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Exosome-Rich Mesenchymal Stem Cell Secretome Improves Strength in Patients with ALS, Kennedy Disease, Congenital Myasthenic Syndrome and Lewy Body Dementia

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Abstract

Amyotrophic lateral sclerosis (ALS) is an increasingly prevalent universally fatal progressive motor neuron disease affecting about 30,000 Americans causing profound muscle weakness, fatigue, fine motor loss, speech disturbance, and respiratory failure. Kennedy Disease, or Spinal and Bulbar Muscular Atrophy (SBMA) is a rare X-linked motor neuron disease causing muscle weakness, pain, fatigue, speech, swallowing, and chewing dysfunction. Congenital Myasthenic Syndrome (CMS) is a rare progressively disabling neuromuscular junction disorder causing fatigable peripheral, and ocular muscle weakness, and respiratory failure. Lewy Body Dementia (LBD) is a degenerative α-synucleinopathy neural disorder with severe cognitive dysfunction with motor dysfunction including tremors, weakness, rigidity, bradykinesia, balance and proprioceptive dysfunction. Current pharmacologic treatments have not improved strength, motor function or been disease modifying for any of these disorders. The best that current medicines have achieved is a minor decline in the rate of progression of ALS. Forty-one preclinical studies have shown safety and efficacy with exosome-secretome intranasal treatment for neurocognitive disorders. AlloEx Exosome® is the exosome, micro RNA and protein rich secretome of AlloRx allogeneic umbilical cord derived mesenchymal stem cells. We hypothesized that intranasal AlloEx Exosome® treatment would be completely safe and also effective in attenuating progression and potentially improving strength in ALS and other progressive motor disorders. 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. There were no adverse events of any kind. All patients except one achieved some degree of clinical and strength improvement, with the longest

improvement recorded at the 6 month follow-up. Intranasally-instilled AlloEx Exosomes® are completely safe, attenuate progression, and improve strength in ALS, Kennedy Disease, CMS, and LBD.

Key Words: Exosomes, Secretome, ALS, Kennedy Disease, Congenital Myasthenic Syndrome, Lewy Body Dementia

Introduction

EPIDEMIOLOGY-PATHOPHYSIOLOGY

ALS

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]. The etiology of ALS is multifactorial, with SOD1, FUS/TLS, TARDBP-43, and C9orf72 as possible genes involved, and pesticide exposure thought to be a major environmental risk factor [3]. Clinical manifestations of ALS due to lower motor neuron involvement include progressive muscle weakness, muscle atrophy, and fasciculation [4]. 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 [4,5,6].

Kennedy Disease

Kennedy Disease, or Spinal and bulbar muscular atrophy (SBMA) is an X-linked disease that is classified as a motor neuron disease like ALS [7]. This disease is a lower motor neuron disorder associated with neuron loss, muscle weakness, atrophy, and fasciculations [8]. 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 [8].

Congenital Myasthenic Syndrome

Congenital Myasthenic Syndrome (CMS) is a rare neuromuscular disorder that is caused by defects in the neuromuscular junction [9]. These defects manifest due to mutations in proteins that affect processes involving the motor end plate [10]. As of 2023, there have been variants identified in 35 total genes in CMS patients [11]. This progressively disabling disease is characterized by fatigable muscle weakness which can involve ocular, respiratory, and limb muscles [9,12]. 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 [13].

Lewy Body Dementia

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 [14]. LBD is considered to be the second-most common form of dementia, after Alzheimer's Disease [15, 16]. 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. [17-19].

CONVENTIONAL PHARMACOLOGIC TREATMENT:

ALS

There is no disease modifying treatment nor any treatment of any type heretofore that has resulted in increased strength or function. The best that has been achieved is a minor decline in the rate of progression of the disease by the few pharmaceutical drugs FDA approved for this disorder. Serious side effects are not uncommon. 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. A common adverse event associated with riluzole however, is hepatic toxicity due to elevated levels of transaminases. With patients showing elevated transaminases before taking Riluzole, treatment is contraindicated [20]. Further, one study treating 35 ALS patients with riluzole showed elevated median systolic and diastolic blood pressures in 28 (85%) patients [21]. In one systematic review and meta-analysis of edaravone for ALS, the drug was not shown to improve functional outcomes of the disease [22]. Edaravone has also been associated with serious adverse events such as dysphagia, dyspnea and respiratory failure [23]. Other management strategies, such as magnesium supplements for muscle cramps, are tailored to individual symptoms. The prognosis of ALS is grim, with no cure available and an average survival of 24 to 50 months after symptom onset [24].

Kennedy Disease, Congenital Myasthenic Syndrome, Lewy Body Dementia

There is no disease modifying strategy for any of these disorders. All 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.

