EE704

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RISDIPLAM FOR THE TREATMENT OF SPINAL MUSCULAR ATROPHY: IMPACT ON THE NATIONAL HEALTHCARE SERVICE DURING THE FIRST 15 MONTHS OF COMMERCIALIZATION IN ITALY

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Objective

- Spinal muscular atrophy (SMA) is a rare, serious, and life-threatening autosomal recessive neuromuscular disorder that, prior to the emergence of treatments with proven efficacy, led to more infant deaths than any other genetic disease [1].
- Risdiplam is the first orally-administered small molecule to be marketed for the treatment of SMA patients [2].
- In Italy, risdiplam is reimbursed for the treatment of SMA 5q in patients from 2 months of age, with a clinical diagnosis of SMA type 1, type 2, or type 3, or having one to four copies of SMN2 [3].
- The objective of this study was to evaluate the impact of risdiplam on the Italian National Healthcare Service (SSN) during the first 15 months of commercialization.

Methods

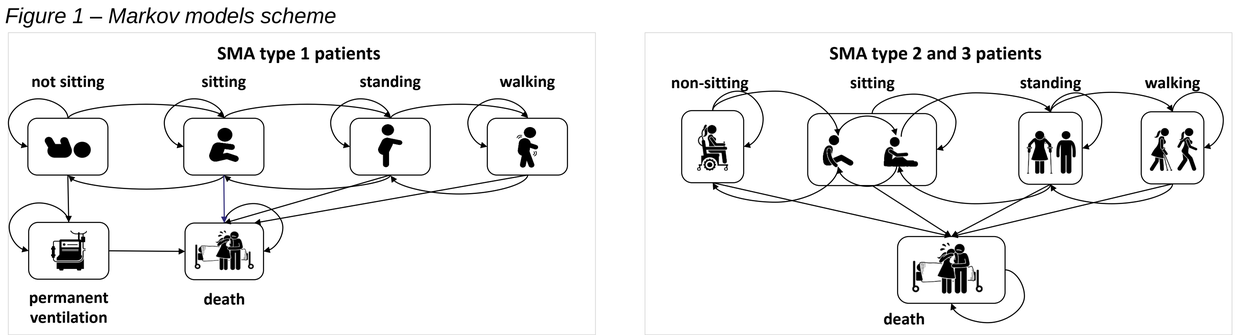
- A Cost Offset Calculator (COC) was developed using Italian Medicines Agency (AIFA) monitoring registry and internal data.
- Two 1-month cycle Markov models were used to estimate clinical outcomes and costs of SMA patients receiving either risdiplam or nusinersen (*Figure 1*).
- Health-state occupancy and treatment discontinuation were determined using risdiplam clinical data and indirect comparisons for nusinersen. For patients who discontinued treatment, the transition to another therapy was not considered (*Table 1*).

Table 1 – Summary of Markov models characteristics

Parameter	Type SMA 1	Type SMA 2 and 3
Patients baseline characteristics	FIREFISH trial	SUNFISH trial
Transition probabilities	2-year follow up FIREFISH data	2-year follow up SUNFISH data
Overall survival	"not sitting" and "permanent ventilation": FIREFISH data Others health states: SMA 2 as proxy	SMA 2: literature data SMA 3: general population
Treatment discontinuation	2-year follow up FIREFISH data	Not considered
Nusinersen efficacy	Indirect treatment comparison	Indirect treatment comparison

- Direct costs included drug acquisition, administration, and disease monitoring while indirect costs such as caregiver and patient productivity loss in terms of missed work and school days. Resource use data and unit costs were retrieved from published literature and Italian sources (*Table 2*).
- The COC considered the first 15 months of commercialization (February 2022 - April 2023) and compared expenses for risdiplam treatment to those that would have been incurred with nusinersen.
- In the nusinersen scenario, for patients coming from risdiplam compassionate use program (CUP) no costs were considered as they were deemed ineligible for nusinersen treatment.

