Has respiratory function assessment higher responsiveness than motor functional evaluation to the positive effect of risdiplam in later-onset SMA patients? The experience of a long-term follow-up in two italian centers

Anthony Gabriele Messina, M. Sframeli, N. Brolatti, F. Trucco, E. La Rosa, R. Lauro, R. Materia, M. Maniaci, N. Longoni, I. Said, C. Allegra, M. Pedemonte, C. Bruno, S. Messina

UOSD Neurodegenerative & Neuromuscular Diseases, AOU Policlinico G. Martino, Univ. Messina– Messina, Italy
Dept. of Neuroscience & Translational Myology, IRCCS Gaslini & Univ. Genoa – Genoa, Italy
Pediatric Neurology & Muscular Diseases Unit, IRCCS Gaslini – Genoa, Italy

INTRODUCTION

Spinal Muscular Atrophy (SMA) is a progressive neuromuscular disease characterized by muscle weakness and respiratory decline, the leading cause of morbidity and mortality. Risdiplam, a SMN2 splicing modifier, is approved for SMA 5q, but long-term data on respiratory function are limited. Motor functional scores often remain stable in advanced SMA, reducing their sensitivity to treatment effects.

OBJECTIVES

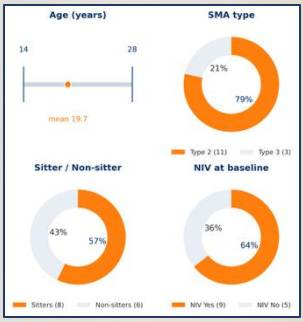
1. To evaluate whether respiratory function (FVC: maximal volume exhaled after full inspiration; PEF: maximal expiratory flow rate, indicator of airway patency & expiratory strength) is more responsive than motor scales (HFMSE, RULM) in later-onset SMA patients treated with risdiplam.
2. To describe the longest available follow-up (>5 years).

METHODS

Population: 14 non-ambulant SMA type 2 and 3 patients (mean age 19.7 yrs; 57.1% sitters, 42.9% non-sitters).
Setting: 2 Italian centers (Messina, Genoa).
Assessments:

- *Motor:* HFMSE, RULM
- *Respiratory:* FVC, FVC%, PEF, PEF%
- *Ventilation:* NIV requirement

Follow-up: mean 5.4 years.

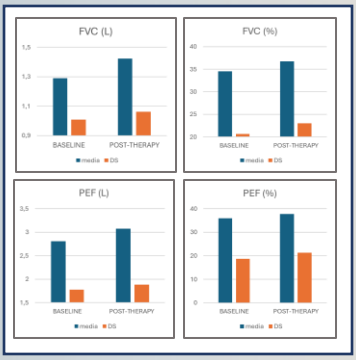


RESULTS

MOTOR FUNCTION:
- Baseline HFMSE ≤ 8 in 13/14 pts; stable after treatment (p=0.6).
- RULM range 2–26; no significant change (p=0.1).

RESPIRATORY FUNCTION:
- FVC: 1.28 L → 1.42 L (Δ+0.14 L, p=0.04)
- PEF: 2.8 L → 3.07 L (Δ+0.27 L, p=0.03)
- FVC% and PEF% improved, but not always significant
- 72% improved FVC; 78% improved PEF

VENTILATION:
- 9 patients on NIV at baseline remained stable.
- 1 patient discontinued nocturnal NIV after 4 years with documented improvement.



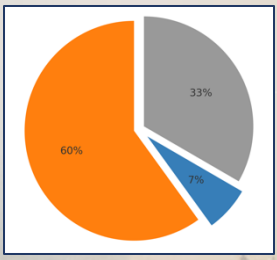
DISCUSSION

1. This is the longest-term report of risdiplam effects on respiratory function in SMA.
2. Motor scales remained stable, while FVC and PEF improved significantly, suggesting respiratory measures are more sensitive.
3. These findings support including respiratory outcomes as standard measures in SMA follow-up.

CONCLUSIONS

- We report the longest respiratory follow-up in non-ambulant SMA type 2–3 patients treated with Risdiplam.
- For the first time, a differential improvement in respiratory function by standard lung tests is shown.
- FVC and PEF appear highly responsive - especially in severely affected patients, where motor outcomes may miss change.

Further studies on larger cohorts are warranted to confirm our results.



60%: stable NIV (9 pts)
33%: no NIV at baseline (5 pts)
7%: discontinued NIV after 4 years (1 pt)

REFERENCES

1. Finkel RS, Mercuri E, Meyer OH, et al. Diagnosis and management of SMA: part 2. Neuromuscul Disord. 2018;28:197–207.
2. Wijngaarde CA, Veldhoen ES, van Eijk RPA, et al. Natural history of lung function in SMA. Orphanet J Rare Dis.2020;15:88.
3. Trucco F, Ridout D, Scoto M, et al. Respiratory trajectories in type 2 and 3 SMA (iSMAC cohort). Neurology.2021;96:587–599.