

Exploring Patient Perspectives of Treatment Choice in Spinal Muscular Atrophy Including acceptability of intrathecal onasemnogene abeparvovec

Executive Summary

This study was conducted by SMA UK to provide patient-reported evidence on attitudes towards intrathecal onasemnogene abeparvovec (OAV101-IT) and to better understand the factors that may influence treatment decision-making in spinal muscular atrophy (SMA).

As effective disease-modifying therapies (DMTs) are already available as routine care, understanding patient preferences, treatment experiences and treatment acceptability is important when considering the role of a new therapy within the treatment pathway.

The study captured responses from 85 adults with SMA and parents/carers of children with SMA Types 1, 2 and 3 across the UK. Treatment uptake was high, with 94.1% of respondents receiving a DMT. Overall satisfaction with current treatment was also high, although 25.9% of participants had previously switched therapies, most commonly from nusinersen to risdiplam. These findings highlight the importance of treatment burden and mode of administration in treatment decision-making.

Attitudes towards OAV101-IT were generally positive, with respondents reporting high levels of willingness to engage with the treatment pathway, including travel to specialist centres and follow-up monitoring. Many viewed a one-time gene therapy as an opportunity to improve quality of life, potentially achieve additional functional gains, or maintain stability where existing treatments were perceived to have plateaued.

However, important considerations were also identified. These included uncertainty regarding long-term durability, concerns about steroid regimens and monitoring requirements, challenges associated with intrathecal administration, and hesitation around moving from an established treatment to a therapy with limited long-term evidence in older populations. Adults and parents/carers often placed different weight on these considerations, highlighting the individualised nature of treatment decision-making.

Overall, the findings suggest that while OAV101-IT is viewed positively by many within the SMA community, treatment decisions are likely to be influenced by a range of practical, personal and clinical considerations. These insights provide important evidence on the acceptability of OAV101-IT and its potential place within the SMA treatment pathway

Introduction and study rationale

Spinal Muscular Atrophy is a rare, neuromuscular condition. It causes progressive muscle wasting (atrophy) and weakness. It may affect crawling and walking ability, arm, hand, head and neck movement, breathing and swallowing. How severely people are affected, and in what way, varies greatly. Over the last ten years, the therapeutic landscape for SMA has transformed dramatically with the introduction of disease-modifying therapies (DMTs) such as nusinersen (Spinraza), risdiplam (Evrysdi), and intravenous (IV) onasemnogene abeparvovec (Zolgensma). However, current disease-modifying treatment options for older children, adults, and heavier individuals Type 1, Type 2, or Type 3 SMA remain limited primarily to ongoing, lifelong administration regimens, either via daily oral dosing or recurring intrathecal injections.

Intrathecal onasemnogene abeparvovec (OAV101 IT) represents a potential single-dose gene therapy designed to deliver functional SMN1 direct to the central nervous system via lumbar puncture. Clinical trials for OAV101 IT target specific paediatric cohorts, resulting in the absence of direct clinical trial data in the full prevalent population of SMA in the UK.

When evaluating new therapeutic options , Health Technology Assessment (HTA) bodies, such as the National Institute for Health and Care Excellence (NICE), must look beyond clinical endpoints alone to understand how a new therapy will fit into routine NHS practice. This includes considering where the treatment fits in the pathway, which individuals are most likely to consider it and the practical and personal factors that influence treatment decisions.

In spinal muscular atrophy (SMA), these questions are particularly important because effective disease-modifying treatments are already available as part of routine care. For patients and families established on existing therapies, the decision to switch to, or choose, a one-time gene therapy may be influenced by a range of factors beyond its clinical profile, including treatment administration, monitoring requirements, immunosuppressive steroid regimens, attitudes towards uncertainty, and how the treatment fits into the lives of patients and families. Understanding the importance of these considerations, and the extent to which they influence treatment preferences, is essential when considering how a new therapy may be received and used in clinical practice.

1.1 Objective of the Study

This study was conducted by SMA UK to gather real-world perspectives directly from the UK SMA community, including adults living with SMA and parents/carers of children with SMA across Types 1, 2, and 3. The study aimed to better understand attitudes towards OAV101-IT and explore the factors that may influence treatment decision-making, including satisfaction with current treatment, perceptions of a one-time gene therapy and the circumstances in which patients and families might consider a one-time gene therapy.

By capturing community perspectives on the potential benefits, burdens, uncertainties and trade-offs associated with OAV101-IT, this report provides important patient-reported evidence to support NICE's evaluation. The findings offer insight into the acceptability of OAV101-IT in the context of existing treatment options and how patients and families may view its role within the SMA treatment pathway.

2.0 Participant Demographics

2.1 Geographical distribution

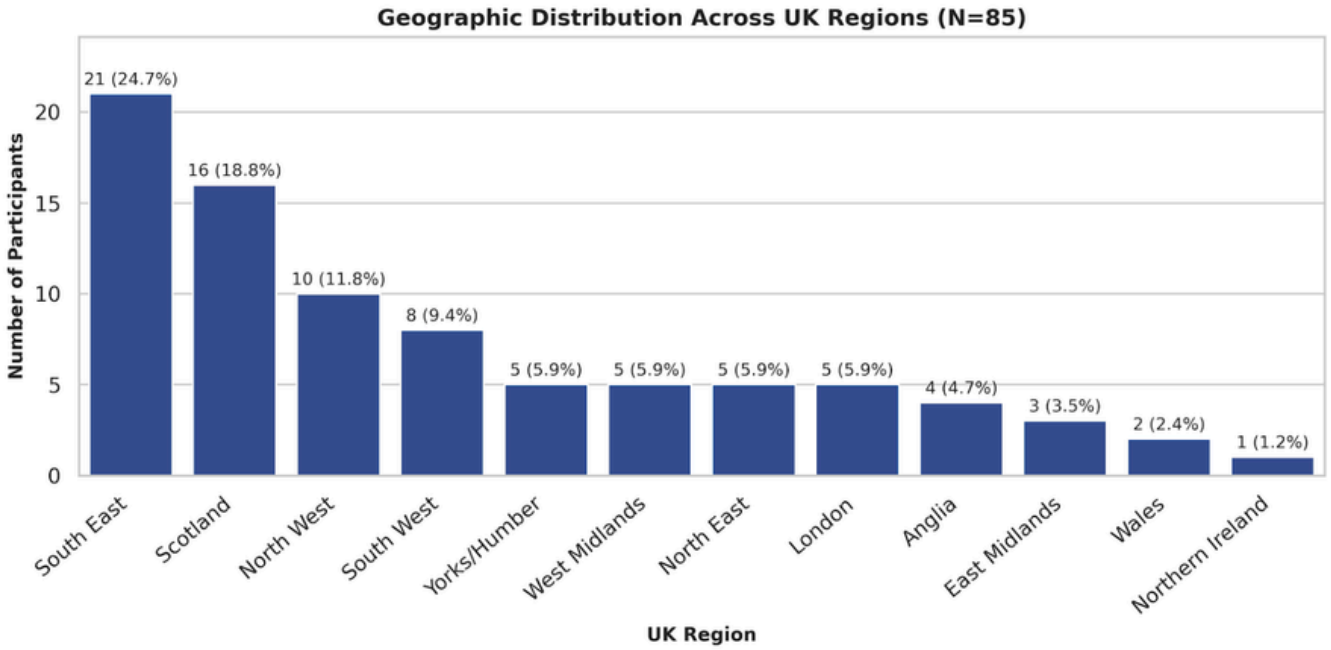


Fig.1

A total of 85 participants across the United Kingdom completed the study. Responses were submitted either directly by:

- Individuals diagnosed with SMA: n= 32 (27.6%)
- Parents/carergivers answering on behalf of individuals with SMA: n=53 (62.4%).

