ASIA San Antonio 2014

Phase I/II Clinical Trial of HuCNS-SC Cells in Chronic Thoracic Spinal Cord Injury

Interim analysis

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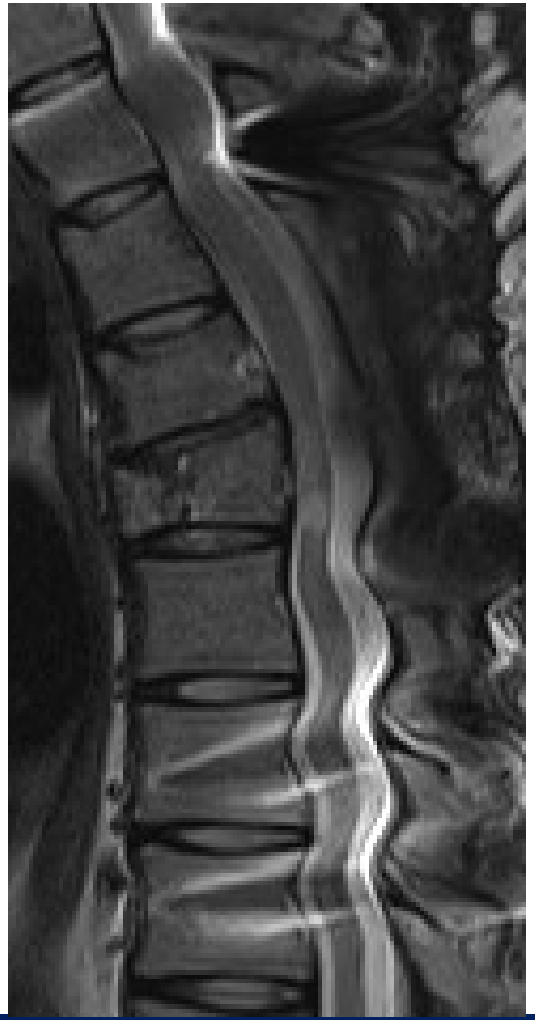
Phase I/II Study Design

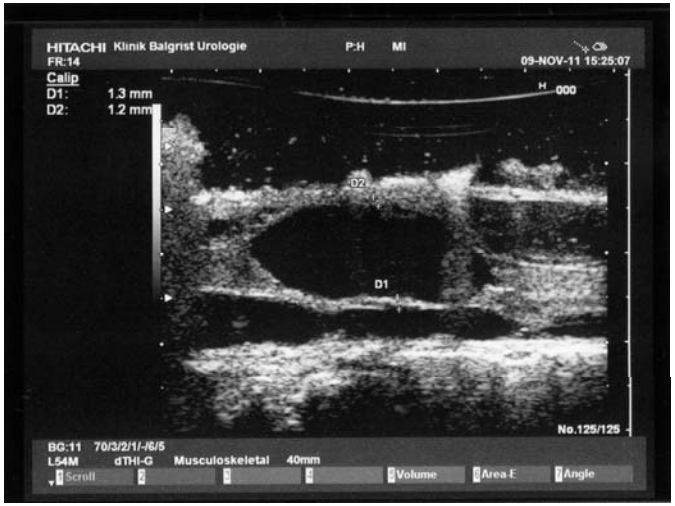
Design

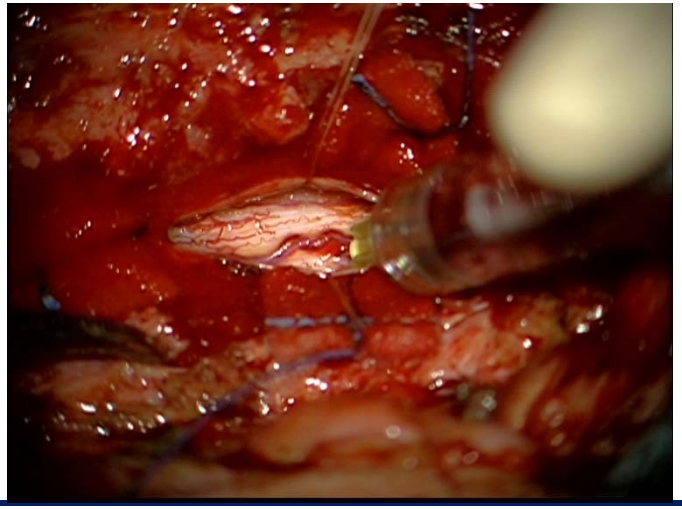
- Open-label, single fixed dose of HuCNS-SC
  - Total intramedullary dose: 20 million cells
  - Immunosuppression: 9 month post-op course
- T2-T11 thoracic SCI: late sub-acute to early chronic
  - AIS A: 3 to 12 months post-injury
  - AIS B: 3 to 24 months post-injury
- Safety and preliminary efficacy endpoints
  - Adverse Events, Serious Adverse Events, Pain Questionnaire
  - Clinical: light touch, pin prick, quantitative sensory testing
  - Evoked Potentials: dSSEPs and CHEPs
  - Radiological: MR imaging

