Hospital Costs Of Treating Infantile-Onset SMA Patients With High Dose Nusinersen (50/28 mg) vs Low Dose Nusinersen (12/12 mg) In Italy

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BACKGROUND

- Spinal muscular atrophy (SMA) is a genetic neuromuscular disease caused by autosomal recessive mutations in the SMN1 gene on chromosome 5, which leads to a reduction in survival motor neuron (SMN) protein that impairs motor neuron function [1,2]. SMA is characterized by skeletal and respiratory muscle weakness, the severity of which is inversely related to SMN2 gene copy number [1,2].
- Clinical evidence has demonstrated that the antisense oligonucleotide nusinersen delivers robust, long-term therapeutic benefits across diverse SMA phenotypes [3,4]. Nusinersen was originally approved at a dose of 12 mg, per intrathecal administration [3,4].
- More recently, clinical efficacy, safety, and tolerability of a higher dose of nusinersen (50 mg as a loading dose and 28 mg as a maintenance dose) were investigated in the DEVOTE trial, a global, 3-part, Phase 2/3 study [5,6,7].
- DEVOTE Part B was a randomized, double-blind, active-controlled treatment trial examining the clinical efficacy of 50/28 mg nusinersen in treatment-naive children with infantile- or later-onset SMA compared with nusinersen 12-mg dose.
- DEVOTE Part B included additional hospital-related secondary endpoints: i) proportion of participants hospitalized for serious adverse events (SAEs); ii) hospital time attributable to SAEs; iii) proportion of participants experiencing serious respiratory events (SREs); and iv) proportion of time participants used ventilation support.
- This analysis used these outcomes to compare hospital and administration costs during the first year of treatment, between the 50/28 mg and 12/12 mg nusinersen regimens, from the Italian NHS perspective.

OBJECTIVES

To compare hospital costs for drug administration and adverse-event management, from the Italian National Healthcare Service (NHS) perspective, using clinical outcomes from the DEVOTE Part B trial, enrolling participants with infantile-onset spinal muscular atrophy (SMA) treated with the 50/28 mg nusinersen dose versus the 12/12 mg nusinersen dose.

METHODS

- A 1-year economic analysis was conducted in a hypothetical cohort of 100 patients with infantile-onset SMA treated with either 50/28 mg nusinersen or 12/12 mg nusinersen.
- Clinical inputs (Figure 1) were derived from the DEVOTE Part B trial (infantile-onset); more specifically, analysis of secondary outcomes showed that [7,8]:
  - 38% of patients in the 50/28 mg nusinersen arm experienced an SAE-related hospitalization, versus 56% in the 12/12 mg nusinersen arm.
  - The adjusted annual rate of SAE-related hospitalizations was 0.8 per patient/year in the 50/28 mg nusinersen arm, versus 1.4 per patient/year in the 12/12 mg nusinersen arm.
  - Average length of stay (LOS) was 30.70 days in the 50/28 mg nusinersen arm, versus 32.90 days in the 12/12 mg nusinersen arm.
  - 52% of patients in the 50/28 mg nusinersen arm experienced a SRE, versus 64% in the 12/12 mg nusinersen arm.
  - Adjusted annual rate of SRE was 1.8 per patient/year in the 50/28 mg nusinersen arm, versus 2.1 per patient/year in the 12/12 mg nusinersen arm.
  - Over the first year of treatment, N=4 administrations per patient were required with the 50/28 mg nusinersen dose, versus N=6 administrations per patient with 12/12 mg nusinersen regimen.

Figure 1a. Clinical inputs of the model [7,8].

