Am J Stem Cells 2025;14(4):217-229
www.AJSC.us /ISSN:2160-4150/AJSC0166665

Original Article

Exosome-rich mesenchymal stem cell secretome improves strength in patients with amyotrophic lateral sclerosis, Kennedy disease, congenital myasthenic syndrome and Lewy body dementia

Chadwick C Prodromos[1], Ruby Del Villar[1], Max Y Jin[3], Alaa Abd-Elsayed[4], Kenneth Candido[1,2]

[1]Prodromos Stem Cell Institute, Glenview, IL, USA; [2]Department of Anesthesiology and Surgery, University of Illinois College of Medicine, Chicago, IL, USA; [3]University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; [4]Department of Anesthesiology, University of Wisconsin School of Medicine, Madison, WI, USA

Received June 9, 2025; Accepted August 30, 2025; Epub October 15, 2025; Published October 30, 2025

Abstract: Aim: Amyotrophic lateral sclerosis (ALS), Lewy Body dementia (LBD), Kennedy disease (KD), and Congenital Myasthenic Syndrome (CMS) are progressive motor disorders for which no disease modifying treatment exists. ALS and LBD are uniformly, and often rapidly, fatal. No treatment of any kind has ever resulted in actual improvement for ALS patients; the best that has been achieved is minor slowing of their progression. Forty-one preclinical studies of intra-nasal instillation of mesenchymal stem cell exosomes have, however, demonstrated complete safety and efficacy for models of a variety of neurocognitive and motor disorders. We hypothesized that intranasal exosomes treatment in humans would be completely safe and also effective for the treatment of motor disorders such as ALS, LBD, KD and CMS. Methods: 18 patients with ALS, Kennedy Disease, Congenital Myasthenic Syndrome, or Lewy Body Dementia had 32 AlloEx Exosome® treatments to assess safety, attenuation of disease, and increase in strength and motor function. The study was conducted under the clinical trial NCT07105371 found at clinicaltrials.gov/study/NCT07105371. Results: There were no adverse events of any kind reported among these treatments. All patients, except for one, achieved some degree of clinical and strength improvement; the longest improvement was recorded at the 6-month follow-up. Conclusion: Intranasally-instilled AlloEx Exosomes® are completely safe, attenuate progression, and improve strength in ALS, Kennedy Disease, CMS, and LBD.

Keywords: Exosomes, secretome, ALS, Kennedy disease, congenital myasthenic syndrome, Lewy body dementia

Introduction

Amyotrophic lateral sclerosis (ALS) is a uniformly fatal progressive motor neuron disease that is growing in prevalence, with over 30,000 Americans affected [1]. It is estimated that approximately 5-10% of ALS cases are familial (FALS), while the majority of cases are sporadic (SALS) [2]. Clinical manifestations of ALS due to lower motor neuron involvement include progressive muscle weakness, muscle atrophy, and fasciculations [3]. On the other hand, upper motor neuron involvement manifests as spasticity, hyperreflexia, and bradykinesia. The pathophysiology of ALS involves the loss of motor neurons in the motor cortex, brain stem, and spinal cord, potentially resulting from defects in proteostasis, RNA metabolism, cytoskeletal structure, and axonal transport [3-5].

Kennedy Disease, or Spinal and bulbar muscular atrophy (SBMA), is an X-linked disease that is classified as a motor neuron disease similar to ALS [6]. This disease is a lower motor neuron disorder associated with neuron loss, muscle weakness, atrophy, and fasciculations [7]. The symptoms include fasciculations in the face and extremities, muscle weakness with difficulty walking and climbing stairs, often with a level of asymmetry, or weakness more dominant on one side. Additionally, SBMA patients commonly have issues with speech, swallowing, and sometimes chewing due to weakness in the jaw muscles [7].

https://doi.org/10.62347/FTXA8845

Congenital Myasthenic Syndrome (CMS) is a rare neuromuscular disorder that is caused by defects in the neuromuscular junction [8]. These defects manifest due to mutations in proteins that affect processes involving the motor end plate [9]. As of 2023, there have been variants identified in 35 total genes in CMS patients [10]. This progressively disabling disease is characterized by fatigable muscle weakness which can involve ocular, respiratory, and limb muscles [8, 11]. CMS can vary in severity, with symptoms manifesting as muscle fatigue, ptosis, swallowing disturbances, and diplopia in mild cases, or as apnea and extreme limb weakness that can lead to loss of ambulation in severe cases [12].

Lewy body dementia (LBD) is a degenerative neural disorder involving a specific presentation of α-synucleinopathy, with a similar pathology and presentation as Parkinson's Disease Dementia [13]. LBD is the second-most common form of dementia, after Alzheimer's Disease [14, 15]. This progressive dementia commonly presents issues with attention, executive function, memory loss, cognitive function, drowsiness, muscular rigidity, tremors, loss of balance and proprioception, and bradykinesia [16-18].

