J04 Efficacy and safety of tiapride for chorea treatment in huntington's disease: a systematic review

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the disorder a suitable candidate for cell replacement therapy (CRT), a process involving the transplantation of donor cells to replace those lost due to disease. Whilst previous trials of CRT in HD have shown proof of principle, further investigation to demonstrate ongoing safety and efficacy is warranted.

Aim Assess the safety and feasibility of transplanting an increased number of human fetal striatal cells into the striatum of people with HD.

Methods TRIDENT (TRIal DEsigns for delivery of Novel Therapies in neurodegeneration) is an open label phase 1 trial using a Trial Within a Cohort (TWiC) design. A minimum of 18 participants will be enrolled in the study observational cohort, and up to five eligible participants will be randomly selected to undergo transplantation of 12-22 million fetal cells in a dose escalation paradigm. Independent reviewers will assess safety outcomes (lack of significant infection, bleeding or new neurological deficit) four weeks after surgery, and ongoing safety will be established before conducting each subsequent surgery. All participants will undergo detailed clinical and functional assessment at baseline, 6 and 12 months. Surgery will be performed one month after baseline, and transplant participants will undergo regular clinical follow-up for at least 12 months.

Results 20 participants have been recruited to the observational cohort. The first transplant surgery is scheduled for July 2021.

Conclusion The data collected in TRIDENT will; 1) enable assessment of the safety and feasibility of fetal cell transplants; 2) inform trial designs for complex intracranial interventions in a range of neurodegenerative conditions and 3) facilitate the development of stable surgical pipelines for delivery of future stem cell trials.

J03 CLINICAL TRANSLATION OF STEM CELL THERAPIES FOR HUNTINGTON'S DISEASE (HD)

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Background The underpinning concept of regenerative medicine is restoration of structure and function. This can be achieved through several approaches, including implantation of cells to either provide support for vulnerable host cells or to integrate and adopt the function of cells lost to the disease process. HD represents an excellent prospect for regenerative medicine, but there are multiple challenges along the translational pipeline, many of which are common across diseases and pertinent to multiple donor cell types.

Aims Provide a consensus document that sets out the challenges for advancing stem cell therapies to the clinic for HD.

Methods Stem cells for Huntington's disease (SC4HD) and the EHDN Advanced Therapies Working Group (ATWG) provide a combined platform for discussion and to share experience in order to generate a robust clinical development plan across a range of stem cell-based therapies for HD.

Results Over a series of meetings, SC4HD/ATWG have produced a consensus white paper (submitted for publication) that identifies the challenges of cell therapy for HD. These include defining criteria for transitioning to clinical studies; scale-up, characterization, quality control and validation of the cell product; design, validation and approval of surgical devices; operative procedures for safe and effective delivery of cell product to the brain; designing clinical trials that incorporate principles of efficient design and disease specific outcomes. All processes must be adaptable in a dynamic regulatory environment.

Conclusions Here we set out the challenges associated with the clinical translation of cell therapies, using HD as a specific example, and suggests potential strategies to address these challenges. This provides the starting point for developing guidance, and highlighting future directions, with the aim to expedite progress towards therapies for clinical benefit in HD.

J04 EFFICACY AND SAFETY OF TIAPRIDE FOR CHOREA TREATMENT IN HUNTINGTON'S DISEASE: A SYSTEMATIC REVIEW

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Background Chorea is a distinct feature of Huntington's Disease (HD) and can be treated with various drugs. Although (deu)tetrabenazine is the only drug endorsed for chorea control by an RCT, it is not suitable for every HD patient due to its side effect profile. (Deu)tetrabenazine is contraindicated in patients with severe depression and/or previous suicidal thoughts. Antipsychotics are then used as off-label alternatives. In Northern Europe, tiapride is therefore regularly prescribed and also highly affordable with € 0.55/day for 200 mg. However, tiapride was recently taken off-market in the Netherlands without rationale. As we have very good experiences with tiapride for HD chorea treatment, we decided to evaluate tiapride by performing a systematic review.

Aims To review the efficacy and safety profile of tiapride in HD.

Methods A systematic search in PubMed, Web of Science, PsychInfo, Embase and the Cochrane Library was performed. Original research on the efficacy or safety profile of tiapride and expert opinions regarding prescribing preferences to treat chorea were included. Tiapride's drug safety profile was additionally examined via national and international databanks.

Results 11 original data articles and 3 expert opinions were included. The majority of studies (7 out of 11) showed an improvement in chorea while on tiapride. No significant worsening of chorea under tiapride was observed. Due to limited sample sizes not all studies performed statistical tests on their results. In the EU, up to 50% of HD experts prefer tiapride as first choice monotherapy to treat chorea. Antipsychotics are unanimously favored to treat chorea when comorbid behavioural symptoms are present. Tiapride is generally well tolerated without major safety concerns. Side effects, such as drowsiness, elevated prolactin levels and fatigue, are often rare (< 10%) and mild.

Conclusions Tiapride can be an effective and safe alternative to tetrabenazine while treating chorea in HD.