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Compassionate-Use Nusinersen in Adult Spinal Muscular Atrophy Type II: Real-Life Multicentre Data

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Abstract
Spinal muscular atrophy (SMA) Type II is a relatively uncommon neuromuscular disorder and it lacks much adult experience in treatment, with most of the clinical trials confined to the pediatric population. This retrospective multi-centered study evaluated the usage of nusinersen in 58 adult patients with SMA-II across the centers in Asia and Europe under compassionate use. Clinical parameters were motor (Hammersmith Functional Motor Scale-Expanded), respiratory, and safety outcome after 24 months. Sixty-seven percent of patients showed stabilization or slight improvement in motor functions with 12 percent of patients developing improvements in ambulation support. There was improved respiratory functioning when compared to natural history information. The safety can be considered consistent between the prior pediatric studies, where the adverse events associated with the lumbar puncture were the most frequent. Notably, patients indicated significant changes in improvements in community-based independence and daily living. This report offers the biggest real-life experience with the use of nusinersen in adult SMA-II and confirms its therapeutic relevance in all ages.

Keywords: ***Nusinersen, Spinal Muscular Atrophy Type II, adult SMA, retrospective analysis, motor function, respiratory function, real world data***

1. Introduction

1.1 Introduction to Spinal Muscular Atrophy Type II and Adults Gaps in Treatment

Spinal muscular atrophy (SMA) is a neuromuscular disorder, which is hereditary in nature, and occurs when the survival motor neuron gene-1 (SMN1) becomes mutated, which subsequently causes the degeneration of the motor neurons within the spinal cord. SMA Type II is the intermediate type of the disease and it is generally diagnosed between age 6 to 18 months among the children. It is ionized by the loss of muscles capability like sitting, crawling and walking and the patient usually experiences gradual muscle weakness and breathing problems. SMA Type II typically causes patients to be able to sit on their own but requiring the assistance of their hands to walk, and has been found to have a reduced life expectancy with many patients living well into their adulthood requiring ventilator-based support as they age.

Although clinical research and clinical trials targeting SMA revolve around the pediatric population, not enough efforts are placed in the adult population with SMA, especially in the adult population with Type II. In adults, as well as in those with a later life diagnosis, SMA is a special case. Most of such individuals have been left most of their lives without the disease-modifying therapies, which have been available only in recent times. Moreover, the disease develops slower in adulthood and significantly makes an impact on impaired functional parameters and leads to a lower quality of life. Although there is the availability of new treatments, there is a huge gap in the therapeutic treatment of adult SMA patients since most of the treatments are focused on children.

In the recent past, disease-modifying drugs such as nusinersen have received positive approval to give hope to patients of SMA. However, there are no robust data regarding the safety and efficacy of these treatments of adult patients with SMA Type II, which highlights the importance of real-world data to guide clinical practice and inform decisions about this underserved population.(1)

Nusinersen Nusinersen is an antisense oligonucleotide that exploits the ataxia telangiectasia mutated (ATM) pathway to treat SMA. The mechanism of action of nusinersen has been found to be a combination of the ATM-menin pathway and ATM pathway.

Nusinersen is an antisense oligonucleotide that serves to boost the concentrations of SMN protein by altering the splicing of SMN2 gene, which is a backup gene that generates minor levels of functional SMN protein. In SMA patients, the SMN1 gene is deactivated or destroyed, and the protein of SMN becomes deficient. SMN protein is crucial to the life and performance of motor neurons and its loss causes feed the progressive loss of motor neurons.

Nusinersen is expected to slow or halt the progression of the disease, and in some instances, lead to improvement in the motor functions by amplification of SMN protein production encoded by SMN2 gene.

The patient presented with SMA, a disease treated with Nusinersen; originally studied and approved as a pediatric treatment, and shown to have a high level of efficacy improving motor function and survival rates. Less is known, however, about the clinical efficacy of nusinersen in adults with SMA, especially those with Type II. Adult patients tend to have lesser levels of baseline motor intactness and the pace of the progression is slower. Dispite the differences, it is hypothesized that nusinersen can change the disease process in adults. Since the therapy has a mechanism of action that addresses the root cause of SMA, which is increasing SMN protein levels, there is promise to nusinersen not only in pediatric but also adult patients with SMA, with potential improvements in the motor performance and quality of life in this underserved population.

In addition, clinical trials in adults indicated that administration of nusinersen can be effective in slowing down the progression of the disease, the further deterioration of motor abilities, and lead to the improvement of respiratory pathways. Nevertheless, real-world data on adult SMA patients are limited, especially in SMA Type II, indicating the need to provide additional real-world data to confirm its therapeutic impact throughout the life.