Pre-op MRI and intra-operative ultrasound

Transplantation



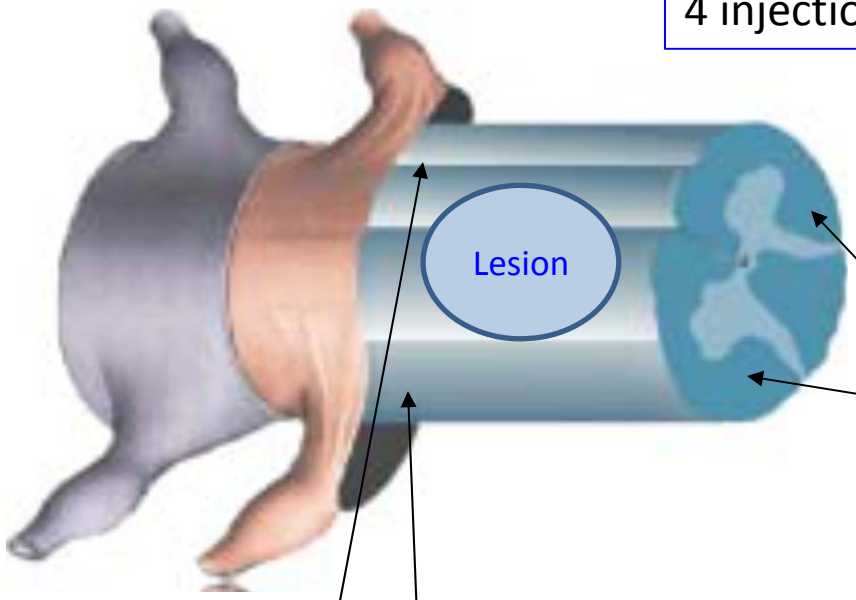




Surgical HuCNS-SC transplantation

Transplantation

Total dose of 20 million cells
Total volume of 280 µL
4 injections of each 70 µL



Superior implant

Inferior implant

caudal ⟷ rostral

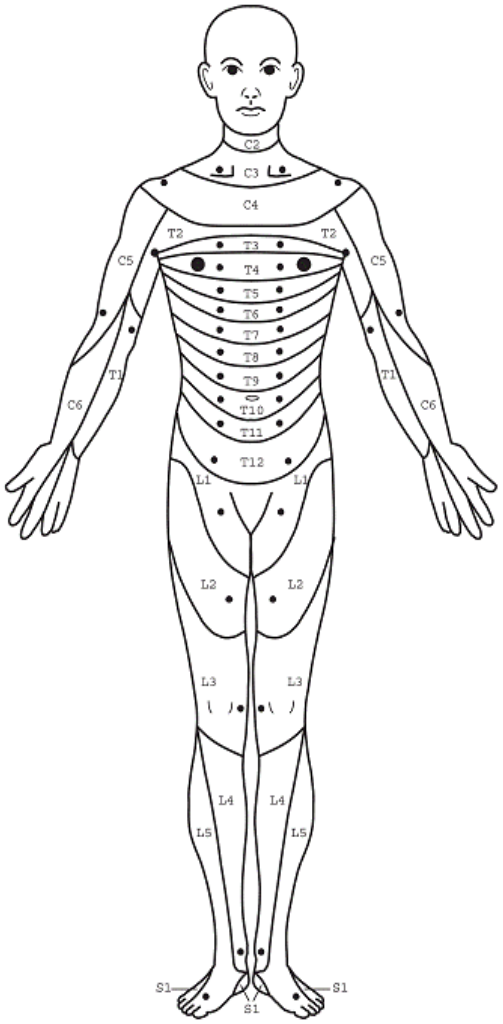
Sensory dermatome testing in SCI

Endpoints

ASIA Scores

Light touch
Pin prick

Normal
Altered
Absent



Quantitative sensory testing and electrodiagnostics

Heat Perception Thresholds
CHEPS

Electrical Perception Threshold
dSSEP

CHEPS	EPT
normal	EPT normal
impaired	3 - 5mA
Highly impaired	5-10mA
absent	10-50 mA
	EPT absent

