Parkinson's Update:
Therapies targeted at augmenting striatal dopamine, the old and the new

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Article by Chris Brearley

The US Food and Drug Administration (FDA) has given fast track designation to BlueRock Therapeutics' (a subsidiary of Bayer AG) investigational cell therapy DA01 which is in a clinical trial in people with advanced Parkinson's disease. FDA's fast track status aims to accelerate a therapy's development and expedite its approval by enabling more frequent meetings and discussion with the FDA regarding the clinical development plan.

Parkinson's disease is a progressive neurodegenerative disorder characterised by worsening motor and non-motor symptoms caused by the loss of dopamine-producing neurons in key areas of the brain. At diagnosis, it is estimated that patients have already lost 60-80% of their dopaminergic neurons. Symptoms include tremor, rigidity, cramping and dyskinesias. Parkinson's disease is the second most common neurodegenerative disorder, affecting more than 7.5 million people worldwide.

DA01 is an engineered dopaminergic neural cell therapy derived from pluripotent stem cells which is expected to increase dopamine levels in the putamen. In the DA01 study (NCT04802733), up to 10 people with advanced Parkinson's disease are being enrolled into a study where DA01 will be surgically implanted into the putamen whilst under general anaesthesia.

In another recent announcement, the Hong Kong-based Forest Hills Lab announced that the FDA have given permission to open a 52-week Phase 2 trial into the tolerability and potential efficacy of FHL-301 in people in the early stages of Parkinson's disease. Forest Hills Lab are repurposing the peroxisome proliferator-activated receptor alpha (PPARα) agonist FHL-301 for use in Parkinson's disease. Once activated, PPARα binds to specific DNA peroxisome proliferator response elements located in the promotor region for the target gene glial derived neurotropic factor (GDNF), turning on GDNF production to support the differentiation, growth and survival of the dopaminergic neurons that are continually lost in Parkinson's disease. Pre-clinical proof of concept data in animal models are said to show that FHL-301 was able to activate the GDNF gene and slow or reverse progression of Parkinson's disease in animal models.

Nearly 20 years ago, Amgen controversially decided to halt clinical trials with their recombinant GDNF in Parkinson's disease, which was given using direct bilateral putaminal infusion of GDNF through programmable pumps. GDNF seemed promising as a treatment for Parkinson's disease in animal studies and a small open-label trial but did not deliver benefits in a 34-patient randomised controlled trial. It will certainly be interesting to see the outcome of these 2 approaches to augmenting striatal dopamine levels for the treatment of Parkinson's disease.

References

1. https://parkinsonsnewstoday.com/2021/07/21/fda-fast-track-da01-a-cell-therapy-advanced-parkinsons/

2. https://www.einnews.com/pr_news/546323892/fhl-announces-phase-2-clinical-trial-for-parkinson-s-drug-korean-medical-device-company-acquisition-and-saudi-jv

3. https://journals.lww.com/neurotodayonline/Fulltext/2005/04000/AMGEN_DECISION_TO_HALT_GDNF_CLINICAL_TRIALS_AND.4.aspx

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