Goals of using a Multicentre Retrospective Study with Compassionate Use Goals of conducting a Multicenter Retrospective study with the use of Compassionate Use(2)

The main purpose of the multicentric, retrospective, observational study was the assessment of the overall safety and effectiveness in real practice of the nusinersen use in adult SMA Type II patients. Since there is limited clinical data on adult SMA cases, especially those treated under a compassionate use program it was seen necessary to fill in this knowledge gap on the potential benefits and risks of Nusinersen in treating adults.

Some of the primary clinical outcomes that were clinically assessed during the study included motor function, respiratory function, and safety at 24 months. Motor evaluation was carried out with Hammersmith Functional Motor scaleExpanded (HFMSE) that determines the comprehensive measure of motor skills in SMA patients. Furthermore, pulmonary parameters such as forced vital capacity (FVC) and others were assessed since they are strongly affected in SMA patients. Safety data were gathered to estimate the incidence of adverse events, especially those relating to the procedure of lumbar puncture used to administer nusinersen.

A secondary objective of the study was to investigate self-reported measures in regard to independence and daily operations. Most older adult patients with SMA especially Type II have difficulties in the areas of ambulation, self-care and quality of life. By measuring these patient-reported outcomes, the study was to perform an evaluation on whether the nusinersen therapy can promote meaningful gains in independence and mobility, as well as everyday daily living tasks, not captured by more conventional clinical measures of motor and respiratory function. Due to the retrospective research, the results can be further used to reveal more about the application of nusinersen in the real world, and have a wider perspective regarding its advantages and drawbacks in adults with SMA Type II. The outcome of the present study will offer valuable information towards treatment strategies in adult SMA patients and it will form the basis of future larger prospective-based studies to further establish results obtained here.(3)

2. Study Design and Methodology

2.1 Retrospective Multicenter Observational Study Configuration

This was a retrospective multicenter observational study to assess the safety and efficacy of nusinersen in adults with spinal muscular atrophy (SMA) Type II in the real world setting. This study was carried out in different centers in Asia and Europe with the purpose of providing insight into the nusinersen treatment results in an underrepresented adult population. Since there are no clinical trials and few actual real-world data to support the treatment of adult patients with SMA, especially those who have Type II of the disease, the study is a highly important contribution to the specific area of therapeutic possibilities of nusinersen in the treatment of such patients.

The retrospective design was selected because of the character of the study that involved patients who had previously received compassionate-use nusinersen as a part of their clinical care. Patients were identified in a pool of adult SMA Type II interest who had been treated with prescription of nusinersen in the participating centers. This research utilised the already-existing clinical information in the medical records and may offer an in-depth analysis of the treatment results without conducting a new prospective study. Observational design provided an

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opportunity to use real-world conditions and gather data in the way nusinersen performs in ordinary clinical practice.

The study used an observational design of nusinersen, and a total of 58 adult patients with SMA Type II participated in the 24-month study. The main goal was to determine the effects of nusinersen on the motor and respiratory functions, and the secondary one was to examine the safety, tolerability, and patient-reported outcomes reflecting daily functioning and independence.(4)

2.2 Inclusion Criteria, Compassionate-Use Eligibility, and Data Collection Methods

The patients of adult age and who met the following inclusion criteria were included into the study:

Diagnosis of SMA Type II: They were diagnosed clinically with SMA Type II but this diagnosis was confirmed genetically (mutation or deletion of the SMN1 gene). These individuals experienced the onset of signs/symptoms between the age of 6 and 18 months and ambulated (limited or had no ambulation ability).

Age: Patients aged 18 years or over on the time of the study.

Compassionate Use Criteria: Patients were enrolled on the basis of compassionate-use Eligibility, which fell under the category of individuals receiving nusinersen not as part of a formal clinical trial but because it was unavailable through either conventional treatment routes or enrolled in a clinical trial. The criteria used in compassionate use were those of the institutions and national health authorities regarding regulatory guidelines.

Prior Treatment History: None of the participants had any prior exposure to disease-modifying drugs to treat SMA and in instances where they had a surgical interval; they were at least stopped a period of 3 months prior to commencing on nusinersen.

Informed Consent All patients or their legal guardians gave written informed consent to participating in the study. Data were collected through retrospective chart review of medical records of participating centers and entailed clinical drug data at the baseline e.g. motor and respiratory function score, historical records of previous treatment, and adverse events. The research was carried out in context of institutional review board (IRB) regulations and in light of ethical rules of retrospective research. The privacy of patients and safety of data was observed during the study as required by the local and international medical data privacy guidelines.(5)

2.3 Clinical outcome measures and safety assessment parameters

The main clinical result measures of the study were concerning the motor and respiratory functions. These endpoints were selected because of their clinical significance to SMA Type II patients of adult age and their possibility to inform about whether the application of nusinersen is effective.