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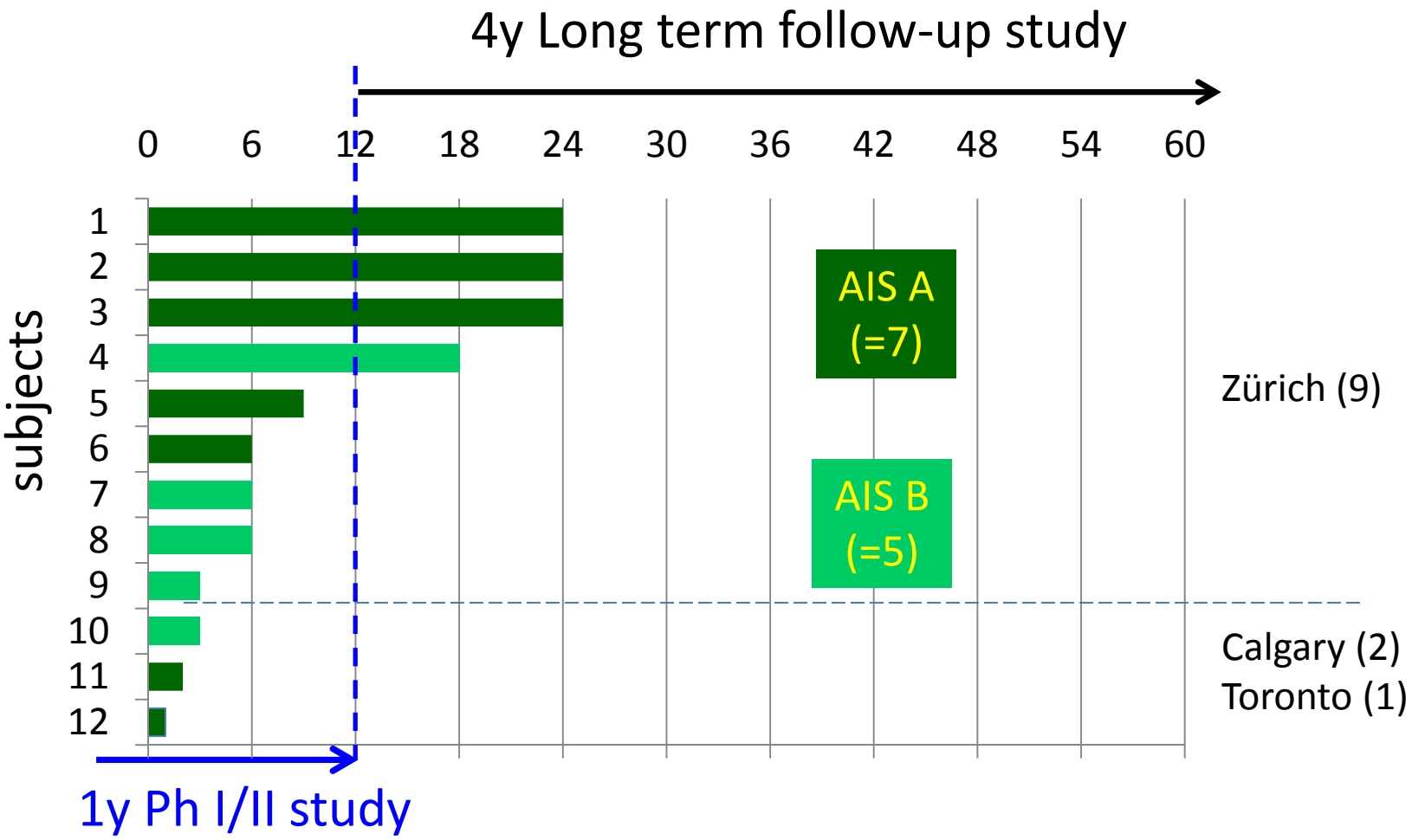
