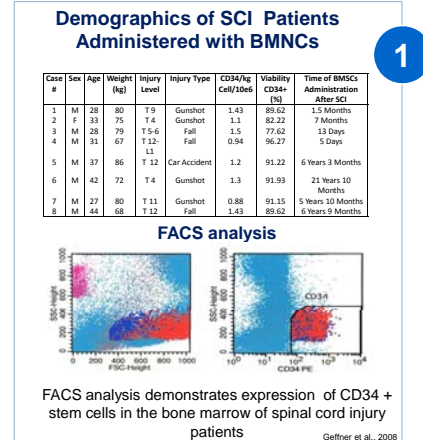


# Administration of Adult Bone Marrow Stem Cells into Spinal Cord Injury Patients via Multiple Routes is Safe and Feasible

Rafael Gonzalez ‡, L. F. Geffner,\* P. Santacruz,\* M. Izurieta,\* L. Flor,\* B. Maldonado,†, A. H. Auad,\* X. Montenegro,\* and F. Silva‡  
 ‡DaVinci Biosciences, LLC, Costa Mesa, CA, USA; \*Hospital Luis Vernaza, JBGYE, Guayaquil, Ecuador; †SOLCA, Guayaquil, Ecuador

## ABSTRACT

Spinal cord injury (SCI) is a devastating disorder with no cure or effective treatment. Presently, the ideal therapy would improve the quality of life for SCI patients. Numerous studies have demonstrated the use of stem cells for treating various pathological states. Clinical studies have demonstrated that transplantation of autologous CD34+ stem cells ameliorate the symptoms of several disorders such as leukemia, cardiomyopathy, diabetes, and autoimmune diseases including multiple sclerosis. Here we report a safety and feasibility trial with 2 years follow up of 8 SCI patients (4 acute, 4 chronic) administered with autologous bone marrow stem cells (BMSCs) via multiple route delivery. The study demonstrated changes in magnetic resonance imaging, improvements in Asia, Barthel (quality of life), Frankel, Ashworth scoring and bladder function following BMSCs administration. These studies demonstrate that BMSCs administration via multiple routes is feasible, safe, meeting our primary end points and may improve the quality of life for patients living with SCI. Presently, we have administered BMSCs into 46 paraplegic patients with greater than 6 months follow up. Our data demonstrates that administration of BMSCs via multiple routes is safe and feasible. Most importantly we had no tumor formations, no cases of infection or increased pain, and few instances of minor adverse events.



## Magnetic Resonance Imaging demonstrates morphological changes in the spinal cord following administration of BMSCs



## Neurological Evaluations

Case Study	Prior to Administration	6 Months after Administration	1 Year after Administration	2 Years after Administration
ASIA IMPAIRMENT GRADE/FRANKEL GRADE/ASHWORTH SCORE				
<b>Acute</b>				
Case 1	A/B/0	C/C/2	C/C/3	C/C/1
Case 2	A/A/3	A/C/1	A/C/1	C/C/2**
Case 3	A/A/0	ND	A/C/1	A/C/1
Case 4	A/A/0	C/C/1	C/C/1	A/C/1
<b>Chronic</b>				
Case 5	B/C/1	B/C/0	C/D/1	C/D/1
Case 6	C/D/3.5	D/D/3	D/D/3.5	D/D/ND
Case 7	A/A/0	C/C/1	C/C/1	C/C/1**
Case 8	C/C/2	C/C/2	C/D/1	C/D/0

ND-Not done \*1 year 3 months \*\*1 year 6 months

SCI Patients were evaluated using the American Spinal Injury Association (ASIA) and Frankel scale. The modified Ashworth scoring system was used to measure changes in spasticity.

