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The Zolgensma: The Future of Gene Therapy With Its Possibilities and Concerns

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Abstract

This study will briefly explain a particular gene therapy called Zolgensma (onasemnogene abeparvovec-xioi), used for treating a rare genetic disease, spinal muscular atrophy (SMA). SMA is a condition that leads to progressive muscle weakness and mobility disorders. It is a major cause of infant fatality, with the type 1 having a fatality rate of approximately 90% before the age of two without treatment. Zolgensma is a genetic therapy that has been developed over the recent years. It is a promising medical advancement specifically designed for children under 2 years old with SMA. The treatment works by delivering a functional copy of the defective SMN1 gene, using an adeno-associated virus (AAV9); therefore, enabling the production of essential proteins for motor neuron activity. Unlike other treatments, Zolgensma targets the root genetic cause, therefore it is administered as a one-time intravenous infusion. Zolgensma's effects, advantages and disadvantages are going to be explained and compared to other therapies such as Spinraza and Evrysdi. In addition, ethical concerns raised by Zolgensma, such as its accessibility, are going to be discussed in this study.

Keywords: *genetics; disease; therapy; gene; science*

1.Introduction

Over the last few decades, genetics have developed and has been used in several areas of life, along with raising ethical concerns and increasing individuals' overall life quality. One of these areas is medicine. Genetic therapies have been helpful for those with rare and fatal medical diseases. One of these diseases is spinal muscular atrophy (SMA) which is a genetic disorder that causes muscles to progressively weaken over time, leading to serious movement loss. For instance, it can lead to individuals not being able to sit, crawl or even lift up their head. It is one of the leading genetic causes for infant death. SMA Type 1 has a fatality rate of approximately 90% before the age of two without treatment (Novartis, n.d.).

2. Zolgensma

2.1 Spinal Muscular Atrophy (SMA)

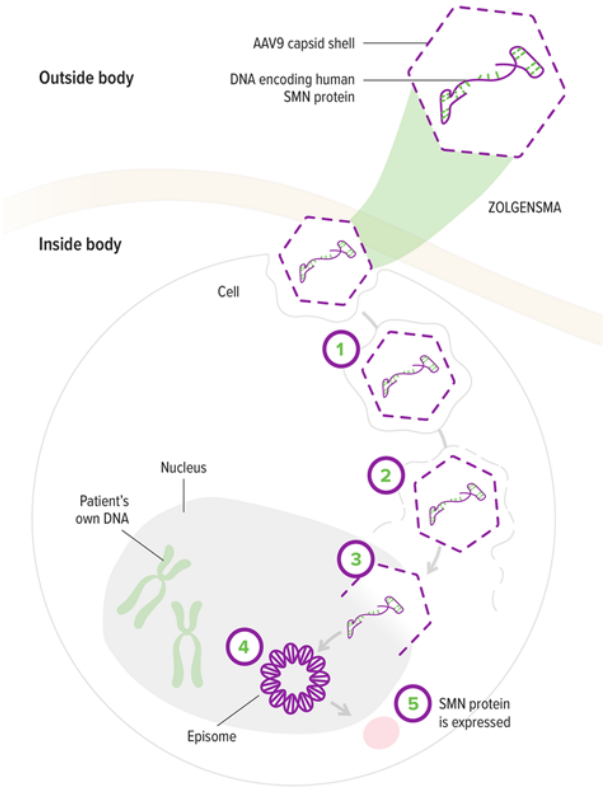
SMA is caused by a problem in the gene called SMN1 gene. SMN1 produces a protein that is necessary for motor neurons — nerve cells that control muscle movement. An SMA patient's SMN1 gene cannot function properly, causing it not to produce enough protein for the body. As a result, motor neurons start to die, resulting in mobility loss and muscle weakness. It can be fatal in infants and children. This disease's prevalence is relatively high in Türkiye. Around 3,000 people are currently SMA patients,

along with 130–180 new patients being diagnosed each year (Topcu Yenercag et al., 2025). This disease's phenotype is classified into four grades of severity (SMA I, SMA II, SMA III, SMA IV) based on age of onset and motor function achieved (Mercuri et al., 2022). It is treated by only a handful of treatments.