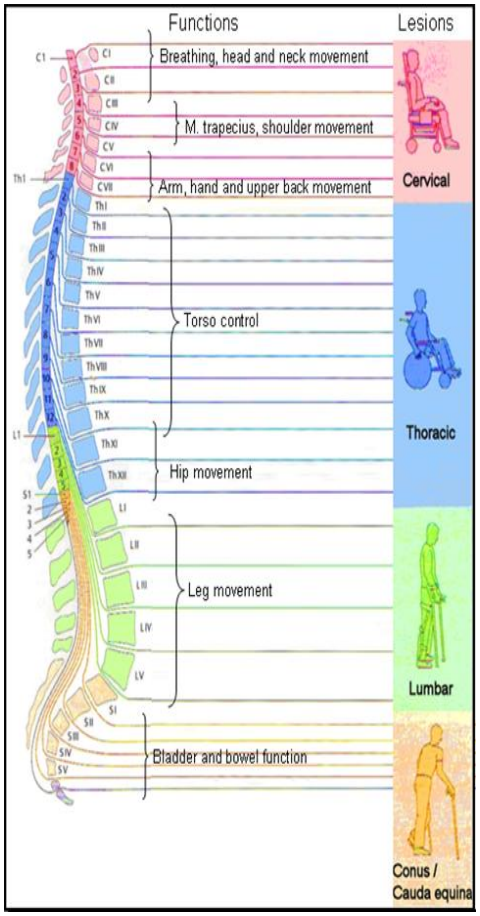
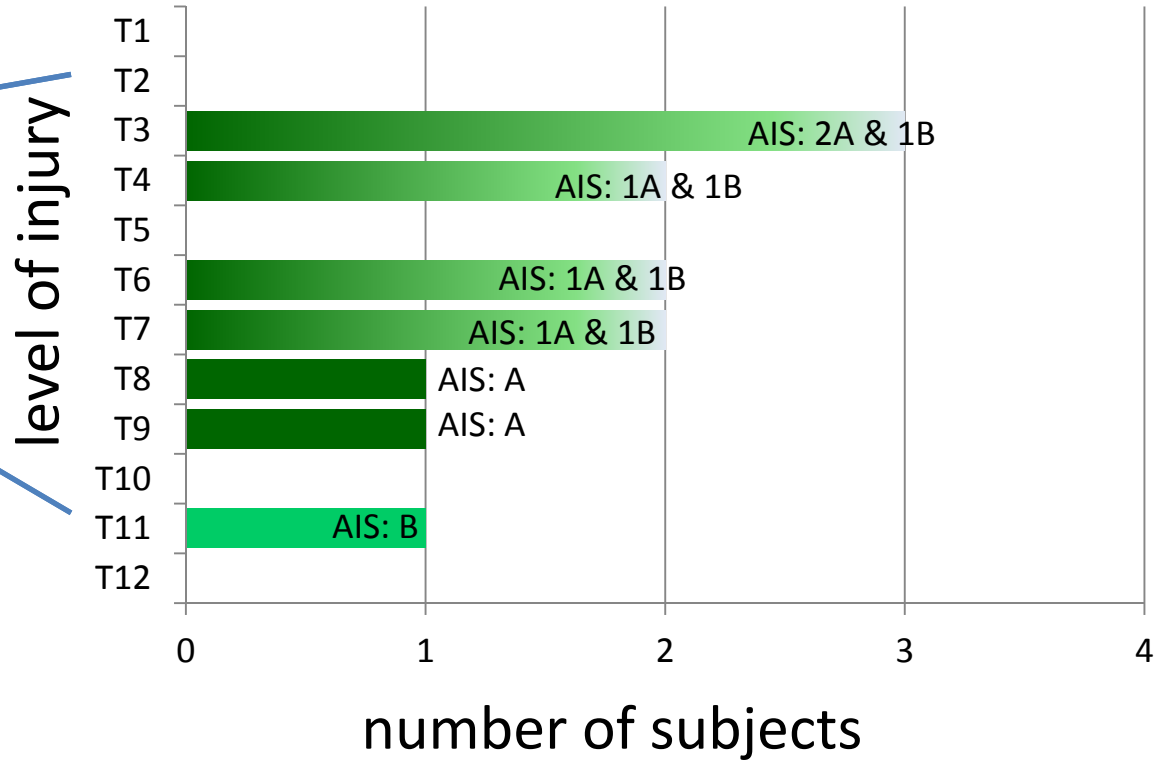
Study design and follow-up

