Budget Impact and Cost-Effectiveness of Introducing Voretigene Neparvovec for Treating Inherited Retinal Diseases in the Kingdom of Saudi Arabia

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Background

Inherited retinal diseases

- Inherited retinal diseases (IRDs) are a diverse group of disorders characterized by various levels of vision loss and retinal degeneration. Approximately 270 gene mutations are linked to IRDs, with an incidence of about 1 in 2000 individuals globally.[1,2]
- Most IRDs cause early and profound vision loss, leading to significant disability. The degeneration typically affects the photoreceptor and retinal pigment epithelium (RPE) complex. IRDs can be stationary, like congenital stationary night blindness (CSNB), or progressive, such as retinitis pigmentosa (RP).[1]
- Leber congenital amaurosis (LCA) is one of the most severe progressive IRDs, causing significant vision decline within the first year of life. Nearly 60% of LCA patients experience severe visual impairment shortly after birth.[3]

Treatment options for IRDs

- Clinically, IRD is primarily managed through best supportive care (BSC) which includes regular eye examination and treatment support to slow down vision loss.
- Voretigene neparvovec (VN) is the first gene therapy approved to treat LCA. It is indicated for children and adults with vision loss due to *RPE65* gene mutations and sufficient viable retinal cells. VN is a one-time treatment option and has been reported to have a favorable safety profile.[4-6]

Objective

This study aimed to assess the cost-effectiveness analysis (CEA) from societal and payer's perspective and budgetary impact analysis (BIA) with and without managed entry agreement (MEA) from the Ministry of Health (MOH) perspective of applying VN for treatment of IRD in the Kingdom of Saudi Arabia (KSA).

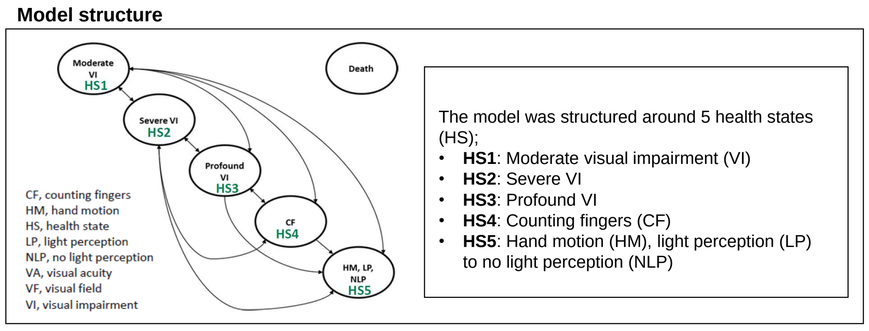
Methods

Cost-effectiveness analysis (CEA)

Model overview

Elements	Input
Key focus	Cost-effectiveness analysis (CEA)
Perspective	Societal perspective and payer perspective
Patient Population	Patients with *RPE65*-mediated IRD who have sufficient viable retinal cells
Duration of VN treatment effect	30 years (based on the global model)
Health states defined by	Visual acuity (VA) and visual field (VF)
Source of baseline data	Phase III Trial[7]
Comparators	Best supportive care (BSC)
Analytical Tools	Microsoft® excel
Time Horizon	Lifetime (maximum age of 75 years)
Discounting	Costs and outcomes are discounted at 3.5%
Currency	Saudi riyal (SAR)

Model structure



The model was structured around 5 health states (HS);
- **HS1**: Moderate visual impairment (VI)
- **HS2**: Severe VI
- **HS3**: Profound VI
- **HS4**: Counting fingers (CF)
- **HS5**: Hand motion (HM), light perception (LP) to no light perception (NLP)

Figure 1: Markov state transition model for CEA

Model inputs: Patient population, clinical data, utility data (health state utility values, adverse event disutility, carer disutility), and cost data (VN costs, eligibility testing costs, adverse event costs, healthcare, and non-healthcare resources costs)

Model outputs: Cost per quality-adjusted life-year (QALY) gained and incremental cost-effectiveness ratio (ICER)

Budget impact analysis (BIA)

