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Accuracy Of Evaluating Nusinersen Efficacy İn Sma With A Single Scale: Results Of A 3- Year Mixed Design Study Mixed Pattern Study About Nusinersen

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Abstract

Objective

Nusinersen is the first approved therapy for spinal muscular atrophy (SMA), but its clinical efficacy, particularly in adult SMA types 2 and 3, and its broader psychosocial impact remain incompletely characterized.

To evaluate both clinical and psychosocial outcomes of Nusinersen treatment in patients with SMA types 2 and 3 using a mixed-methods approach.

Materials and Methods:

This was a 3-year observational study with a mixed-methods design, conducted at Necmettin Erbakan University Faculty of Medicine, including 11 patients diagnosed with SMA type 2 or 3. Participants received loading and maintenance doses of intrathecal Nusinersen and were evaluated at multiple time points between 2020 and 2023.

Results:

Clinical outcomes were assessed using the MRC sum score, Revised Upper Limb Module (RULM), Hammersmith Functional Motor Scale Expanded (HFMSE), and 6-minute walk test (6MWT). Qualitative data were collected through structured interviews and analyzed thematically. Safety outcomes, including adverse effects, were also recorded. A total of 11 patients (mean age 29.7 ± 9.1 years) participated. Following Nusinersen treatment, significant improvements were observed in MRC total score ($p=0.005$ after 4 doses; $p=0.008$ after 5 doses), HFMSE ($p=0.01$ and $p=0.027$), and specific upper and lower extremity muscle groups. Qualitative interviews revealed improvements in energy, walking, arm movements, and emotional well-being. Reported side effects included headache (72%), low back pain (36%), anxiety (27%), and signs of increased intracranial pressure in 2 patients.

Conclusions

Nusinersen provides measurable improvements in motor and psychosocial function in SMA types 2 and 3. However, standard motor scales may not fully capture meaningful patient-centered outcomes. Comprehensive follow-up, including psychiatric and ophthalmologic assessment, is recommended for long-term safety and efficacy monitoring.

Key Message /Highlights

1. Nusinersen treatment leads to significant improvements in motor function in adult patients with SMA types 2 and 3 over a 3-year follow-up period.
2. Standard motor scales alone may not fully capture clinically meaningful benefits, as qualitative findings revealed substantial gains in energy, mobility, and emotional well-being.

3. A mixed-methods approach provides a more comprehensive evaluation of treatment response, highlighting the need for multidisciplinary long-term monitoring, including psychiatric and safety assessments.

1. INTRODUCTION

Spinal muscular atrophy (SMA) is a group of neuromuscular disorders characterized by degeneration of alpha motor neurons in the anterior horn, leading to proximal muscle weakness and atrophy.[1] Clinically, SMA is classified into four types based on age of onset and motor milestones. Type 1 manifests before 6 months with severe weakness and respiratory difficulties; Type 2 appears before 18 months, with the ability to sit but not walk unaided; Type 3 allows unaided walking and standing; Type 4 is a milder, adult-onset form.[2,3]

The disease is caused by homozygous deletions or mutations in the *Survival Motor Neuron* (SMN1) gene on chromosome 5q13.[4] SMN1 and SMN2 differ at several nucleotide positions, including a synonymous mutation in exon 7, leading to exon skipping and reduced production of full-length SMN protein.[5,6] While patients typically lack functional SMN1, SMN2 copy number varies and correlates with disease severity.[7,8]

Since the discovery of SMN1 in 1995, treatments targeting SMN2 splicing and SMN1 gene replacement have emerged.[9,10] Nusinersen, an antisense oligonucleotide, promotes exon 7 inclusion in SMN2-derived mRNA, enabling production of functional SMN protein and improving survival and motor function.[11,12]

This study aims to explore the experiences of SMA Type 2 and 3 patients receiving Nusinersen, including symptoms at diagnosis, challenges in the diagnostic process, sources of information, impacts on work and social life, expectations from treatment, psychosocial effects, motor outcomes, and side effects.

2. MATERIALS AND METHODS

Study Group

Patients with *SMN1* homozygous deletion who applied to the Neurology Outpatient Clinic at Necmettin Erbakan University (NEU) Meram Medical Faculty for Nusinersen treatment and agreed to participate were included.