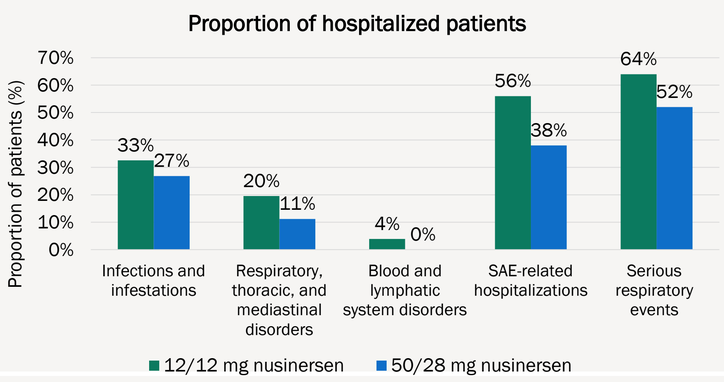
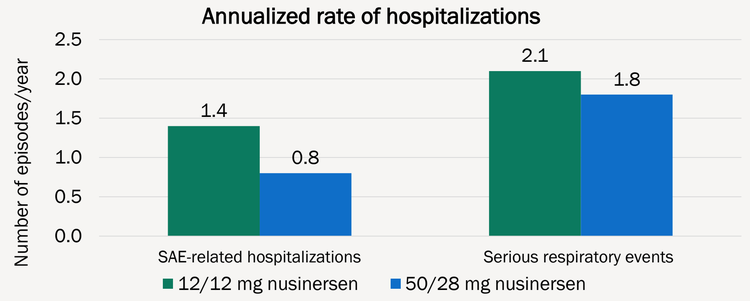


Figure 1b. Clinical inputs of the model [7,8].



- Cost analyses were conducted using Italian NHS unit costs (i.e., per episode; Table 1):
- For each cause of SAE-related hospitalization, a weighted average diagnosis-related group (DRG) tariff was calculated using the number of hospital discharges as weights [9,10]: infections and infestations; respiratory, thoracic, and mediastinal disorders; and blood and lymphatic system disorders.
- For SREs, the unit cost of an emergency room (ER) visit was retrieved from Italian economic literature [11] and inflated to March 2026 [12].
- For treatment administration (intrathecal), the tariff of lumbar puncture was used [13].

- Table 1. Economic inputs of the model.

Economic input	Unit cost (€)	Description	Source
SAE-related hospitalizations			
Infections and infestations	5,468.17	Weighted average DRG tariff (number of hospital discharges used as weights)	Elaborated from [9,10]
Respiratory, thoracic, and mediastinal disorders	4,581.07		
Blood and lymphatic system disorders	2,438.28		
Hospital cost, per day	158.43	Daily charge for hospitalizations exceeding LOS threshold	
Serious respiratory events	341.20	Unit cost of an emergency room (ER) visit (inflated to March 2026)	Elaborated from [11,12]
Nusinersen administration	482.10	90% of administrations outpatient: € 2,850 (DRG 12) 10% of administrations outpatient: € 219 (MAC 11)	Elaborated from [13]

- Drug acquisition costs were not included in the analysis.
- The base-case analysis compared total hospital costs between the two scenarios.
- One-way sensitivity analysis (OWSA) was conducted versus the base-case, varying both clinical and economic inputs by ± 10%.
- An alternative analysis was conducted, by applying hospital daily costs instead of fixed DRG tariffs (base-case, standard approach in Italy), to estimate total costs from the hospital perspective.

RESULTS

As described in methods, a lower proportion of patients receiving 50/28 mg nusinersen experienced SAE-related hospitalization and SREs, compared with patients receiving 12/12 mg nusinersen. Similarly, annualized rates of SAE-related hospitalization and SREs were lower in the 50/28 mg nusinersen group, versus the 12/12 mg nusinersen group.

Base-case analysis

- Assuming that 100 patients were treated with either 12/12 mg or 50/28 mg nusinersen, the 50/28 mg nusinersen dose was associated with fewer SAE-related hospitalizations (30.4 versus 78.4; difference: -48.0 admissions; -61%), cumulative length of stay (933 days versus 2,579 days; difference: -1,646 days; -64%), and fewer SRE cases (93.6 versus 134.4; difference: -40.8 cases; -30%), compared with 12/12 mg nusinersen.
- In addition, during first year of treatment, 50/28 mg nusinersen reduced the number of administrations by 200 (400 versus 600; -33%) due to the lower number of loading doses required.
- These clinical improvements and the reduction in administrations generated considerable cost offsets, with total hospital costs of €383 thousand for 50/28 mg nusinersen versus €739 thousand for 12/12 mg nusinersen, resulting in potential savings of €356 thousand (relative reduction: -48%; Table 2).

