FREQUENTLY ASKED QUESTIONS (FAQ)

Vesemnogene lantuparvovec rAAV9-SMN1 gene therapy for Spinal Muscular Atrophy (SMA)

Contents

01 INTRODUCTION

#	Questions	Answer
1.	What is this new gene therapy Vesemnogene lantuparvovec for SMA? Is it the same as Zolgensma?	Vesemnogene lantuparvovec consists of rAAV viral vector to deliver a normal copy of the SMN1 gene (rAAV9-SMN1) to treat SMA, just like AdV the viral vector in the AstraZeneca or CanSino vaccines which deliver the SARS-Cov2 spike protein gene to induce an immune response (vaccination). Just like AdV vaccine, various manufacturers can produce the same therapy (or vaccine) using the same technology, which is NOT exclusive to any company. Yes, Vesemnogene lantuparvovec is similar to Zolgensma. Vesemnogene, for now, is available only (a) under clinical trial in China or Low-Middle Income country which has in-licensed the technology, or (b) early access use for patients unable to enroll in the trial.
2.	How effective is it? Does it work as well as Zolgensma?	Vesemnogene lantuparvovec is similar to Zolgensma, so the efficacy is expected to be the same. As shown in the scientific data provided to your doctor, the vector design and construction of Vesemnogene is very similar to Zolgensma. We have completed pre-clinical studies in mice & Cynomolgus monkey, which showed that the treatment works. We have also completed enrollment for a Phase 1 trial of Vesemnogene in patients with SMA Type 1 and 2. Early preliminary data suggest the treatment is efficacious. Refer interim report at: https://www.medrxiv.org/content/10.1101/2025.04.13.25325764v2.full.pdf
3.	How safe is it? Is its safety profile the same as Zolgensma?	Vesemnogene lantuparvovec is similar to Zolgensma, so the safety profile is expected to be the same as Zolgensma. The most common and serious adverse reaction is elevated liver enzymes, rarely this may lead to ***acute serious liver injury***.

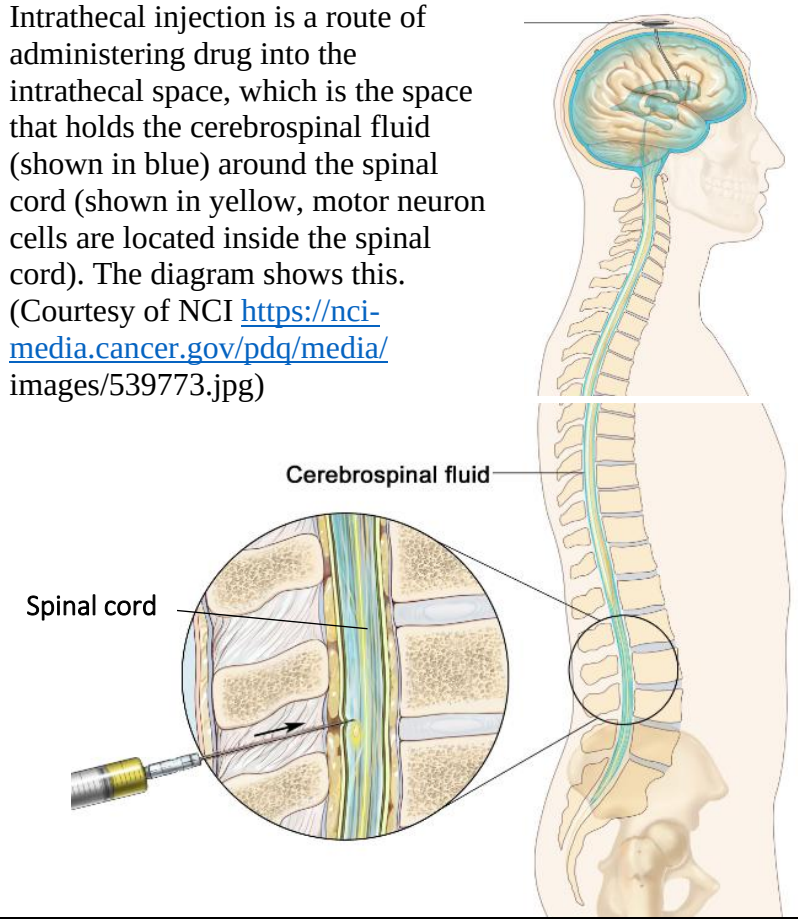
		In the above-mentioned Phase 1 trial of Vesemnogene in patients with SMA Type 1 and 2, we used ~10x lower dose via intrathecal (IT) route than Zolgensma given intravenously. As expected, with the lower dose and IT route, the safety profile of Vesemnogene was highly favorable; no patients had serious liver toxicity at all (markedly elevated transaminases requiring prolonged steroid prophylaxis). Other side effects which have been observed though without apparent clinical effects are: • Elevated Troponin-I (heart enzyme) • Presence of anti-AAV9 antibody. AAV9 is the viral vector used to deliver the SMN1 gene.
4.	What happens when there is serious adverse reaction?	The healthcare provider who administers the treatment will manage all adverse reactions and other health related issues. For patients treated under the clinical trial, the manufacturer will agree to support the cost of healthcare required to manage any adverse reactions.