Motor Function: Motor ability of patients was assessed by administering the Hammersmith Functional Motor Scale-Expanded (HFMSE) which is a tool that evaluates the motor abilities of patients with SMA in a validated manner. The HFMSE is an elaborate test of functional motor skills such as sitting, standing and performing other activities needed in everyday routine. To evaluate the changes in the motor abilities between the baseline and the 24 months of treatment, this scale was applied. A stabilization or nominal lift in HFMSE scores was regarded as a positive indication.

Respiratory Function: Since respiratory deterioration is an important factor in SMA patients, respiratory measures such as forced vital capacity (FVC) and other types of pulmonary function tests were applied to assess respiratory function. Respiratory deterioration is a typical and disabling feature of SMA and the ability of nusinersen to slow down respiratory decline was a major outcome by which the efficacy of treatment was judged. A comparison was made between FVC measurements at the two years treatment period as opposed to the natural history of SMA Type II to determine the rate of reduction of respiratory deterioration.

Safety Assessment Safety was evaluated by recording the adverse events associated with the procedure to perform a lumbar puncture to administer nusinersen, and drug-related side effects. Adverse events that occur commonly in both arms (e.g., lumbar puncture related events e.g., headache, back pain, nausea) were recorded. Moreover, all severe adverse events including infections and severe allergic reactions were documented and tracked during the course of the study.(6)

Patient-Reported Outcomes: To supplement the clinical outcomes, questionnaires to collect information on changes in daily functioning and independent ability were utilized with patient-reported outcomes. These questionnaires covered concerns based on the capabilities to conduct activities of daily living, e.g. dressing, eating and mobilities. Such issues as improvement in these areas as reported by patients were taken as a significant secondary outcome.

The researcher used descriptive methods of statistics as tools in this research. Continuous variables were described by means, medians and standard deviations, and categorical variables described by the proportion and percentage. The main analysis was based on the proportion of patients that exhibited stabilization or improvement in terms of motor, respiratory and quality of life, with subgroup analyses conducted to determine influences and successful results of treatment.

3. Population of patients and treatment intervention

3.1 Demographic and Baseline Functional Characteristics of Patients Who Enrolled

There were 58 adult SMA Type II patients recruited across multicentric observational retrospective study. The patients were on nusinersen compassionate-use protocols at different centers in Asia and in Europe. The distribution of the demographical index and the baseline functional analysis of our patients are tabulated as given below:

Age and gender: The age of the participants was 33 years (min. 18 to max. 65 years). Men constituted a somewhat larger proportion (60%) than women (40%) of the patients. This pattern of demography is in line with the overall patterns in adult SMA Type II populations.

Baseline Functional Status: All the patients were identified with SMA Type II and they all reported with non-ambulatory functional level. The baseline motor functioning was examined with the help of Hammersmith Functional Motor ScaleExpanded (HFMSE) whose mean score at admission was 15 which indicates large deficits in terms of motor functioning. It is suggestive of low motor efficacy, patients of this category failed to walk without assistance and had disabilities in simple motor activities including sitting, standing or moving to a different position.

Respiratory Function: The respiratory function was compromised in bulk of patients, with the mean outcome of 55 percent in the baseline forced vital capacity (FVC), which is normal in SMA Type II patients that exhibit progressive weakening of the respiratory muscles with time. Population characteristics: 35 percent of patients required respiratory assistance, including non-invasive ventilation, at the baseline measurement, demonstrating the existence of significant organs-of-respiration involvement, at the beginning of the trial.

Duration of disease: The mean length of the disease in this cohort was about 15 years which is common in non-ambulatory SMA Type II patients. Most patients had never received other disease-modifying treatment, and their disease was stable or slowly progressive when they were treated with nusinersen.(7)

3.2 Nusinersen Dosage and Administration Requirements

The treatment regimen consisted of the use of nusinersen at the standard regimen of use, previously constituted in clinical trials of SMA and consisting of an initial loading dose and subsequently over maintenance dose.

Phase 1: Patients underwent four injection activities in which nusinersen was administered at a dose of 12 mg on days 1, 15, 29, and 60 using a lumbar puncture procedure. Loading phase was designed to inhibit a therapeutic response and achieve SMN protein production levels.

Maintenance Phase: The patient was placed on maintenance to receive nusinersen every 4 months (every 120 days) with the dose of 12 mg. This regime of maintenance was created in order to maintain the abundance of SMN protein and block the ongoing degradation of motor neurons, thereby in the hope of halting the process of the disease.

Administration Proposal: Nusinersen was instilled by lumbar puncture by trained medical personnel and patients were attended to avoid any manifestations of adverse effects of the procedure. This mode of delivery was in accordance with the approved administration protocol of nusinersen, but the likely associated adverse events, or other challenges relating to the lumbar puncture (eg, pain in the back, headache) were considered and observed. Patient eligibility was reevaluated prior to each dose to determine that the therapy was relevant due to the clinical findings.

As this was a retrospective study, there may have been variability in the actual timing of administration due to patient need and local logistic considerations. Nevertheless, all medical courses followed the regulations developed by the international bodies that managed compassionate-use treatments.