Figure 1 – Markov models scheme



- The SMA type 1 Markov model considers the possibility of motor-function milestone gains/lost, and survival in 6 discrete health states: non-sitting, permanent ventilation, sitting, standing, walking and death. The SMA type 2 and 3 Markov model considers the possibility of motor-function related declines, stabilization, improvements, and survival in 6 discrete health states: non-sitting, sitting (supported), sitting (unsupported), standing, and walking.
- Patients can die from any health state and proceed to death.
- The costs associated with each health state are calculated on a monthly basis.

Table 2 – Unit costs

Direct cost	*Not sitting*	*Permanent ventilation*	*Sitting*	*Standing*	*Walking*
Disease monitoring (annual cost)	56.238	23.725¶	20.667	14.181*	7.694
Indirect cost					
Missed work and school days (annual)	24.00	24.00‡	14.50	12.33*	8.82

* Estimated as the mean of "sitting" and "walking". ¶ To be added to the "not sitting" cost [8]. ‡ Conservatively assumed same as "not sitting".

Drug consumption and administration

Ex-factory prices net of confidential discounts negotiated with AIFA were considered [4]. Posology reflected the Summary of Product Characteristics. For oral administration a cost of zero was assumed. For intrathecal administration literature data was used [5].

Disease monitoring

Annual cost were retrieved from literature [6]. Estimates reported for SMA types 1, 2, and 3 were used as proxies for "not sitting", "sitting", and "walking" respectively.

Missed work and school days

Data were retrieved from literature. [7] The model included one additional day lost for each nusinersen infusion.

Results

- During the **initial 15 months** of commercialization, **514 patients** received treatment with risdiplam (*Figure 2*):
  - 66 treated while risdiplam was not yet classified for reimbursement (Cnn);
  - 171 coming from CUP;
  - 32 coming from clinical trials;
  - 75 switching from nusinersen.
- Considering the SSN perspective, the COC estimated **savings of €15.3 million for drug acquisition and administration** along with **savings of roughly €256.000 for** healthcare resources consumed for **disease monitoring** (*Table 3*, *Figure 3*).
- In addition to these economic results, there were also a **gain of almost 1.600 days of work and school** compared to treatment with nusinersen.

Table 3 – Estimated costs and related offset for the first 15 months of commercialization (costs in €)

	Risdiplam	Nusinersen*	Offset
Drug acquisition	56.634.024	69.613.493	- 12.979.470
Drug administration	-	2.334.028	- 2.334.028
Treatment cost	**56.634.024**	**71.947.521**	**- 15.313.498**
Disease monitoring	13.078.580	13.334.780	- 256.199
Total cost	**69.712.604**	**85.282.301**	**- 15.569.697**

* In the "Nusinersen" scenario the following treatment costs were considered:
- New and Cnn patients: loading and maintenance.
- Clinical trials and switchers patients: only maintenance. It was assumed that these patients had already received 12 months of treatment.
- CUP patients: no cost. These patients were deemed ineligible for nusinersen treatment, therefore no costs were considered.

Figure 2 – Risdiplam treatments initiated from Feb-22 to Apr-23 (cumulative)

