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

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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

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AST-OPC1: Phase 1 Safety Study in Complete Thoracic SCI

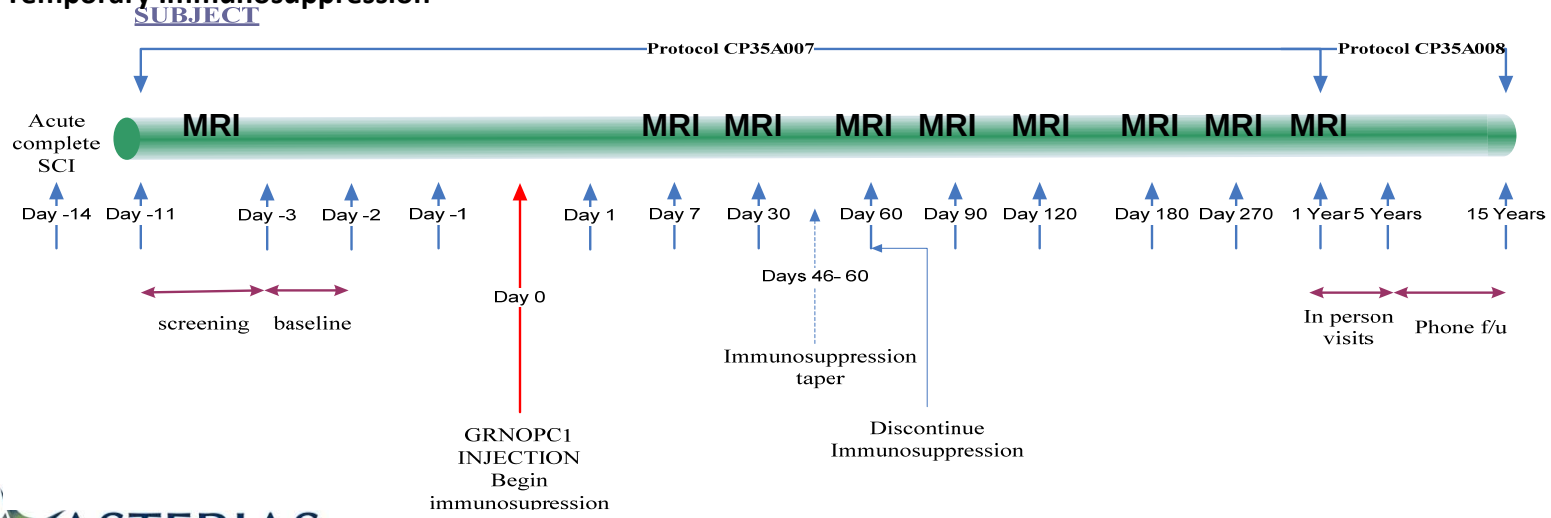
- **Open Label Trial**
- **Multi-Center (7 sites)**
- **5 Subjects received AST-OPC1**
- **Neurologically Complete T3-T11 Lesions**
- **$2x10^6$ Cells**
- **Transplant 7-14 Days Post Injury**
- **Temporary Immunosuppression**

Primary Assessment: Safety

Secondary Assessment: ISNCSCI exams

Exploratory Assessments

- UAB-IMR / SCIM
- SCI Pain Basic Data Set
- Bowel and Bladder Basic Data Set



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Summary of Phase 1 Thoracic Safety Study of AST-OPC1

Well Tolerated

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

No Immune Responses

- 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

Activity

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

No Changes Neurological Function

- 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)

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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

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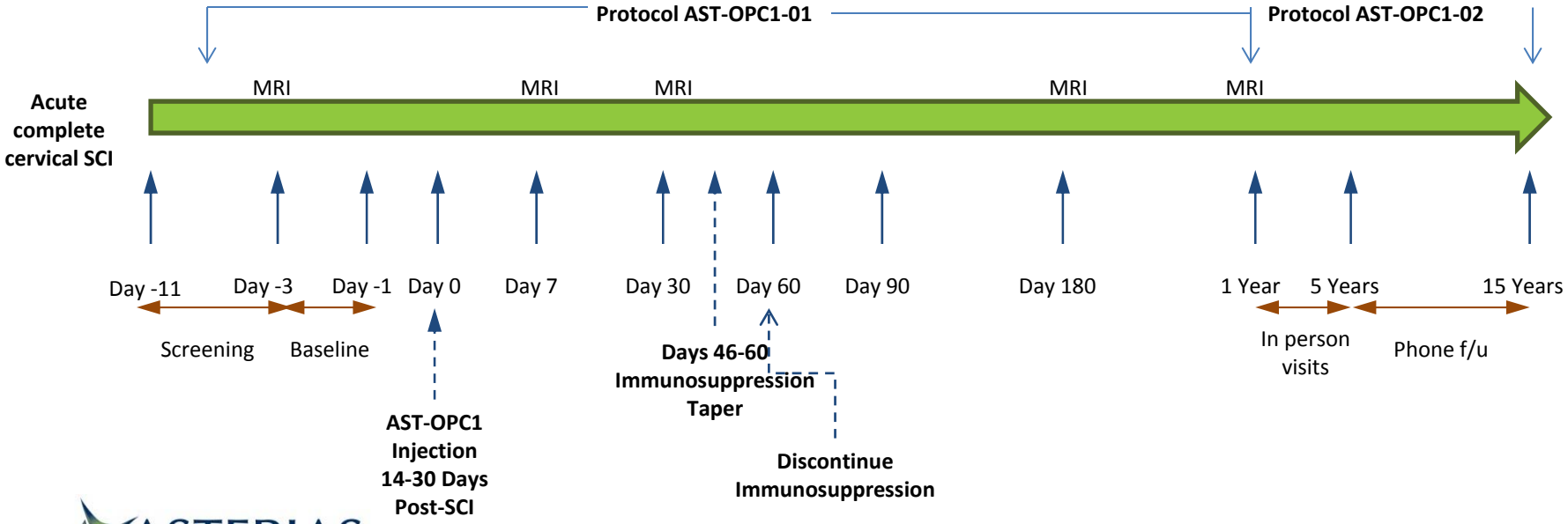
AST-OPC1 Phase 1/2a Study Schema

