NTCELL® (immunoprotected [alginate-encapsulated] porcine choroid plexus cells for xenotransplantation) in patients with Parkinson’s disease (PD): 26 weeks follow-up

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Background

NTCELL® comprises of neonatal porcine choroid plexus cells encapsulated in alginate microgels. The Auckland Islandbank, which was the source of the choroid plexus, is an island with no chickens for screening and for pathogens. NTCELL® is effectively a xenograft, a transplant of material from a different species of multiple organism classes. On the other hand, NTCELL® replaced only the striatum of rats and non-human primates staying the following:

• SAFETY
  • Abnormal of Pericardial Effusion (PPE) (transmission across or into heart muscle)
  • No major organ toxicity or shortening of lifespan
• LONGLITUDE
  • Survival of NTCELL for 18 months in rats
• EFFICACY
  • Histological evidence of corresponding inflammation of scalp wound
  • No major organ toxicity or shortening of lifespan
  • Survival of NTCELL for 18 months in rats compared to age-matched controls

Methods

Our clinical trial was approved by the Ministry of Health (NZ) and the Auckland Ethics Committee in New Zealand (NT/11/06).

The trial was conducted at Auckland City Hospital. The results were an extension and an updated version of the previous consent procedure which was approved by the independent Data Monitoring Committee participating in this trial.

Patients aged between 45-70 years who had previously been treated for Deep Brain Stimulation (DBS) participated in this trial.

We implanted 60 NTCELL microparticles (200) choroid plexus cells per patient which were contraindicated to the fact that the striatum in each of the four patients.

The primary endpoints of this trial were:

• Clinical and laboratory evidence of PERV transmission in patients and partners

The secondary endpoints included:

• Parkinson’s Disease Rating Scale (UPDRS) at the end of 26 weeks

• Unified Parkinson’s Disease Rating Scale (UPDRS) in the off state

• Parkinson’s Disease Quality of Life Questionnaire (PDQ-39) scores

• Positive Emotion Tryptophan (PETP) [intracerebral] and in serum

The results of 26 weeks follow-up implantation were compared with those of the sham group.

Informed consent was obtained from the patients. After each follow-up, there was a list of traumatic or emergent adverse events that were considered related to the investigations procedure, rather than NTCELL®. The PETP assessments showed no evidence of inflammation.

Table 1: Adverse events related to the implant procedure

<table>
<thead>
<tr>
<th>Event</th>
<th>Grade</th>
<th>Bradykinesia</th>
<th>Dyskinesia</th>
<th>Headache</th>
<th>Mental Fatigue</th>
<th>Pain</th>
<th>Rash</th>
<th>Temperature Rise</th>
<th>Urinary Retention</th>
<th>Nausea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
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<tr>
<td>Grade 2</td>
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The results of the study were evaluated on the basis of a randomized clinical trial of patients with Parkinson’s disease comparing the effects of NTCELL® implantation on levodopa dosage.

The dosage remained the same from the beginning to the end of the first needle pass. This may have had a significant impact on the results of the study.

The primary endpoint was the improvement in clinical features of PD.

Results

Table 2: Adverse events related to the implant procedure

<table>
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The sustained improvement at Week 26 post-implant is not likely to be due to re-implantation of dopaminergic neural terminals.

Efficacy could be slowed by the result of recovery in function of other means impaired in dopaminergic and compensatory mechanisms known to occur in the striatum. NTCELL® is encapsulated choroid plexus cells with potential for production of signals that will trigger the release of neurotransmitters that modulate the demand to the dopaminergic response of the patients.

The improvement in the DBS score would be consistent with histological improvement seen in animal studies. Moreover, the improvement in the motor function of the patient.

Conclusion

NTCELL implantation was safe and well-tolerated.

While the study is small, in scale, the results obtained are sufficiently encouraging to support further studies with NTCELL® for patients with Parkinson’s disease.

Discussion

The primary endpoint of this clinical trial was to determine the efficacy of NTCELL® implantation in patients with Parkinson’s disease. All adverse events were attributable to the implant procedure and must not be over-interpreted in only four patients.

The marked improvement immediately after the procedure would require further validation.

The cause of this change is unclear and must not be over-interpreted in only one patient.

The mechanism of improvement could be the result of recovery in function, removal of waste products such as amyloids and proteins.

NTCELL® would have been considered a potential response to dopaminergic augmentation in Parkinson’s disease, due to a placebo effect within the brain.