02 WHO CAN AND HOW TO GET THE TREATMENT?

5.	Who is eligible to receive treatment?	All children below age 5 who have SMA are ***potentially eligible***, and treatment should be initiated as early as possible. However, some children will be too ill to undergo treatment, while others will have too advanced disease to benefit from treatment. Children will also require testing for the presence of AAV antibody in the blood sample, and will not be eligible to receive treatment if they are tested positive. We will consider whether to treat older child on a case-by-case basis.
6.	When will the treatment be given for those who are eligible to receive treatment?	Treatment should be given as soon as possible after a child is tested negative for AAV antibody. Early treatment is crucial because gene therapy for SMA can improve the survival of motor neurons, the nerve cells controlling voluntary movement that gradually die off in SMA. However, gene therapy cannot revive motor neurons that have already died. For this reason, outcomes from treatment are highly dependent on when they are started — in almost all cases, initiating treatment as early as possible tends to lead to the best clinical outcomes. And because of inevitable delay in administering the gene therapy (waiting for test result, seeking approval, making travel arrangement etc), we encourage all children to be started on Risdiplam as bridging therapy while awaiting to receive the gene therapy.
7.	What is the cost?	Vesemnogene lantuparvovec is undergoing clinical trial. The treatment is therefore free for patients enrolled in the trial. For patients who receive the treatment under early access use, your healthcare providers who administer the therapy and care for

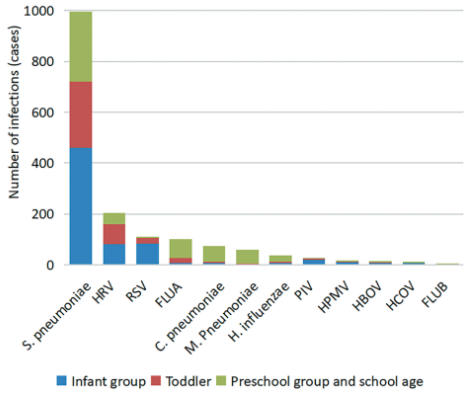
		you will charge for their professional services. The manufacturer may also require you to share the manufacturing and logistic cost.

