# Simvastatin does not slow progression of Parkinson's disease, should not be investigated further as therapy

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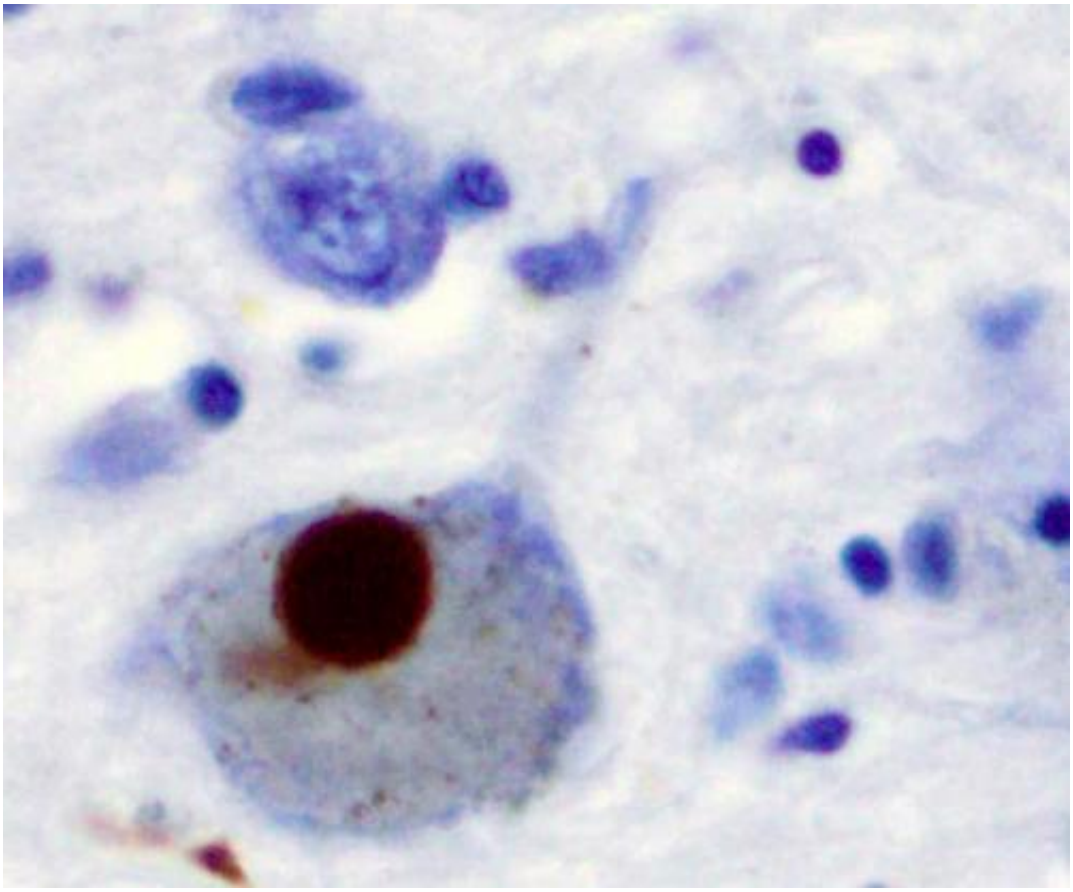

Immunohistochemistry for alpha-synuclein showing positive staining (brown) of an intraneural Lewy-body in the Substantia nigra in Parkinson's disease. Credit: Wikipedia

A major clinical trial of a potential new treatment for Parkinson's disease (PD) has found that the statin under investigation holds no promise as a protective therapy in PD.

PD-STAT has been running since 2016, and at its start was the largest academic study in the UK investigating neuroprotective drugs in PD.

It examined whether simvastatin, a widely-used cholesterol-lowering drug, had the potential to reduce the rate of neurodegenerative decline in patients with PD of moderate severity.

The study has now provided robust evidence that simvastatin, in comparison with a placebo, was "futile" in slowing the rate of progression of Parkinson's disease and that a phase III trial should not be recommended. A futility study is designed to test a new treatment over a relatively short period to determine whether it is worthy of larger and longer-term studies or should be abandoned.

