zolgensma®
(onasemnogene abeparvovec-xioi)
suspension for intravenous infusion

A CAREGIVER'S GUIDE TO ZOLGENSMA

A one-time-only dose for the treatment of SMA in children under the age of 2 years old.

Ryker, treated with ZOLGENSMA at 5 months old and pictured at 2 years old with his father, Glen, was diagnosed with SMA Type 1. Before receiving treatment with ZOLGENSMA, Ryker received another SMA treatment.

Indication

ZOLGENSMA® (onasemnogene abeparvovec-xioi) is a prescription gene therapy used to treat children less than 2 years old with spinal muscular atrophy (SMA). ZOLGENSMA is given as a one-time infusion into a vein. ZOLGENSMA was not evaluated in patients with advanced SMA.

Important Safety Information

ZOLGENSMA can increase liver enzyme levels and cause acute serious liver injury or acute liver failure which could result in death. Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function. Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, if the patient misses a dose of corticosteroid or vomits it up, or if the patient experiences a decrease in alertness.

Please see additional Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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Click the page number for detailed information on these topics about ZOLGENSMA® (onasemnogene abeparvovec-xioi) and more.

Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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FACTS ABOUT SMA

“Treatment day gave us hope for Brady’s future. We celebrate that day because we feel like that’s the day Brady got the chance to be a kid again.”

Nicole, Brady’s mother

Brady, treated with ZOLGENSMA at 14 months old and pictured at 2 years old, was diagnosed with SMA Type 2.

Important Safety Information

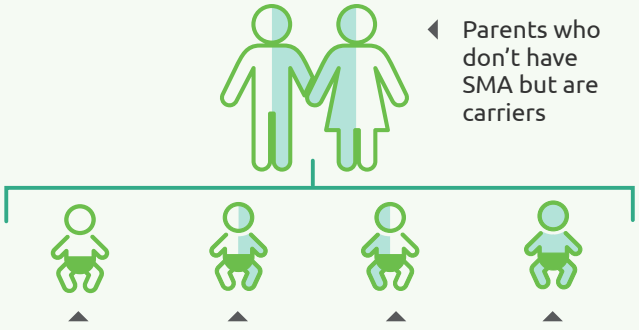
Infections before or after ZOLGENSMA® (onasemnogene abeparvovec-xioi) infusion can lead to more serious complications. Caregivers and close contacts with the patient should follow infection prevention procedures. Contact the patient’s doctor immediately if the patient experiences any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

SMA is a rare genetic disease and, if diagnosed early, can be treated quickly to stop the progression of the disease

How SMA is inherited

Spinal muscular atrophy (SMA) is an autosomal recessive disorder. This means that in order to have SMA, a person must have 2 copies of a nonworking *survival motor neuron 1* (*SMN1*) gene or be missing both copies of the *SMN1* gene.



About 1 in 50

people in the United States (or 6.6 million* Americans) is a genetic carrier of SMA, and most don't know it.

*Calculations are based on an estimated US population of 330 million.

/11K

SMA affects about 1 in every 11,000 babies born in the US.

As more children are diagnosed early through newborn screening, treatment can be started immediately to stop the progression of SMA and improve outcomes.

Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

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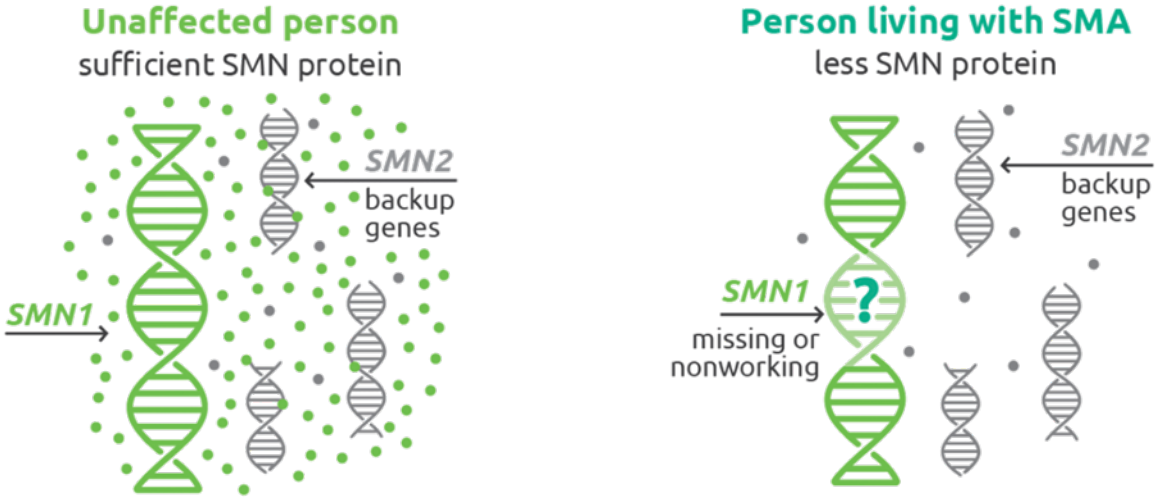
What causes SMA?

The genetic root cause of SMA is the *SMN1* gene that is missing or not working properly. When this main gene is missing or not working properly, the body cannot make enough survival motor neuron (SMN) protein, which is needed for motor neuron cell survival. Everyone is born with a certain amount of motor neuron cells, which are responsible for communicating with the arms, legs, throat, and many other areas in the body to tell them to work properly. Without enough SMN protein, select motor neuron cells throughout the body may lose function and die. As a result, children with SMA experience muscle weakness and may develop difficulty in breathing, swallowing, or speaking.