Overview



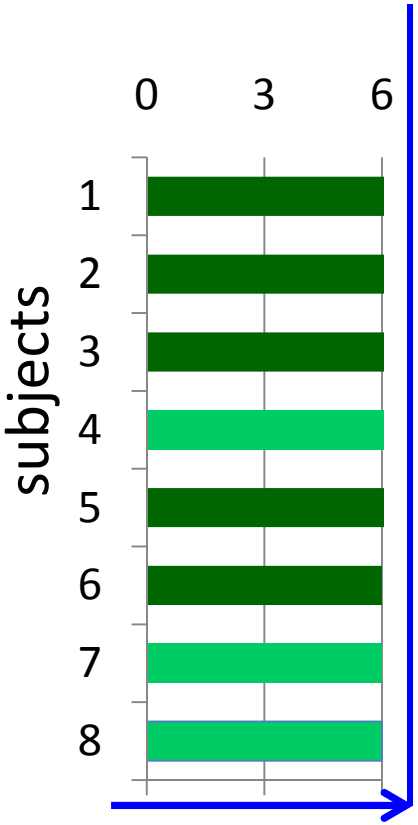
ASIA neurological level



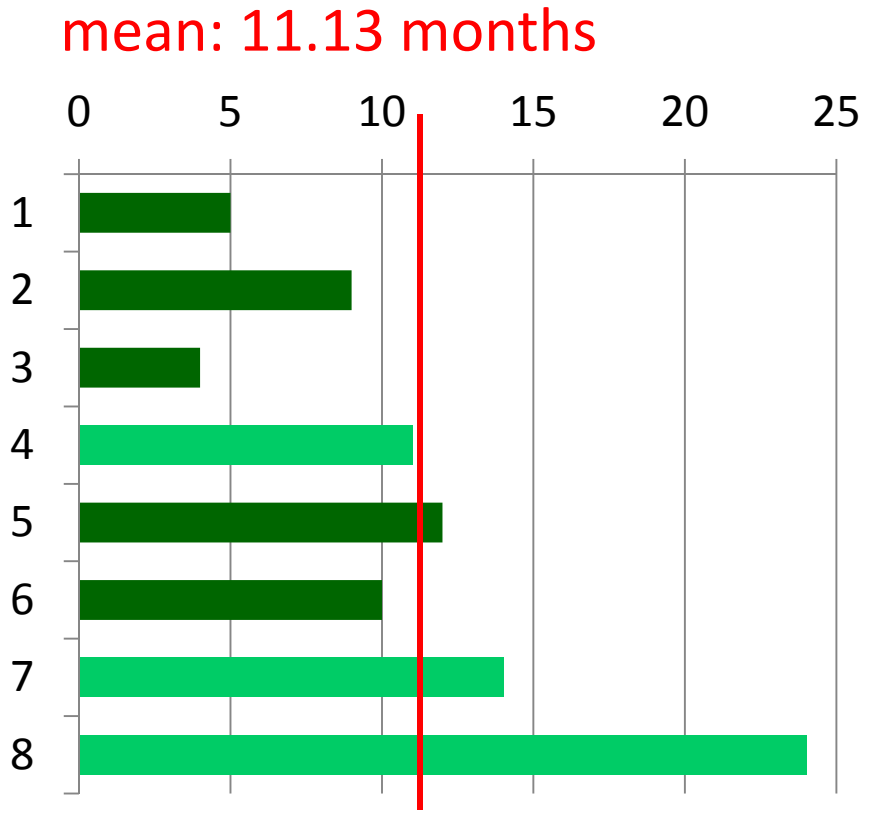


Interim report 6 month follow up

interim data



Phase I/IIa study



Timing of transplant after injury

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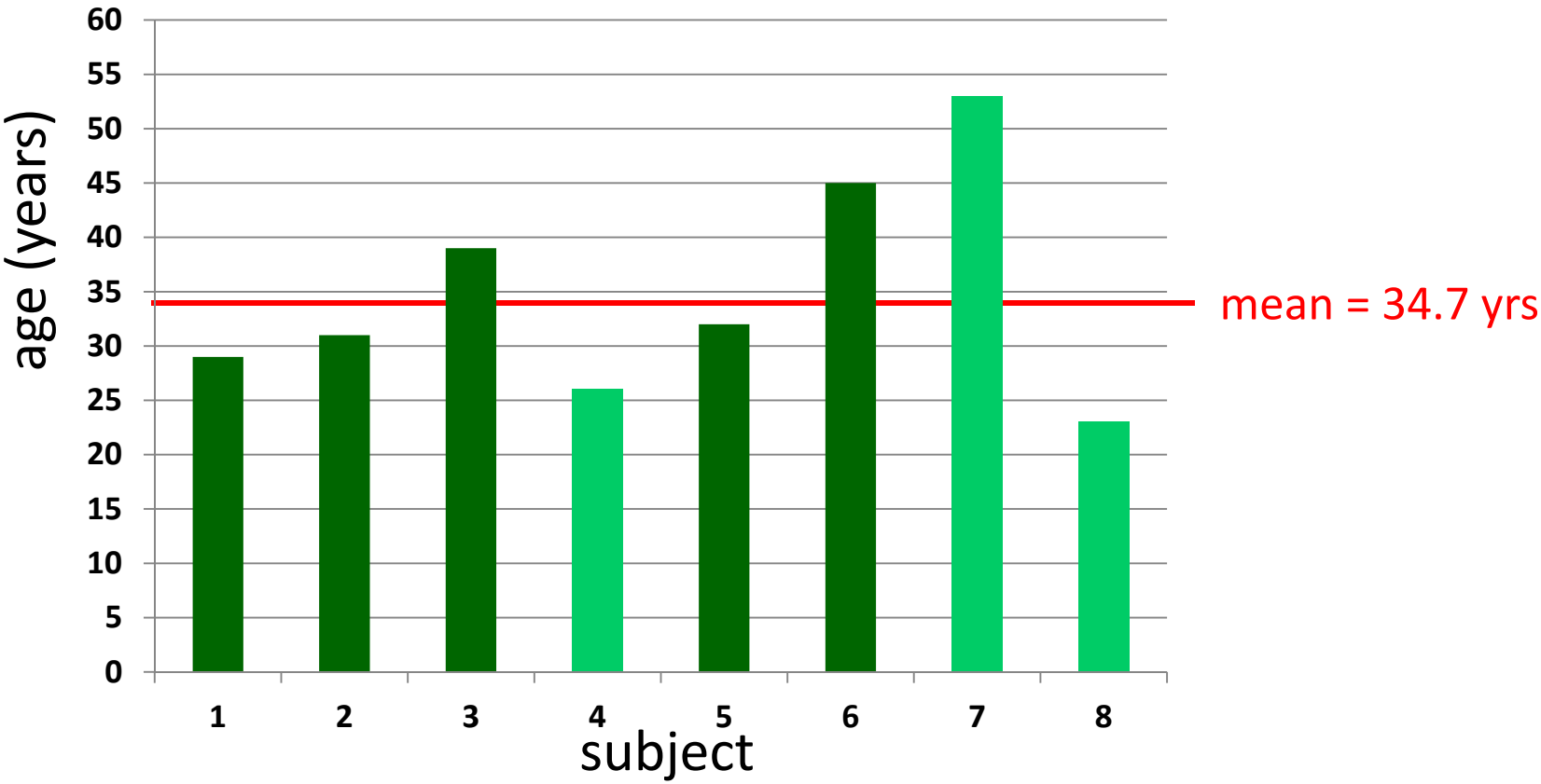
Subject age at enrollment