PD-STAT was led by Dr. Camille Carroll, Associate Professor in the University of Plymouth's Faculty of Health and Honorary Consultant Neurologist at University Hospitals Plymouth NHS Trust (UHP). It was managed by the Peninsula Clinical Trials Unit (PenCTU), part of the University's Faculty of Health, and sponsored by UHP.

Dr. Carroll said, "Although the result of PD-STAT did not show that simvastatin has promise as a protective therapy in Parkinson's, it is very helpful to be able to present robust data and a definitive answer on this important question. There are lots of positives to come out of this study, particularly the extent to which we were able to involve participants across the country, and the very positive feedback received from them and staff in the hospitals involved. PD-STAT has taught us a huge amount about how to improve the way we design and deliver clinical trials in Parkinson's and this knowledge will be very useful in designing

future trials."

Parkinson's disease (PD) is a progressive neurodegenerative condition affecting more than 145,000 people in the UK. No drug has been shown to slow, stop or reverse the neurodegenerative process of PD, and most treatments act to relieve symptoms, with a limited lifespan of effectiveness.

Statin use has been associated with lower PD incidence, and in toxin and genetic cell culture and animal model studies has been shown to influence several pathways thought to be relevant to PD pathogenesis. Simvastatin has also been shown to reduce the rate of brain atrophy in people with secondary progressive multiple sclerosis.

For these reasons, the drug was identified as worthy of investigation by The Cure Parkinson's Trust's International Linked Clinical Trial Initiative. The initiative identifies compounds that have biochemical potential to slow, stop or reverse PD to bring into clinical trials.

PD-STAT was conducted at 23 hospitals across England, with 235 participants recruited, who attended up to eight study visits at their local hospital over 26 months, interspersed with regular phone calls from research nurses. The participants were randomized to receive either simvastatin or a placebo (dummy drug) for 24 months, followed by a final study visit at 26 months.

Dr. Richard Wyse, director of research and development at The Cure Parkinson's Trust, said, "Given the strength of pre-clinical evidence, and the progress with simvastatin already being made in MS, this is a disappointing result. However, we now have a definitive answer, and that enables us to move forward to test a number of other drugs of interest, many of which have been used to treat other diseases, and all of which we have determined have compelling evidence they each have the

potential to modify Parkinson's progression. This has been an important trial as we have not only tested a study medication and evaluated novel outcomes, but we have also used this as an opportunity to understand the impact of involvement in clinical trials on participants and their loved ones. As a result of this trial we now have motivated an active network of researchers who are keen to participate in running future studies of drugs of interest, evaluated and prioritized through the International Linked Clinical Trials process."

Helen Matthews, Deputy CEO of The Cure Parkinson's Trust, added,

"This trial reached its conclusion thanks to the dedicated participants and network of committed study centers across the country. A huge thank you must go to the participants who not only contributed to this trial but also to the numerous sub-studies that have been part of this wider project. The commitment of participants enables us to secure the definitive answers needed in Parkinson's trials and we cannot undertake this research without them."

Katherine Bewsey, one of the trial participants, said, "Taking part in this trial was very easy, all the people I dealt with were pleasant and keen to make sure I was always comfortable. I also received a few extra check-ups as a result of taking part, which was a plus. The only way we'll find out more about which drugs are effective is to do these trials—someone has to be willing to take part, and it really is for everyone's benefit. At any rate, this is a drug that is well known and already taken by many, although for different illnesses. It's the people trialing new classes of drugs that are the brave ones. All in all, I'd be very happy to recommend taking part in a similar trial to other people."

Dr. Pauline McGlone, chief operating officer of NIHR Clinical Research Network South West Peninsula, praised the research team for the way in which it had dealt with the coronavirus outbreak. She said, "I

am delighted to see research activity continuing despite the challenges the COVID-19 pandemic has presented research teams. It's particularly encouraging to hear of the creative solutions the team quickly devised to ensure the study data collection continued. Innovations such as converting to a remote assessment process, including video motor assessments for sites across the country show the flexibility and extra effort teams are going to ensure that the study continued and was not delayed by the pandemic."

Provided by University of Plymouth