Model overview

Elements	Input
Key focus	Budget impact
Perspective	Ministry of Health (MoH) - Kingdom of Saudi Arabia
Intervention	VN administered as two subretinal injections (one in each eye)
Comparators	Best supportive care (BSC)
Population	Individuals with *RPE65*-mediated IRD who have sufficient viable retinal cells
Analytical Tools	Microsoft® excel
Time Horizon	5 years
Currency	SAR

Model structure

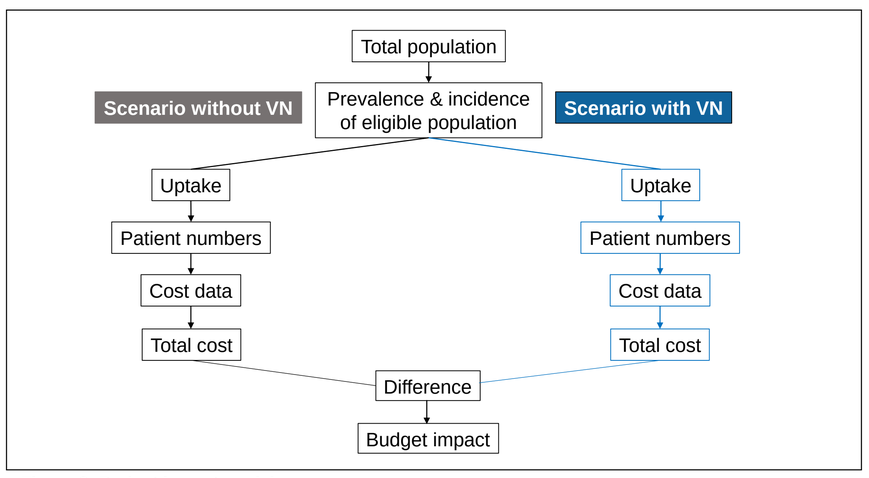


Figure 2: Budget impact model

Model inputs: Patient population, market share data, clinical data, cost data with and without MEA, adverse events costs, healthcare and non-healthcare resources use, eligibility testing costs

Model outputs: Total budget impact and total incremental cost over five years with and without MEA

Results

Cost-effectiveness analysis (CEA)

Societal perspective

- CE results demonstrated that in the base case-societal perspective **the total cost is lower with VN (SAR 5,571,527)** as compared to BSC (SAR 6,215,952).
- The **total QALYs gained are higher with VN (14.9)** than with BSC (9.2)
- For **a willingness to pay threshold (WTP) of 75,000**, **VN has the dominant ICER** (Table 1). The ICER results are the same for WTP of 50,000, 150,000, and 225,000.
- **Sensitivity analysis:** Four of the ten most influential parameters are those describing the utility values (Acaster Lloyd, EQ-5D-5L) for all five health states (**Figure 3**).

Payer perspective

- For the base case-payer perspective**, the total cost is higher with VN (SAR 3,091,239)** compared to BSC (SAR 342,815) for the same **total QALYs gained.**
- For **a willingness to pay threshold (WTP) of 75,000**, **VN has an ICER of SAR 487, 561** (Table 2). The ICER results are the same for WTP of 50,000, 150,000, and 225,000.
- **Sensitivity analysis:** For the payer perspective also, five of the ten most influential parameters are those describing the utility values (Acaster Lloyd, EQ-5D-5L) for all five health states (**Figure 4**).