There is no disease-modifying treatment nor treatment of any type heretofore that has resulted in increased strength or function in ALS patients. The best that has been achieved is a minor decline in the rate of progression of the disease by the few FDA-approved pharmaceutical drugs for this disorder. So bleak are the treatment options that a 25% reduction in the rate of decline is considered satisfactory for approval of treatment. Current management options for ALS include riluzole and edaravone. Overall, the prognosis of ALS is grim, with no substantial cure available and an average survival of 24 to 50 months after symptom onset [19].

Kennedy disease, LBD, and CMS are characterized by weakness. No treatment has been shown to increase strength or motor function except for a small minority of LBD patients who respond to L-Dopa precursors.

Forty-one preclinical studies have shown safety and efficacy with exosome-secretome treatment. One such study utilized adipose-derived mesenchymal stem cells to treat a SOD1 murine model, comparing intravenous and intranasal routes of administration [20]. In this study, repeated administration of ASC-exosomes improved motor performance and protected lumbar motor neurons, the neuromuscular junction, and muscle tissue. A second study also showed significant improvements in motor performance and survival in SOD1 mice after intranasal administration of exosomes sourced from MSCs induced from human urine epithelial cells [21]. This study showed that administration attenuated the elevation of proinflammatory cytokines and glial responses. Further, proteomics and transcriptomics revealed overactivation of the complement and coagulation cascades, and that the NF-κB signaling pathway was inhibited by exosome delivery, representing a potential avenue for ALS therapy.

AlloEx Exosome® is the exosome-rich secretome of AlloRx allogeneic umbilical cord-derived mesenchymal stem cells. It contains exosomes, micro-RNA, and various cytokines and proteins. Mesenchymal stem cell secretomes and exosome solutions have been shown to improve motor function in pre-clinical trials of multiple neurocognitive disorder models when instilled intranasally. No serious adverse events have been reported in any of these preclinical trials.

This current series looked to expand on the success of mesenchymal stem cell exosomes and translate to a clinical model. The objectives were to analyze the safety and efficacy of AlloEx Exosomes as a potential therapeutic option for patients with ALS and other motor disorders. We hypothesized that this treatment would be completely safe and effective.

Methods

Inclusion criteria

Patients needed a neurologist-verified diagnosis of a progressive motor disorder. In addition, LBD patients must have failed a trial of dopamine precursors. Patients must have been 18 years old or older, able to travel to Antigua for the treatment, and capable of informed consent.

Exclusion criteria

Patients were excluded from the trial if they were pregnant or had active cancer at the screening consultation.

Table 1. Patient baseline demographics

Patient No.	Age	Sex	Diagnosis
1	60	M	ALS
2	64	M	ALS
3	66	M	ALS
4	59	M	ALS
5	68	M	ALS
6	63	M	ALS
7	35	M	ALS
8	37	F	ALS
9	56	M	ALS
10	84	F	ALS
11	51	M	ALS
12	47	M	ALS
13	49	M	ALS
14	51	M	ALS
15	66	M	Kennedy Disease
16	47	F	Congenital Myasthenic Syndrome
17	72	M	Lewy Body Dementia
18	65	M	Lewy Body Dementia

By design these were our only inclusion and exclusion criteria. If participants had the relevant disorder, we could learn from treating them. For example, we did not limit inclusion to a certain degree of severity, as we sought to understand whether this treatment was safe and effective for the full range of severity. The same is true of age and all other patient variables.

Patient cohorts

14 patients with ALS, 1 patient with Kennedy Disease, 1 patient with Congenital Myasthenic Syndrome, and 2 patients with Lewy Body Dementia were selected. All patients were treated in our treatment facility located in Antigua. Patient demographics can be observed in **Table 1**.

ALS

The clinical course is characteristic. Presentation involved weakness in all. In some, it was primarily bulbar, while many others had weakness of their hands or of core and respiratory muscles. All had been progressive prior to treatment. All had brain MRIs which ruled out other causes of weakness such as Multiple Sclerosis (MS) or stroke. Below is a breakdown of the presentation of each patient.

Patient 1: A 60-year-old male presented with weakness of the arms and some fasciculations. He had trapezius pain on the right side. The patient was also previously diagnosed with hypertension and was taking medication to manage it. The patient reported that the onset of his symptoms began around January 2024, and he was diagnosed with ALS in August 2024.

Patient 2: A 64-year-old male presented with difficulties in swallowing and frequent choking episodes. He was ambulatory with assistance and was diagnosed with ALS in June 2024.

Patient 3: A 66-year-old male presented with ambulatory difficulties and used an assistive device. He reported the onset of symptoms beginning in November 2023 and was diagnosed with ALS in April 2024. He was taking medications to manage his symptoms, including 105 mg of edaravone- two days on one day off for two weeks- and 50 mg of riluzole twice daily.

