a dummy drug(a difference of 21%). Patients in the trial, which was funded by drug company Novartis, had had MS for an average of 17 years – an average of four years with secondary progressive MS, Most needed assistance with walking before the trial began.

When standard measures of disability were used to track their progress, there was a 21% lower risk of walking or arm movements getting worse for those given the drug, compared with those taking the placebo. But the international research team found the drug had no effect on maintaining patients' walking speed.

Lead author Prof Ludwig Kappos, from the University of Basel, said: "Although the results are not as good as we wanted to see, it is a very large study, which is robust. It means siponimod is one option to delay the disease in the advanced stage."

Dr Susan Kohlhaas, director of research at the MS Society, said: "This trial showed that siponimod had a modest but significant effect in slowing disability progression, which is incredibly encouraging." But Dr Luanne Metz, from the University of Calgary, in Canada, said a second trial was needed to confirm the benefits of the drug and its impact beyond three to six months. She said: "Although siponimod seems to reduce the time to confirmed disability in secondary-progressive MS, the treatment effect was small.

Before the drug becomes available on the NHS, it would need to be approved by the European Medicines Agency and then recommended as cost-effective by NICE in the UK but given there are few treatment options for secondary progressive MS this seems likely. If siponimod passes these tests is could be available on the NHS towards the end of 2019 at the earliest.

For further details of all news stories go to page 1



Exoskeletons are rapidly becoming an alternative to wheelchairs for prog - MSers

Walking devices such as "exoskeletons" are fast becoming an alternative to wheelchairs for MSers and others with walking problems.

One disabled woman used an exoskeleton to take part in the Great North Run last year and at least one exoskeleton is used by an NHS Trust in Britain. Yhings are starting to move elsewhere in the UK .

However, the speed of change is faster in North America particularly in Canada where there was recent news of a Canadian firm, B-Temia, opening clinics to train people to use its walking assistance device. B-Temia announced the launch of its "b-Klinic Mobility" business unit, offering clinical services, information, training, and ongoing support to patients and healthcare professionals who use the company's Keeogo walking assistive device (pictured).

The company, based in Quebec, opened its first b-Klinic Mobility clinic in Quebec City, and additional ones are scheduled to open in Montreal and Toronto. Staffed by certified kinesiologists and applied engineers, the clinics will offer a range of services designed to train and support Keeogo users and healthcare workers in using the device to help them take full advantage of its features. Clinic kinesiologists will meet with patients to evaluate if Keeogo is of benefit, assess their walking gait, and explain how Keeogo might help them regain personal autonomy. Training sessions are provided for home users, covering issues like how to put the device on, how to use it best, and how to care for it.

Continued on p9



The Keego walking assistance device has a wide range of uses outside and indoors

Continued from page 8 : " The b-Klinic Mobility service will also offer clinicians education and information about Keeogo and related topics, in-service presentations, and training sessions on identifying patients who could benefit from Keeogo, and configuring the device's support software to optimally match a patient's gait and muscular strength.

Keeogo utilizes sensors at the knee and hip joints to read a person's body position and desired movement, and to provide the needed assistance to help complete that action. Keeogo does not initiate movement, but waits for the wearer's lead and first indication, then assists in executing it — like pushing up when the wearer begins to stand up, or slowly supporting a person who is starting to sit down. Keeogo's adjustable motorized power complements its wearers' own muscle strength to manage body movements naturally and more effectively, while offering stability and security, the company reports.

Keeogo is B-Temia's first product in the class of exoskeletons, designed to assist persons with mobility-related problems such as walking, climbing or descending stairs, sitting down, or standing up. Commercially available for purchase at around CAN $20,000 (£11,400) or rental at CAN $1,500 (£850) for 12 months in Canada, Keeogo is under investigation in a multicenter clinical trial (NCT02904382) aimed at obtaining the U.S. Food and Drug Administration (FDA) clearance needed to enter the U.S. market.

