A PHASE 1,2a STUDY SHOWING THAT ASCELLOS IS SAFE AND EFFECTIVE FOR THE TREATMENT OF NEUROCOGNITIVE DISORDERS

Chadwick Prodromos, Ruby Del Villar, Andrew Striegel, Gerard Pena

From the Foundation for Regenerative Medicine, Glenview Illinois

research@ismoc.net

December 1, 2025

INTRODUCTION

Intravenous or intrathecal mesenchymal stem cell (MSC) secretome or exosome formulations are ineffective for the treatment of neurocognitive disorders in humans. However, at least 41 pre-clinical studies have shown efficacy when these substances are instilled intranasally. For instance, studies have shown that intranasal exosomes protect motor neurons in mice with SOD1-linked amyotrophic lateral sclerosis (ALS), leading to an increase in motor function [1-2]. We hypothesized that intranasal instillation of Ascellos (RegenOMedix, Boca Raton, FL), an MSC-concentrated exosome product, would be safe and also effective for the treatment of neurocognitive disorders in humans. In our extensive ongoing study of intranasal exosome/secretome treatment for neurocognitive disorders in humans, we have consistently observed that any beneficial clinical effect that occurs will always manifest during the first twenty-four hours after treatment. We therefore also hypothesized that any efficacy after Ascellos treatment would manifest within the first 24 hours after treatment.

MATERIALS AND METHODS

After informed consent, 23 patients with ALS, Parkinson's disease (PD), Multiple Sclerosis (MS), Lewy Body dementia (LBD), idiopathic cognitive decline (CD), congenital myasthenic syndrome (CMS), or essential tremor (ET) were treated. Baseline patient characteristics are reported in Table 1. Prior to treatment, frozen vials of Ascellos were thawed for 15 minutes in a 37°C water bath. Patients were placed in the supine position, and either five, nine, or

ten cc were instilled intranasally by a licensed physician. The patients were observed for 15 minutes post-instillation. They were instructed to call after leaving the clinic if they had any adverse events. They were all followed up the next day in person or by telephone, and at one week and one month after treatment by telephone. Patients were asked specifically about improvement in the symptoms their disease manifested before treatment. For ALS patients this included bulbar, motor, and respiratory symptoms as well as muscle pain. For PD patients, common issues included balance problems, stiffness, tremors, muscle cramps, as well as olfactory, gustatory, cognitive, GI, and GU symptoms. For MS, primary symptoms were motor. For LBD patients, primary symptoms were motor, balance, tremor, and cognition related. For ET, the magnitude of tremors was evaluated.

RESULTS

Twenty-six treatments were administered among the 23 patients. Two ALS patients and one PD patient who had initially responded to Ascellos also received a second treatment. Both ALS patients were treated one month after the first treatment, while the PD patient was treated two months after the first treatment. Fifteen patients also received a different secretome or exosome formulation on the day after their Ascellos treatment. Therefore, only their clinical result in the first twenty-four hours after treatment was felt to be a reliable indicator of the isolated effect of Ascellos. No patient experienced any pain at the time of treatment nor after treatment. There were no adverse events of any kind after treatment out to one month.

After one day, 14 patients (60.9%) reported substantial clinical improvement, six of whom (42.9%) remained improved compared to baseline after one month. All patients who had a positive response to Ascellos after one month also had a positive response after one day. Among ALS patients, the most common response was an improvement in speech, occurring in 6 of the 7 responders. In patients with PD, improvements often occurred in tremor size, pain/cramps, and mental clouding. The doses and areas of clinical improvement for each patient are shown in Table 2.

DISCUSSION

This study demonstrates that intra-nasal Ascellos instillation is completely safe in human patients with neurocognitive disorders and has clinical efficacy in a majority of such patients. Since many patients in this study had a different exosome or secretome treatment in addition to Ascellos after Ascellos, the one-month improvement cannot be necessarily ascribed to Ascellos alone. However, the one-day results can only be the result of Ascellos treatment. While combining treatments makes data analysis more difficult, our top priority is to effectively treat our patients. Using more than one treatment was deemed

to give the patient the best chance to improve. However, as described above it is still possible to break out the efficacy of Ascellos focusing on the initial treatment before other treatment was tried. These results may be the first demonstration of disease modifying activity by any treatment for ALS, PD or LBD. Studies are ongoing to further analyze the efficacy and longevity of efficacy of Ascellos and other treatment for neurocognitive disorders.

