Assessing Risdiplam Cost-Effectiveness for Spinal Muscular Atrophy Types I, II, and III in Chile

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BACKGROUND

Spinal Muscular Atrophy (SMA) is a rare, autosomal recessive neuromuscular disorder primarily affecting newborns and children. It is caused by the deletion or mutation of the SMN1 gene on chromosome 5q, with disease severity modulated by the number of SMN2 gene copies. Despite the incurable nature of the disease, recent advancements in genetic therapies have demonstrated significant clinical benefits.

OBJECTIVE

The present study aims to conduct a cost-effectiveness analysis of risdiplam compared to other therapies for the treatment of patients with SMA in stages I, II, and III in the public health sector from a social perspective, to compare outcomes between the alternatives and, thus, generating scientific evidence to support decision-making related to the selection and funding of these technologies.

METHODS

Adapting a pre-existing Markov model developed by Roche, this study evaluated a hypothetical cohort of patients diagnosed with Spinal Muscular Atrophy (SMA) types I, II, and III. Separate models were constructed for SMA type I and for SMA types II & III, designed to simulate the natural course of the disease and its progression through different stages.

This study focuses on the Chilean public healthcare sector (i.e. FONASA) with a 10-year time horizon from a social perspective. Treatments, including risdiplam, nusinersen, and AVXS-101, were assessed for costs and effectiveness within the public healthcare system. Full adherence to treatment is assumed, and adverse events are considered to occur at equal rates across different states. Indirect comparisons are conducted due to the absence of head-to-head studies. Clinical effectiveness outcomes include quality-adjusted life years (QALYs), with costs and health outcomes discounted at an annual rate of 3%. A cost-utility analysis compared treatments in terms of costs and quality-adjusted life years (QALYs), evaluated against willingness-to-pay thresholds. Sensitivity analyses, including Monte Carlo simulations, tested the robustness of findings.

Model overview

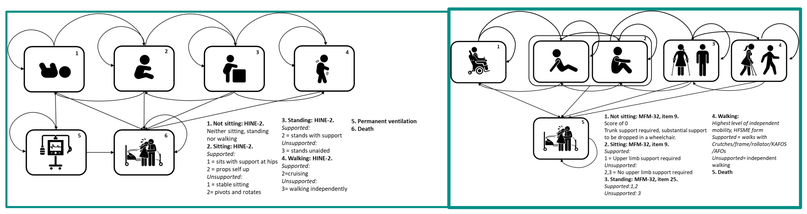

Figure 1. Markov model for SMA type I (Left), SMA type II & type III (Right)

Model structure. For SMA type I, the model encompassed potential motor function gains and survival across six states: non-sitting, permanent ventilation, sitting, standing, walking, and death, with monthly transitions between states. For SMA types II & III, the model tracked declines, stabilization, improvements, and survival across states: non-sitting, sitting (with/without support), standing, and walking, with transitions occurring once per cycle. Population characteristics, such as age, gender distribution, weight, and SMA type distribution, were identified and specified at the study's outset. External experts with experience managing SMA patients validated the transitions and parameter selection utilized in this economic modeling.

Transition probabilities between motor function states were derived from clinical trials, with data from the FIREFISH and SUNFISH studies informing the probabilities for SMA type I and types II & III, respectively. Continuous-time multi-state models were employed to estimate transition probabilities, capturing the dynamic nature of disease progression. Survival estimates were based on KM data for SMA type I and external sources for SMA types II & III, with parametric survival analyses conducted to extrapolate survival beyond the study period. Adverse event incidences, including grade 3-5 events, were integrated into the model, with higher rates observed for SMA types II & III. Utilities representing the health-related quality of life for patients and caregivers were incorporated to assess the impact of the treatment on overall well-being.

Intervention and comparators. Risdiplam, developed by Roche, is an oral medication designed to increase SMN protein levels, thereby supporting motor neurons and muscle function. Clinical studies indicate that risdiplam enhances motor function and survival in infants with SMA type I, while motor function gains in SMA types II and III remain stable or improve over time. Comparators include onasemnogene abeparvovec (AVXS-101), a single-dose intravenous gene therapy for infants and patients up to 21 kg, and nusinersen, an intrathecal treatment that increases functional SMN protein production.