## Administration of BMSCs following SCI Improves ASIA Motor and Sensory Scores

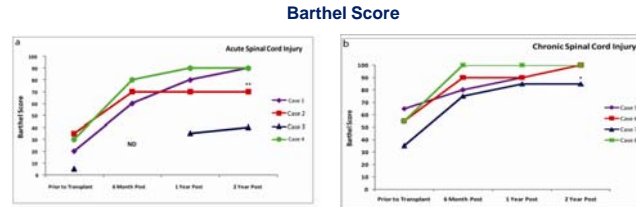
Case Study	Prior to Administration	6 Months after Administration	1 Year after Administration	2 Years after Administration
ASIA Motor Score/Sensory Light Touch Score/Sensory Pin Prick Score				
<b>Acute</b>				
Case 1	50/64/64	54/72/72	54/83/80	56/90/90
Case 2	50/49/49	52/50/50	52/54/54	52/54/57*
Case 3	50/42/42	ND	51/58/58	51/60/64
Case 4	50/76/76	52/78/78	56/80/82	58/80/84
<b>Chronic</b>				
Case 5	52/88/88	54/88/88	64/100/101	68/100/101
Case 6	62/66/66	62/80/80	78/94/94	85/94/94
Case 7	50/70/70	54/70/70	54/70/73	61/72/73**
Case 8	58/86/86	58/88/88	66/98/98	70/98/98

ND-Not done \*1 year 3 months \*\*1 year 6 months

ASIA motor and ASIA sensory (light touch and pin prick) scoring demonstrate improvements following administration of BMSCs into spinal cord injury patients

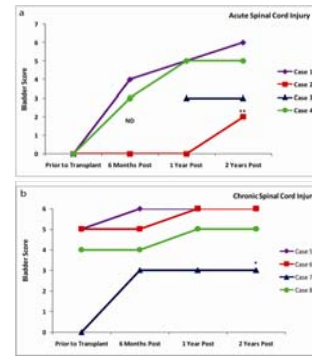


## Administration of BMSCs into SCI patients may Improve their Quality of Life



**Barthel Score**  
 Feeding - 0, 5, 10; Bathing - 0, 5; Grooming - 0, 5; Dressing - 0, 5, 10; Bowel - 0, 5, 10; Bladder - 0, 5, 10; Toilet use - 0, 5, 10; Transfers, bed to chair and back - 0, 5, 10, 15; Mobility on level surfaces - 0, 5, 10, 15; Stairs - 0, 5, 10  
 Maximum score of 100

### GGSF Bladder Function Scale

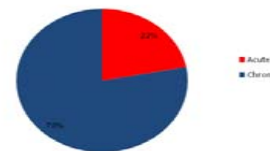


**Geffner, Gonzalez, Santacruz, and Flor (GGSF) Bladder Function Scale**

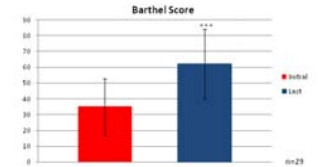
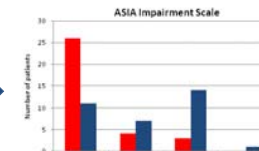
- No urinary bladder sensation or function <sup>a,b,c,d</sup>
  - Patients with cystostomies that when are closed may involuntarily void through the urethra <sup>a</sup>
  - Bladder sensation or autonomic symptoms and inability to void <sup>a,b,c,d</sup>
  - Bladder sensation or autonomic symptoms and passive voiding (spontaneous release of urine) <sup>a,b,c</sup>
  - Patients with open cystostomies that have bladder sensation or autonomic symptoms and passively void through the urethra (spontaneous release of urine) <sup>a</sup>
  - Bladder sensation with incomplete voiding (needs catheterization to complete voiding) <sup>b,c,d</sup>
  - Bladder sensation with active ability to void; however no control while voiding <sup>a</sup>
  - Complete bladder control
- <sup>a</sup> Patients use a suprapubic cystostomies in order to void their urinary bladder.  
<sup>b</sup> Patients use a catheter in order to void their urinary bladder  
<sup>c</sup> Patients with a urine collector  
<sup>d</sup> Patients that manually compress (massage) the hypogastric region in order to void their urinary bladder

## Data on Larger Cohort of Patients Administered with BMSCs Following SCI

Percentage of Chronic and Acute Patients



6 month follow up of 29 patients demonstrates improvements in ASIA scale following administered of BMSC



Barthel scoring demonstrates improvements in quality of life following BMSCs administration

## SUMMARY

- Administration of bone marrow stem cells via multiple routes is feasible and safe.
- Two year follow up of administration of bone marrow stem cells demonstrates that it may improve the quality of life for acute and chronic spinal cord injury patients.
- Presently we have administered 46 patients with bone marrow stem cells without any cases of infection, tumor formation, or increased pain.