2.2 SMA Type and age demographics

Fig.2

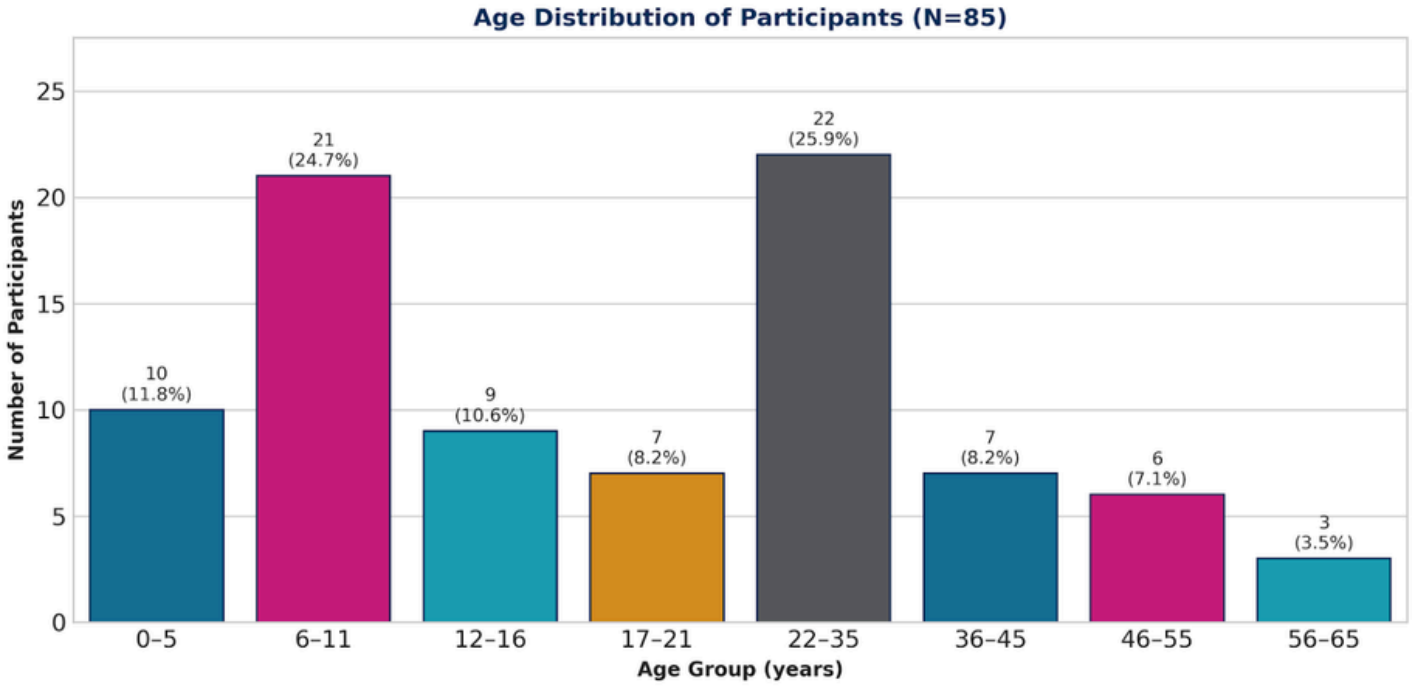
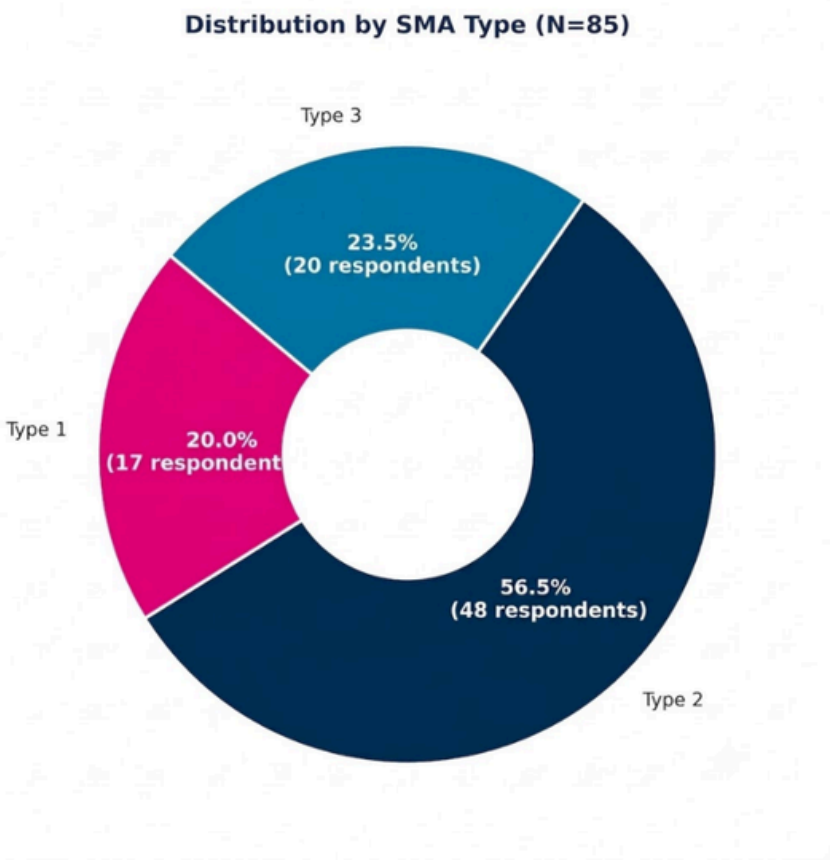