interim data



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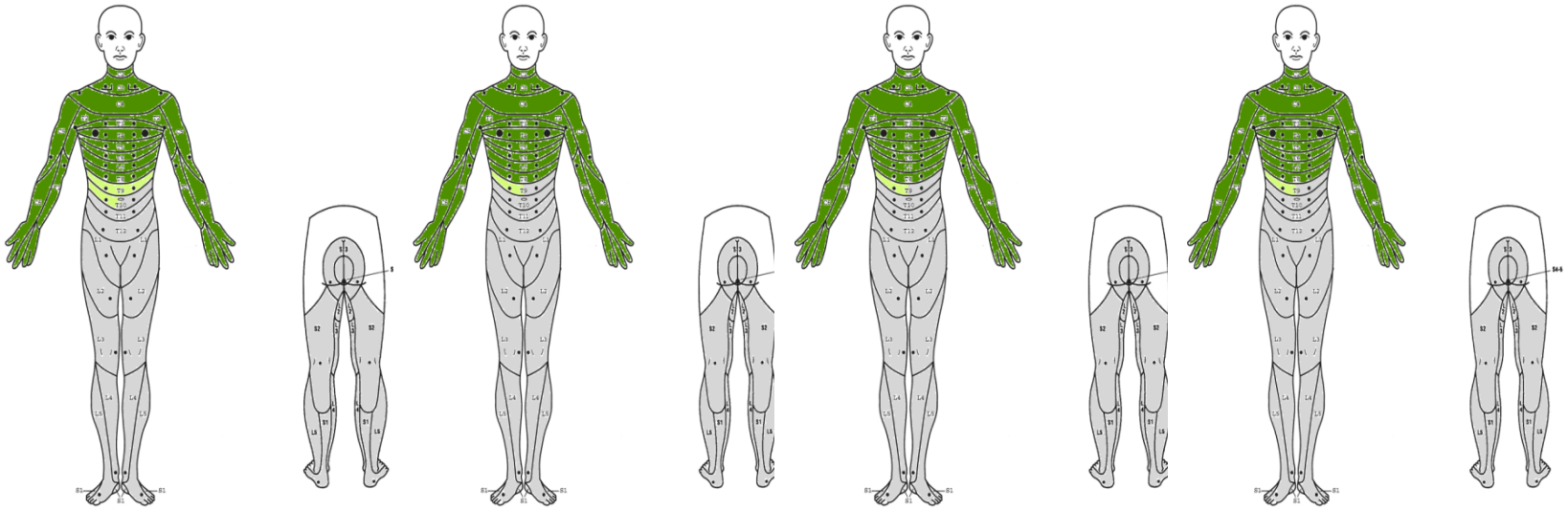
STEMCELLS

AIS A (3 of 5): Stable

Light Touch: Pre-op to Month 12

Subject 1



Pre-op | Month 3 | Month 6 | Month 12

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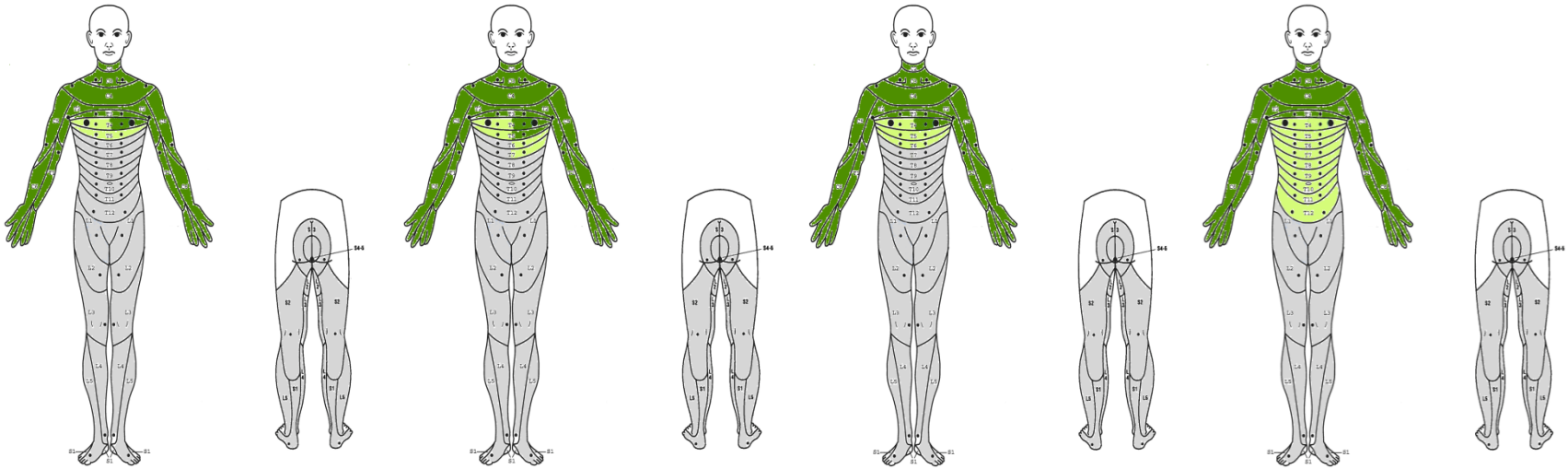
AIS A (2 of 5): Sensory gains