Table 1: WTP: SAR 75,000

Incremental costs	**-SAR 644,425**
Incremental QALYs	5.64
ICER	**-SAR 114,319**

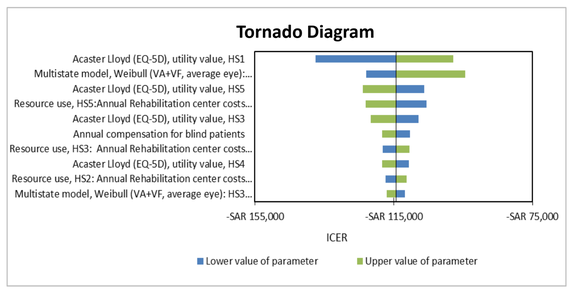


Figure 3: Univariate sensitivity analysis for the societal perspective

Table 2: WTP: SAR 75,000

Incremental costs	**SAR 2,748,424**
Incremental QALYs	5.64
ICER	**SAR 487,561**

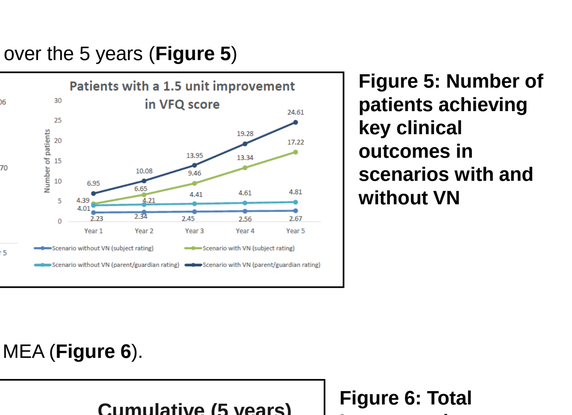


Figure 4: Univariate sensitivity analysis for the payer perspective

- **VN provides substantial health benefits compared to BSC, with total QALYs gained being significantly higher.**
- **The ICER remains consistent across various WTP thresholds, indicating robust cost-effectiveness within the evaluated range.**

Budget impact analysis (BIA)

Clinical outcomes

- The introduction of VN for the treatment of IRD is expected to improve the clinical outcomes significantly over the 5 years (**Figure 5**)

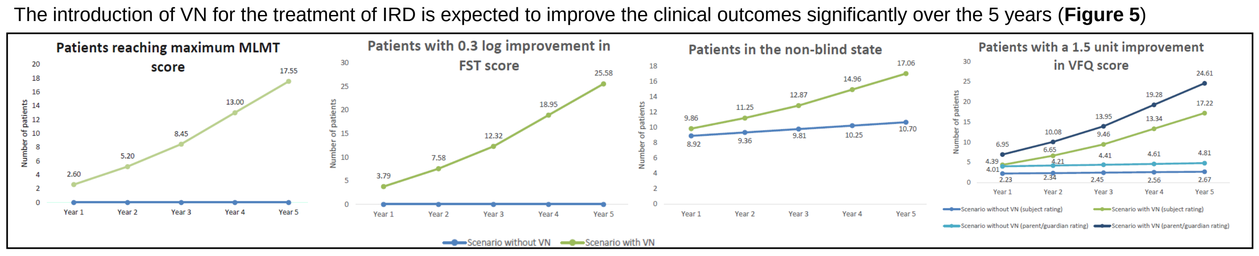


Figure 5: Number of patients achieving key clinical outcomes in scenarios with and without VN

Scenario 1: BSC vs VN without MEA

The introduction of VN resulted in a total incremental cost of **SAR 69 million (387.6%)** over 5 years without MEA (**Figure 6**).