2.2 Zolgensma

One of these treatments that has been developed over the past years is Zolgensma (onasemnogene abeparvovec-xioi), which is a genetic therapy used to treat children less than 2 years old who have SMA Type 1. Zolgensma works by delivering a healthy copy of the SMN1 gene into the patients' cells, using a modified virus that is harmless, called adeno-associated virus, AAV9 (adeno-associated virus serotype-9). AAV9 is used as a carrier to transport the gene into motor neuron cells. This process allows the body to produce the SMN1 gene again. This protects neurons and prevents further damage (Novartis Pharmaceuticals Corporation, n.d.).

Fig. 1: The Mechanism of Zolgensma at the Cellular Level

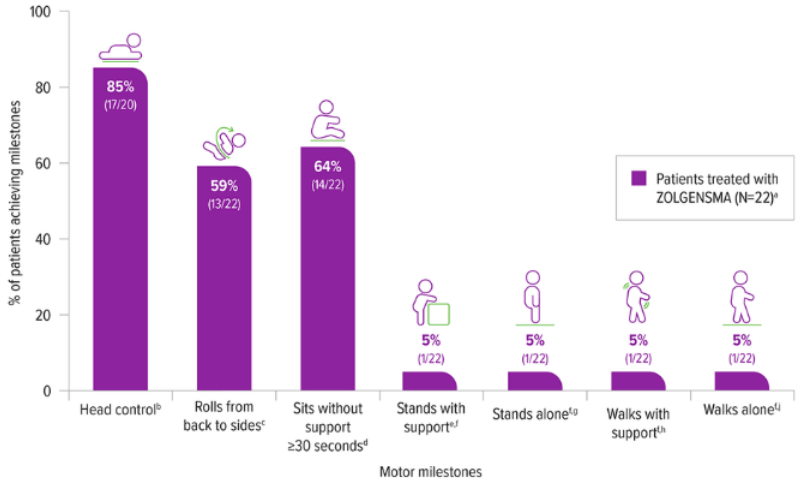


2.3 Advantages of Zolgensma

Zolgensma has unique advantages as a gene therapy. One of these is that it treats the genetic cause of SMA, rather than focusing on treating the symptoms of it. Producing a working copy of the SMN1 gene allows the body to restore nerve function and stop the progression of the disease (European Medicines Agency, 2025). Unlike other therapies such as Spinraza, where lifelong intrathecal injections every 4 months are required, Zolgensma is given as a single intravenous infusion (NBScience, n.d.). Because of this advantage, Zolgensma also provides a one-time treatment. This can also lead to improvement of patients' and their families' life quality due to reducing long-term medical care, such as less respiratory support and fewer hospital treatments. According to studies, patients treated with Zolgensma have

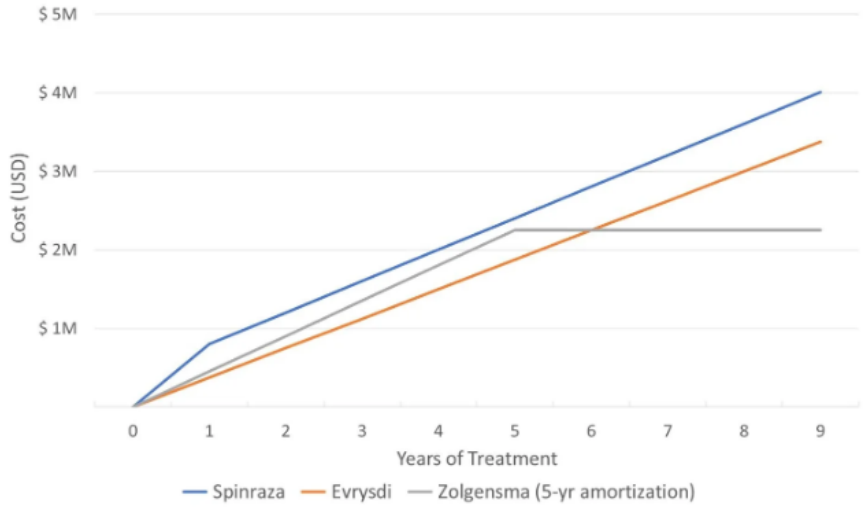
achieved successful results amongst motor control: 59% (13/22) of patients achieved sitting without support for ≥30 seconds at 18 months of age (Novartis Gene Therapies, n.d.).