REFERENCES

[1] Bonafede R, Turano E, Scambi I, Busato A, Bontempi P, Virla F, Schiaffino L, Marzola P, Bonetti B, Mariotti R. ASC-Exosomes Ameliorate the Disease Progression in SOD1(G93A) Murine Model Underlining Their Potential Therapeutic Use in Human ALS. International Journal of Molecular Sciences. 2020; 21(10):3651.

[2] Zhou J, Li F, Jia B, Wu Z, Huang Z, He M, Weng H, So K, Qu W, Fu Q and Zhou L. Intranasal delivery of small extracellular vesicles reduces the progress of amyotrophic lateral sclerosis and the overactivation of complement-coagulation cascade and NF-κB signaling in SOD1G93A mice. J Nanobiotechnol 22, 503 (2024).

TABLES

Table 1. Baseline Patient Demographics.

Patient No.	Sex	Age	Diagnosis
1	M	68	ALS
2	F	58	ALS
3	M	35	ALS
4	M	48	ALS
5	M	50	ALS
6	M	43	ALS
7	M	39	ALS
8	M	59	ALS
9	F	69	ALS
10	M	55	ALS
11	M	79	ALS
12	M	39	ALS
13	M	59	ALS
14	M	82	ET
15	M	65	CD
16	M	69	LBD
17	F	47	MS
18	M	78	PD
19	F	65	PD

20	M	91	PD
21	M	55	PD
22	M	62	PD
23	F	47	CMS

Table 2. Response characteristics one day and one month after Ascellos treatment. $_2$Results from second treatment. *Patient received a different product more than 24 hours after Ascellos.

Patient	**Dose**	**1-Day Response**	**1-Month Response**
1	10cc	No Response	N/A*
2	10cc	Respiratory, Muscle Movement, Vision, Speech, Sleep	N/A*
3	10cc	Bulbar (Speech), Gait, Energy	N/A*
4	10cc	No Response	N/A*
5	10cc	Muscle Movement (L fingers/toes), Speech	N/A*
6	10cc	Speech	N/A*
7	9cc	No Response	N/A*
8	9cc	No Response	N/A
9	9cc	No Response	N/A
9_2	9cc	No Response	N/A
10	9cc	Speech, Respiratory, Energy, Sleep, Reduced Pain (neck)	Bulbar (Speech), Respiratory
10_2	9cc	Speech, Respiratory, Reduced Pain (neck/feet)	Respiratory
11	9cc	No Response	N/A*
12	9cc	Bulbar (Speech, Swallowing), Muscle Movement/Strength (shoulder/legs)	N/A
13	9cc	Mood, Muscle Movement (R Leg, L hand)	N/A*
14	9cc	No Response	N/A*
15	10cc	No Response	N/A*
16	10cc	Vision, Muscle Movement/Strength (hands), Balance, Reduced Pain (back, toes, neck, legs), Sleep, Reduced Mental Clouding	N/A*
17	9cc	Reduced Pain (legs/hips)	Reduced Pain (shoulders/back /legs/hips)
18	10cc	Sleep, Reduced Tremor, Reduced Stiffness, Reduced Pain (neck), Gait	Gait, Reduced Sialorrhea
18_2	9cc	Gait, Reduced Pain (neck)	N/A

19	10cc	Reduced Cramps (leg), Gait, Reduced Mental Clouding	N/A*
20	9cc	No Response	N/A*
21	9cc	Reduced Mental Clouding, Reduced Tremor	N/A
22	9cc	Reduced Cramps (foot), Smell	Smell
23	5cc	Bulbar (Speech, Swallowing), Vision	Gait