For details of all news stories and features go to page 13

Umbilical cord stem cell treatment has sustained benefit in progressive MS

Treatment with umbilical cord stem cells led to sustained improvements in disability and brain lesions in 20 MS patients, five of whom had progressive MS, four of the five had primary progressive MS and one secondary progressive MS .

The study, "Clinical feasibility of umbilical cord tissue-derived mesenchymal stem cells in the treatment of multiple sclerosis," was published in the Journal of Translational Medicine. Mesenchymal stem cells (MSCs) are adult stem cells found in multiple tissues, such as umbilical cord, bone marrow, and fat. These cells are able to mature into bone, cartilage, muscle, and fat tissue cells. Recent results with placenta or umbilical cord MSCs showed improvements in patients' level of disability.

The current trial, carried out in Panama included 20 MS patients with an average age of 41, 60 percent of whom were women. Fifteen participants had relapsing-remitting MS, four had primary progressive MS, and one had secondary progressive MS. Patients' disease duration was an average of 7.7 years.

Participants received seven intravenous infusions of umbilical cord MSCs over seven days. The treatment's effectiveness was evaluated at the start, at one month, and at one year after treatment.

Improvements were most evident at one month after treatment, namely in the level of disability, non-dominant hand function, and average walk time, as well as bladder, bowel, and sexual dysfunction. Patients also reported improved quality of life. MRI scans at one year after treatment revealed inactive lesions in 15 of 18 evaluated patients. One patient showed almost complete elimination of lesions in the brain, which "is a particularly encouraging finding," the researchers wrote. After a year improvements in disability levels were also still present, and could translate into improved ability to walk and work without assistance**.**

For details of all news stories go to page 13

Targeting Blood-clotting Protein Can Restore Brain's Potential to Repair Myelin Layer, Study Shows

A blood-clotting protein called fibrinogen prevents myelin production and blocks the neuron remyelination repair process in mice.

That's the finding of a study, "Fibrinogen Activates BMP Signaling in Oligodendrocyte Progenitor Cells and Inhibits Remyelination after Vascular Damage," which appeared in the journal Neuron. Its conclusions offer new insights and open new therapeutic avenues for treating MS

Attempting to add new insights, a research team led by Katerina Akassoglou, senior investigator at Gladstone Institutes and professor of neurology at the University of California, San Francisco (UCSF), tested if the blood-clotting protein fibrinogen could be involved in MS.

"We realized that targeting the blood protein fibrinogen could open up the possibility for new types of therapies to promote brain repair." Akassoglou said in a press release. In a previous study, the UCSF research team showed that when fibrinogen crosses the brain-blood barrier it can induce autoimmune responses in the brain, similar to those involved in MS. In this new study, the team revealed that fibrinogen can also trigger signals that block development of oligodendrocytes, the cells that produce myelin. This not only stops myelin production but also prevents the brain from repairing and rebuilding the protective myelin layer that is destroyed during the autoimmune-inflammatory process.

Inhibition of fibrinogen signals in experimental cells and mice models showed it is possible to reverse the adverse effects of the protein and promote remyelination. These results further support the pursuit of strategies targeting fibrinogen to boost the brain's regenerative potential.

"Repairing myelin by eliminating the toxic effects of vascular damage in the brain is a new frontier in disease therapeutics," said Dr. Lennart Mucke, director of the Gladstone Institute of Neurological Disease and professor of neurology at UCSF. "This study could change the way we think about how to repair the brain."

For details of all news stories go to page 13

Trial starts for new MS walking drug – results are expected next year

The first participant has enrolled on a Phase 3 trial testing an once-a-day — ADS-5102 (amantadine) extended release tablet — in MS patients who have walking difficulties.

The multi-centre, double-blind study (NCT03436199) will assess ADS-5102 in 570 US patients, half of who will take a dummy pill or placebo. Effectiveness will measured using the timed 25-foot walk (T25FW) test and in the 2-Minute Walk Test (2MWT).