Fig. 2: Achieved Muscular Behaviours After Zolgensma Treatment in Patients



Total cost of Zolgensma is lower than Spinraza and Evrysdi, which are other leading gene therapies that require lifetime treatment. Novartis is also offering payment plans for up to 5 years (Iannacci, 2023).

Fig. 3: Total Cost of Treatment (Millions USD) in Zolgensma, Evrysdi and Spinraza Over Years



Source: (Iannacci, 2023)

2.4 Disadvantages of Zolgensma

Although Zolgensma has advantages, it also comes with disadvantages and risks. One of the most noticeable disadvantages is the extremely high cost of 2.1 million dollars, even though it is a single dose, making it one of the most expensive medications in the world for a one-time dosage. Although some

researchers concluded that onasemnogene appears to be an efficacious therapy for younger pediatric patients with SMA Type 1, drug cost and potential hepatotoxicity are major concerns (Ogbonmide et al., 2023). Experiencing liver toxicity due to elevated liver enzymes is one risk. Immune response to AAV9 is another possible effect for patients with pre-existing antibodies to AAV9, causing reduced efficacy (NBScience, n.d.). It should also be considered that long-term effects have not been studied yet, as Zolgensma received FDA approval only in 2019, meaning there has not been sufficient time to fully assess long-term effectiveness and safety.

Fig. 4: Comparison of Cost and Administration Between Zolgensma and Nusinersen (Spinraza)

Medication	Zolgensma	Nusinersen
Frequency of Dosage	Single Dose	Every 4 months
Estimated Cost per Dose	$4.2 million	$125,000
Injection Type	Intravenous	Intrathecal
Estimated Total	$4.2 million	$6 million

Source: (Ogbonmide et al., 2023)

3. Conclusion

Zolgensma is a highly discussed medication as a one-time treatment for SMA. However, it is more cost-effective than comparable therapies, Evrysdi and Spinraza, and requires less time for treatment. The unique and effective features of Zolgensma will most likely cause this medication to become popular among physicians in the future. There is substantial evidence of improved outcomes when Zolgensma is administered early to children under two years of age. With the efficacy of this treatment option, physicians treating patients with SMA can be more confident in making an early diagnosis of SMA, which will improve the chances of survival and quality of life for their patients.

The range of patients who have access to Zolgensma is currently limited by age and weight due to the intravenous administration route. Future clinical trials will potentially make Zolgensma available for older and heavier patients. Extensive studies focused on detecting the disease early in life will continue to improve the overall efficacy of Zolgensma in the affected population, even though there are toxicity risks amongst certain groups of gene-carrier patients. Considering all things, Zolgensma is one of the best treatments for SMA Type 1 available to date (Ogbonmide et al., 2023).

It is certain that gene therapy is advancing. Future developments of such medications may refine accessibility, safety and efficacy. Along with raising ethical questions, it should not be forgotten that they redefine the quality of our lives and the world around us. Zolgensma, along with other leading therapeutic innovations such as Evrysdi and Spinraza, demonstrate the great range of possibilities the human mind can explore to solve or minimize the effect of rare genetic diseases.

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