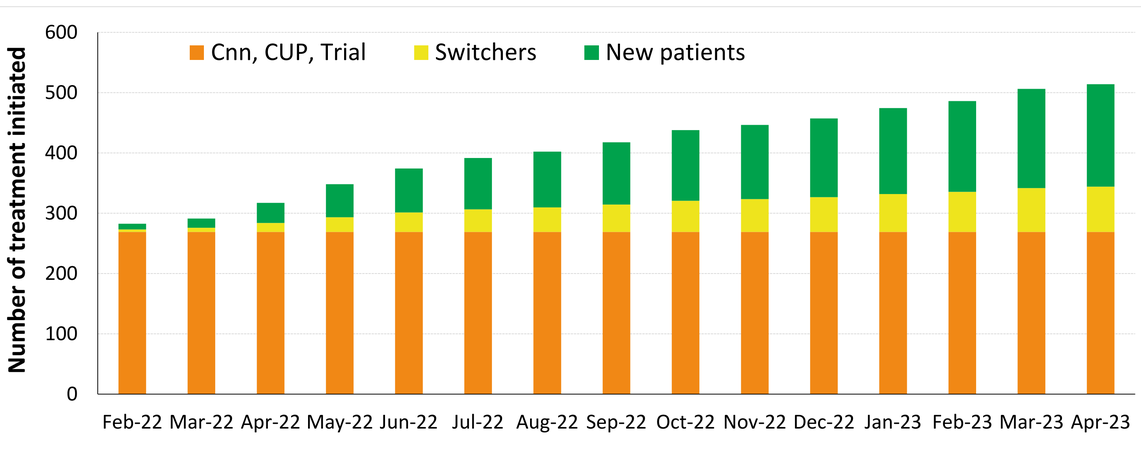
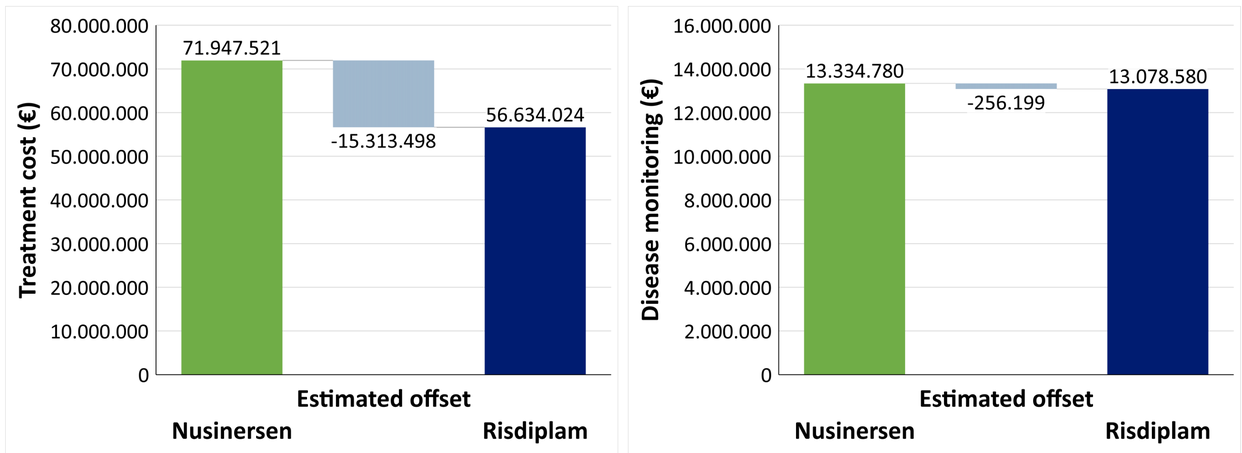


Figure 3 – Estimated costs and related offset for the first 15 months of commercialization



Conclusions

The introduction of **risdiplam** during its first 15 months of commercialization led **to significant overall savings for the SSN**.

References

1. Spinal muscular atrophy. Nat Rev Dis Primers. 2022 Aug 4;8(1):51. doi: 10.1038/s41572-022-00385-3
2. European Medicines Agency. Evrysdi. Online link
3. Gazzetta Ufficiale. Serie Generale n.31 del 07-02-2022
4. So.Re.Sa. Tender process 20/03/2023
5. Calabrò GE et al. La gestione value-based del paziente con Atrofia Muscolare Spinale: il disease burden in Italia. Osservatorio nazionale sulla salute nelle regioni italiane. 2021. Online link
6. Belisari A et al. Healthcare costs of patients with spinal muscular atrophy. Presented at ISPOR Europe 2018
7. Sutherland CS et al. Burden of illness related to motor function in Types 2 and 3 spinal muscular atrophy (SMA). Presented at International Scientific Congress on Spinal Muscular Atrophy 2022
8. Vitacca M et al. Advanced COPD patients under home mechanical ventilation and/or long term oxygen therapy: Italian healthcare costs. Monaldi Arch Chest Dis. 2011 Dec;75(4):207-14. doi: 10.4081/monaldi.2011.208.

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