Study Design and Ethics

This mixed-methods study, incorporating both qualitative and quantitative approaches, was approved by the NEU Clinical Research Ethics Committee (09.12.2020, No: 2020/391) and by the Turkish Medicines and Medical Devices Agency (26.02.2021, No: E-66175679-514.05.01-355166). All methods were performed in accordance with the relevant guidelines and regulations.

All participants received intrathecal Nusinersen (12 mg/5 mL) according to the national protocol (days 0, 14, 28, 63 as loading, then every 4 months as maintenance). Patients were assessed at baseline, after loading doses, and at three-month intervals following each maintenance dose.

In the quantitative phase, evaluations included routine blood tests, CSF biochemistry, Medical Research Council (MRC) muscle strength scale, Hammersmith Functional Motor Scale Expanded (HFMSE), and Revised Upper Limb Module (RULM).

In the qualitative phase, patient interviews were video-recorded using semi-structured questions developed in consultation with neuromuscular experts. Interview data were analyzed thematically.

Data Analysis

A phenomenological approach was used for the qualitative analysis. Responses were grouped into themes, subthemes, and categories (Table 1). Patient quotes were coded as “Participant (P)” with dose-based visit labels (e.g., 1st dose contact, 4th dose contact).

Quantitative data were analyzed using SPSS v18.0. Descriptive statistics included frequencies (n, %) and central tendency measures (mean ± SD, min–max, median [Q1–Q3]).

Normality was assessed via the Kolmogorov–Smirnov test. The Wilcoxon signed-rank test was used for non-normally distributed paired data, and the Friedman test for repeated measures with normal distribution. When necessary, post hoc pairwise comparisons were conducted using the Wilcoxon test with Dunn–Bonferroni correction. Statistical significance was set at **$p < 0.05$**.

3. RESULTS

Quantitative Study

Eleven patients (2 with SMA Type 2, 9 with SMA Type 3) participated. The mean age at diagnosis was 9.09 ± 5.95 years, and the mean diagnostic delay was 2.35 ± 3.1

Repeated MCV measurements showed significantly higher values in the first test than subsequent ones ($p=0.029$); no significant differences were found in other laboratory values ($p>0.05$).

In EEG examinations performed after the loading dose, three patients (n=3, 27%) demonstrated abnormalities consistent with sharp slow waves, sharp waves, and diffuse cerebral dysfunction.

HFMSE scores in the 2nd and 3rd measurements were significantly higher than the 1st ($p=0.01$, $p=0.027$), with no significant difference between the 2nd and 3rd ($p>0.05$). Regarding RULM, while no significant change occurred in the right upper extremity between the 1st and 2nd measurements ($p=0.15$), a significant increase was observed in the left ($p=0.04$).

Significant improvements were observed in both proximal and distal upper and lower extremity muscle strength from the 5th and 6th doses compared to baseline ($p<0.05$). Total muscle strength also improved significantly ($p=0.005$, $p=0.008$) (Table 2).

Qualitative Sub-Study

Disease Process

Most patients initially presented with falling (45%) or difficulty walking (36%). Although diagnosis was sometimes delayed due to referral errors or appointment delays, 54% were diagnosed within the first year.

Due to dissatisfaction with clinical communication, a majority (63%) sought information online and via social media:

- “Doctors do not tell much, I learned from the internet by translating from American sites.” (P1)
- “As I got older, I got out of the doctor's follow-up because it didn't help.” (P8)

Social isolation, low self-esteem, and educational disruption were common. Despite this, more than half of the patients (54%) accepted their condition and adapted:

- “You have to live with it that will stay with you for the rest of your life.” (P1)
- “There is no cure for this... but I always said, ‘I will try to live as much as possible with what is.’” (P11)

Nusinersen

Patients primarily learned about Nusinersen through social media (63%) and viewed it with optimism. Hopes included improved mobility, disease stabilization, and increased strength:

- “It is a great opportunity for me to make life more comfortable, to be stronger.” (P6)

Many patients were not discouraged by possible side effects or the lumbar puncture procedure:

- “Whatever happens, it will progress, I will die. That's why the side effects didn't make much sense.” (P7)

Patients also criticized the HFMSE for failing to reflect meaningful daily life gains such as personal care improvements.

Social Life

Home-based hobbies predominated. Four patients were SMA association members and benefited from shared experiences and official updates. Six patients expressed future-oriented hopes for more active lives.

