Background

Multiple Sclerosis (MS) is a chronic neuroinflammatory and neurodegenerative disorder of the central nervous system. Progressive MS is defined by the gradual accumulation of neurological disability independent of relapses, typically with lack of or incomplete recovery.1

Therapies addressing regeneration and repair may offer an innovative treatment option in progressive MS.2

Autologous MSC-NTF cells are bone-marrow derived mesenchymal stem cells (MSCs) propagated and differentiated in culture to secrete high levels of neurotrophic factors. In the experimental autoimmune encephalomyelitis mouse model, intracerebroventricular administration of autologous MSC-NTF cells were shown to delay the onset of motor impairment and improve survival.3

MSC-NTF cells are currently being evaluated in a 200 patient US phase 3 placebo-controlled, repeated intrathecal dose study in Amyotrophic Lateral Sclerosis (ALS).

Study Design

This open label, single-arm Phase 2 study, conducted at 5 US MS clinical centers, will evaluate the safety and efficacy of repeated doses of MSC-NTF cells using clinical outcome measures and paired CSF and blood biomarker analyses.

Study population: N=20 Progressive MS patients with Expanded Disability Status Scale (EDSS) 3.0-6.5, based on the 2017 revised McDonald Criteria.5

Inclusion Criteria

- Clinical progression of MS (Primary and Secondary) based on the 2017 revised MacDonald Criteria; disease entered progressive stage for at least 6 months prior to enrollment
- No evidence of clinical MS relapse or corticosteroid treatment within 6 months prior to screening
- Disability status at screening with an Expanded Disability Status Scale (EDSS) 3.0-6.5
- Able to walk 25 feet in 60 seconds or less
- Stable dose of non-excluded MS Disease Modifying Therapy for 6 months prior to screening visit

Eligible subjects will undergo a bone marrow aspiration (BMA) with the first IT transplantation ~12 weeks later. The next two transplantation visits occur 2 months apart with a 12 week follow-up period.

Primary Endpoint:

- To evaluate safety and tolerability of 3 intrathecal doses of NurOwn®

Secondary Endpoints:

- To evaluate the efficacy of NurOwn® as measured by MS assessments
- To evaluate the modulation of CSF and blood biomarkers following NurOwn® transplantation

Safety Outcome Measures

- Changes in vitals and physical exam, safety labs, AEs, concomitant medications and MRI T1- and T2-weighted lesions
- Key safety data will be reviewed 1) when 50% of subjects have completed one treatment and 2) after all subjects complete the study

Efficacy Outcome Measures

- Timed 25 Foot Walk (T25FW), 9-Hole Peg Test (9HPT), Expanded Disability Status Scale (EDSS), Low Contrast Letter Acuity (LCLA) and Symbol Digital Modalities Test (SDMT)
- Biomarkers paired Blood plasma and CSF
- Physical function measured with wearable sensor and 12–item MS Walking Scale

Biomarkers: CSF and Blood Samples

- CSF and serum samples will be collected prior to and with the first IT transplantation ~12 weeks prior, with the second IT transplantation ~24 weeks after the first IT transplantation.
- Biomarkers and paired blood samples will evaluate the safety and efficacy of repeated intrathecal dosing of autologous MSC-NTF cells in progressive MS patients and will inform the design of a subsequent Phase 3 pivotal trial.

Study Status

Enrollment began in the first quarter of 2019 with topline clinical data expected in the first half of 2020.

Outcomes from a large contemporary, matched natural history cohort will be used in the data analysis.

Conclusion

This phase 2 open-label study was designed to provide preliminary data on the safety and efficacy of repeated intrathecal dosing of autologous MSC-NTF cells in progressive MS patients and will inform the design of a subsequent Phase 3 pivotal trial.

References


Conflicts of Interest

Dr. Cohen reports personal compensation for consulting for Conexos and Gossamer Bio, speaking for Mylan, and serving as an Editor of Multiple Sclerosis Journal. Dr. Cohen has served on advisory boards for Biogen, Novartis, and Sosef-Genzyme; received research support from Biogen, Novartis, Octave, Sosef, and Verity; has participated in clinical trials sponsored by Sosef-Genzyme and Novartis; and has served as an investigator in studies involving Sanofi-Genzyme, EMD Serono, Biogen, and Novartis. Dr. Cohen has also served as a consultant to MD Anderson Cancer Center, Genzyme, Sosef, and Sanofi-Genzyme. Dr. Cohen reports consulting fees for InterX Inc.

Dr. Lock reports consulting fees for InterX Inc, and Diagnose Early. Served as scientific advisory board member or speaker for Biogen, Sanofi Genzyme, and EMD Serono. Dr. Lock has received a grant from the Motor Neuron Disease Association.

Dr. Pelletier serves as scientific advisor to Convelo and Gossamer Bio; consulting for Mylan; and reporting personal compensation for consulting for Novartis.

Dr. Cohen, reports personal compensation for consulting for Conexos and Gossamer Bio, speaking for Mylan, and serving as an Editor of Multiple Sclerosis Journal. Dr. Cohen has served on advisory boards for Biogen, Novartis, and Sosef-Genzyme; received research support from Biogen, Novartis, Octave, Sosef, and Verity; has participated in clinical trials sponsored by Sosef-Genzyme and Novartis; and has served as an investigator in studies involving Sanofi-Genzyme, EMD Serono, Biogen, and Novartis. Dr. Cohen has also served as a consultant to MD Anderson Cancer Center, Genzyme, Sosef, and Sanofi-Genzyme. Dr. Cohen reports consulting fees for InterX Inc.

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