Light Touch: Pre-op to Month 3

Subject 3



Pre-op | Day 14 | Day28 | Month 3

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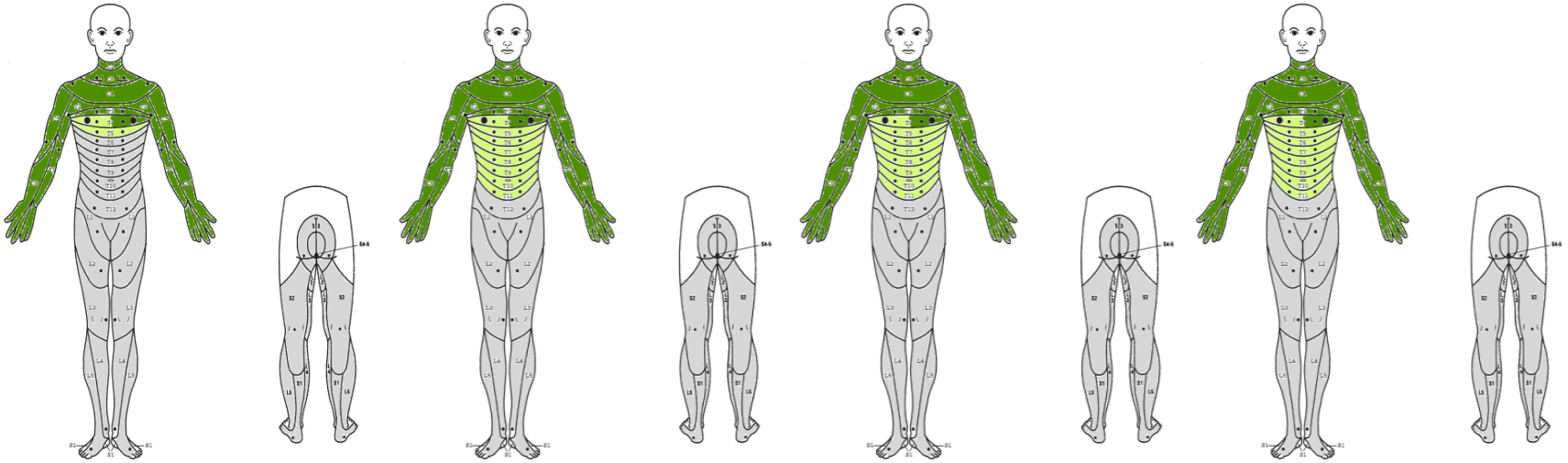
AIS A (2 of 5): Sensory gains

Light Touch: Pre-op to Month 12

Subject 3



Pre-op | Month 6 | Month 9 | Month 12

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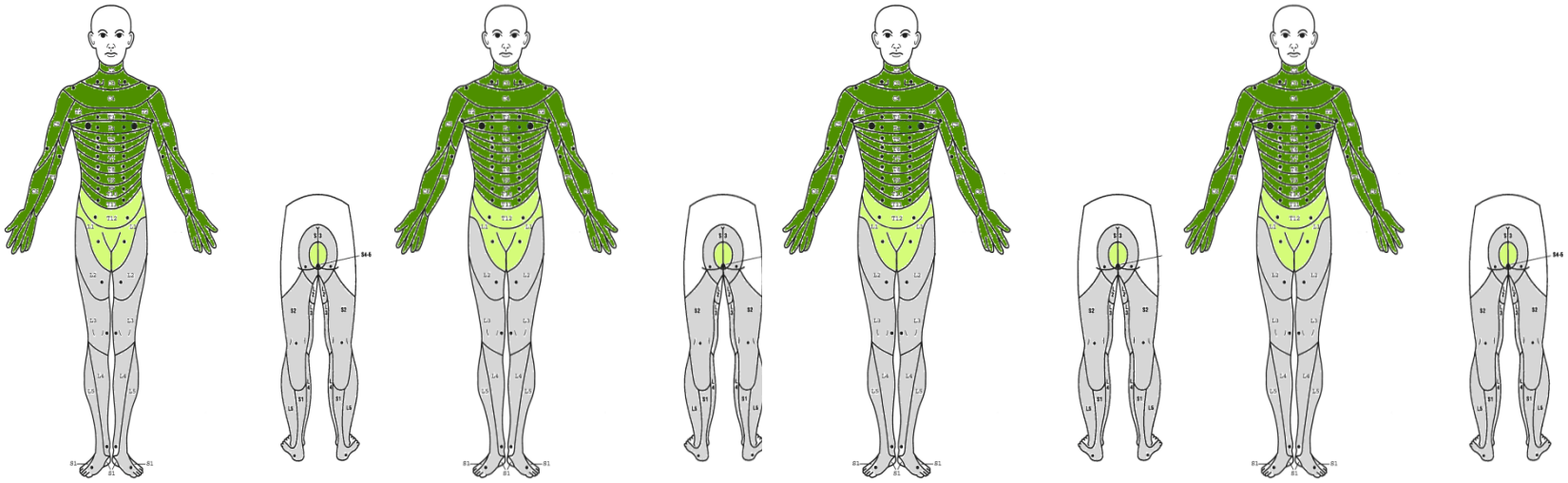
AIS B (1 of 3): Stable