Patient 4: A 59-year-old male presented with muscular weakness in the arms and legs. He had a complete foot drop on the left and partial foot drop on the right. The patient's distal function appeared worse than his proximal. He also presented with weakness in his hip flexors, core muscles, biceps, and deltoids. He was able to walk with the assistance of a walker.

Patient 5: A 68-year-old male presented with weakness in both ankles, as demonstrated by foot drops of both feet. He also presented with weakness of his deltoids, hands, and torso. His speech was slightly slurred although he reported no breathing or swallowing problems. The patient reported that the onset of his symptoms began around November 2022.

Patient 6: A 63-year-old male presented with ambulatory difficulties that required him to use a wheelchair. He was able to stand and bear weight to transfer from the chair, but only for short periods. The patient was diagnosed with ALS on January 21st, 2021, and had been taking 50 mg of riluzole twice a day and 10 mg of baclofen, a muscle relaxer, three times a day to manage his symptoms.

Patient 7: A 35-year-old male presented with weakness in both arms and was able to lift one arm more than the other. The patient reported that the onset of his symptoms began around September 2021 and was diagnosed with ALS in January 2023.

Patient 8: A 37-year-old female presented with slight difficulties in speech and arm strength. She reported that her symptoms began with her knees and caused her to have impaired balance and walking abilities. She was diagnosed with ALS in 2019.

Patient 9: A 56-year-old male presented with ambulatory and speech issues. He used assistive devices to be able to walk and was experiencing weakness in his hands. The patient reported that the onset of his symptoms began around January 2023, and he was diagnosed with ALS in January 2024.

Patient 10: An 84-year-old female presented with shortness of breath and difficulties with swallowing, causing her to frequently choke. Her voice and right hand also exhibited impaired function, and she demonstrated ambulatory difficulties that required her to use a walker. The patient reported that the onset of her symptoms began in the early summer of 2023, and she was diagnosed with ALS on October 4th, 2024.

Patient 11: A 51-year-old male presented with speech difficulties and impaired function of his left hand. He reported frequently feeling winded and noted that the onset of his symptoms began around October 2023. He was then diagnosed with ALS in February 2024.

Patient 12: A 47-year-old male presented with weakness of his arms and legs that was more pronounced on his right side. The patient reported that the onset of his symptoms began around March or April of 2023, and he was diagnosed with ALS on July 24th, 2023.

Patient 13: A 49-year-old male presented with significantly decreased function of his hands and feet. He was not ambulatory and reported the onset of his symptoms beginning in August 2021.

Patient 14: A 51-year-old male presented with impaired speech and balance. He also demonstrated left arm weakness, fasciculations, and overall muscle stiffness. The patient was diagnosed with ALS in February 2024.

Kennedy disease

The clinical course is characteristic. Presentation involved muscular atrophy in the limbs and bulbar muscles that progressed slowly, compared to the quick decline associated with ALS. All patients were diagnosed by an independent physician prior to treatment.

Patient 15: A 66-year-old male presented with muscle weakness and atrophy throughout his body. He reported experiencing difficulties with walking, speech, and sleeping. The patient was diagnosed with KD.

CMS

The clinical course is characteristic. Presentation involved ptosis, fatigue, respiratory problems, and muscle weakness. All patients were diagnosed by an independent physician prior to treatment.

Patient 16: A 47-year-old female presented with intermittent weakness and myotonic-like problems that caused muscle pains and cramps. She reported having a shortness of breath, droopy eyelids, and double vision. She required oxygen and had a general lack of energy. She was diagnosed with CMS.

Lewy body dementia

The clinical course is characteristic. Presentation involved fluctuating cognitive abilities, visual hallucinations, and Parkinsonism symptoms, rather than issues with memory and language skills, which are associated with Alzheimer's Disease.

Patient 17: A 72-year-old male presented with progressive gait problems along with muscle pains and cramps. He was diagnosed with LBD and had been taking 10 mg of donepezil daily and 50 mg of carbidopa-levodopa twice daily to manage his symptoms.

Patient 18: A 65-year-old male presented with rigidity of arms/elbows and knees. He was only able to partially bear weight on his legs and was experiencing issues with his speech. The patient was diagnosed with LBD.

Objectives

The primary study objectives were demonstration of safety through observation of adverse events, and measurement of efficacy using the ALSFRS-R rating, muscle grade testing, pulmonary testing, electroencephalogram (EEG)

tests, Neurofilament Light Chain (NfL) Serum Z scores, and detailed interviews with patients.

Adverse events

Generally, an adverse event would refer most commonly to heart attack, stroke, deep vein thrombosis, pulmonary embolus, allergic reaction, or psychosis. However, any significant deviation in their normal health would be listed if it occurred.

Statistical analysis

Descriptive statistics (mean, median, etc.) were calculated for each of the numerical measurements of efficacy. No other statistics were appropriate for this study. Interviews with patients were analyzed for various parameters and were evaluated by using Likert scales to quantify changes from the treatment.