EXOSOME TREATMENT

Preclinical Exosome Treatment

Forty-one preclinical studies have shown safety and efficacy with exosome-secretome treatment. One such study utilized adipose-derived mesenchymal stem cells to treat SOD1 murine model, comparing intravenous and intranasal routes [25]. In this study, repeated administration of ASC-exosomes improved motor performance; protected lumbar motor neurons, the neuromuscular junction, and muscle within murine models. A second study also showed significant motor performance and survival in SOD1 mice after intranasal administration of exosomes sourced from MSCs that were induced from human urine epithelial cells [26]. 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 cascade and NF-kB signaling pathway was inhibited by exosome delivery,

and is a potential avenue for ALS therapy. In addition, one clinical case report showed a good result after intranasal exosome treatment [27].

AlloEx Exosome Treatment

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 models of a variety of neurocognitive disorders when instilled intranasally. No serious adverse events have been reported in any of these preclinical trials.

RATIONALE/HYPOTHESIS

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 sought to investigate the ability of intranasal AlloEx Exosome® treatment to improve strength and motor function in progressive motor diseases for which no prior treatment has had success in doing so. We hypothesized that this treatment would be completely safe and also effective.

Methods

Inclusion Criteria

Patients needed a physician verified diagnosis of a progressive motor disorder. For Lewy Body Dementia they must have failed a trial of dopamine precursors. Patients must have been 18-years old or older, cancer free, not pregnant, and capable of informed consent.

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 below.

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

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, EEG tests, Neurofilament Light Chain Serum Z scores, and detailed interviews with patients.

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. They also have international ISO 9001 and 13485 certifications. They 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 showing efficacy [25,26]. Additionally in the process of performing 176 treatments in 97 unique patients in total 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 below.