Fig.3

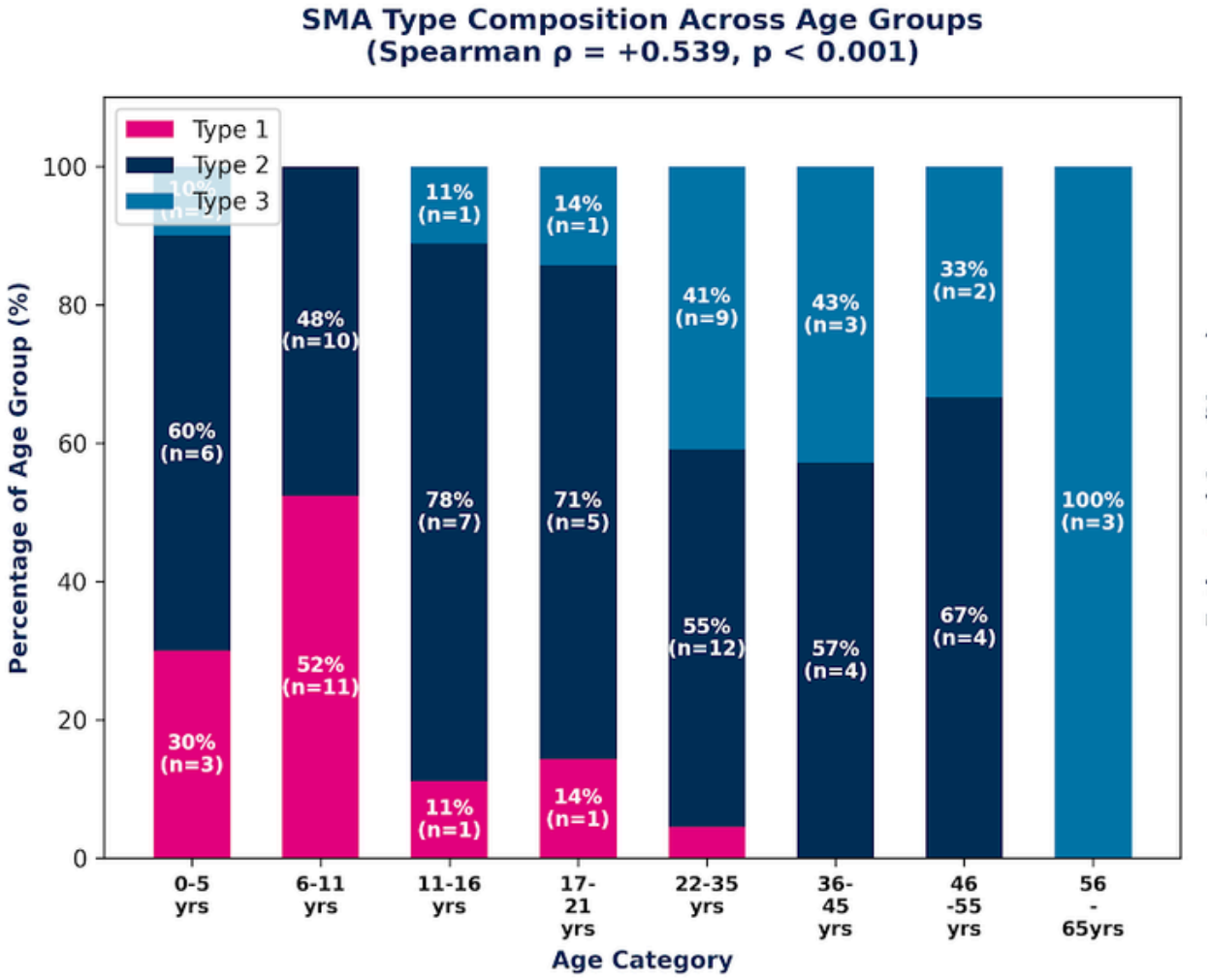


Only those people who had not already accessed gene therapy participated in this survey,

Mean Estimated Age by Subtype:
SMA Type 1: 9.5 years (SD = 6.25)
SMA Type 2: 20.7 years (SD = 14.37)
SMA Type 3: 34.8 years (SD = 15.69)

The mean age for respondents with SMA Type 1 reflects an older cohort of children and young adults who were unable to access Zolgensma because they exceeded the treatment's weight-based safety threshold.

Fig.4



2.3 SMA types and SMN2 copy numbers

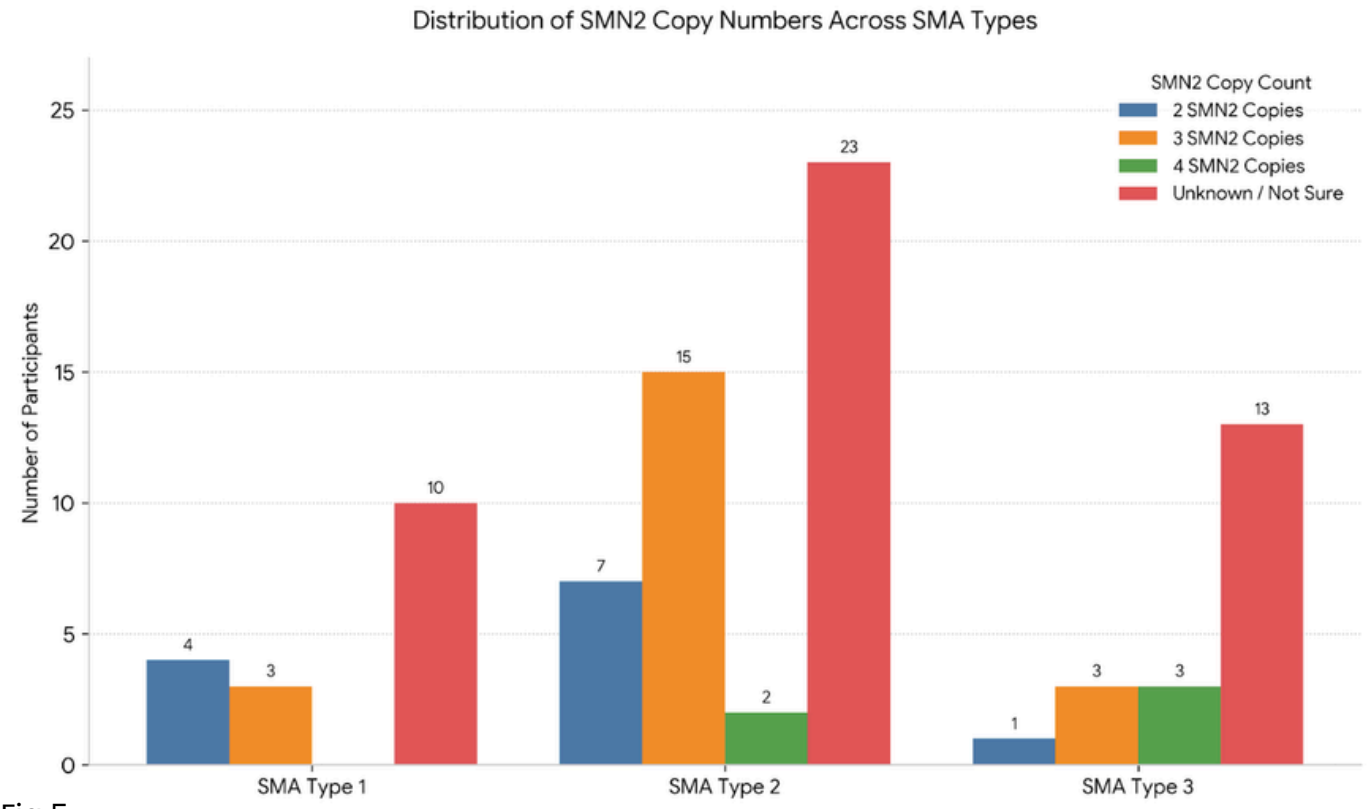


Fig 5.

While higher known SMN2 copy numbers generally correlate with milder clinical phenotypes over half of survey respondents (54.1%) do not know their exact copy count, whereas 100% identify with their diagnosed SMA Type. This high rate of unknown copy counts across all subtypes demonstrates that clinical typing currently remains the universally recognised identifier within the UK patient community and NHS clinical practice.

Furthermore, the data highlights that copy number is not a rigid predictor of disease severity: phenotypic overlap exists across subtypes, and rare outliers, such as a participant with SMA Type 3 reporting only 2 SMN2 copies, underscore the presence of protective genetic modifiers, historical testing inaccuracies, or self-reporting misconceptions.