ALS functional rating scale - revised: ALSFRS-R

This test was given to each patient digitally by one of our team members remotely. The score is then simply calculated from their response. This is the standard procedure for this test.

Muscle grading test

This was evaluated in each case by Chadwick Prodromos MD, a board-certified orthopaedic surgeon. Some were done in person, but most were done by remote video tele-medicine evaluation. The muscles tested were selected because they allowed remote strength evaluation based on visual assessment of lack of motion, flicker, motion with gravity, and motion against gravity. All evaluations, whether in person or remote, were performed directly by Dr. Prodromos.

Pulmonary function test

These were standard PFT's ordered by their local physician or by our team.

EEG

These were carried out by Timothy Royer, Ph.D. He is a board-certified neuropsychologist with extensive experience in this field. Tests were carried out directly by him in Antigua before treatment. After treatment, he performed some sessions when patients returned to Antigua for further treatment, or remotely with the portable EEG kit sent to patients where it was administered locally.

Neurofilament light chain

These were ordered by the patients' local doctor or by Dr. Prodromos, both before and approximately six weeks after treatment.

Exosomes

All patients were treated with the umbilical cord-derived mesenchymal stem cell secretome known as AlloEx Exosomes®, from Vitro Biopharma (www.vitrobiopharma.com) in Golden, Colorado. Vitro Biopharma is an FDA-registered biomanufacturing firm whose cells have been FDA-authorized for use in human patients. They use cGMP technique, have international ISO 9001 and 13485 certifications, and have an active MSC IND with the US FDA. Their cells and exosomes have been repeatedly approved for compassionate use for various patients in the United States.

Dose determination

The dose determination was extrapolated to human size from murine model preclinical studies that demonstrated efficacy [20, 21]. Additionally, in the process of performing 176 treatments for 97 unique patients in Antigua for various neurocognitive and neurodegenerative disorders, we have determined the appropriate dose in the study of those patients with 1-6 months of follow-up, based on our dose escalation trials as seen in **Figure 1** and **Table 2**.

Instillation protocol

Patients were instructed to take a single baby aspirin on the morning of treatment, unless they were on other anticoagulants or had a contraindication to baby aspirin. The administration route for treatment was intranasal instillation in each nostril. For treatment preparation, the frozen conditioned medium was thawed for 1 hour to room temperature. A dose of exosome solution was instilled into each nostril. Patients were observed for ten minutes and then discharged.

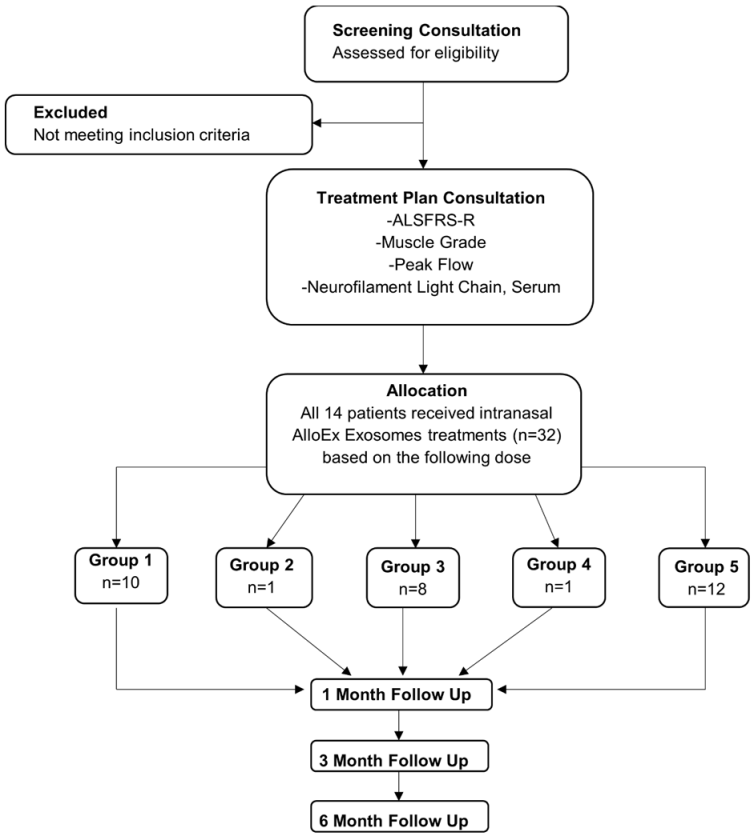

Figure 1. CONSORT flow chart. Patients in Group 1 received a single dose of AlloEx Exosomes. Patients in Group 2 received 1.25× single dose of AlloEx Exosomes. Patients in Group 3 received a double dose of AlloEx Exosomes over the course of two consecutive days. Patients in Group 4 received a total dose of 2.25× AlloEx Exosomes over the course of two consecutive days. Patients in Group 5 received a total dose of 2.5× AlloEx Exosomes over the course of two consecutive days.