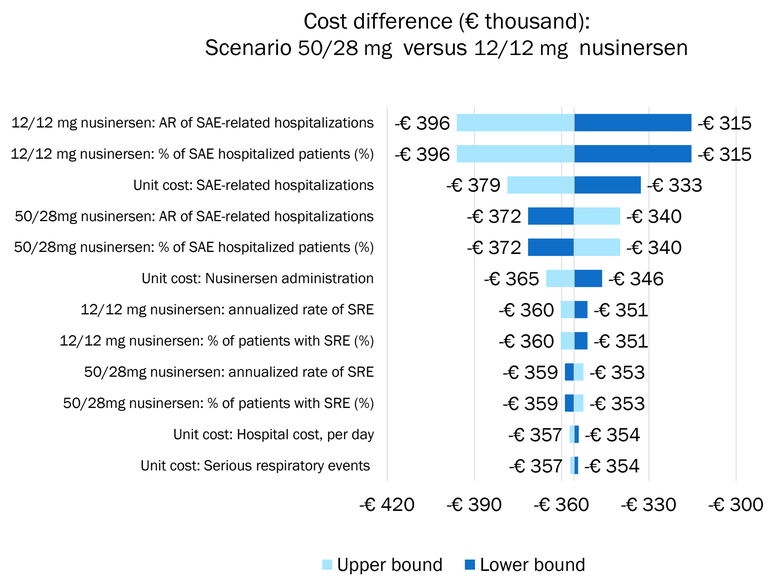
Table 2. Results of the base-case analysis.

Economic output	Scenario with 100 patients treated with 12/12 mg Nusinersen	Scenario with 100 patients treated with 50/28 mg nusinersen	Absolute difference 50/28 mg versus 12/12 mg nusinersen (relative difference)
SAE-related hospitalizations	**€ 387,871**	**€ 158,301**	**-€ 229,570 (-59%)**
Infections and infestations	*€ 249,247*	*€ 117,340*	*-€ 131,906 (-53%)*
Respiratory, thoracic, and mediastinal disorders	*€ 125,287*	*€ 40,960*	*-€ 84,327 (-67%)*
Blood and lymphatic system disorders	*€ 13,337*	*€ 0*	*-€ 13,337 (-100%)*
Additional costs for hospitalizations exceeding LOS threshold	**€ 15,805**	**€ 0**	**-€ 15,805 (-100%)**
Serious respiratory events	**€ 45,858**	**€ 31,937**	**-€ 13,921 (-30%)**
Nusinersen administration	**€ 289,260**	**€ 192,840**	**-€ 96,420 (-33%)**
Total costs	**€ 738,793**	**€ 383,077**	**-€ 355,716 (-48%)**

Alternative analyses

- The OWSA confirmed robustness of the base-case analysis, with all scenarios being favourable to 50/28 mg nusinersen (i.e., 50/28 mg nusinersen cost-saving versus 12/12 mg nusinersen; Figure 2).
- In the alternative scenario, in which daily costs were applied (instead of fixed DRG tariffs), total hospital costs were €532 thousand for 50/28 mg nusinersen versus €1,132 thousand for 12/12 mg nusinersen, resulting in potential savings of €601 thousand (relative reduction: -53%).

Figure 2. Results of one-way sensitivity analysis.



CONCLUSIONS

50/28 mg nusinersen has the potential to generate substantial cost savings for the treatment of infantile-onset SMA patients in Italy, by reducing the clinical and economic burden of hospital admissions and administration frequency during the first year of treatment. Future real-world studies on patients treated with 50/28 mg nusinersen should be conducted to confirm the findings of this economic evaluation. In fact, the outcomes observed in DEVOTE, including clinical events may not be fully representative of real-world practice in Italy, where SMA treatment and management practices may differ from those experienced by participants in the study.

Acronyms: AR: annualized rate; ER: emergency room; LOS: length of stay; MAC: complex outpatient intervention; NHS: National Healthcare Service; OWSA: one-way sensitivity analysis; SAE: serious adverse event; SMA: spinal muscular atrophy; SMN: survival motor neuron; SRE: serious respiratory event.

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Disclosures: FG: is an independent consultant and under contract with Biogen Italia. OC, MG, SL: are employees of and may hold stock in Biogen.

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