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

Primary Assessment: Safety

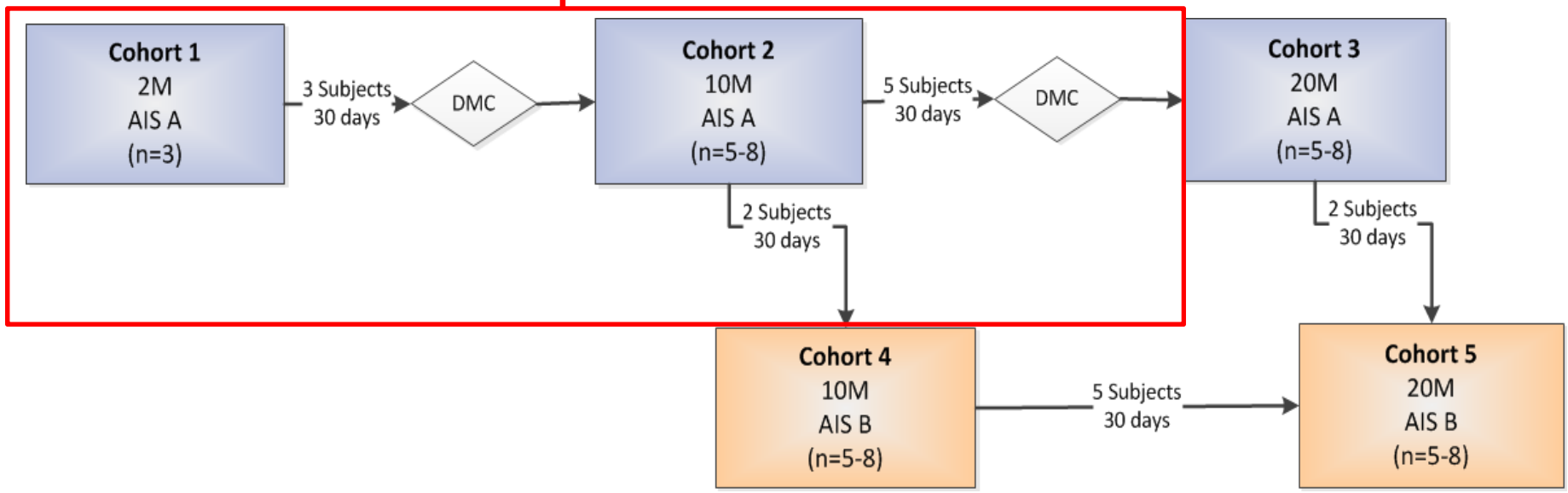
Secondary Assessment: ISNCSCI exams

Exploratory Assessments: SCIM, GRASSP



AST-OPC1 Current Study Design

Completed



Currently recruiting patients for both Cohorts 3 & 4

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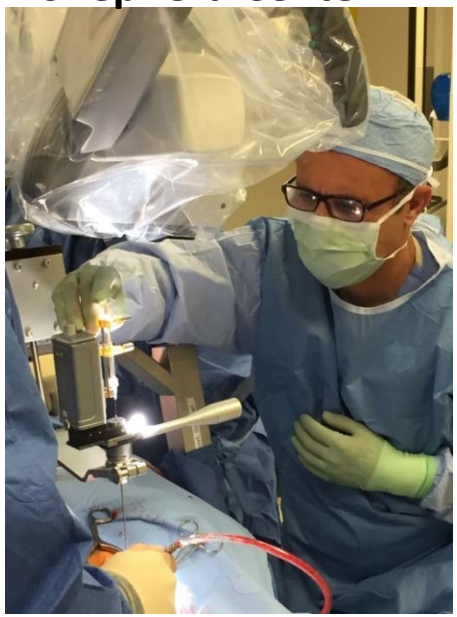
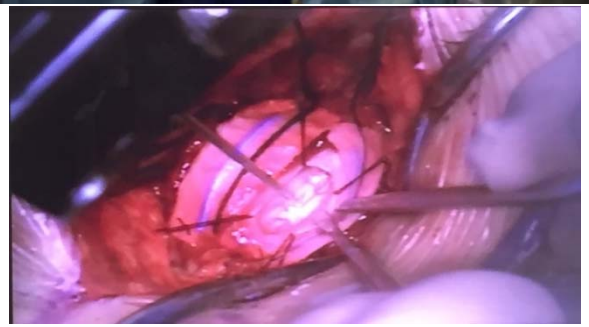
AST-OPC1 Injection Procedure