Post-treatment protocol

To assess the safety of the treatment, patients were observed post-treatment and vital signs were monitored for 30 minutes. They were then observed on the evening of treatment, and again on the day after treatment. All patients were stable and without side effects at all observation points.

Results

18 patients had a total of 32 treatments throughout the trial. One patient did not show improvement, while the other patients all had some clinical improvement regarding one or more of the following: muscle strength, dyspnea, deglutition, sensorium, muscle stiffness, sexual function, and/or fasciculations.

ALS functional rating scale - revised: ALSFRS-R

An increase was observed in the mean ALSFRS-R scores at one month after each treatment as seen in **Table 3**.

Strength, stiffness, and fasciculations

Strength: 13 of 14 ALS patients had some improvement in strength after treatment. Most had improvement in their ALSFRS-R score. Seven patients had some measurable improvement in strength as seen in specific muscle grade testing without an improvement in the ALSFRS-R score. Changes in muscle grade score for each category can be observed in **Table 4**.

Stiffness: Stiffness is not measured on the ALSFRS-R assessment. Two patients had clinically significant improvement in stiffness, which was independently measured and listed in **Table 4**.

Fasciculation: Similarly, fasciculation is not measured on the ALSFRS-R score. However, one ALS and one Kennedy Disease patient noticed significantly decreased fasciculations, which are also listed in **Table 4**.

EEG data

EEG scans were collected before and after treatment for Patients 1, 2, 3, and 7. Unfortunately, the data from Patient 3's post-treatment EEG is unavailable due to electrical interference during the scan. This patient will be retested on a later date. EEG data were interpreted and reported by a neuropsychologist on our team for the other three patients.

Patient 1: The results of the patient's EEG scans indicated a statistically significant increase in the post-treatment Theta ratio in

Table 2. Patient dosing regimen

Patient No.	Rx 1	Rx 2	Rx 3	Rx 4
1	Nov 2024	Jan 2025 x2	Mar 2025 x2	-
2	Nov 2024	Jan 2025 x2	Mar 2025 x2	-
3	Nov 2024	Jan 2025 x2	Mar 2025 x2	-
4	Jan 2025	Mar 2025 x2	-	-
5	Jan 2025	Mar 2025 x2	-	-
6	Jan 2025	Mar 2025 x2	-	-
7	Jan 2025	Mar 2025 x2	-	-
8	Jan 2025 x 2	-	-	-
9	Mar 2025 x2	-	-	-
10	Mar 2025 x 2	-	-	-
11	Mar 2025 x2	-	-	-
12	Mar 2025 x2	-	-	-
13	Mar 2025 x2	-	-	-
14	Mar 2025 x2	-	-	-
15	Mar 2025 x2	-	-	-
16	Mar 2025	-	-	-
17	Aug 2024	Nov 2024	Jan 2025	Mar 2025 x2
18	Nov 2024	Mar 2025 x2	-	-

Patients that received double dose treatment over the course of two consecutive days are indicated by "x2".

Table 3. Mean ALSFRS-R scores (for ALS patients)

Time	Mean ALSFRS-R Score
Pre-Treatment (n = 14)	30.93
1 Month Post First Treatment (n = 14)	31.38
1 Month Post Second Treatment (n = 8)	33.00
1 Month Post Third Treatment (n = 3)	34.00

the T3 region, which is a strong indicator of improved mental recovery, cognitive clarity, and calmness. Additionally, post-treatment High Beta ratios decreased in the CZ, T3, and T4 regions, suggesting improvements in stress regulation. These results were consistent with the patient's increased ALSFRS-R scores following treatment.

Patient 2: The patient's post-treatment EEG scans demonstrated a considerable increase of the Theta ratio, which had previously been well below the healthy range prior to treatment. This suggests strong neurological recovery, improved attentional capacity, and enhanced cognitive resilience. The patient also demonstrated a decrease in High Beta ratios following treatment, indicating improved emotional regulation, greater resilience, and reduced anxious reactivity. These results were consistent with the patient's increased ALSFRS-R scores after treatment.

Patient 7: The patient's EEG scans showed a decrease in Theta across the CZ, T3, and T4 regions, indicating reduced brain recovery and balance after treatment. Additionally, the post-treatment High Beta ratio increased across all three regions, suggesting potential effects on right hemisphere processing and an elevated stress response. These findings do not align with the patient's ALSFRS-R score, which increased by 1 point in March 2025. However, this patient did not exhibit an improvement as clinically significant as the others, which may correspond to the EEG data reported.

Kennedy disease

The Kennedy Disease patient is a 66-year-old male who presented with complaints of muscle weakness and atrophy throughout his body after being diagnosed with Kennedy Disease in 2010. Since his diagnosis, the patient had been treating his symptoms only with physical therapy. He stated that physical therapy alleviated the tingling in his limbs by 10%, but it did not alleviate the muscle weakness and pain in his lower back and legs. In January of 2025, the patient presented for a screening consultation and was prospectively enrolled in the trial as Patient 15.