2.4 Functional Groups

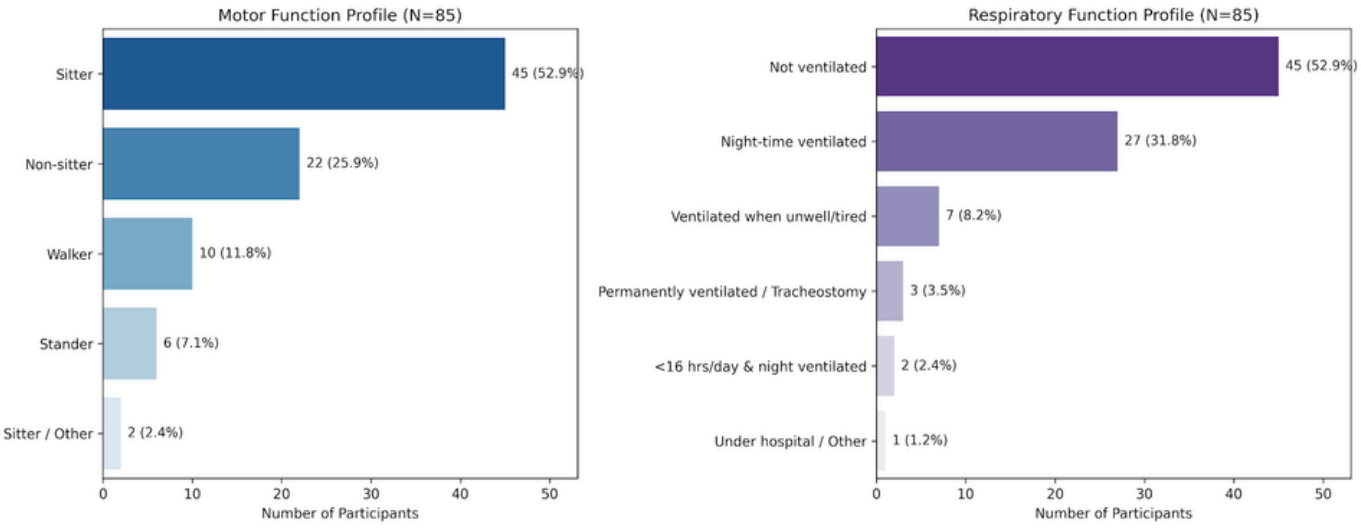


Fig.6

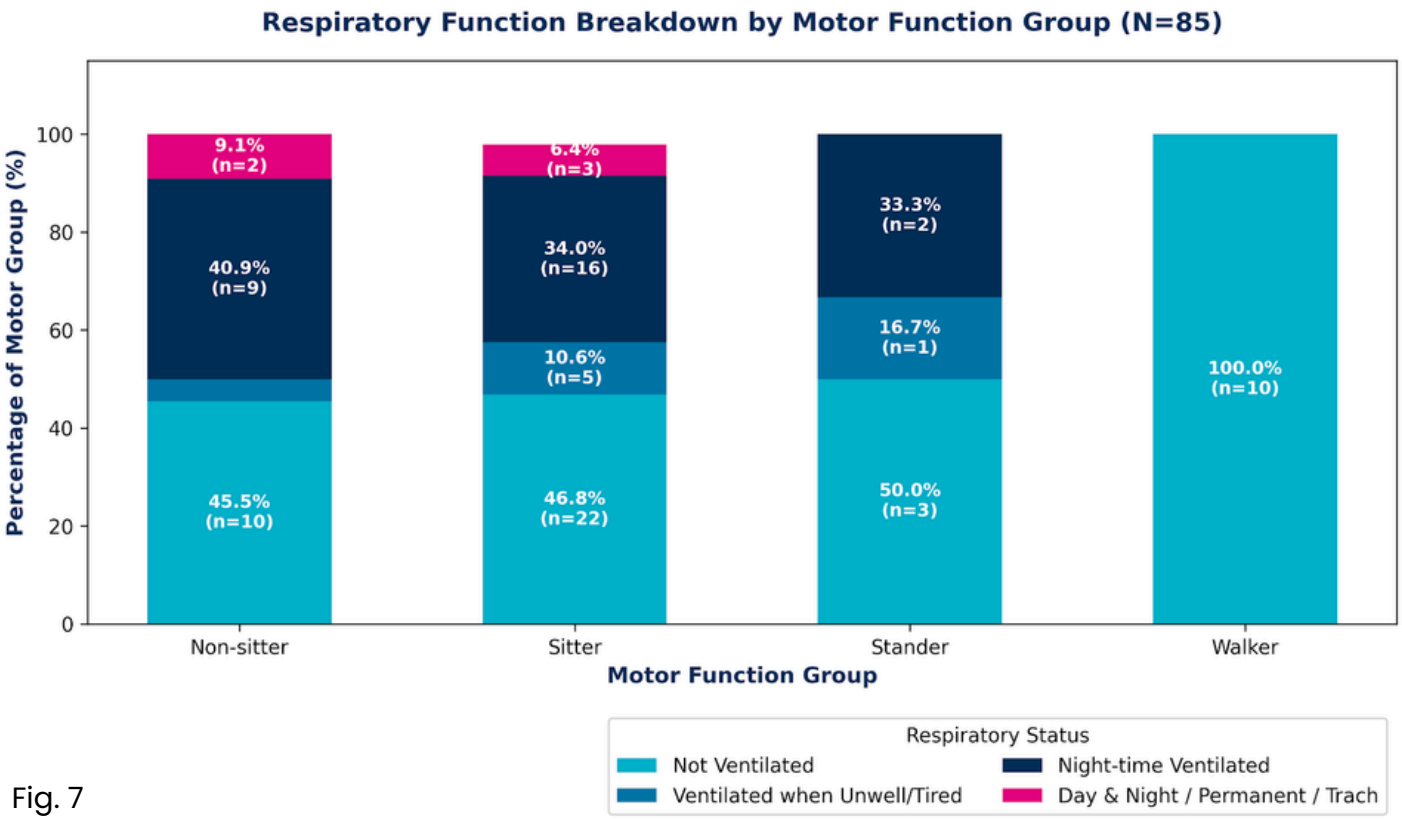


Fig. 7

In this data set, daytime and permanent ventilation is exclusive to non-ambulatory groups. Walkers have complete respiratory independence, non-sitters and sitters require the highest level of respiratory support.

As motor function improves (from Non-sitter Sitter Stander Walker), reliance on respiratory support decreases. However, night time ventilatory support is required across significant proportions of the non-sitter, sitter and standing groups.