03 UNDERGOING TREATMENT & IIMEDIATE POST-TREATMENT CARE

8.	How is the treatment administered?	Vesemnogene is administered intrathecally, instead of intravenously (injection into the vein). Through this route, the gene therapy reaches the spinal cord directly to transfer a normal copy of the gene to reach the motor neuron cells (these are the cells in the brain and spinal cord that control our movement including speech, swallowing and breathing). It further allows us to use a much lower dose (~10x lower dose than intravenous dosing) to lessen risk of liver injury.
		Intrathecal injection is a route of administering drug into the intrathecal space, which is the space that holds the cerebrospinal fluid (shown in blue) around the spinal cord (shown in yellow, motor neuron cells are located inside the spinal cord). The diagram shows this. (Courtesy of NCI https://nci-media.cancer.gov/pdq/media/images/539773.jpg) 
9.	Anything I should prepare prior to undergoing treatment?	Intrathecal injection of Vesemnogene is a simple and safe procedure. No special preparation is required. You should continue the your usual physiotherapy and Risdiplam treatment. If you had purchased the Risdiplam, you may continue the Risdiplam until the open bottle is finished and/or re-sell remaining bottles to other patients. The following examination, test and procedure will be performed prior to administering the gene therapy:

		• Blood tests consisting of liver function, troponin-I and platelet counts. The first may increase while the last may decrease after treatment. • One day prior to treatment, oral corticosteroids (prednisolone 1 mg/kg of body weight per day) will be given for a total of 14 days, which will then be stopped gradually if the liver function is normal. • For young children, intrathecal injection is conducted under sedation (typically Midazolam and Ketamine) given by an anesthetist.
10	What to do after treatment?	For the first month after treatment, please adhere to the following: • Regular blood test to check on **liver enzyme levels (**liver function) which could increase after gene therapy. Consult your healthcare provider immediately if your child's skin and/or whites of the eyes appear yellowish. • Regular blood test to check on **blood platelet count** which could decrease after gene therapy, and increase the risk of bruising or bleeding. Consult your healthcare provider immediately if your child experiences unexpected bruising or bleeding • You and other close contacts of your child should follow **infection prevention practices** (e.g., hand hygiene, coughing/ sneezing etiquette, limiting potential contacts). • **Temporary shedding of the virus vector** (rAAV9-SMN1) can occur up to one month after gene therapy administration. Shedding occurs primarily through body waste. Observe proper procedure in disposing the patient's feces (sealing disposable diapers in disposable trash bags and then discarding into regular trash). Observe good hand hygiene when coming into direct contact with the patient body waste.

04 AFTER TREATMENT CARE BEFORE RECOVERY: CHEST HEALTH

11	How to protect the chest of young babies, especially non-sitters, after treatment?	It takes a few months for the chest (respiratory) muscles of young baby to gain strength after gene therapy. Be aware that a **viral respiratory infection** (e.g., cold, flu, or RSV) could lead to more serious complications despite gene therapy. Watch for signs of a possible viral respiratory infection, such as coughing, wheezing, sneezing, runny nose, sore throat or fever. Consult your healthcare provider immediately if you see any of these symptoms **Please adhere to the following recommendations:** • You and other close contacts of your child should follow **infection prevention practices** (e.g., hand hygiene, coughing/ sneezing etiquette, limiting potential contacts). • **Consult your chest physiotherapist & physical therapist** regularly; perform **respiratory exercises** regularly every day (singing, breathing, coughing and blowing into positive expiratory pressure (PEP) device or simple Lung Exerciser device) • Consult your healthcare provider to adjust your child's **vaccination schedule** to accommodate treatment with corticosteroid. • *Respiratory infections among infants are commonly caused by pneumococcus, respiratory syncytial virus (RSV), Flu-A, H. influenzae*.  **Vaccines against Influenza, Haemophilus influenzae type b (Hib) & Pneumococcal (PCV 15 or 20) and Nirsevimab** prophylaxis against RSV are recommended. • **Young non-sitting babies (SMA Type 1)** requires particular attention on their chest care: a. Monitor ***O2 saturation*** during sleep and where available sleep study to determine need for BIPAP/breathing machine. b. Assess ***airway clearance*** (weak chest & difficulty in coughing) to determine need for intensive chest physiotherapy, suctioning, Cough Assist machine and/or Mechanical Percussion. c. Assess ***swallowing, reflux, retained secretions*** & saliva or drooling, which increase risk of aspiration into lung, to determine need for suctioning to remove secretions/saliva and tube feeding.