Research news January 2025

This document aims to clarify the complex world of medical research. There are two prerequisites for this document: the first is a basic understanding of Parkinson's disease. The second is to have a view of how a scientific discovery translates to innovation in medical treatment

Parkinson's basics

Parkinson's disease is a degenerative neurological condition where dopamine-producing brain cells are damaged or destroyed. Current treatments, like dopamine replacement therapy (levodopa, dopamine agonists) and surgical interventions such as brain stimulation, do not halt disease progression. However, new drugs that may slow the disease are nearing regulatory approval. Additionally, stem cell therapy shows promise in repairing and replacing damaged nerve cells.

The journey from Scientific Discovery to clinical treatment

Why Basic Medical Science is important

Medical history contains numerous examples of how basic scientific discovery underpins and enables medical treatment. The gold standard treatment for Parkinson's disease is levodopa, which was developed based on the discovery that post-mortem examination of individuals with Parkinson's showed a loss of dopamine-producing neurons in a part of the brain called the substantia nigra. In the 1960s, the biochemical processes leading to the destruction of these brain cells were not understood. Currently, some of these biological mysteries are being unravelled, leading to the development of new drugs with the potential to slow disease progression.

How do new scientific discoveries lead to new drugs and new treatments

Description	
Biomedical Basic Science	New scientific discovery
	Identification of possible therapeutic target
Phase 1	Small scale Clinical trial to establish safety
Phase 2	Intermediate scale clinical trial to establish safety in a larger group,
Phase 3	Large scale Clinical trial Usually multicentre to assess Benefit and potential side-effects
Reglators	Treatment is assessed by regulators In the NHS For treatment effectiveness and cost-effectiveness
Available for use	Treatment is available for use in the NHS

The journey from scientific discovery to clinical treatment requires significant time. Similar to constructing a building, it is essential to have a strong foundation before advancing to more complex stages. Medical treatments undergo a complex regulatory process to ensure patient safety. Once a scientific discovery is made, a potential treatment must pass through rigorous clinical trials and be assessed by regulatory authorities. In the UK, this is particularly important as treatment is free to the public at the point of delivery. Therefore, a regulatory process evaluates the clinical and cost-effectiveness of a treatment before it becomes available for use in the NHS. A description of the trial process is provided in the colour-coded box, utilizing a red-amber-green grading system to indicate the progress of a particular treatment through this process.

Important notes

- This document is intended to provide insights into the latest advancements in Parkinson's disease treatment and the medical research process. It is not a substitute for professional medical advice. For personalized treatment options, please consult your neurological healthcare team
- This document does not cover the causes of Parkinson's. Future versions may include this based on feedback.

Disease modifying drugs

GLP-1 Agonists exenatide lixisenetide

This class of drugs was initially developed for the treatment of diabetes and weight management. They are thought to potentially impact Parkinson's disease by mitigating cellular damage associated with the condition. These drugs do not have any relation to levodopa or dopamine but may influence disease progression.
The initial compounds that progressed through phase 1 safety trials included exenatide and lixisenatide. In 2017, exenatide underwent a phase 2 study which showed significant benefits compared to a placebo in terms of Parkinson's symptoms over time. The phase 2 study of lixisenatide also indicated similar benefits, particularly among individuals under 60 years of age. However, a subsequent phase 3 multicentre study conducted in the UK did not meet its primary endpoint, making it impossible to draw definitive conclusions about its efficacy. Further phase 3 trials are anticipated to publish results in 2025.

Ambroxyl

This small molecule inhibits an enzyme called G-Case, which is linked to cell damage in Parkinson's disease. Ambroxol, already used in Europe for respiratory symptoms like cough, requires a higher dose to be effective for Parkinson's. It is about to enter a multicentre phase 3 clinical trial in the UK.

Azathioprine

AZA-PD is a phase 2 study investigating the effects of azathioprine in individuals with Parkinson's disease (PD). Azathioprine is a potent immunosuppressant, believed to suppress brain inflammation associated with the release of toxic chemicals from cells affected by Parkinson's. Results are expected in 2025.

I need to be on my way

DAPA – PD is a phase 2 clinical trial investigating dapansutrile's effects on the NLRP3 inflammasome in Parkinson’s disease (PD). This inflammasome plays a critical role in the inflammation damaging brain cells in PD. Recruitment begins in 2025.

Symptom Control Drugs

Produodopa (foscarbidopa foslevodopa)

This is a form of dopamine replacement therapy administered as a continuous subcutaneous infusion. It has completed phase 3 trials and is currently in the process of being implemented throughout the NHS. It is intended for individuals with advanced

symptoms of Parkinson's disease, where significant on-off phenomena cannot be managed with tablet dopamine replacement therapy.

A-Dopamine

In Brain Pharma take a similar approach with continuous infusion, however they use A-Dopamine given direct into the brain. They are in phase 1 clinical trials

Surgical Intervention

Adaptive Deep Brain Stimulation

This refines the existing deep brain stimulation procedure. Conventional deep brain stimulation uses fixed output electrodes to disrupt circuits causing tremors or dyskinesia. Adaptive brain stimulation is different as it continuously monitors the disrupted circuits, allowing for auto-tuning.

Stem Cell Treatment

Major biotechnology companies are starting phase 3 trials for implanting stem cells into the brain. Results will take years as these cells need time to integrate. Stem cell therapy does not address the initial cause of cell death, and due to Parkinson's slow progression, it will take decades to see if new brain cells resist the disease.