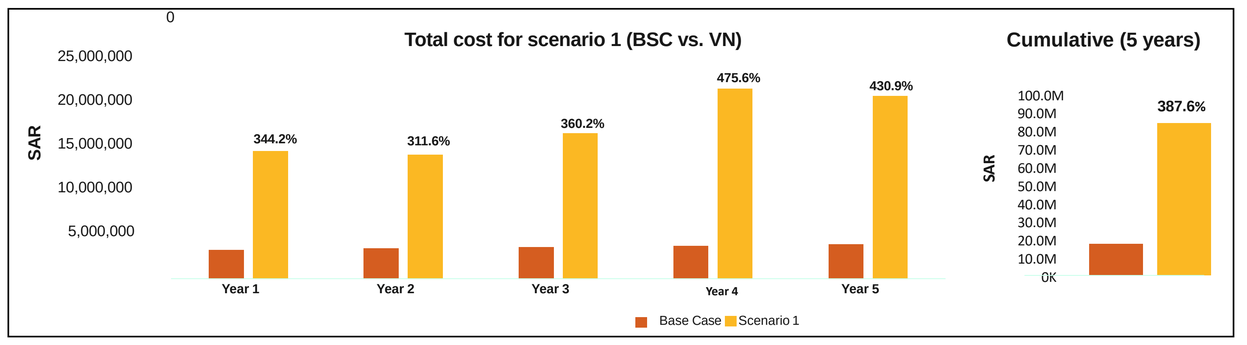


Figure 6: Total Incremental cost associated with VN over 5 years without MEA

Table 5: Total incremental cost for BSC and VN

Year	Year 1	Year 2	Year 3	Year 4	Year 5	Cumulative
BSC (Without VN)	SAR 3,280,909	SAR 3,444,424	SAR 3,607,938	SAR 3,771,452	SAR 3,934,966	**SAR 18,039,688**
With VN	SAR 14,575,173	SAR 14,176,773	SAR 16,601,939	SAR 21,710,192	SAR 20,890,357	**SAR 87,954,433**
Total Incremental cost	**SAR 11,294,264**	**SAR 10,732,349**	**SAR 12,994,001**	**SAR 17,938,740**	**SAR 16,955,391**	**SAR 69,914,745**

Scenario 2: BSC vs VN with MEA

The introduction of VN resulted in a total incremental cost of SAR **64 million (356%)** over 5 years with MEA (**Figure 7**).

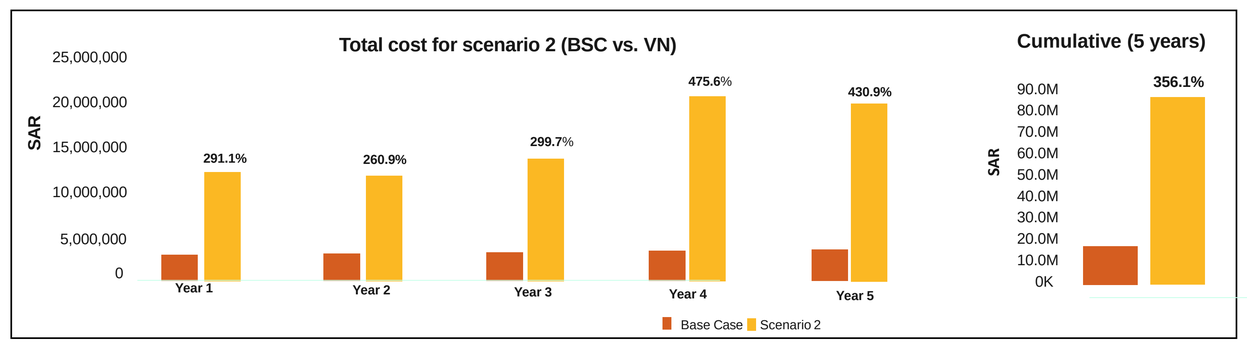


Figure 7: Total Incremental cost associated with VN over 5 years with MEA

Table 6: Total incremental cost for BSC and VN

Year	Year 1	Year 2	Year 3	Year 4	Year 5	Cumulative
BSC (Without VN)	SAR 3,280,909	SAR 3,444,424	SAR 3,607,938	SAR 3,771,452	SAR 3,934,966	**SAR 18,039,688**
With VN	SAR 12,830,434	SAR 12,432,034	SAR 14,421,016	SAR 21,710,192	SAR 20,890,357	**SAR 82,284,033**
Total Incremental cost	**SAR 9,549,525**	**SAR 8,987,610**	**SAR 10,813,078**	**SAR 17,938,740**	**SAR 16,955,391**	SAR 64,244,345

- **Over a period of 5 years, the introduction of VN will result in significantly improved clinical outcomes and a lower budget increase with Scenario 2; i.e., with the MEA. The increase will be the highest in the base case scenario without any MEA.**

Conclusions

- The introduction of VN for the treatment of *RPE65*-mediated IRDs in KSA is both cost-effective and beneficial from a budgetary perspective, particularly when supported by market access agreements.
- VN offers superior health outcomes at a nominal increase of the total budget compared to the BSC, demonstrating significant value in terms of both patient health and economic impact.
- Policymakers and healthcare providers should consider adopting VN, leveraging MEAs to optimize the balance between immediate financial investments and long-term clinical benefits.
- This comprehensive evaluation supports VN as a valuable addition to the healthcare options for managing IRDs in KSA, promising enhanced quality of life for patients and sustainable healthcare expenditure.

References

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