The patient received a double dose of exosomes over two consecutive days in March of 2025. A week after treatment, the patient reported a 45% increase in energy compared to his energy level before receiving treatment. The patient also reported that he had an improvement in his myopia. Two months after treatment, the patient reported no regression in his improvements (**Table 5**), and also noticed a 50% improvement in his muscle fasciculation and walking endurance compared to his pre-treatment condition.

Table 4. Change in muscle strength, stiffness, and fasciculations

Category (Muscle Strength)	Total Change in Muscle Grade Score (Δ)
Left Hand Strength (n = 5)	+5
Right Hand Strength (n = 3)	+3
Left Shoulder Strength (n = 1)	+1
Right Shoulder Strength (n = 3)	+3
Core Strength (n = 4)	+5
Left Hip Strength (n = 1)	+1
Right Knee Strength (n = 1)	+1
Left Knee Strength (n = 1)	+1
Right Foot Strength (n = 1)	+1
Left Foot Strength (n = 1)	+1
Category	Negative Point Score = Decreased Stiffness
Stiffness (n = 2)	-3
Category	Negative Point Score = Decreased Fasciculations
Fasciculations (n = 2)	-3

Table 5. Qualitative overview of Kennedy Disease patient parameters

	Before Treatment	2 months after Treatment
Speech	Most words understandable with difficulty	Easily understandable
Ambulation	Could not walk on sand, used cane regularly, fell frequently	Able to walk on sand, rarely uses cane, no falls
Muscle Pain	Level 8 out of 10	Level 1-2 out of 10
Muscle Burning	Constant	Decreased 65%
Sleep	4.5 hrs/night, pain	6 hrs/night, no pain, improving
Brain Fog	Moderate/Severe	Mild
Balance	Severe Impairment	Mild Impairment
Grip Strength	5 kg Left, 10 reps 5 kg Right, 2 reps	6.5 kg Left, 15 reps 5 kg Right, 5 reps

Table 6. Quantitative overview of congenital myasthenic syndrome patient parameters

	MIP (cmH_2O)	MEP (cmH_2O)	Lt Grip Strength (lbs.)	Rt Grip Strength (lbs.)	Sit-to-Stand Test
Before Treatment	26	23	35	35	6 times
2 months After Treatment	73	30	50	60	12 times

Maximal Inspiratory Pressure (MIP) and Maximal Expiratory Pressure (MEP) in cmH_2O, were measured one month before treatment and one month after treatment. Grip strength was measured for both hands in units of pounds. The sit-to-stand test measured how safely the patient stood from a chair within 30 seconds, one week before and after treatment.

Congenital myasthenic syndrome (DOK7)

The patient is a 47-year-old female who complained of progressive muscle weakness, tremor, progressive muscle atrophy, fasciculations, chronic respiratory failure, lack of endurance, and double vision. The patient elected to receive a dose of 2.5× exosomes over two consecutive days for her motor disorders, and also opted to receive a single dose of AlloRx Stem Cells intravenously, to address her ongoing pulmonary disease, on her third day.

The patient had dramatic improvement in all parameters for 3-4 weeks with some regression subsequently in most parameters but not to pre-treatment levels, and with some parameters not showing regression (**Tables 6** and **7**).

Table 7. Qualitative overview of Congenital Myasthenic Syndrome patient parameters

	Before Treatment	4 Weeks After Treatment	7 Weeks After Treatment
Muscle Pain	Moderate	0%	40% Reduced
Muscle Atrophy	Progression	Not Progressive	Progression
Strength	Baseline	100% Improvement	60% Improvement
Deglutition/Choking	Moderate	Absent	Mild
Chewing fatigue (ability to eat solid food meal)	Limited	Unlimited	Unlimited
Gait Asymmetry	Intermittent	Absent	mild
Tremor	Every other day	Absent	Absent
Endurance (weekly step average)	2400	5315	4260
Meters Traversed in 6 Minutes	260	378	393
Calories Consumed per Week	220	340	282
Intermittent Diplopia with prism glasses	Moderate	Absent	Mild
Ptosis	Intermittent	Absent	Absent
Oxygen Dependence	Constant	1-2 hrs/day	1-2 hrs/day

Lewy body dementia

Patient 17: The first Lewy Body Dementia patient was a 71-year-old male who presented with complaints of balance and gait as well as decreased strength. Due to continued decline in the patient's state, the patient elected treatment with intranasal AlloEx Exosome®.

In August of 2024, the patient received a single intranasal dose of AlloEx Exosome®. One month after treatment, the patient showed marked improvement in balance and motor function. He also stated that he was more alert cognitively and felt overall substantially improved. Nightmares also stopped. Shortly after, motor function began to decline slightly, thus a decision was made to proceed with another treatment.

Two months later in November of 2024, the patient received another single dose of AlloEx Exosome®. One week after, the patient showed further improvement and maintenance from the first treatment. Motor function returned to the previous improvement level, while cognition remained better. The patient reported that his sleep was better after treatment.