3.0 Treatment choice

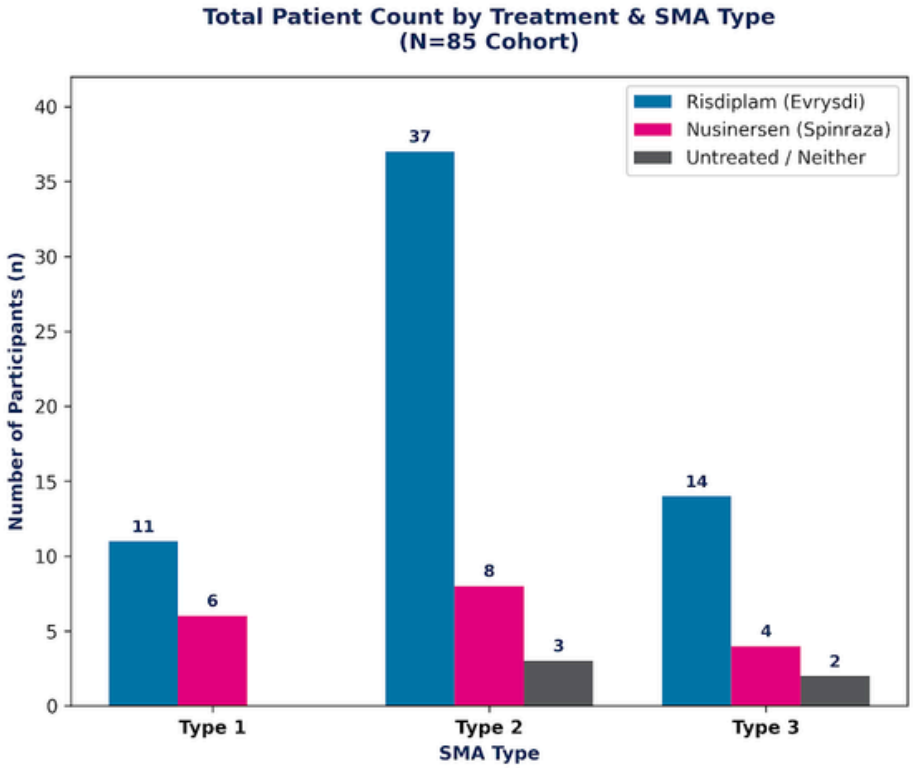


Fig. 8

Across the survey cohort, DMT adoption is high at 94.1% with daily oral risdiplam serving as the predominant choice across all clinical classifications, ranging from 64.7% in Type 1 to 77.1% in Type 2 and 70% in Type 3. Nusinersen maintains its highest retention among SMA Type 1 participants (35.3% vs. 16.7% vs. 20% in Type 2 and Type 3 respectively), reflecting earlier historic access and long-term stability on intrathecal therapy.

Due to the fast progression of the disease at the severe end of the spectrum, active treatment coverage is complete (100%) among Type 1 individuals, whereas untreated cases are confined to Type 2 (6.2%) and Type 3 (10%). However, because overall treatment distribution does not statistically differ by diagnosis, therapy choices in the UK are primarily driven by patient and caregiver preferences regarding route of administration, such as avoiding repeated lumbar punctures and historical switching trends rather than clinical subtype constraints.

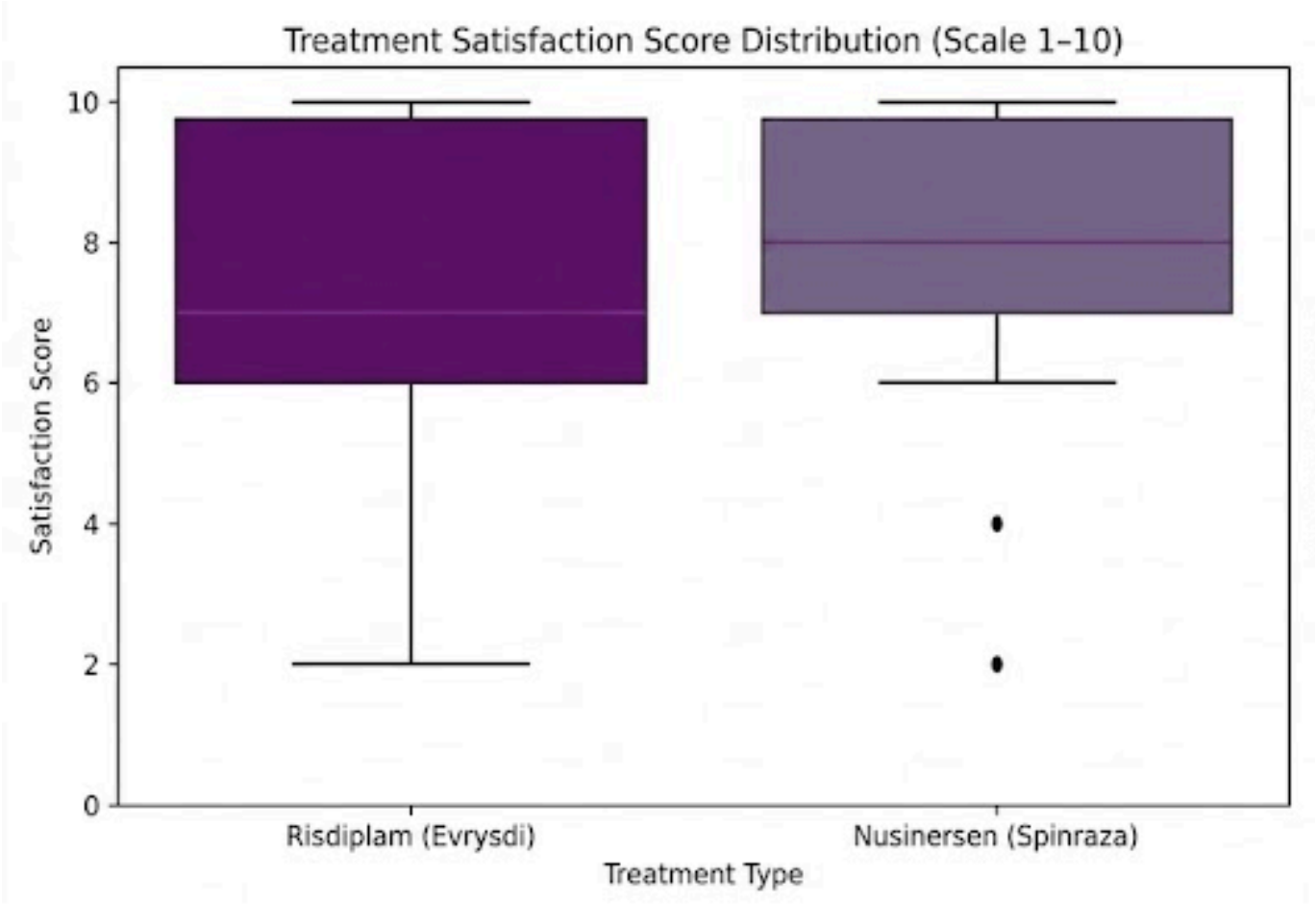


Fig. 9

Out of 85 total study participants, 80 provided a numerical rating (scale 1–10) for satisfaction with their current treatment. The remaining 5 participants were not currently receiving treatment and did not complete this rating.
There was a higher average satisfaction for nusinersen**,** with patients reporting a higher mean satisfaction rating (8.2/10) compared to those receiving Risdiplam (7.4/10). Nusinersen satisfaction ratings showed less variation, ranging from 6.0 to 10.0, with no respondents reporting scores of 5 or below. In contrast, risdiplam satisfaction ratings showed greater variability, ranging from 2.0 to 10.0, and 16.1% of respondents reported scores of 5 or below.

Statement Agreement "I am content with my current treatment":

- **Nusinersen:** 72.2% agreed or strongly agreed (13/18), 27.8% were neutral (5/18), and 0% disagreed.
- **Risdiplam:** 43.5% agreed or strongly agreed (27/62), 45.2% were neutral (28/62), and 11.3% disagreed (7/62).

