Initial Clinical Trials of hESC-Derived Oligodendrocyte Progenitor Cells in Subacute Spinal Cord Injury

ISCoS Meeting
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AST-OPC1: hESC-Derived Oligodendrocyte Progenitor Cells (OPCs)

AST-OPC1 (formerly GRNOPC1)

- Cryopreserved Allogeneic Cell Population
- Derived from Human Embryonic Stem Cells (hESCs)
- Characterized Composition of Cells:
  - Oligodendrocyte progenitors
  - Neural progenitors
  - Infrequent mature neural cells and
  - Rare other characterized cell types
- Three identified functions
  - Produces neurotrophic factors
  - Induces remyelination
  - Induces vascularization
- “Off the shelf” administration
- First indication: spinal cord injury
- Potential line extensions in other neurodegenerative diseases
AST-OPC1: Phase 1 Safety Study in Complete Thoracic SCI

- Open Label Trial
- Multi-Center (7 sites)
- 5 Subjects received AST-OPC1
- Neurologically Complete T3-T11 Lesions
- 2x10^6 Cells
- Transplant 7-14 Days Post Injury
- Temporary Immunosuppression

Primary Assessment: Safety
Secondary Assessment: ISNCSCI exams

Exploratory Assessments
- UAB-IMR / SCIM
- SCI Pain Basic Data Set
- Bowel and Bladder Basic Data Set
Summary of Phase 1 Thoracic Safety Study of AST-OPC1

- AST-OPC1 well tolerated, with no SAEs to date deemed related to the cells, delivery method, or immunosuppressive regimen

- No evidence of immune responses to AST-OPC1, even 10 months after removal of all immunosuppression
  - Despite significant HLA mismatches between AST-OPC1 and subjects

- MRI results consistent with activity in injection site in 4 of 5 subjects at 4-5 years post-transplant

- No evidence of significant changes in neurological function
  - No evidence for ascending loss of function from cells or delivery
  - Efficacy not anticipated in this study due to low dose (5-10x below predicted efficacious range) and suboptimal patient population (complete thoracic injuries)
A Phase 1/2a Dose Escalation Study of AST-OPC1 in Subjects With Subacute Cervical Spinal Cord Injury

Six Sites Currently Enrolling

ClinicalTrials.gov: NCT02302157
AST-OPC1 Phase 1/2a Study Schema

- Open Label Trial
- Multi-Center (8-12 sites)
- Complete cervical SCI (C5-C7)
- Temporary Immunosuppression

Primary Assessment: Safety
Secondary Assessment: ISNCSCI exams
Exploratory Assessments: SCIM, GRASSP

In person visits
Phone f/u

AST-OPC1 Injection
14-30 Days Post-SCI

Days 46-60
Immunosuppression Taper

Days 60
Discontinue Immunosuppression

MRI

Day -11
Screening

Day -3
Baseline

Day 0

Day 7

Day 30

Day 60

Day 90

Day 180

1 Year

5 Years

15 Years

Years 15

Years 5

Years

Day 0

3 Day

‐11

‐11

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Currently recruiting patients for both Cohorts 3 & 4
AST-OFC1 Injection Procedure

Shepherd Center

Rush University

• Injections performed using a table-mounted syringe positioning device (SPD)
• Direct intra-parenchymal injection into the spinal cord lesion
• Single 50µL injection for both the 2M & 10M doses
• No intraoperative complications to date
Upper Extremity Motor Recovery to Date

Upper Extremity Motor Score (UEMS)

Motor Level Recovery at Day 90 Follow Up

* N=4 at Day 90 (fifth subject has only reached Day 60)
Cohort 1: 2 million AST-OPC1 cells
Cohort 2: 10 million AST-OPC1 cells
## Upper Extremity Motor Score (UEMS) – Per Subject Data to Date

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<th>Baseline</th>
<th>Day 90</th>
<th>Day 365</th>
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### Cohort 1
- Avg. time from SCI to AST-OPC1 Injection:
  - Cohort 1: 27 days
  - Cohort 2: 28 days

### Cohort 2

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</table>

- No correlation between degree of recovery and baseline UEMS
- Has not reached Day 90
Motor Recovery Summary

- All subjects in Cohorts 1 & 2 have exhibited improved upper extremity motor scores (UEMS) relative to baseline

- The average UEMS improvement at Day 90 was 5.0 points in Cohort 1 (N=3) and 9.5 points in Cohort 2 (N=4)

- At 1-year of follow up, all subjects in Cohort 1 have improved one motor level on at least one side

- At Day 90 of follow up, 2 of 4 subjects in Cohort 2 have improved one motor level and 2 of 4 have improved two motor levels on at least one side (one patient has improved two motor levels on both sides)

- Cohort efficacy target of 2 of 5 patients improving two motor levels within 6-12 months post-administration has already been met, despite 4 patients only at Day 90 and 1 patient not yet even at Day 90
Conclusions

• AST-OPC1 can be safely administered to patients in the subacute period after severe cervical SCI

• There have been no serious adverse events related to AST-OPC1, the injection procedure, or immunosuppression with low-dose tacrolimus

• A dose response effect on upper extremity motor recovery appears to be emerging by Day 90 of follow up, much earlier than we expected

• These data are early, but very encouraging; We look forward to the UEMS & motor level 6-month readouts in Cohort 2 in January 2017

• Concurrent enrollment of both AIS-B patients with 10M cells and AIS-A patients with 20M cells is in progress to further elucidate the dose response of OPC1
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AST-OPC1 Team

The Trial Participants

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Data Monitoring Committee  
Radiology Committee  
Outcomes Committee

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