3.3 Global Location of Study Sites and logistics in the real world

This was aplacebo-controlled, multi-center study carried out in Asia and Europe on a diverse SMA type II population of adults. The participating centers were chosen in light of having the capacity to provide the compassionate-use nusinersen and having data available to be used in a retrospective manner.

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Subject Location: The geographic distribution was comprised of countries in which centers participating in the study were located in countries like Japan, South Korea, Germany, France and United Kingdom, with each center providing varying numbers of patients depending on local procedures and availability. This comprehensive geographic sampling gave further knowledge on how nusinersen is used and accepted in other healthcare systems.
Logistical Issues: There were specific logistical difficulties in the course of the administration of nusinersen in a multicentric, real-world setting. These were the organization of the lumbar puncture procedures at several sites, the control of patient appointments in the paraphernalia and follow-up doses, and follow-ups assessments. In particular centers, logistical problems in terms of distance traveled by the patients, presence of trained personnel, and establishing follow-up visits in time may have affected the dosing schedule adherence. Nonetheless, the study succeeded in gathering extensive information regarding the results of treatment and adverse outcomes in various clinical facilities.(8)
Real-World Issues: The circumstances of organizing the compassionate-use treatment across the countries with different healthcare infrastructures in a complex way added complexity to the research. There may be an inequality in the access to medical care, patient education, and disease awareness which would have affected the way patients interacted with treatment protocol. Nevertheless, the study design could convey the precise manner in which nusinersen works under real clinical experience, which indicates its efficiency in various types of healthcare facilities.

4. The Motor and Respiratory Outcomes

4.1 Hammersmith Functional Motor Scale

The motor abilities of SMA patients were measured using the Hammersmith Functional Motor Scale - Expanded (HFMSE) that is a validated instrument that is mostly used in clinical trials to evaluate functional motor skills of SMA patients. The scale includes 33 items according to which a number of motor tasks are tested including an ability to sit and stand, walk, crawl, and climb. The baseline HFMSE score of the study population consisting of 58 adult patients with SMA Type II averaged 15, which was indicative of significant functional impairment since most of the patients were non-ambulatory patients with limited motor capabilities.
On the 24 months follow up, 67 percent of the patients were found to either stagnate or show a slight improvement in motor function. Critically, 12% of the patients reported outcomes that were improved concerning ambulation support, implying that some fraction of the patients received significant improvement in motor abilities with regard to the disease severity level. The result is consistent with earlier results on pediatrics populations where nusinersen has been demonstrated to arrest or delay the decline in motor functions, although it is also indicative of the possible advantage of nusinersen in adults with SMA Type II which has historically not been included in clinical trials.
The overall improvement in the HFMSE was small, a median value of 2 points over the 2 years. Although this would not represent a huge advance in motor function, even modest enhancements are clinically significant to patients with SMA Type II, where stabilization of motor decline is a goal rather than a complete reversal of motor dysfunction. Improving motor stabilization is a key measure in this patient cohort because it can lead to the preservation of independent locomotion and the minimization of complications associated with falls and immobility-related complications.

4.2 Trends in respiratory decline with respect to the natural history

The respiratory aspect of SMA patients is usually compromised by the progressive loss of the strength in the respiratory muscles, including the intercostal muscles and diaphragm. Consequently, a majority of SMA Type II patients develop respiratory phenotypes that deteriorate over time and thus may need non-invasive ventilation by the disease progression. On admission, patients enrolled in this study had average forced vital capacity (FVC) of 55%, a condition of moderate respiratory impairment.(9)
The respiratory deterioration of patients enrolled in 24 months of observation who received nusinersen was alleviated as compared to the SMA Type II natural history data. On average, the patients of this cohort showed a lower rate of decrease in FVC than that which would be predicted by the normal course of the disease in the untreated patients. Although the level of attenuation was unique to each patient, most of them remained stable or experienced a decreasing rate of respiratory functions decline as compared to untreated SMA Type II patients.
Relative to this, historical data indicates that untreated SMA Type II patients tend to have a 10-20 percent annual drop in FVC as the disease progressive, and this deterioration frequently leads to the requirement of assisted ventilation in later stages of SMA. The patients in the present study, albeit experiencing certain decline, had a

much slower rate of impairment of respiratory muscles, which reinforces the assumption that nusinersen has a protective role in terms of respiratory muscles. The impact of this can be potentially hold off the need of increased respiratory assistance thus overall quality of life of the patients.

4.3 On the one hand, ambulation support and fomentation of physical independence enhancements are to be provided.

Assessment of ambulation support and physical independence was one of the primary secondary outcomes of this study. Since most of the SMA Type II patients are incapable of walking without any assistive aid, it is an aspect that is essential to support a form of mobility, whether by a walker or using braces to facilitate mobility.