Qualitative responses from the survey illustrate the primary themes driving patient satisfaction across both treatments:

1. Stopping progression and achieving disease stability
For many participants, preventing further loss of motor function is considered a success.

Risdiplam (Rating: 8/10):
" I scored at 8 as the treatment has improved lots of measures however we have now stabilised and the progression has stopped."
Parent/Carer on behalf of child living with SMA type 2 (6-11 yrs)

Nusinersen (Rating: 7/10):
*"I have remained stable with arguably a few gains which are not captured by the data collection. No decline is good in my view**."***
Adult living with SMA type 2 (46-55yrs)

2. Functional Gains & Independence in Daily Tasks
Patients who gave high satisfaction scores frequently highlighted meaningful functional improvements.

Risdiplam (Rating: 10/10):
"I can now brush my hair and teeth."
Adult living with SMA type 3 (22-35yrs)

Nusinersen Rating: (10/10):
"Before treatment he could not sit independently, could not roll, and struggled to hold his head up. He does all with ease now and do not get fatigued doing so."
Parent/Carer of child living with SMA type 2 (6-11yrs)

3. Non-motor improvements (breathing, swallowing, stamina)
Beyond limb motor scores, participants noted significant enhancements in endurance and bulbar/respiratory function**.**

Nusinersen (Rating: 8/10):
"Pretty much all of his physical capabilities have improved, from swallowing to lifting to an increase in general energy levels."
Parent/Carer of child living with SMA type 2 (6-11 yrs)

Risdiplam (Rating: 7/10):
"I'm having to turn down my BiPAP!!!"
Adult living with SMA type 2 (36-45yrs)

4. Plateaus after initial gains
A recurrent theme among moderate satisfaction scores (6–8/10) is an initial surge in progress followed by a plateau.

Risdiplam (Rating: 7/10):
"When I first started treatment, my ability to perform daily tasks improved significantly, which made me less reliant on others to help me or retrieve things for me. After the initial improvements, I did not notice any further gains, but my condition has remained stable since then. Overall, I am satisfied with the treatment as it has improved my independence and helped prevent further decline"
Young person living with SMA type 2 (11-16 yrs)

Risdiplam (Rating: 8/10):
"I scored at 8 as the treatment has improved lots of measures however we have now stabilised and the progression has stopped."
Parent/carer of child living with SMA type 2 (6-11 yrs)

5. Dissatisfaction & Unmet Expectations
Lower ratings (2–4/10) stem from a lack of noticeable functional gains or uncertainty regarding whether progression has actually slowed.

Risdiplam (Rating: 4/10):
"Slowed down deterioration but had hoped for a bit of strength improvement."
Adult living with SMA type 2 (46-55 yrs)

Risdiplam (Rating: 2/10):
"Personally, I have not seen any improvement in my daughter's ability since starting risdiplam and feel that she has lost some abilities since taking this."
Parent or carer of adult living with SMA type 2 (22-35yrs)

3.1 Treatment switching

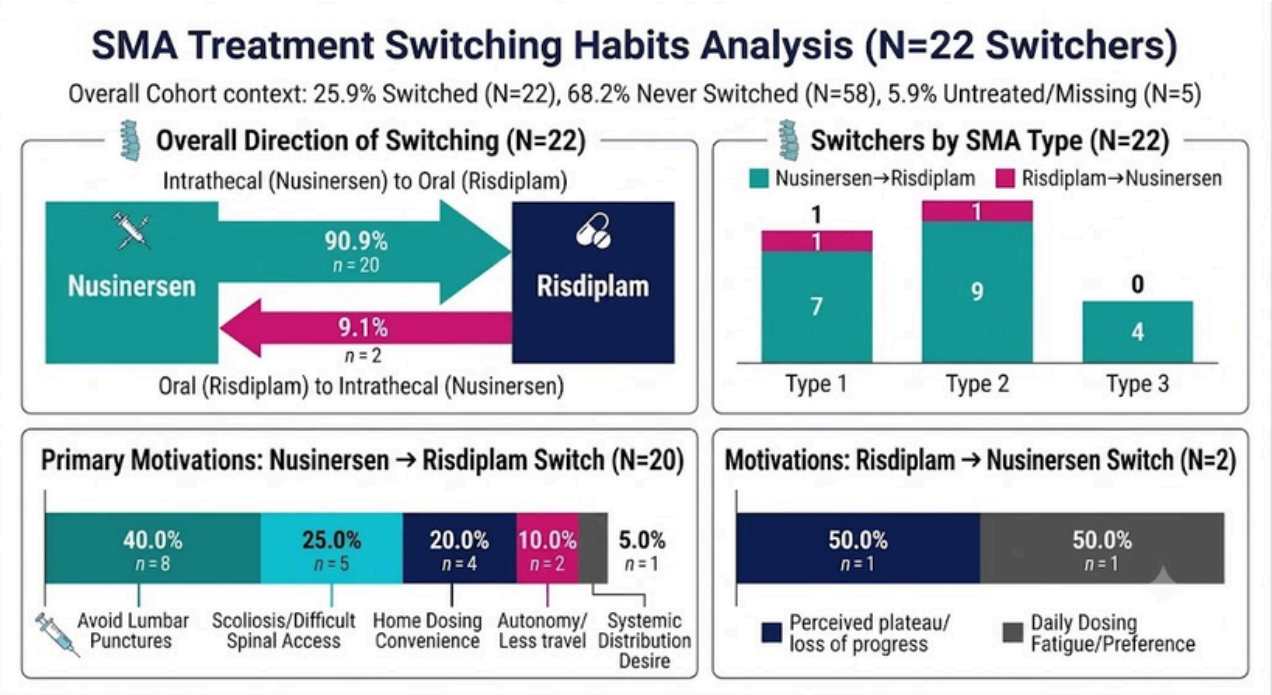


Fig. 10

Treatment switching is a major factor shaping current therapy distribution across the survey cohort, with 25.9% of all participants (22/85) having changed their DMT. Switching is predominantly one-directional: 90.9% of switchers (20/22) transitioned from intrathecal nusinersen injections to daily oral risdiplam, whereas only 9.1% (2/22) moved from risdiplam to nusinersen.

Beyond single switches, the data captures complex, multi-step care pathways:

Nusinersen > Risdiplam > Nusinersen: 1 participant (4.5%) of switchers returned to nusinersen after experiencing a perceived plateau on oral therapy.

Nusinersen > Risdiplam > Discontinuation: 1 participant stopped active treatment entirely following an initial switch to oral therapy.

1. Switching from nusinersen to risdiplam
The primary driver for switching to oral risdiplam was eliminating the clinical burden and physical trauma of intrathecal delivery.