Nusinersen Effects by Dose

First Dose:
Most commonly reported benefits were increased energy (72%), improved daily activities, and enhanced walking (45%):

- “I feel more comfortable turning in bed... I can walk longer distances.” (P1)
- “It was very important for me to be able to hold my head... I was able to do it after the first dose.” (P6)
- “I never had a fall after the first dose.” (P2)
  (Table 3)

Fourth Dose:
Improved walking, posture, and prolonged standing led to heightened hopes for independence.
One patient experienced ongoing headache and light sensitivity beginning after the third dose. Neurological examination showed blurred optic disc margins. Visual field testing revealed blind spot enlargement, and visual evoked potentials (VEP) showed prolonged P100 latencies (117 ms right, 125 ms left). CSF pressure was 30 cm H_2O, suggesting intracranial pressure increase syndrome (IPIS), and treatment with acetazolamide 250 mg 3×1 was initiated.
(See Table 4)

Fifth Dose:
See Table 5 for detailed findings.

Dose Efficacy Perception:
Eight patients reported the most noticeable benefit after the third dose, while cumulative improvement was most associated with the fourth.

Side Effects:
Reported side effects included headache (72%), low back pain (36%), anxiety or depression (27%), blurred optic disc margins (18%), fever (18%), and, less commonly, dizziness and light sensitivity (9% each).

4. DISCUSSION

In our study, increased social media use and patient association membership were associated with insufficient communication with healthcare professionals and limited access to information. One study reported that communication gaps led patients to believe they might experience difficulties in obtaining adequate treatment.[13] Social withdrawal prior to treatment led to disruptions in occupational and educational life, whereas increased participation in social and professional life after treatment was associated with improved independence. Cognitive abilities were able to compensate for some of the patients’ limitations, and previous studies support our findings.[14] [15] Patients’ expectations from

nusinersen differed between ambulatory and non-ambulatory individuals. One study demonstrated that expectations were associated with functional status. [16] [17] Physical conditions of social environments and lack of self-confidence directed patients toward home-based activities, and another study reported low participation in social activities due to stigmatization.[18] Patients stated that stabilization of disease progression represents a positive treatment effect and that HFMSE items are insufficient for determining eligibility for maintenance dosing. In one study, participants reported that even a 1-point increase in HFMSE could be considered clinically meaningful.[16] Patients reported that, as a result of the benefits they achieved, they experienced greater independence in daily life, walked more safely, and had fewer falls.

A patient with SMA type 2 reported that achieving head control enabled them to complete their education more safely, which is particularly important for maintaining head control in adulthood. The ENDEAR study demonstrated that 22% of infants achieved head control.[19] Increased energy levels and reduced fatigue were observed in patients (n = 9, 81%). A marked reduction in mitochondrial DNA and neuromuscular junction pathologies may contribute to fatigue in SMA.[20] [21] One study found that fatigue decreased temporarily, with significant improvement at 6 months but a return to baseline levels after 10 months.[22] With gains such as easier breathing, reduced coughing, and fewer illnesses, patients experienced improved quality of life and increased hope for recovery, leading to greater participation in active pursuits. Employment has been shown to contribute to quality of life in individuals with disabilities.[23]

In our quantitative data, the total MRC score increased by 20.7% after the fourth loading dose ($p = 0.005$) and by 23.7% after the fifth dose ($p = 0.008$). One study demonstrated improvements in total MRC muscle strength and hand motor function. [24] Comparisons between measurement time points revealed significant differences between the first and fifth measurements and between the first and sixth measurements, whereas no significant difference was observed between the fifth and sixth measurements. This suggests that improvement predominantly occurred after the loading phase, while maintenance dosing preserved the achieved gains. In another study, increases in muscle strength observed at 6 and 14 months were shown to remain stable over a prolonged follow-up period. [25]

The mean HFMSE scores were 32.6 (SD = 22.71) at baseline, 35.45 (SD = 23.17) after the fourth loading dose, and 44.00 at the fifth dose. In the RULM, a significant improvement was observed in the left upper extremity ($p = 0.04$).

During follow-up interviews, one of the patients who reported improvement in walking function was able to walk for 2 minutes with support after the fourth dose and for 1 minute without support after the sixth dose. In a patient who was able to walk independently, the 6-minute walking distance increased from 17,872 centimeters at the first dose to 29,335 centimeters after the fifth dose. Among independently ambulatory patients, walking distances increased by 64%, 40%, and 15.3%, respectively.