In January 2025, the patient received another single dose of AlloEx Exosome®. One week after treatment, he reported an overall 80% improvement in cognitive function and 60% improvement in motor function compared to baseline prior to the first treatment. The patient also noted a reduction in brain fog. Two months later, he reported sustained improvements in all areas, although there was some regression in motor function and slight decline in cognition. Consequently, the decision was made to administer a double dose of exosomes over two days.

In March of 2025, the patient received a double dose of exosomes over two consecutive days. One week after, patient follow-up was conducted as an in-person visit, and the following observations were recorded. The patient reported that his cognitive and motor function was better than his baseline prior to the very first treatment. Slight balance issues were observed on his right side but still very much improved. One month after treatment, the patient reported continued maintenance of the improvement he had from treatment. The patient's level of impairment over time can be observed in **Figure 2**.

Patient 18: The second Lewy Body Dementia patient was a 65-year-old male who presented with complaints regarding difficulty with his speech, coordination, and movement due to a clinical diagnosis of Lewy Body Dementia and Corticobasal degeneration. The patient was non-ambulatory and supported in a wheelchair. He was unable to speak and unable to wipe his mouth when eating. The patient presented for a screening consultation in September of 2024, and the decision was made to enroll him in the trial, where he would receive multiple treatments of AlloEx Exosome®.

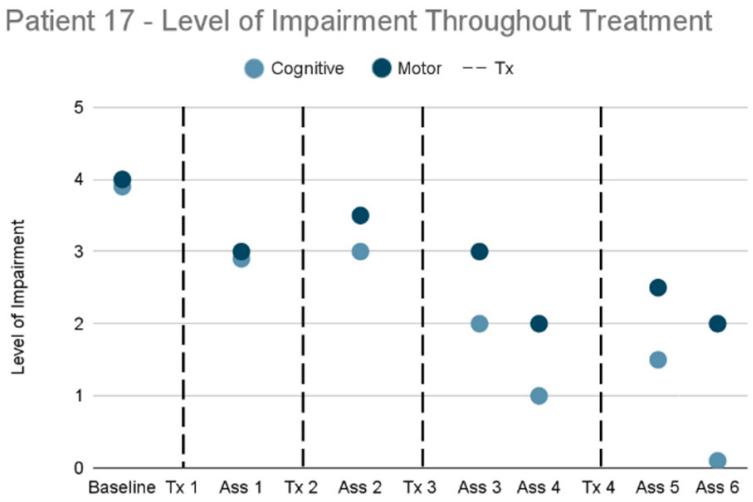

Figure 2. Level of impairment in Patient 17 over time. The levels of impairment were categorized as follows: 0 = Normal, 1 = Very Mild, 2 = Mild, 3 = Moderate, 4 = Severe, and 5 = Very Severe. Baseline was assessed in August of 2024 before Treatment 1 (Tx 1). Assessment 1 (Ass 1) was conducted 1 week after Tx 1. Tx 2 was administered in November of 2024, and Ass 2 was conducted 1 week after. Tx 3 was administered in January of 2025. Ass 3 and Ass 4 were conducted 1 week and 1 month after Tx 3, respectively. Tx 4 was administered in March of 2025. Ass 5 and Ass 6 were conducted 1 week and 1 month after Tx 4, respectively.

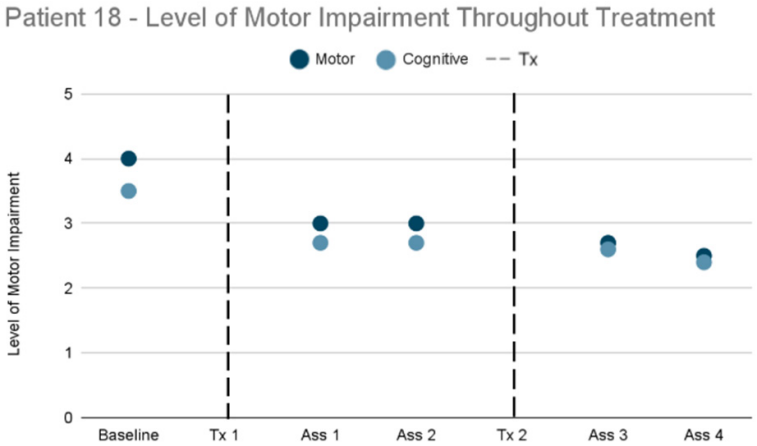

Figure 3. Level of motor impairment in Patient 18 over time. The levels of impairment were categorized as follows: 0 = Normal, 1 = Very Mild, 2 = Mild, 3 = Moderate, 4 = Severe, and 5 = Very Severe. Baseline was assessed in November of 2024 before Treatment 1 (Tx 1). Assessment 1 (Ass 1) was conducted 1 week after Tx 1 and Ass 2 was conducted 1 month after Tx1. Tx 2 was administered in March of 2025. Ass 3 and Ass 4 were conducted 1 week and 1 month after Tx 2, respectively.

