Drug shown to improve sight for patients with inherited blindness

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A clinical trial led by Newcastle University shows that the drug, idebenone (Catena), improved the vision and perception of colour in patients with Leber's Hereditary Optic Neuropathy (LHON). The inherited condition means patients, who can see normally, lose the sight in one eye then within 3 to 6 months lose the sight in their other eye.

In some severely affected patients such as those who were unable to read any letters on the chart, the treatment with idebenone resulted in a marked improvement in their vision. In nine patients (12 eyes) out of 36 patients (61 eyes) taking idebenone, vision improved to the extent that patients were able to read at least one row of letters on the chart. In contrast not a single patient of the 26 who were taking the placebo improved to that extent.

Inherited from the mother, and mainly affecting men, LHON is caused by damage to the mitochondria in the eyes – the 'batteries' which power their cells. It is one of the most common causes of inherited blindness and is thought to affect around 2,000 people in the UK, around 10,000 in Europe and a further 10,000 in the USA.

"This is the first proven treatment for a mitochondrial disorder. We have seen patients who couldn't even see an eye chart on the wall go on to read the first line down – and some even attempted the second line. For these patients, it can mean a vast improvement in their quality of life," said Professor Patrick Chinnery, a Wellcome Trust Senior Fellow in Clinical Science at Newcastle University who also works at the Royal

Victoria Infirmary in Newcastle – part of the Newcastle upon Tyne Hospitals NHS Foundation Trust.

Released today in the journal *Brain* published by Oxford University Press, the authors describe how patients with LHON were recruited from Newcastle Hospitals in the UK, in Munich, Germany and in Montreal, Canada for a double blind trial. Patients were either given idebenone for 24 weeks or a placebo.

At the end of the six months, some patients who were taking idebenone had improved vision and this is the first time a successful treatment has been found. The greatest improvement was seen in patients who had deteriorated in one eye more than the other.

Professor Chinnery explained: "We saw most progress in people who had better vision in one eye than the other - this tends to indicate that they are at an earlier stage of the condition. While we know that their vision is not what it once was, we also know that this treatment can dramatically improve their lives – some were able to move around more easily or even see family photos again."

Idebenone penetrates into the mitochondria and is thought to mop-up toxic free radicals and enhance mitochondrial function. Previous research had provided anecdotal reports of improvements in vision but this is the first time it had been put to the test in a clinical trial. The drug company which sponsored this trial, Santhera Pharmaceuticals, is now seeking marketing approval from the European Medicines Agency for it to be offered as a standard form of treatment.

"We are hearing from patients that they still have improved vision – even though they are no longer taking the drug but we would like to verify this and study the effect further," said Professor Chinnery. "There may also be a case for offering idebenone from the first moment that

LHON is diagnosed – preferably before any symptoms are shown - and a further trial would ideally examine this."

"I lost the sight in my left eye in just five days"

Mike Scholes, 58 from Lindfield in West Sussex, UK and a graduate of Newcastle University took part in the trial. He said: "I was training for a freefall parachute jump five years ago when I noticed I was having problems with my eye. I went for an eye test at the optician and on the way to pick up my glasses five days later, I nearly crashed the car. The optician tested my right eye and there was no problem, when he came to the left eye I asked him to switch on the machine – and he said he already had. I had lost the sight in my left eye in just five days.

"This meant an abrupt change in my life - I had a very successful hot air balloon business and I had to stop flying. I had to sell my cars as I could no longer drive.

"Following seven months of tests including CAT scans, X-Rays, MRI scans and a lumbar puncture, I was finally given a DNA test which revealed I had Leber's hereditary optic neuropathy.

"It was around this time that my vision started to go in my second eye. I couldn't see in an increasingly large area in the centre of my eyes and gradually colours disappeared. At worst the only colours I could make out were shades of blue.

"Soon after friends spotted a clinical trial in Newcastle, I volunteered to take part and started taking the tablets three times a day – not knowing whether I was taking a placebo or the drug.

"After just a month and a half I noticed that the area affected in the centre of my vision was smaller. The improvement continued and I

began to appreciate colours again seeing yellow and most reds.

"Having Leber's hasn't stopped me enjoying life to the full - I run marathons with a guide, I've hiked to the North pole - but the noticeable improvement in my vision means daily life is easier. I can use a computerised viewer to help me read, I can get dressed without having to use a detector for the colours of clothes and while initially I couldn't even see the eye chart, now if I get really close to a street sign I can read it."

More information: A randomized placebo-controlled trial of idebenone in Leber's hereditary optic neuropathy, Thomas Klopstock, Patrick Yu-Wai-Man, Konstantinos Dimitriadis, Jacinthe Rouleau, Suzette Heck, Maura Bailie, Alaa Atawan, Sandip Chattopadhyay, Marion Schubert, Aylin Garip, Marcus Kernt, Diana Petraki, Christian Rummey, Mika Leinonen, Günther Metz, Philip G Griffiths, Thomas Meier and Patrick F Chinnery. *Brain* 2011-00800.

For interested patients, further information can be seen here: www.ncl.ac.uk/press.office/press.release/lhon.htm

Provided by Newcastle University