Avoiding lumbar punctures and medical trauma: Participants consistently cited the distress and pain of regular spinal procedures:
"The psychological toll and physical pain of repeated lumbar punctures every four months became overwhelming"
Adult living with SMA type 2 (25-34 yrs)

"She was not coping with being put under anaesthetic to receive her nusinersen and it began to affect her home life and behaviour. Switched to risdiplam to avoid future hospital visits and hope it would help her emotional and mental well being"
Parent/carer of child living with SMA type 2 (6-11 yrs)

Scoliosis and severe spinal access Issues : Complex spinal anatomy made injections increasingly difficult or clinically unsafe:
"Due to spinal fusion I had to change to risdiplam as there was no longer any access to between my vertebrae"
Parent/carer of child living with SMA type 2 (6-11 yrs)

Convenience, autonomy, and systemic reach : Home administration significantly reduced life disruption:
"Risdiplam has been safe, reliable, and easy to administer at home."
Parent/carer of child living with SMA type 2 (6-11 yrs)

"Nusinersen was physically invasive and required repeated lumbar punctures. It also took up most of the day due to travel to the hospital, the procedure itself, and the journey home. I switched because risdiplam offers similar benefits while being much more convenient and less disruptive to everyday life"
Young person living with SMA type 2 (11-16 yrs)

2. Switching from risdiplam to nusinersen
For the one person returning to intrathecal nusinersen, decision-making centred on perceived clinical efficacy and routine preferences.

Perceived plateau / loss of progress :
"Started with Spinraza at 4, moved to risdiplam upon clinician recommendation age 9, moved back to Spinraza aged 12"
Parent/carer of young person living with type 2 SMA (11-16yrs)

4.0 Patient Perceptions of OAV101 IT treatment pathway
Overall, respondents across the cohort demonstrated strong willingness to consider a one-time gene therapy. When asked "How open are you to the concept of having a one-time gene therapy?" on a scale of 0 to 10, the average response was 8.4. Among young adults and adults, aged 17 to 65 years old, (45/85 respondents), the average score was similarly high at 8.3.

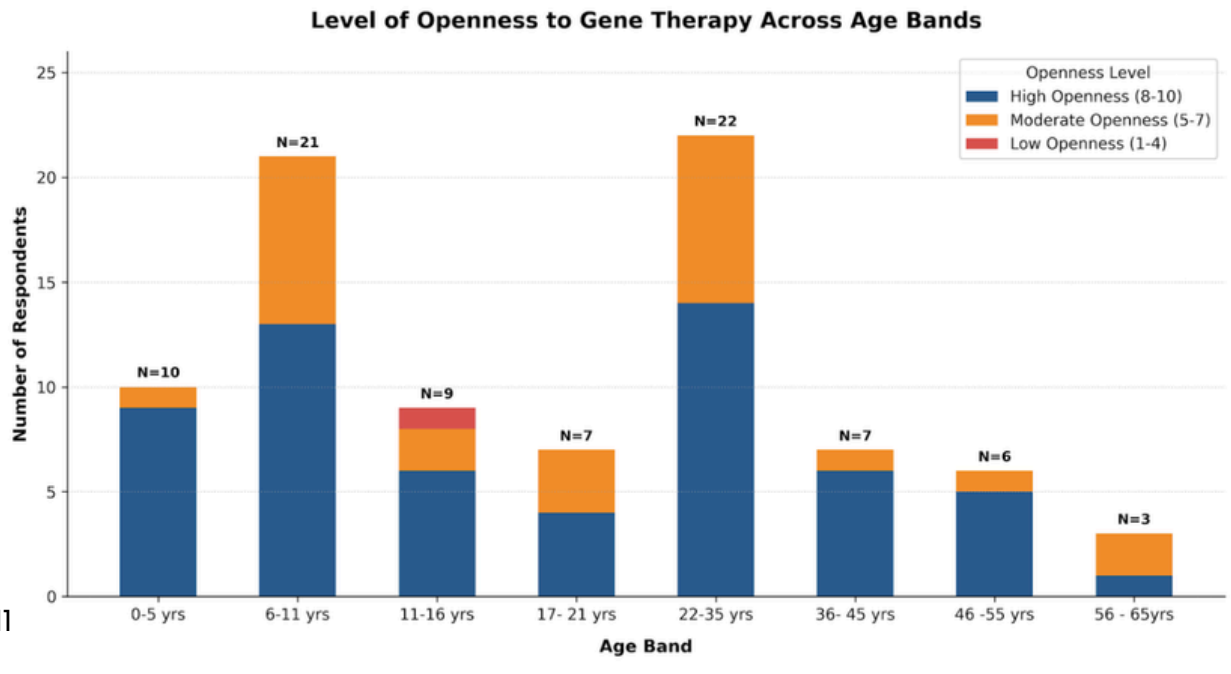


Fig 11

To further understand views of OAV101 IT, respondents answered how much they agreed with a statement about the treatment. Below is a summary of these attitudes (n=85 respondents). Responses were collected on a standard 5-point Likert scale (Strongly Disagree = 1, Disagree = 2, Neutral = 3, Agree = 4, Strongly Agree = 5).

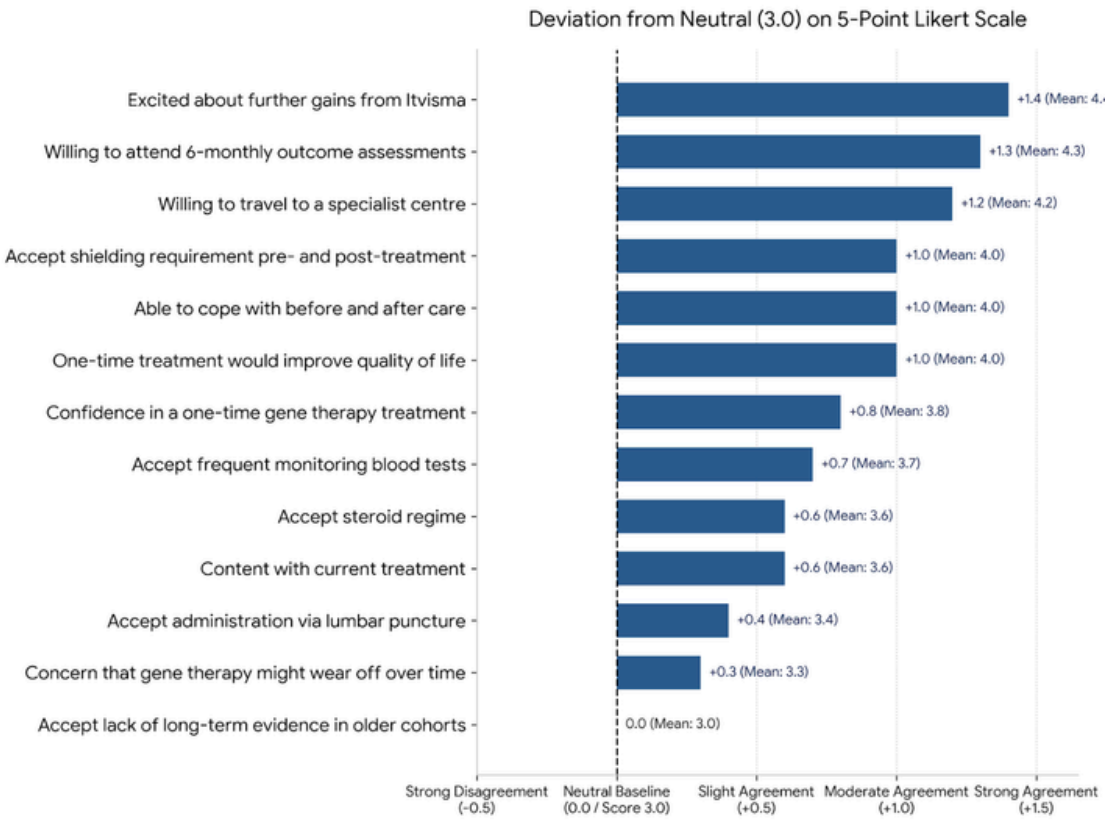


Fig 12.