Light Touch: Pre-op to Month 12

Subject 4



Pre-op | Month 3 | Month 6 | Month 12

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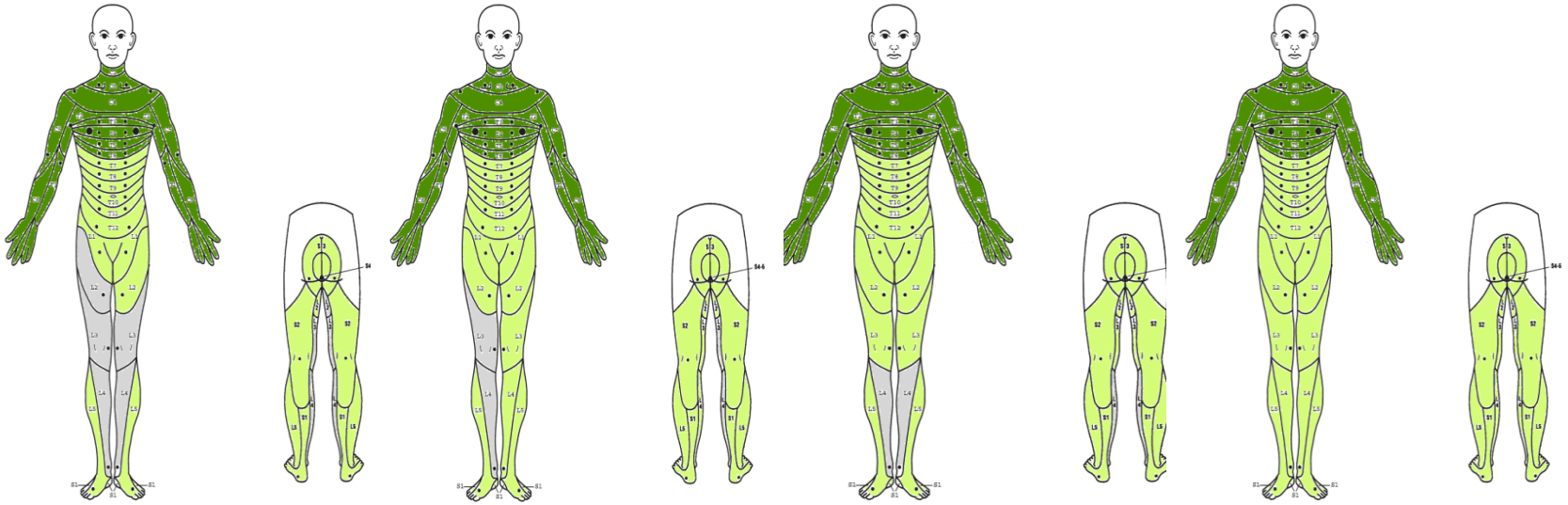
AIS B (2 of 3): Sensory gains

Light Touch: Pre-op to Month 6

Subject 7



Pre-op | Day28 | Month 3 | Month 6

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Adverse Events

Safety

59 AEs: 9 Zurich subjects to date

60% attributed to underlying SCI or intercurrent illness

17% attributed to surgery or immunosuppression

Most Frequent (>2 events)

-UTI n=12

-Decubitus ulcer n=5

-Headache n=5

4 SAEs: All expected and unrelated to HuCNS-SC

-CSF leak *(prolonged hospitalisation)*

-Pseudomeningocele *(prolonged hospitalization)*

-Constipation *(required hospitalization)*

-UTI *(required hospitalization)*

No post-transplant deterioration

Safety

Neurological
- No segmental deterioration in AIS A/B
- No segmental or below level deterioration in AIS B
- No ascending deterioration

Functional
- No loss of overall functional capacity (ADLs)
- No deterioration of bladder sensation in AIS B

Pain
- No change or induction of novel pain syndromes
- No exacerbation of pre-existing pain
- No unexpected or unknown pain conditions

Spasticity and muscle tone
- No exacerbation of pre-existing spasticity
- No induction of novel spasticity

PH I/II preliminary efficacy

Efficacy

Sensory changes

- Segmental improvements at/below level of lesion in AIS A
- Below level improvements in AIS B
- Observed sensory changes supported by QST/EP

Timing of changes

- First changes observed 1 - 3 months after transplantation

Summary of Interim Analysis

- Completed enrollment under Swiss, Canadian and US approval
- Minimum 6m data demonstrates safety and feasibility
  - surgical route of administration, immunosuppression, technique and cell dose
- Gains in multiple sensory modalities and segments
  - 4 out of 8 subjects show signs of segmental sensory improvement
- Interim data suggests first signs of a biological and clinical effect with HuCNS-SC transplantation in spinal cord injury
- Next step
  - randomized controlled PH II study in complete and incomplete cervical SCI