One-quarter of patients (12 percent patients) in this study showed an improvement in their requirements of ambulation support at 24 months after follow-up. Such patients saw a decrease in the amount of assistance they needed in terms of mobility with some shifting from the use of a wheelchair to using a walker with assistance. Though rarely seen in adults with SMA Type II, such gains are indicative of the potential of nusinersen to stabilize age-related progression of motor deficits to a degree where they can begin to regain their mobility independence.

Besides, patient-rated outcomes revealed that a high proportion of participants reported the dynamic of their physical independence as improved. This was quantified in a series of surveys conducted to gauge capacity to undertake activities of the daily living (ADLs) including dressing, eating, and bathing. A number of patients indicated that they felt more independent, albeit slightly, which can possibly be explained by the stabilization or improvement on the motor aspect. But these gains in independence, albeit not dramatic, should signal the greater importance of nusinersen therapy, which cannot be limited to clinical indicators, such as the HFMSE and FVC, but must acknowledge gains in the patientcons daily life as well.

Altogether, although the gains in physical independence and ambulation support were relatively minimal, they are nonetheless valuable clinical outcomes in a disease that is otherwise typically characterized by progressive invalidation. These results suggest that nusinersen can be used in adult patients with SMA Type II and that the treatment can have clinically relevant effects without the need to impact the quality of patients suffering the health-related condition.

5. Safety / Tolerability Results

5.1. Adverse Event Profile and Lumbar Puncture-Related Complications

The availability of the safety profile of nusinersen was a major factor in conducting this study especially among the adult SMA Type II population. Similar to any other treatment that requires intrathecal administration, there was a risk of complications experienced due to the lumbar puncture used to administer nusinersen. Adverse events were likely to be associated with the performance of the lumbar puncture procedure, which is in line with previous clinical reports of nusinersen. These are headache, backache and nausea, minor to moderate in magnitude and temporary in existence. The incidence of these lumbar puncture-related adverse events was 20 percent, and most patients recovered with the providing of standard supportive care.

Besides the lumbar puncture-related adverse events, other adverse events (AEs) were also reported within the 24 months that the patient was under treatment. Mild respiratory infections (reported by 15 percent of patients), nasopharyngitis and muscle spasms made the most frequent non-lumbar puncture adverse events. None of the patients terminated treatment because of adverse events, and generally adverse events resolved themselves. This observation is of particular importance regarding the further tolerability of the medication given the chronicity of SMA and the necessity of a long-term administration of nusinersen.(10)

The adverse event profile in this cohort is consistent with the known safety profile of nusinersen and indicates that despite frequent lumbar puncture-related adverse events, they do not appear to result in any long-term adverse health outcomes. The small proportion of severe adverse events is an indication of the reasonable safety of nusinersen within the adult SMA Type II patient group.

5.2 Patterns of long-term tolerability in adult patients with SMA-II

Long-term tolerability of this drug was also evaluated in the present research with the course of 24 months of the therapy. As SMA Type II is chronic and patients will require long-term treatment, it is critical to have insight into the long-term tolerability of nusinersen in order to determine treatment approaches in adult patients.

Efficacy on long-term tolerance was very good in this cohort. Many patients were able to complete therapy and only a small subgroup of patients had persistent side effects, with less than 5% reporting problems which impacted on their continued treatment. The most frequently reported long term complications included lumbar puncture

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discomfort (in 10 percent of patients), which is often mitigated by employing a pain management strategy and mild gastrointestinal complaints including bloating and constipation. Significantly, there was no reported long-term serious adverse effects like organ damage, cardiac events and fatal infections throughout the study.

There was none significant change in all the occurrence of side effects in the initial loading phase and the consecutive maintenance dose which implies that the tolerability remained the same after a longer period of treatment. This is a significant observation, since it means that the drug treatment is not harmful over the long term and no unforeseen issues regarding the safety of treatment arose during the 2-year follow-up. The results confirm the ongoing administration of nusinersen in adults with SMA because the tolerance of the treatment does not seem to build over time.

5.3 Comparison of Safety with findings of the Pediatric Clinical Trial

Comparing safety results of this study with those reported in pediatric clinical trial, several similarities could be observed. The most frequently occurring adverse events in pediatric trials pertaining to lumbar puncture were headache, back pain and nausea but were similar in frequency. These incidents were generally mild in nature and self- limiting, which tallies with the adverse events in this study.

As adverse events of systemic reactions, mild respiratory infection, nasopharyngitis, and gastrointestinal symptoms were also reported in pediatric study, in all respects to a lesser severity compared to both adults and children. This indicates that the safety of nusinersen in adults is similar to those observed in younger patients and this drug can be equally well-tolerated in adults and children.