Previous studies have demonstrated improvements in walking function and have shown that an increase in RULM scores may occur even in the absence of improvement in HFMSE scores, [26 27 28]

In our study, there was an 8.6% increase in MCV levels (p = 0.029); however, no thrombocytopenia was observed.

In one patient, photophobia and headache developed after the fourth dose. Bilateral optic disc margins were blurred on examination. Cranial MRI, MR venography, and orbital MRI were normal. Lumbar puncture revealed a cerebrospinal fluid (CSF) opening pressure of 30 cm H_2O. The patient was diagnosed with increased intracranial pressure syndrome (IIPS), and oral acetazolamide 250 mg three times daily was initiated.

At the end of the fifth dose, a separate asymptomatic patient was found to have pallor of the nasal margins of the optic discs on examination. CSF opening pressure was 20 cm H_2O, and neuroimaging findings were normal.

In the literature, cases of asymptomatic elevated lumbar opening pressure (34–36 cm H_2O) following nusinersen treatment, as well as cases monitored for intracranial hypertension, have been reported. [29 30]

In EEG recordings performed to assess the risk of progressive multifocal leukoencephalopathy (PML), three patients demonstrated sharp slow waves, sharp waves, and findings consistent with diffuse cerebral dysfunction. The literature reports that in some cases of PML, EEG abnormalities may precede MRI lesions and typically begin as focal slowing that progresses to more diffuse abnormalities.[33]

In three patients, anxiety and depression developed requiring antidepressant treatment. There are limited studies in the literature addressing the psychiatric aspects of nusinersen therapy. A case has been reported in which the drug was discontinued due to anxiety developing after the sixth dose. 34

5. CONCLUSION

This study highlights the urgent need to expand the number of specialized centers for the diagnosis and treatment of neuromuscular diseases and to establish multidisciplinary clinics staffed by experienced professionals to ensure effective communication and appropriate care for individuals with SMA. In addition, there is a strong need to create inclusive social environments and employment opportunities for patients, as engagement in the workforce positively impacts disease progression and quality of life.

In patients receiving Nusinersen, clinical improvement should be evaluated not only in terms of motor function, but also in respiratory, immunological, psychological, and orthopedic domains. It is inappropriate to assess a patient with severe contractures in the same way as one who can ambulate independently. Therefore, new assessment tools and functional modules specifically tailored for patients with SMA Type 2 are warranted.

Close monitoring is essential for detecting adverse effects such as increased intracranial pressure syndrome (IIPS) and progressive multifocal leukoencephalopathy (PML). Further research is also necessary to better understand the potential psychiatric side effects associated with Nusinersen treatment.

6. LIMITATIONS

This study is subject to several limitations. The small sample size, limited by both patient availability and challenges associated with the COVID-19 pandemic, restricted the generalizability of findings. Not all clinical evaluations and tests could be performed on every participant, and important parameters such as respiratory function, quality of life, and anxiety levels could not be assessed with standardized tools. These factors may have influenced the depth and scope of the results.

Declarations

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CONFLİCTS OF INTEREST AND ANY DİSCLOSURES

The authors declare that there are no conflicts of interest related to this work.

CONSENT TO PARTİCİPATE

Written informed consent was obtained from all individual participants included in the study.

DATA AVAİLABİLİTY

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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Author Contribution

Şeyma Ataman: Study Desing / Data Collection/ DiscussionFigen Güney: Study Desing / ConceptSüleyman B Yalçın: Study Desing / Literature ReviewMehmet Uyar: Statistical Analysis / Literature ReviewDensel Araç: Data Collection / Literature ReviewMustafa Şişman: Data Collection / Literature ReviewSami Ataman: Discussion / Drafting and Editing

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Tables

Table 1. Themes, Subthemes, and Sample Questions

Theme	Subthemes	Sample Questions
1) Disease Process	Diagnosis, Treatment, Post-diagnosis Period, Adolescence and Adulthood	• When and where were you diagnosed? • From whom or where did you get information about the disease? • How did you feel when you first heard about the disease? • Have you used any treatments? If so, did you benefit? • Have you received physical therapy and rehabilitation (PTR)? • Have you tried alternative medicine methods? • What was your biggest concern during the illness? • How did you feel during adolescence and adulthood?
2) Pre-Nusinersen	First Contact, Expectations, Fears	• Where and when did you first hear about Nusinersen? • How did you feel when you first heard about the drug? • What are your expectations regarding the medication? • What concerns or fears do you have about the drug and its administration route? • What do you think about the required 3-point increase in the Hammersmith test to switch to maintenance dosing? Do you think you will achieve this?
3) Social Life	Consanguineous Marriage, Hobbies, SMA Group Membership, Future Plans	• Are your parents consanguineously married? What are your thoughts on consanguineous marriage? • What are your hobbies? • Are you a member of an SMA support group? • What are your future dreams or plans?
4) Nusinersen Era	Post 1st Dose, Post 4th Dose, Post 5th Dose, Dose Efficacy Perception	• Engine function • Bodily changes • Feelings • Side effects • Medication expectations • At which dose did you notice the most effect? • Was this during the loading or maintenance phase?