Amantadine extended release capsules, marketed by Adamas under the trade name Gocovri, were approved by the U.S. Food and Drug Administration in August 2017 to treat the uncontrolled jerky movements that affect Parkinson's patients on levodopa-based therapy so licensing the drug for MS should present relatively few problems as the drug's safety profile is already known . The trial is set to conclude in September 2019.

Researchers will test the efficacy of two doses, 274 mg or 137 mg, of ADS-5102 given at bedtime against each other and against a placebo. Effectiveness will be analyzed as a primary goal using the timed 25-foot walk (T25FW) test — a measure of mobility and leg function — at week 12. Changes in the Timed Up and Go (TUG) test — a measure of mobility — and in the 2-Minute Walk Test (2MWT) will also be assessed.

The multi-center, double-blind study (NCT03436199) will assess ADS-5102 in about 570 such patients at five sites across the U.S. Eligible patients are being recruited at sites in Colorado, Georgia, New York, North Carolina and Washington.

In an earlier phase II trial ADS-5102 significantly improved T25FW scores in patients by 16.6 percent, and led to at least a 20 percent improvement in walking speed compared to placebo.

"Initiating this Phase 3 study of ADS-5102 in MS patients with walking impairment is a significant milestone for Adamas, as it could potentially advance the approval of Gocovri (amantadine) extended release capsules as a treatment for this MS population," Rajiv Patni, chief medical officer at Adamas, said in a press release.

"The goal of the study is to confirm the results of our Phase 2 proof-of-concept study and to demonstrate the efficacy and safety of ADS-5102 using several measures of walking in MS patients," Patni added.

For details of all stories go to page 13

References

Page 2

ATA 188 story

Source: https://multiplesclerosisnewstoday.com/2017/04/28/small-study-shows-unexpected-reversal-of-some-ms-symptoms/#at_pco=tst-1.0&at_si=5accbf8923fb7fc9&at_ab=per-2&at_pos=0&at_tot=2

Page 3 MS retrovirus story

Source: http://www.ms-uk.org/gnbac1-may-provide-safe-treatment-option-against-neurodegeneration-ms

Page 4 Assisted dying feature

Sources: https://exitinternational.net/

Page 6 Ibudilast story

Source: https://multiplesclerosisnewstoday.com/2018/04/19/aan2018-ibudilast-slows-brain-atrophy-progressive-multiple-sclerosis-phase-2-trial/??utm_medium=desktop-push-notification&utm_source=Notifications&utm_campaign=OneSignal

page 7 siponimod story

Source http://www.bbc.co.uk/news/health-43502845

Page 8-9 Exoskeletons

Sources

Sources: https://multiplesclerosisnewstoday.com/2016/11/10/b-temia-opens-clinics-in-canada-to-train-and-support-keeogo-walking-assistance-users#at_pco=tst-1.0&at_si=5ab025389117996d&at_ab=per-2&at_pos=0&at_tot=2

https://keeogo.com/about-keeogo/what-is-keeogo

Page 10 stem cell story

Source: https://multiplesclerosisnewstoday.com/2018/03/20/umbilical-cord-stem-cell-ms-treatment-safe-effective-clinical-trial/?utm_medium=desktop-push-notification&utm_source=Notifications&utm_campaign=OneSignal

Page 11 Fibrinogen story

Source: https://multiplesclerosisnewstoday.com/2017/11/07/ms-patients-could-benefit-from-fibrinogen-protein-that-restores-brain-potential-to-repair-myelin-layer/2/

Page 12 MS walking drug

Source: Source: https://multiplesclerosisnewstoday.com/2018/04/05/first-ms-patient-enrolls-in-phase-3-trial-gocovri-amantadine-for-walking-ability-adamas-announces/?utm_medium=desktop-push-notification&utm_source=Notifications&utm_campaign=OneSignal

In the next (July/August) edition **My journey to find out about mobility scooters – class 2 or class 3? To buy or to rent?**	

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