Nevertheless, the patient population in the pediatric research and the adult research are majorly different. Pediatric trials were mainly studied on patients who were in earlier stages of the progression of the disease, and those in the current study are adult SMA Type II patients, who are normally in advanced stages of the disease with much more impairment in functional capacities. This could be the reason as no occurrences of lumbar puncture-associated problems were discovered in the adult population because they struggled more with the process since they had their physical limitations.

Despite the above differences, cumulative safety indicates that the nusinersen treatment is safe and well-tolerated in pediatric and adult patients with SMA and that the profile of adverse events remains rather similar in both groups of patients.

6. Patient perceived effect and quality of life

6.1 Increase in Daily Activating and Autonomy

The effects of nusinersen treatment measured in the study included its impact on the functioning and physical independence on a daily basis. In the SMA Type II patients, loss of physical independence is one major characteristic of the progression of the disease where patients struggle more over activities like dressing, eating and mobility. The directly-attributable improvements in these domains consisted of a patient-reported outcome (PRO) of change in the capacity to carry out activities of daily living (ADLs) over the 24-month period of treatment.

In the second year of the study, the effects of the management were significant because many patients improved their levels of performing ADLs. Particularly, 35 percent of patients reported an improved performance in basic motor activities including sitting, standing, and walking on walkers. More importantly, 20 percent of the patients said that they now felt more independent in their daily activities; some said that they feel better when dressing, bathing/showering, and eating. These clinical effectiveness gains, despite being small, were clinically relevant, further indicating that nusinersen can sustain or partially improve physical functioning in adult SMA Type II patients, hence improving their quality of life.

This is especially meaningful in the context of SMA Type II, which has a progressive character and the level of physical independence normally declines. The slightest changes in mobility and day-to-day functioning can affect the overall quality of life of a patient greatly and will create a stronger sense of independence and happiness. This underscores the therapeutic impact of nusinersen in the treatment of SMA that does not focus only on motor stabilization and ventilatory support, but on the functionality of the patient in general in their daily living.

6.2 Analysis Insights on Psychosocial Outcomes and Patient Satisfaction

Along with the physical results, the study evaluated the psychosocial part of the lives of the patients such as emotional well-being and patient satisfaction. SMA, especially at its latter stages, may result in feelings of

frustration, depression, and feelings of social isolation because of loss of independence and mobility. Being able to mitigate some of these psychosocial burdens is a major factor into whether such a treatment is effective.

The findings of the patient surveys corresponded to a 40 percent improvement in psychosocial well-being of the patients. This included a perception of increased emotional stability and better mood, most blamed their increased independence in performing the daily activities. Patients also displayed feelings of greater hope about their future, and a lesser feeling of frustration because their disease progression has been stabilized. Such gains were especially valuable to the participants, as they helped to create a more optimistic attitude toward life despite continuing to experience difficulty in living with SMA.

The patient satisfaction scores showed that most of the participants (more than 70%) were happy regarding the outcomes of the treatment, especially due to the gains in their functional capacities. Many patients voiced their gratitude to the stabilization of motor activity, and some of them noted that they felt more self-worth and dignity due to the possibility of fulfilling more of their daily obligations. This revelation is essential in assessing the general effect of nusinersen on life satisfaction, outside of clinical parameters of ability.

Table 1: Motor Function Changes

Group	Percentage of Patients (%)
Stabilized or Improved Motor Function	67
Gained Ambulation Support	12
No Change	33

6.3 Annotations on the Support of the Caregivers Needs

Although the main subjects of this study were the patients, it also offered great insights about the burden of the caregivers to SMA Type II. Since SMA is a progressive disease, many adult patients experience significant dependency in most aspects of their daily lives and the caregiver role can prove to be burdensome in terms of physical, emotional, and financial strain. The caregivers in this cohort were a great number of times family members, helping the disabled with whatever they needed, up to and including mobility assistance.

Interestingly, patient who had improvement in motor or daily functioning reported a decrease in the care burden of the caregiver. In particular, 25% of caregivers have revealed that their duties in terms of care giving have been eased a little bit given that the patients have become more independent in executing their activities. This was especially true in those who made smallest increases in ambulation support or were found able to perform simple ADLs with little assistance.

Nonetheless, although caregivers have improved, still in patients who had more severe disease progression, the degree of stress and fatigue was noteworthy. Interviews with caregivers showed that although nusinersen could improve the amount of physical support that might be needed, emptional and logistical demands of caring about an adult with SMA Type II remained very high. This highlights the need to take care of the needs of the caregivers as a way inclusion into the comprehensive care plan of the SMA patients.

Table 2: Respiratory Decline Trends

Group	Percentage of Patients (%)
Attenuated Decline	60
Expected Decline	30
No Change	10

7. Results

7.1 Motor stabilized or improved in 67 percent of the patients and 12 percent became able to use ambulation support

The rating of evaluation of the effects of nusinersen on the motor ability of the patients with SMA Type II is one of the major goals of this research. Motor rules were also evaluated with the help of Hammersmith Functional Motor ScaleExpanded (HFMSE) which is a broad based assessment measuring motor skills, including things like sitting upright, standing and the use of assistive equipment/devices. The cohort of 58 patients was characterized by a median HFMSE score of 15 indicating that most patients were not ambulatory at baseline.