Costs. The study includes direct healthcare expenses like medications, consultations, and hospitalizations, as well as indirect costs such as lost productivity and informal caregiving. Treatment costs vary with therapeutic technologies: risdiplam is administered orally; nusinersen intrathecally, requiring additional resources; and AVXS-101 incurs costs for intravenous infusion. Living space adaptations and equipment provision, such as braces and wheelchairs, are tailored to patient needs. Consultation, tests, hospitalizations and equipment costs are assessed using the Institutional Care Modality (FONASA's MAI) tariffs. Medication costs are sourced from the public price database of the Chilean National Supply Center of Medications (Observatorio CENABAST). Indirect costs from lost caregiver productivity are estimated using expert responses.

	Total Cost	QALYs	ΔCosts	Δ QALYs	ICER
Risdiplam	$1,712,956,907	16.68	-	-	-
Nusinersen	$1,950,035,249	15.28	$(237,078,341)	1.3959	Dominant
AVXS-101	$1,767,745,732	16.64	$(54,788,824)	0.0354	Dominant

Table 1. SMA type I Results

	Total Cost	QALYs	ΔCosts	ΔQALYs	ICER
Risdiplam	$2,171,074,171	7.06	-	-	-
Nusinersen	$2,176,751,222	6.94	$(5,677,051)	0.1206	Dominant

Table 2. SMA type II & type III Results

RESULTS

Results indicate risdiplam dominance over comparators in terms of both effectiveness and costs across SMA types. For SMA type I, risdiplam showed a ΔQALYs of 1.40 and negative incremental costs, rendering it dominant in the Chilean public system. For SMA types II & III, risdiplam remained dominant with a ΔQALYs of 0.12 and reduced costs.

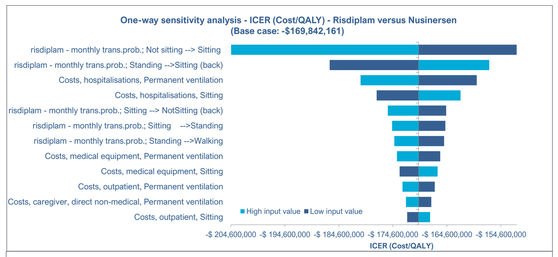

Figure 2. SMA type I Deterministic analysis (Left), SMA types II & III Deterministic analysis (Right)

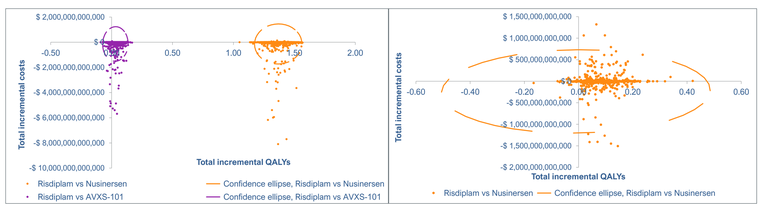

Figure 3. SMA type I Probabilistic Sensitibity Analysis (Left), SMA types II & III PSA (Right)

CONCLUSIONS

Risdiplam shows higher overall survival and quality-adjusted life years (QALYs) compared to nusinersen and AVXS-101 in SMA type I, and higher QALYs compared to nusinersen in SMA types II and III. It has the lowest direct medical costs for SMA type I and lower total costs for SMA types II and III. Sensitivity analyses confirm the robustness of risdiplam's dominance over nusinersen and AVXS-101 in SMA type I, and over nusinersen in SMA types II and III. Additionally, risdiplam's dominance is consistent in other countries, showing extended survival and lower costs. However, SMA treatment is not covered under special financial programs in Chile, raising concerns among patient associations and policymakers. The analysis provided insights into the economic implications of SMA treatments in Chile, aiding healthcare decision-making and highlighting the importance of having funding alternatives for risdiplam given its results in quality-adjusted life years, survival, and costs for the Chilean healthcare system.