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

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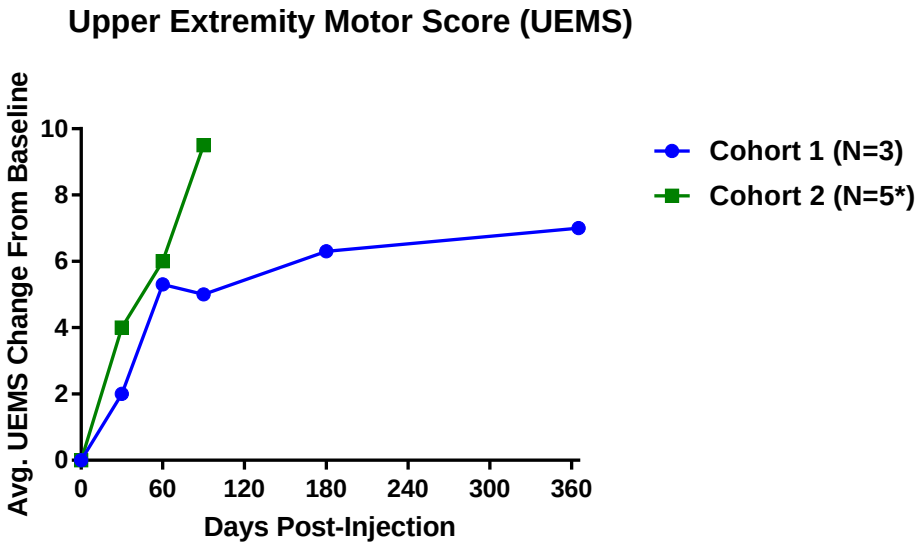
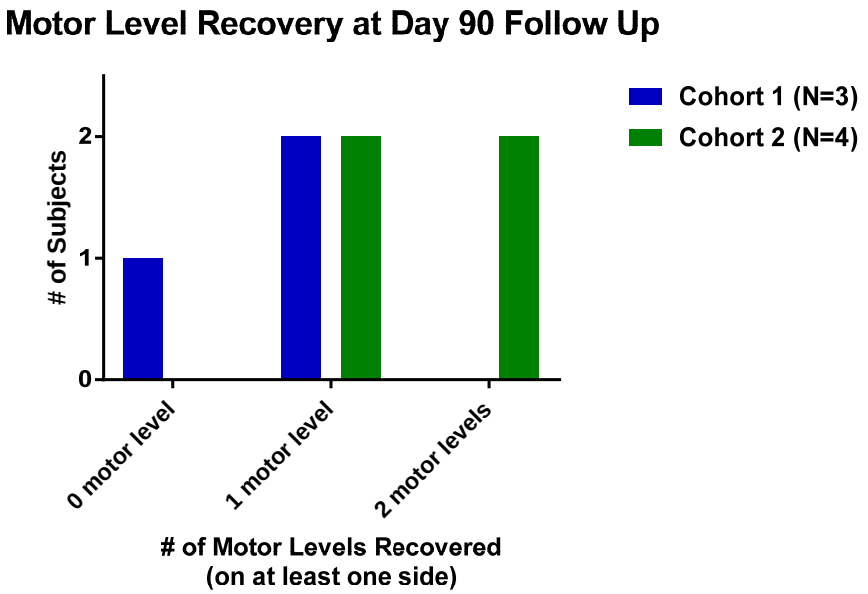
Upper Extremity Motor Recovery to Date





* 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

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Upper Extremity Motor Score (UEMS) – Per Subject Data to Date

Cohort 1

Subject	Baseline	Day 90	Day 365
2001	24	26	28
2101	20	24	27
2102	8	17	18

Avg. time from SCI
to AST-OPC1 Injection
Cohort 1: 27 days
Cohort 2: 28 days

Cohort 2

Subject	Baseline	Day 90	
2501	30	41	
2003	20	26	
2301	24	38	
2502	32	39	
2202	15	---	Has not reached Day 90

No correlation between degree of recovery and baseline UEMS

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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

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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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Committees

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Data Monitoring Committee
Radiology Committee
Outcomes Committee

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