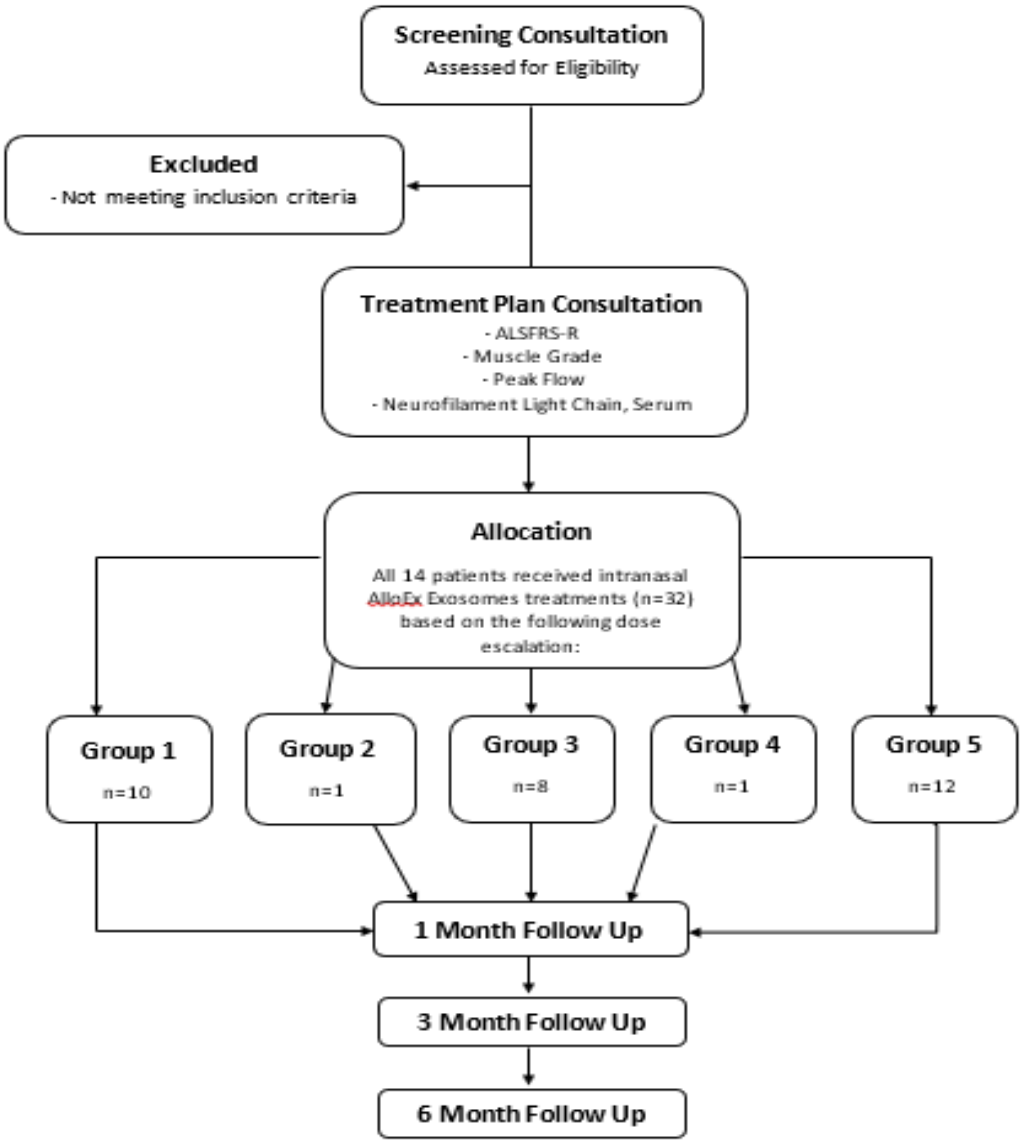

Figure 1. CONSORT Flow Chart. Patients in Group 1 received a single-dose of AlloEx Exosomes. Patients in Group 2 received 1.25x single-dose of AlloEx Exosomes. Patients in Group 3 received a double dose of AlloEx Exosomes over the course of two consecutive days. Patients in Group 4 received a total dose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

Table 2. Patient dosing regimen. Patients that received double dose treatment over the course of two consecutive days are indicated by "x2."

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	-	-

Instillation Protocol

Administration route for treatment was intranasal instillations via the Tian Tx360 Nasal Applicator in both nostrils. For treatment preparation, the frozen conditioned medium was thawed for 1 hour to room temperature. Instillation was then made into each nostril with multiple 0.7cc doses using the Tian Nasal Applicator.

Post-Treatment Protocol

To assess the safety of the treatment, patients were observed post-treatment while monitoring vital signs 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, the other patients all had some clinical improvement regarding one or more of 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.

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

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 below.

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.

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

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

Patient 2

The results of the patient's EEG scans after treatment demonstrated a considerable increase of the post-treatment Theta ratio after being well below the healthy range before receiving treatment. This indicates a strong neurological recovery, improved attentional capacity, and meaningful cognitive

resilience. This patient also demonstrated a decrease in High Beta ratios after receiving treatment, which suggests better emotional regulation, resilience, and a decrease in anxious reactivity. These results conformed with the patient's increased ALSFRS-R scores after receiving treatment.

Patient 7

The results of the patient's EEG scans showed a decrease of Theta across the CZ, T3, and T4 regions, which indicated a decrease in brain recovery and balance after treatment. Additionally, the post-treatment High Beta ratio increased across all three regions, suggesting potential consequences affecting right hemisphere processing and a rising stress response. These results do not conform with the patient's ALSFRS-R score which increased by 1 point in March of 2025. However, this patient did not have as clinically significant an improvement as the other patients, 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 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 pointed out that he also noticed a 50% improvement in his muscle fasciculation and walking endurance compared to his pre-treatment condition.

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	5kg Left, 10 reps 5kg Right, 2 reps	6.5 kg Left, 15 reps 5kg Right, 5 reps

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 2.5x exosomes over two consecutive days for her motor disorders, but 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 6: Quantitative overview of Congenital Myasthenic Syndrome patient parameters

	MIP (cmH2O)	**MEP (cmH2O)**	**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.

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 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 of 2025, the patient received another single dose of AlloEx Exosome®. One week after this treatment, the patient reported that he felt an overall 80% improvement in cognitive function and 60% improvement in motor function when compared to baseline prior to the first treatment. The patient also stated that he was not experiencing brain fog as much as before treatment. Two months later, the patient reported that he was still better in all regards, though stated there was a regression in the motor effects, and slightly regarding cognition. Thus, the decision was made to give the patient 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 there was continued maintenance of the improvement he had from treatment. The patient's level of impairment over time can be observed in Figure 2 below.

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.

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. He was 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®.

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 2.5x 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 below.