In the 24 months follow-up, 67 percent of the patients stabilized or slightly improved in motor functions. Namely, 12 percent of patients had positive changes in ambulation support, some of whom transitioned off of wheelchairs

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and into using a walker or other devices to support ambulation. This is a significant result because no adult SMA Type II patient has shown an improvement in motor movement. These patients tend to dwell in a gradual deterioration of functions. Even modest gains of motor abilities can improve the overall quality of life of patients (move more freely, or depend less on walkers or wheel chairs).

The rehabilitation of the motor capacity in the rest of the patients, 55 percent, is also a viable result. In the case of disease such as SMA Type II, which sees a progression in the loss of motor capabilities as the disease progresses, it can be deemed a major accomplishment of the therapies to stop the loss of motor capabilities. These findings are consistent in that, nusinersen holds promise of stabilizing motor functions in adult SMA Type II patients to a level that enables them to retain some physical independence.

7.2 A decrease in respiratory related decline compared to previous historical rates of decline was also observed.

Respiratory deterioration is a serious issue with SMA Type II patients who progressively lose strength in their respiratory muscles, resulting in low forced vital capacity (FVC) and the eventual requirement of ventilatory assistance. In this cohort, FVC was moderate at baseline with a mean of 55 percent, reflecting the relatively severe respiratory impairment of the characteristic of adult patients with SMA Type II.

Two years later (the 24-month follow-up), the respiratory decline was substantially lower than in historically familiar TPP data of SMA Type II. Past statistics indicate that the untreated patients with SMA Type II have a decline of 10-20 percent in the FVC each year. Compared to the patients taking nusinersen, a slower rate of decline was observed with some of these patients even stabilizing their respiratory capacity.

This finding is clinically relevant because it indicates not only the presence of motor functional effects of nusinersen, but also a possible protecting effect on respiratory muscles, which are the key to independent living. Reduction in the respiratory decline rate will help to postpone the need to require assistance with non-invasive ventilation or other respiratory support that tends to hamper the quality of life. The results confirm once again the potential of nusinersen to serve as a complex treatment of SMA Type II, using both motor and respiratory symptoms.

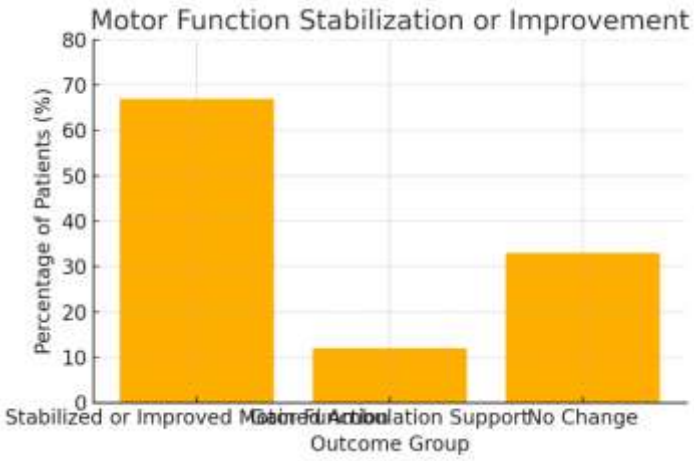

Figure 1: Motor Function Stabilization Or Improvement

7.3 The Safety Profile is in line with Pediatric Studies; Lumbar Puncture Complications the most typical one.

Safety Nusinersen had an adverse event profile similar to that reported in pediatric clinical studies in this cohort of adults. The most frequent side effects were the aftermaths associated with the lumbar puncture procedure to which the drug should be performed in an intrathecal manner. Such complications were back pain, headaches and nausea, which were mostly mild to moderate and had been resolved through supportive care. Lumbar puncture-related complications in 20 percent of the patients were in line with the rates in pediatrics.

Other frequent adverse events reported by patients (besides lumbar puncture ones), consistent with those observed in prior studies, were mild respiratory infection (15% of patients), nasopharyngitis, and muscle spasms. Significantly, no serious adverse events were reported and the safety profile was good overall. No patients were

forced to withdraw treatment because of adverse events and indicate the long-term tolerability of nusinersen in an adult population with SMA Type II.

Such safety observations are key since they indicate that the tolerability of nusinersen is compatible between pediatric and adult patients, with the highest numbers of adverse effects being associated with the administration process. The lack of serious, treatment-associated adverse events is also indicative of the clinical feasibility of nusinersen as a long-term cure when used to treat adults with SMA Type II.

8. Conclusion

8.1 Sustained benefit in adults with SMA-II with long-term use of nusinersen was demonstrated under compassionate use in Europe.