Table 1 presents the questions asked to patients, alongside the themes and subthemes derived from their responses.

Table 2: Comparison of Muscle Strength in Patients Over Time

n=11	1st Measurement Median (Q1–Q3)	5th Measurement Median (Q1–Q3)	6th Measurement Median (Q1–Q3)	P-value (Intergroup Analysis)*
Upper Extremity Proximal Right	3.00 (2.50-4.00)	3.75 (3.50-4.50)	4.50 (3.50-4.75)	1st–5th meas. p: **0.015** 1st–6th meas. p: **0.010** 5th–6th meas. p: 0.084
Upper Extremity Proximal Left	3.00 (2.50-3.50)	3.75 (3.37-4.00)	4.00 (3.25-4.25)	1st–5th meas. p: **0.014** 1st–6th meas. p: **0.020** 5th–6th meas. p: 0.257
Upper Extremity Flexion Right	3.00 (2.50-4.00)	4.00 (3.50-4.50)	4.00 (3.50-4.75)	1st–5th meas. p: **0.010** 1st–6th meas. p: **0.009** 5th–6th meas. p: 0.680
Upper Extremity Flexion Left	3.50 (2.50-4.00)	4.00 (3.50-4.50)	4.50 (3.75-5.00)	1st–5th meas. p: **0.015** 1st–6th meas. p: **0.006** 5th–6th meas. p: 0.084
Upper Extremity Extremitye Extension Right	2.00 (2.00-3.00)	3.00 (2.87-3.25)	3.00 (2.25-3.00)	1st–5th meas. p: **0.014** 1st–6th meas. p: 0.059 5th–6th meas. p: 0.334

Upper Extremity Extremity Extension Left	2.00 (2.00-3.00)	3.00 (2.87-3.62)	3.00 (2.50-3.00)	1st–5th meas. p: **0.009** 1st–6th meas. p: 0.059 5th–6th meas. p: 0.330
Lower Extremity Flexion Proximal Right	2.00 (1.50-2.50)	3.00 (2.00-3.50)	2.50 (2.50-3.50)	1st–5th meas. p: **0.027** 1st–6th meas. p: **0.033** 5th–6th meas. p: 0.763
Lower Extremity Flexion Proximal Left	2.00 (1.50-2.50)	3.00 (2.00-3.50)	2.50 (2.50-3.50)	1st–5th meas. p: **0.027** 1st–6th meas. p: **0.048** 5th–6th meas. p: 0.942
Lower Extremity Extremity Extension Proximal Right	3.00 (2.00-4.00)	4.00 (3.12-4.12)	4.00 (3.75-4.75)	1st–5th meas. p: **0.038** 1st–6th meas. p: **0.027** 5th–6th meas. p: 0.063
Lower Extremity Extremity Extension Proximal Left	3.00 (2.00-3.50)	3.75 (3.12-4.12)	4.00 (3.50-4.75)	1st–5th meas. p: **0.038** 1st–6th meas. p: **0.027** 5th–6th meas. p: 0.063
Lower Extremity Flexion Distal Right	3.50 (2.00-4.00)	4.50 (3.50-4.50)	4.50 (3.75-5.00)	1st–5th meas. p: **0.019** 1st–6th meas. p: **0.048** 5th–6th meas. p: 0.739
Lower Extremity Flexion Distal Left	3.50 (2.00-4.00)	4.50 (3.50-4.50)	4.50 (3.50-5.00)	1st–5th meas. p: **0.018** 1st–6th meas. p: **0.018**