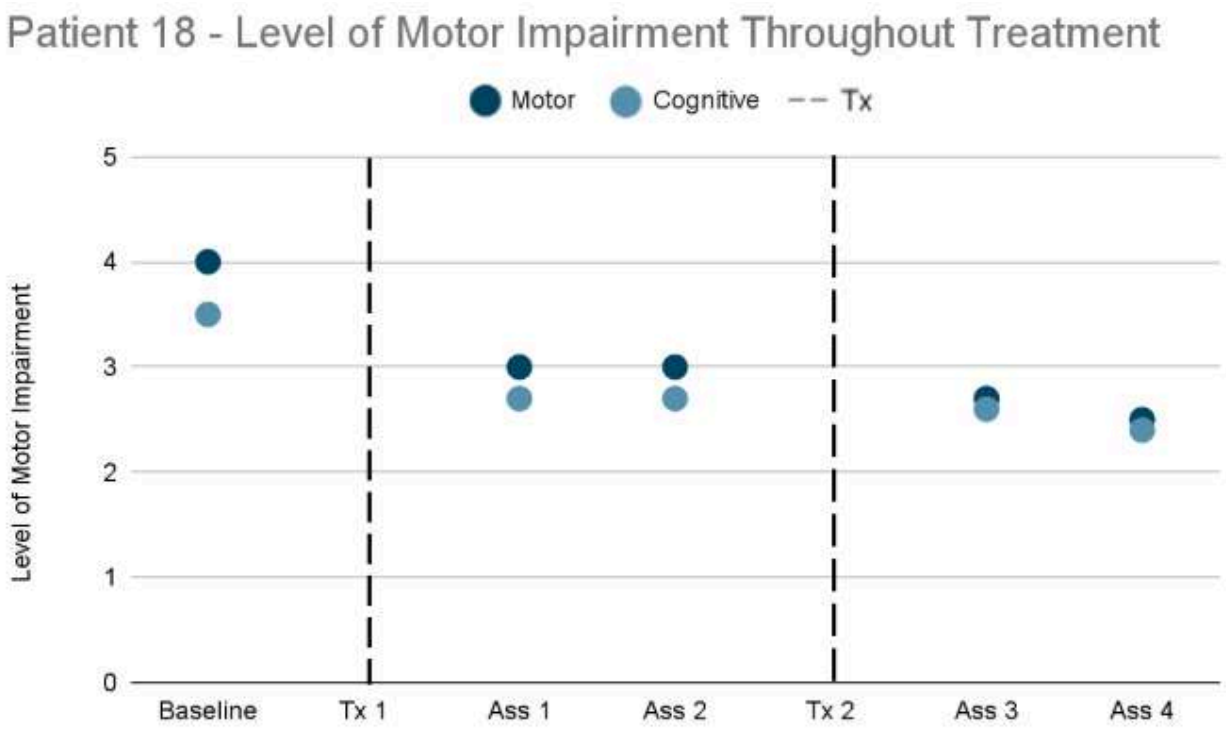

Figure 3. Level of motor impairment in Patient 18 over time. The levels of impairment were categorized as follows: 0 = Normal, 1 = Very Mild, 2 = Mild, 3 = Moderate, 4 = Severe, and 5 = Very Severe. Baseline was assessed in November of 2024 before Treatment 1 (Tx 1). Assessment 1 (Ass 1) was conducted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

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. 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 extraordinarily 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 treated patients, 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, 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. Study weaknesses is also the lack of follow-up of more than six months at the time of this writing.

We do not know if over time treatment benefits will continue to increase with continued treatment, plateau or even wane. However, after 6 months of follow-up results have generally continued to improve.

Based on our more than one year history of treatment of Parkinson's disease where we have seen little backsliding following a good initial response, and continuing additive improvement with subsequent treatment, we are hopeful that continued treatment of ALS and the other motor diseases described will either result in continued improvement, or at a minimum, stabilization of the disease. Either result would be a quantum improvement relative to any prior ALS treatment ever seen - especially since intranasal exosome treatment has a complete absence of side effects. Obviously more patients treated and longer follow-up are necessary. To this end we are continuing to treat and will report further results as they become available.

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.

Abbreviations

ALS - Amyotrophic Lateral Sclerosis

SOD1 - Superoxide Dismutase 1

FUS/TLS - Fused in Sarcoma/Translocated in Liposarcoma

TARDBP-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

Declarations

Funding

The study was patient funded.

Competing Interests

The authors declare that they have no competing interests.

Ethics Approval and Consent to Participate

Name of the Institutional Approval Committee or Unit (IRB): The Foundation for Regenerative Medicine and Orthopaedics IRB

Date of Ethics Approval: July 14th, 2024

This study was approved by an ethics committee before trial initiation. All subjects signed an informed consent form stating that they were aware of the risks and benefits of the procedures and that they consented to take part in the research study.

This study was conducted under the appropriate ethical guidelines. It was reviewed and approved by the IRB board for the Foundation for Orthopaedics and Regenerative Medicine. Informed consent was obtained from all patients before initiation of treatment.

Human and Animal Rights

No animals were used for studies that are the basis of this research. All humans were used in accordance with the IRB board for the Foundation for Orthopaedics and Regenerative Medicine and the Helsinki Declaration of 1975.

Consent for Publication

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

Standards of Reporting

CARE guidelines were followed.

Availability of Data and Methods

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author's Contributions

RD and AA performed data acquisition, data analysis, literature search, and literature analysis.

MJ, and AAE all performed literature search and literature analysis.

CP performed patient clinical evaluation, patient procedures, follow-up, and contributed to the study design.

KC performed patient clinical evaluation, patient procedures, and contributed to the study design.

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