4.1 Key Takeaways

1. **Highest enthusiasm and willingness:**
   - **Excitement for gains:** 90.6% agreed/strongly agreed they are excited about potential gains, with 0% disagreeing.
   - **Clinic assessments and travel :** Participants showed overwhelming willingness to travel to specialist centres (86.9%) and attend 6-monthly follow-up visits (89.4%). Although respondents living further away (>2 hrs) reported slightly lower mean agreement, the vast majority across all distance groups were still willing to travel to a specialist centre for pre and post-treatment monitoring.

1. **Perceived benefits vs. current contentment:**
   - **Quality of Life Impact:** 71.4% felt a one-time gene therapy would improve their quality of life.
   - **Current Satisfaction:** While 47.1% were content with their current treatment, 43.5% remained neutral, leaving room for alternative options.

1. **Key Concerns and hesitations:**
   - **Lack of long-term data:** The most split item in the set (Mean: 2.99), where 40.5% were neutral and 29.8% expressed hesitation regarding limited long-term evidence in older children and adults.
   - **Administration and durability :** Waning efficacy over time was a concern for 45.9%, and 22.6% objected to administration via lumbar puncture.

4.2 Trends across types of SMA

Several distinct statistical trends emerge across SMA Types regarding attitudes toward gene therapy and current treatments:
Type 1 respondents (or parents/carers of type 1 children) expressed the highest concern that gene therapy might wear off over time. Concern steadily decreases for Type 2 and Type 3.

Type 2 and Type 3 individuals reported significantly higher agreement that a one-time gene therapy would improve their quality of life compared to parents and carers of Type 1.

Type 2 respondents expressed the highest excitement for additional functional gains, closely followed by Type 3, whereas Type 1 was slightly lower.

Type 2 and Type 3 are notably more accepting of ongoing blood monitoring regimes than Type 1.

4.3 Trends across age groups

Younger paediatric cohorts (or parents/carers of younger children 0–11 yrs) worry most about efficacy wearing off over time, compared to teens/young adults aged 12–35 and older adults aged over 36 years of age.

Parents/carers of paediatric patients (0–11 yrs) reported higher contentment with current treatment options than adults aged over 36 years of age or teens and young adults 12–35. Paediatric parents/carers (0–11 yrs) were most comfortable with intrathecal / lumbar puncture administration. In contrast, teens and young adults (12–35 yrs) expressed the highest hesitation toward lumbar punctures.

Willingness to undergo the required steroid protocol increases steadily with age.

4.4 Patient optimism vs. caregiver caution

Overall, the survey of 85 community members reveals strong enthusiasm for gene therapy highlighted by 90.6% of respondents expressing excitement for potential functional gains and high willingness to comply with demanding trial logistics like specialist travel (86.9%) and 6-monthly assessments (89.4%).

However, key demographic and role-based nuances emerge across the pathway: parent and carer proxy decision-makers demonstrate significantly higher caution than adult patients, showing greater anxiety regarding long-term efficacy waning (52.8% vs. 34.4%,) and steroid regimes, whereas individuals living with SMA report higher optimism for quality of life improvements (78.1% vs. 67.3%) but greater fear of invasive lumbar puncture procedures (34.4% vs. 61.5% acceptance). Additionally, concerns about durability are most pronounced among SMA Type 1 families and paediatric cohorts.

4.5 Qualitative insights

The qualitative feedback from community members regarding gene therapy reflects a complex balance between strong enthusiasm for potential functional gains, stability and practical hesitations surrounding treatment administration, protocol burdens, and clinical uncertainty.

A prominent theme across the responses is optimism for enhanced quality of life and the possibility of regaining or maintaining physical function, particularly among individuals who feel their current treatments have stabilised or reached a plateau. As one adult living with Type 3 SMA noted,

"As I get older things are starting to get harder to do. Anything that may help me would be a huge benefit to my quality of life."

This sentiment was shared by carers and patients alike who view gene therapy as a critical opportunity for improvement, with one caregiver asking,

"If a treatment is available which could significantly improve your quality of life why would you not want to take it?"

Another adult participant highlighted the contrast with existing options, sharing,

"I have seen the improvements in children having Zolgensma and the opportunity for improvement is very exciting as I feel current treatment is now stagnant."

Adults living with SMA repeatedly highlight that preventing decline and holding onto existing abilities is paramount.

“I have remained stable with arguably a few gains which are not catured by the data collection. No decline is good in my view.”"Gains more at start of treatment but still have ability to drive my car which I may not have without treatment."

Despite this widespread interest, significant anatomical and procedural barriers remain top of mind for many in the community. Adults and teenagers with prior spinal surgeries expressed deep concern regarding intrathecal delivery via lumbar puncture. One participant explained,

"I’d be worried about the lumbar puncture due to my spinal fusion," while another noted, *"I have magnetic rods in my spine which is why I couldn't have Nusinersen, I worry this may impact my chances of having the new treatment."*

Beyond surgical history, the day-to-day burdens of the broader treatment pathway, including prolonged steroid regimens, required shielding, and difficult venous access, were frequently cited as friction points. A teenage respondent emphasized these trade offs, stating,

"the requirement for frequent blood tests would be a significant drawback, as I dislike needles. The need for shielding and taking steroids would also put me off... For me, any potential benefits would need to clearly outweigh these burdens."

Finally, a strong sense of caution persists regarding treatment switching and the limited long term evidence available for older populations. Parents currently managing stable paediatric patients expressed fear over abandoning proven therapies, with one parent asking,

"What if he has the gene therapy and it doesn't work? Can he go back to taking risdiplam?"

Another parent reflected on the anxiety of transitioning, noting,

"Since we have been on Spinraza for 4 plus years and we know it works… it would be very nerve wracking to change."

Consequently, respondents consistently underscored the necessity for robust clinical data prior to making a switch, with an adult participant emphasising,

"I would need very strong, clear long-term safety and efficacy data before switching."

5.0 Conclusion

In conclusion, the findings demonstrate that while the UK SMA community strongly welcomes the prospect of a single-dose gene therapy like OAV101 IT, driven by high optimism for functional gains and an overwhelming willingness to engage with demanding monitoring schedules, successful clinical integration requires navigating complex patient and carer trade-offs. Crucially, this high optimism for clinical gains largely stems from outcomes observed in children treated with IV Zolgensma, despite a current lack of clinical evidence showing that similar gains can be achieved in older populations or those with more progressed forms of the disease.

Key disparities between proxy decision-makers and adult patients highlight that community acceptance is not uniform; carers prioritise long-term treatment durability and caution surrounding immunosuppressive protocols, whereas adult patients seek quality of life gains but face physical barriers to intrathecal delivery due to spinal fusions and rods. Furthermore, for families currently stabilised on existing disease modifying therapies like risdiplam or nusinersen, the hesitation to swap a proven benefit for an uncertain long term outcome remains a critical threshold. Ultimately, treatment decisions will remain highly individualised and nuanced; community perspectives are likely to shift dynamically as more long-term data becomes available and adaptable administration protocols are developed to address complex physical barriers.