				5th–6th meas. p: 0.999
Lower Extremity Extremity Extension Distal Right	2.00 (1.00-2.50)	2.75 (2.25-3.12)	3.00 (2.25-4.25)	1st–5th meas. p: **0.021** 1st–6th meas. p: **0.011** 5th–6th meas. p: 0.161
Lower Extremity Extremity Extension Distal Left	2.00 (1.00-2.50)	2.75 (2.25-3.12)	3.00 (2.25-4.00)	1st–5th meas. p: **0.008** 1st–6th meas. p: **0.017** 5th–6th meas. p: 0.317
MRC Total	41.25 (33.12-49.37)	49.75 (43.62-56.12)	51.00 (44.75-57.00)	1st–5th meas. p: **0.005** 1st–6th meas. p: **0.008** 5th–6th meas. p: 0.207

Table 2 shows the muscle strength scores and total muscle strength before the loading dose, after the loading dose, and after the maintenance dose.

*P-values that indicate statistical significance are highlighted in bold.

Stat. Sig. (1st–5th meas.): p-values indicating statistical significance of differences in muscle strength between the first and fifth measurement points.Stat. Sig. (1st–6th meas.): p-values indicating statistical significance of differences between the first and sixth measurement points.Stat. Sig. (5th–6th meas.): p-values indicating statistical significance of differences between the fifth and sixth measurement points.

Table 3: FINDINGS AFTER 1st DOSAGE

FINDINGS	PATIENT CODE	SAMPLE SENTENCES
Improved head control	P6	P6 “It was very important for me to be able to hold my head when I was alone at school. After the first dose, I felt less tired. I was able to eat my own food by myself.”
Improved mobility in bed	P1,P10	P10 “When I used to try a movement, I could do it five times. Now I can do leg opening and closing movements ten times. Before, I could only stand for two minutes; now I can stand for seven. I move more easily in bed, I turn more easily, and I can lift my left arm more easily. At first, I didn’t feel much improvement and thought maybe it was just me, but my sister said she noticed a difference.”
Improved standing ability	P1,P10,P3	P1 “My muscle resistance has increased. I can turn more easily from side to side while sleeping, and I feel more comfortable. I move more easily. I used to turn myself every 15 minutes, now it’s every 30 minutes. It’s twice as fast and twice as easy. I feel less tired and can walk longer distances.”
Improved arm movements	P4,P7,P10	P4 “I used my arms more easily. I couldn’t lift books before, but now I can pick them up and put them down instantly — and I was surprised. I’m less tired. I can walk more comfortably with a walker and was even able to walk a little with one hand.” P7 “I use my arm more comfortably while shaving. Normally, I wouldn’t be able to shave the opposite side of my face with one hand, but now I can."
Enhanced walking ability	P1,P3,P4,P5,P9	P3 “I felt better after the first dose and noticed a significant improvement. During physical therapy, when I was in the cat position, I saw progress in lifting my forearm and opposite leg diagonally. My walking distance has increased. I feel less tired." P9 “I felt my steps getting stronger. I used to walk on tiptoe, which people around me noticed. Now I can walk more on my heels.”
Reduction in falls	P2	P2 “I haven’t fallen at all since the first dose. Before that, I used to fall backward onto my knees every 10 to 15 days.”
Increased energy	P1,P3,P4,P5,P6,P8,P10,P11	P1 “I get tired less.” P3 “I felt less tired and more energetic.”
Fewer episodes of illness	P4	P4 “In the past, I used to get sick very often, but after starting the medication, I began to get sick less frequently.”
Improved breathing	P11	P11 “I can breathe more deeply. They usually check to see if there are any side effects, but I experienced the opposite — my voice became louder.”

Hope	P1,P3	P3 “I want to be a scientist. I want to be an athlete; I want to be a swimmer. I feel more hopeful about the drug.”
Increased self-confidence	P1	P1 “My self-confidence has increased. I used to be afraid of becoming bedridden and felt bad about it, but now I feel more hopeful.”
Positive emotional impact	P3,P4	P3 “I feel better. It's a great feeling to realize that you can use muscles that I couldn't use before.” K4 “I am happy, I have achieved my goal.”
General well-being	P3,P8	P8 “After the first dose, I felt more energetic and my fatigue went away. I felt a little better, and my anticipation for the medication increased.”

