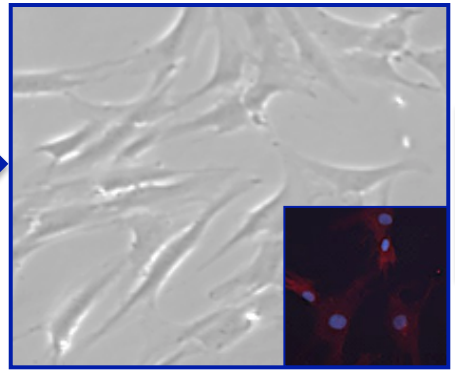
PHASE I TRIAL OF INTRATHECAL MSC-NEURAL PROGENITOR CELLS – AN INTERIM ANALYSIS

TISCH MS

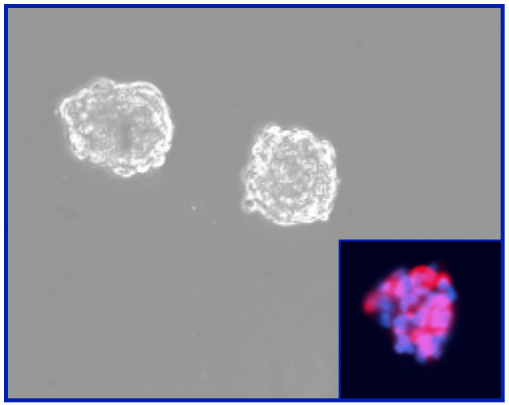
RESEARCH CENTER OF NEW YORK

Cell Source - MSC-NPs

Autologous Bone Marrow



EGF/bFGF



nestin+

MSC

plastic adherent mesenchymal stem cells

MSC-NP

MSC-derived neural progenitors

Phase I Open Label Clinical Trial

Study aim: **Safety and Tolerability of autologous IT MSC-NP**

Dose: **3 injections of up to 10 million cells q 3 months**

Enrollment: **20 MS patients (14 F; 6 M) with 'stable' disability, EDSS 3.5 to 8.5; 16 SPMS; 4 PPMS ; Ages 27-65**

Primary Safety outcomes: **Clinical, MRI, and lab testing, 2 year follow-up**

Secondary Efficacy outcomes: **EDSS, MSFC, EPs (VER, ABER, SER), QOL urodynamic studies**

Unique Aspects of our Study

- Use of MSC-NP cells
- IT route of administration
- Multiple dosing
- Delivery of MSC-NPs in culture to patient within 30 minutes of harvesting. Minimizes physiological stress of freeze-thawing and maximizes cell viability

Adverse Events

- No safety issues to date
- No serious adverse events
- Minor adverse events:

  80% of patients experienced at least one transient headache (< 2 days post-RX)

  20% report transient fever (less than 100^{o} F -first 24 hours)

  One incident of post-spinal headache
- DSMB/IRB/FDA have approved continuation of Phase I study

Results - Efficacy Parameters

- ≥ 0.5 point improvement in EDSS score
- >20% improvement in 25 foot timed walk
- >20% improvement in nine hole PEG test
- >20% increase in bladder capacity
- Abnormal →Normal Visual Evoked Potentials

10/15 Patients Improved

Study subject number	EDSS baseline	EDSS post-tx	% Improvement of 25 ft walk (>20% considered significant)	% Increase bladder capacity (>20% considered significant)	Other Area of Improvement
03	3.5	1.5	23.3%	10.9%	D/C bladder meds; abnormal→normal VEP, D/C Bioness
04	8.0	8.0	n/a	523.4%	D/C bladder meds
05	7.0	6.5	n/a	201.5%	n/a
06	8.0	8.0	n/a	10.9%	58.3% improvement in nine hole peg test (>20% considered significant)
07	6.0	5.5	17.2%	10.5%	D/C unilateral cane
08	7.5	7.5	n/a	69.5%	n/a
10	7.5	6.5	Unable→Able	40.3%	D/C bladder meds; scooter→ walker
12	6.0	5.5	1.1%	-7.0%	D/C unilateral cane
14	5.5	4.0	57.0%	n/a	
15	6	5.5	29.2%	n/a	D/C hip flexor sling, Bioness, and cane

Summary – Interim analysis

- MSC-NP IT use is well tolerated and safe in the short term
- First MS “stem” cell trial to show functional improvement in majority of treated patients
- It appears that less disabled patients do better as 5/6 patients with EDSS of 6.5 or less improved compared to 5/9 patients with EDSS >6.5

Next Steps

- Complete Phase I 20 patient study in 2016
- Planning a double-blind, placebo-controlled, multi-center, phase II study designed to determine efficacy (FDA-approved)

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