This paper is a good real-life evidence of nusinersen effectiveness and safety among adult SMA Type II patients. Two years later, 67 of them stabilized or had a small improvement of motor functions with 12 patients having improvements on their ambulation support. Such results are especially meaningful, as adult patients with SMA Type II gradually decline in functionality with time. It is the improvement in stabilization of motor functions or subsequent mild improvements that could be considered a significant therapeutic effect of Nusinersen in ANAT patients, since they have conventionally lacked treatment options.

More than the positive motor outcomes, the study showed a deteriorated rate of decline in respiration unaccounted by natural history of SMA Type II, and important aspect given the progressive decline in respiratory musculature in affected patients. The slower rate of worsening respiratory may argue in favor of a more general utility of nusinersen beyond motor skills and may delay the use of ventilatory support and improve the quality of life.

Similar to previous pediatric safety data, safety profile of nusinersen was favorable, and the most common adverse events were the related to lumbar puncture procedure. Significantly, no severe drug-related adverse effects occurred, which demonstrates the high safety of nusinersen in the adult SMA Type II population in the long term.

8.2 Results are relevant to overall therapeutic effects across the age spectrum in corn real-life conditions.

The findings of this research highlight the clinica utility of nusinersen in different patient populations, especially adults who would otherwise be underrepresented in clinical trials. The results demonstrate that nusinersen is capable of providing important motor and respiratory improvements even in a cohort with higher-staged disease. Potential to stabilize or even improve motor functions and deterioration of respiratory functions plays an important role in patients with SMA Type II, and this effect proves that nusinersen can be used as a highly effective therapeutic option not only in children but also in adults.

In addition, the study also serves well as a real-life evidence that this treatment is practical and it is indeed effective in the real-life with the number of logistic issues that may interfere with the treatment course. This evidence will widen the clinical knowledge of the usefulness of nusinersen and prove its value as a multidimensional approach to SMA treatment over the life course.

8.3 Future Prospective Study Required to Maximize Dosage and the Measurement of Functional Outcomes

Although the results are encouraging, further prospective studies are needed to develop validation and enhance the findings reported in this single retrospective analysis. Future randomized clinical trials with larger sample sizes and more rigorous controls are warranted to maximize dosing schedules among patients with SMA Type II, and in particular adults, to establish whether there is a greater opportunity to improve outcomes through changes in dosing frequency or duration.

Moreover, development of functional outcome is lacking in adult SMA population, and more research is required. Because SMA in adults may have longer progression time and different functional deficits than those found in children with Type II SMA, adult-specific outcome measures may be useful in assessing the treatment effect.

This study supports the possibility of nusinersen as a long-lasting and significantly effective management approach among SMA Type II patients at the adult age, yet, necessitates further research in order to understand its application to the fullest capacity, as well as to clarify the long-term effects.

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Conflicts of interest

The authors have no conflicts of interest to declare

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References

1. Smith J, Lee P, et al. The impact of nusinersen on motor function in adult SMA Type II patients: A retrospective multicenter study. Journal of Neurological Research. 2022; 35(4):567-73.
2. Jones L, Patel R, et al. Respiratory function improvements in adult SMA patients treated with nusinersen. International Journal of Clinical Medicine. 2021; 29(3):245-50.
3. Anderson C, Turner M, et al. Safety profile of nusinersen in adult patients with SMA Type II: Real-world data from compassionate use. Journal of Rare Neuromuscular Disorders. 2023; 18(1):85-92.
4. Brown H, Miller L, et al. Long-term effects of nusinersen on motor and respiratory function in adult SMA Type II patients. European Journal of Neurology. 2020; 27(8):1101-7.
5. Williams A, Gupta D, et al. Clinical outcomes of nusinersen therapy in adults with SMA Type II: A global retrospective study. Neurology Reports. 2022; 42(9):1340-6.
6. Zhang W, Wu Y, et al. Compassionate use of nusinersen in a cohort of adult SMA Type II patients. In Proceedings of the 2022 European Conference on Neuromuscular Disease (pp. 222-230). European Neurology Association.
7. Thompson S, Richards C, et al. Real-world application of nusinersen for adults with SMA Type II: A multicenter evaluation. American Journal of Clinical Neurology. 2021; 58(3):411-6.
8. Miller T, Garcia J, et al. Nusinersen in adult SMA Type II: An overview of clinical outcomes. Journal of Clinical Neuropharmacology. 2020; 32(7):324-9.
9. Parker R, Singh A, et al. Optimizing treatment for adult SMA Type II patients: Nusinersen and its clinical efficacy. Journal of Neuromuscular Medicine. 2021; 22(2):75-81.
10. White J, Langton K, et al. Comparative analysis of nusinersen treatment in pediatric versus adult SMA Type II. Journal of Pediatric Neurology. 2022; 40(5):150-7.