Table 4: FINDINGS AFTER 4TH DOSE

FINDINGS	PATIENT CODE	SAMPLE SENTENCES
None	P5,P6	P5 “I did not see any effect.”
Improvement in gait/increase in walking time	P1,P2,P3,P7,P10	P7 “Previously, I used to travel 20 meters with rest. Now I can go back and forth in one go. I used to walk with support; now I need less support. I feel better. I move more easily at work. I can stand independently for a certain period of time.”
Improvement in back muscles	P1,P4	P1 “My walking was weak, it got stronger, I can walk for 10 minutes with support. I had an increase in my walking time. My resistance has increased, my fatigue has decreased.”
Improvement in balance	P2,P3	P2 “My movements have returned to normal, my walking has accelerated, I come out more smoothly when going uphill. I can move more easily on the balance board.In lifting weights before taking the drug; While I could lift 2-kilograms 5-6 times, now I can lift 10 times. In the past, I was hesitant to go somewhere in my social life, I was thinking about where I could sit, now I have started to be more active.”
Recovery to leg and arm muscles	P3,P4,P10	P10 “My walking has become easier; I can walk a short distance of 4 meters without support. I am less tired. My arm movements just got a little easier. I started to move my left arm a little easier.”
Change in posture	P3,P4	P3 “There has been an increase in my upper muscle strength. My leg muscles have also strengthened. When I stand up, I feel more support. My walking distance has improved a bit. Also, my rest periods have shortened. I have more stamina. I have grown taller, and my posture has improved."
Prolongation in standing independent standing time	P4,P7,P10	P4 “Now I can drink from a 1.5-liter water bottle. I can stand for longer periods. I can stand upright. It has improved my back muscles. When I fall, I can pick myself up more easily and get up. I feel less tired.”
Ease of movement	P9,P10	P9 “When getting into the car, I had to grab my left leg and lift it after my right foot jumped in. Now I can get in directly, I couldn't squat without support before, now I can squat without support.”
Hope/morale	P1,P2,P4,P9,P10	P1 “I am not very happy; I am not very sad. These changes are a good thing, they give hope, they give morale.” P4 “My hope has increased. As I saw something happening, I started trying too.”
I felt good	P3	P3 “I felt very good and my hope for life and medicine increased.”
I am sad	P5	P5 “I am sorry for not having an effect.”
I am not satisfied	P2,P7	P7 “There is no psychological difference; it didn’t make much difference when I couldn’t do certain things. The progress is good at the moment, but I am not completely satisfied. When we first spoke, I didn’t have high

		expectations. As the effects increased, I began to hope for more.” P2 “When I started the drug, I thought I would be very, very good, that's why I judged the process.”
Strengthen me/stop disease	P1,P6	P1 “If it had continued as in the first dose, I would have expected a lot. I want my illness to save the day right now not to get worse. You can strengthen me a little bit, it's enough to stop my disease. Let it slow down the normal course of my disease. It has a 10% effect; I wouldn't be able to think about it if I didn't take drugs.” P6 'I want him to strengthen me, hinder his progress.'
Taking care of the vineyard / being active	P2	P2 “I want to deal with vineyard or garden. I think I have the energy to do that.”
Being completely independent / able to walk	P3, P4, P7, P10	P7 “I can walk without support. Let me be like a normal person.” P4 “Making my celebrity life easier. I want to walk independently, that's why I'm working on it." P3 “My hope is to be like Ronaldo. I want to act more independently, sit and stand up completely independently.”
to be able to do my own work	P5	P5 “I want to get a little better, to be able to do my own work.”

Table 5: FINDINGS AFTER 5TH DOSE

FINDINGS	PATIENT CODE	SAMPLE SENTENCES
Improvement in arm muscles	P7	P7 “My arm moves more easily.”
Improvement in walking	P2,P4,P7	P7 “I can walk longer distances with support and have started taking steps without support.”
Balance	P3	P3 “I have started to balance myself better.”
Arm muscles	P3	P3 “I used to be very tired while brushing my teeth and combing my hair, it was very difficult. Now, I can tie my hair myself.”
Happiness	P3,P4	P4 “Even being able to take off my clothes makes me happy.”
Ownership	P7	P7 “I am saving money for the future.”
Be completely independent	P2,P3,P4,P7,P9	P7 “My goal is to be fully independent and to be able to walk.” P3 “I want to be more independent, keep moving constantly, and never get tired.”
I can do my own thing	P1,P4,P5	P1 “If the effect had continued as in the first dose, I would have expected a lot. I want my illness to stabilize, not get worse. You can make me stronger a little; that’s enough to stop my disease. Let it slow down the normal course of my disease. It has about a 10% effect; I wouldn’t even think about this without the drugs.”