The patient presented for intranasal AlloEx Exosomes® treatment in November of 2024, where he received a single dose of exosomes. One week after this treatment, the patient's wife reported that he had significant improvement in his speech such that he was able to speak a little and body movements such that he was, for example, able to now wipe his mouth which he could not do before. Shortly after, the patient broke his ankle in an unrelated event, but his wife reported that there was no regression from his previous improvements. Three months after this treatment, the patient's wife reported that all previous improvements had been maintained and that he had further improvements in his communication with others.

In March of 2025, the patient presented for a second treatment of intranasal AlloEx Exosome®, receiving a dose of 2.5× exosomes over two consecutive days. One week after this treatment, the patient's wife reported that he had further improvement in his speech, but that the effects of this treatment were not as prominent as the effects from his first treatment in November of 2024. One month after this treatment, the patient's wife reported further improvements in his speech, movement, and energy. The patient's level of impairment over time can be observed in **Figure 3**.

Discussion

Intranasal exosome treatment, as reported here, is the first treatment ever shown to result in actual improvement in strength and function in ALS, as well as in other motor disorders such as Kennedy Disease, Congenital Myasthenic Syndrome and carbidopa/levodopa resistant Lewy Body Dementia. The best any prior treatments had shown was only a slightly decreased rate of decline for ALS, but without improvement. There are currently six

FDA approved drugs available to treat ALS: Rilutek (riluzole), Exservan (riluzole oral film), Tiglutik (thickened riluzole), Radicava (evaradone), AMX0035 (Relyvrio), and Nuedexta, all of which have no clear evidence of disease reversal. One study analyzing the use of Riluzole, showed that varying doses of the drug were not significantly different than the placebo in alleviating peripheral neuropathic pain associated with ALS [22]. In one systematic review and meta-analysis of edaravone for ALS, the drug was not shown to improve functional outcomes of the disease [23].

In this study, there was also found to be a complete absence of adverse events of any kind in any patient. The success rate of treatment was high with only one patient of 18 treated not showing some significant response. Repeat treatment generally showed incremental improvement above the improvement from prior treatment. The limited backsliding seen in general was able to be ameliorated by repeat treatment. Out of the 18 patients treated, 15 had net improvement after treatment at their most recent follow-up, which ranged from 2 to 6 months. Two had a partial response with decreased rate of decline, and one had no response. Strengths of this study are the 100% follow-up of patients with ALSFRS-R scores and other ratings achieved for all targeted follow up times, the follow-up to 6 months in the first treated patients, and the significant 18 patient cohort. A study weakness is the lack of follow-up of more than six months at the time of this writing.

This is the first study to demonstrate actual strengthening of ALS patients and improvement of symptoms because of treatment. All other prior studies [19, 20, 23-25] have either shown no effect or a slight decrease in the rate of decline. Strengths of this study include the robust 14-person size of the cohort and the length of follow-up, over 6 months for some of the patients. A limitation is that we do not know how long the effect can be maintained with continued treatment or if improvement will continue to be maintained over time. Our results are so important for this dreaded disease, however, that we thought it was imperative to report our results as quickly as possible once it was clear the improvement was real and maintained for a period that is clinically useful. We intend to use this published data to request both accelerated approval for United States use as well as for third party reimbursement. It appears possible that with continued treatment, patients may show even great improvement going forward, as has been shown with prior repeated treatment in our study. To that end, we will be reporting our longer-term follow-up data for this cohort and for additional patients being treated going forward.

Conclusion

Nasal instillation of exosome rich mesenchymal stem cell secretome produces increased strength and reduction in other symptoms in most patients with ALS, as well as in Kennedy disease, congenital myasthenic syndrome, and dopamine-resistant Lewy body dementia, with a complete absence of side effects or adverse events.

Acknowledgements

The study was patient funded.

Informed consent was obtained from all patients before initiation of treatment.

Disclosure of conflict of interest

None.

Abbreviations

ALS, Amyotrophic Lateral Sclerosis; SOD1, Superoxide Dismutase 1; FUS/TLS, Fused in Sarcoma/Translocated in Liposarcoma; TAR-DBP-43, TAR DNA-binding protein 43; MSC, Mesenchymal Stem Cell; RNA, Ribonucleic Acid; ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised; FDA, Food and Drug Administration; cGMP, Current Good Manufacturing Practice; ISO, International Organization for Standardization; CC, Cubic Centimeter; UC-MSC, Umbilical Cord-derived Mesenchymal Stem Cell; MIP, Maximal Inspiratory Pressure; MEP, Maximal Expiratory Pressure.

Address correspondence to: Dr. Chadwick C Prodromos, Prodromos Stem Cell Institute, 1714 Milwaukee Avenue, Glenview, IL 60025, USA. E-mail: chadprodromos@outlook.com

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