The role of a backup gene

There is a backup gene for the *SMN1* gene called the *SMN2* gene. People can have 1 or more copies of this backup gene. This gene, like the *SMN1* gene, tells the body to make SMN protein. For people with SMA, the *SMN2* gene is the only source of SMN protein; however, it is unable to produce as much working protein as the *SMN1* gene. **In fact, the *SMN2* gene makes only about 10% of working protein compared to the protein produced by the *SMN1* gene. That is why it is essential to address the genetic root cause of SMA by replacing the function of the missing or nonworking *SMN1* gene.** Even people with several copies of the *SMN2* gene may not produce as much SMN protein as those with the working *SMN1* gene, and their motor neuron cells may not work as they should. Usually, the more copies of the *SMN2* gene a person has, the less severe his or her SMA is.

The *SMN1* and *SMN2* genes



Important Safety Information

Thrombotic microangiopathy (TMA) has been reported to generally occur within the first two weeks after ZOLGENSMA infusion. Seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

There is a theoretical risk of tumor development with gene therapies such as ZOLGENSMA. Contact the patient's doctor and Novartis Gene Therapies, Inc. (1-833-828-3947) if a tumor develops.

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ABOUT ZOLGENSMA

“She received treatment and that gives me hope for the future. She’s only a toddler now, but I want her to feel like she can do anything she wants.”

Aaron, Natalie’s father

Natalie, treated with ZOLGENSMA at ~14 months old and pictured at 1½ years old, was diagnosed with SMA Type 2.

Watch family videos and hear caregivers share their experiences.

Important Safety Information

Talk with the patient’s doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid. Protection against influenza and respiratory syncytial virus (RSV) is recommended and vaccination status should be up-to-date prior to ZOLGENSMA administration. Please consult the patient’s doctor.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

The one-time-only dose for the treatment of SMA

With one dose, ZOLGENSMA® (onasemnogene abeparvovec-xioi) can stop the progression of SMA. It is a gene therapy that is designed to replace the function of the missing or nonworking *SMN1* gene that causes SMA. ZOLGENSMA is not a cure and cannot reverse damage already caused by SMA before treatment.

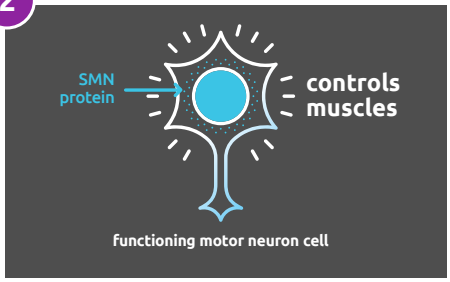
ZOLGENSMA targets the genetic root cause of SMA

1

A targeted approach

ZOLGENSMA targets the genetic root cause of SMA by replacing the function of a missing or nonworking gene called the *SMN1* gene. This gene is critical for making SMN protein.

2



The importance of SMN protein

SMN protein is essential to motor neuron cell survival. These cells control muscle function. Without SMN protein, motor neuron cells die, causing muscles to become so weak that breathing, eating, and moving become difficult, and the condition can become life-threatening in its most severe forms.

Important Safety Information

Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with patient body waste for one month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

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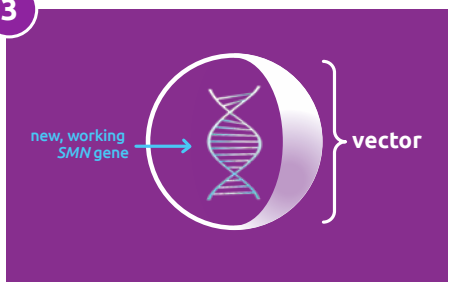
ZOLGENSMA targets the genetic root cause of SMA (continued)

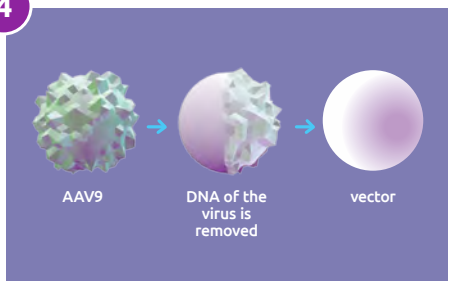
3



The role of the vector

ZOLGENSMA® (onasemnogene abeparvovec-xioi) is made up of a new, working copy of a human *SMN* gene that is placed inside a vector. A vector's job is to take the new, working *SMN* gene to the motor neuron cells in the body.

4



Delivery of the *SMN* gene

The vector that delivers the *SMN* gene is made from a virus called adeno-associated virus 9, or AAV9. This type of virus is not known to make people sick. To make the vector, the DNA of the virus is removed so that the new *SMN* gene can be put inside. Vectors are used because they can travel throughout the body and deliver the new, working gene to the cells where it is needed.

5

Production of SMN protein

When the new gene reaches its destination, it tells the motor neuron cells to start making SMN protein. This happens throughout the body, delivering a new, working copy of the *SMN* gene to motor neuron cells.

6

Motor neuron cells maintained

With the motor neuron cells now able to make sufficient SMN protein, motor neuron cells that have not died may survive, function, and be maintained.

Watch an animated video of how ZOLGENSMA works.

Important Safety Information

The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

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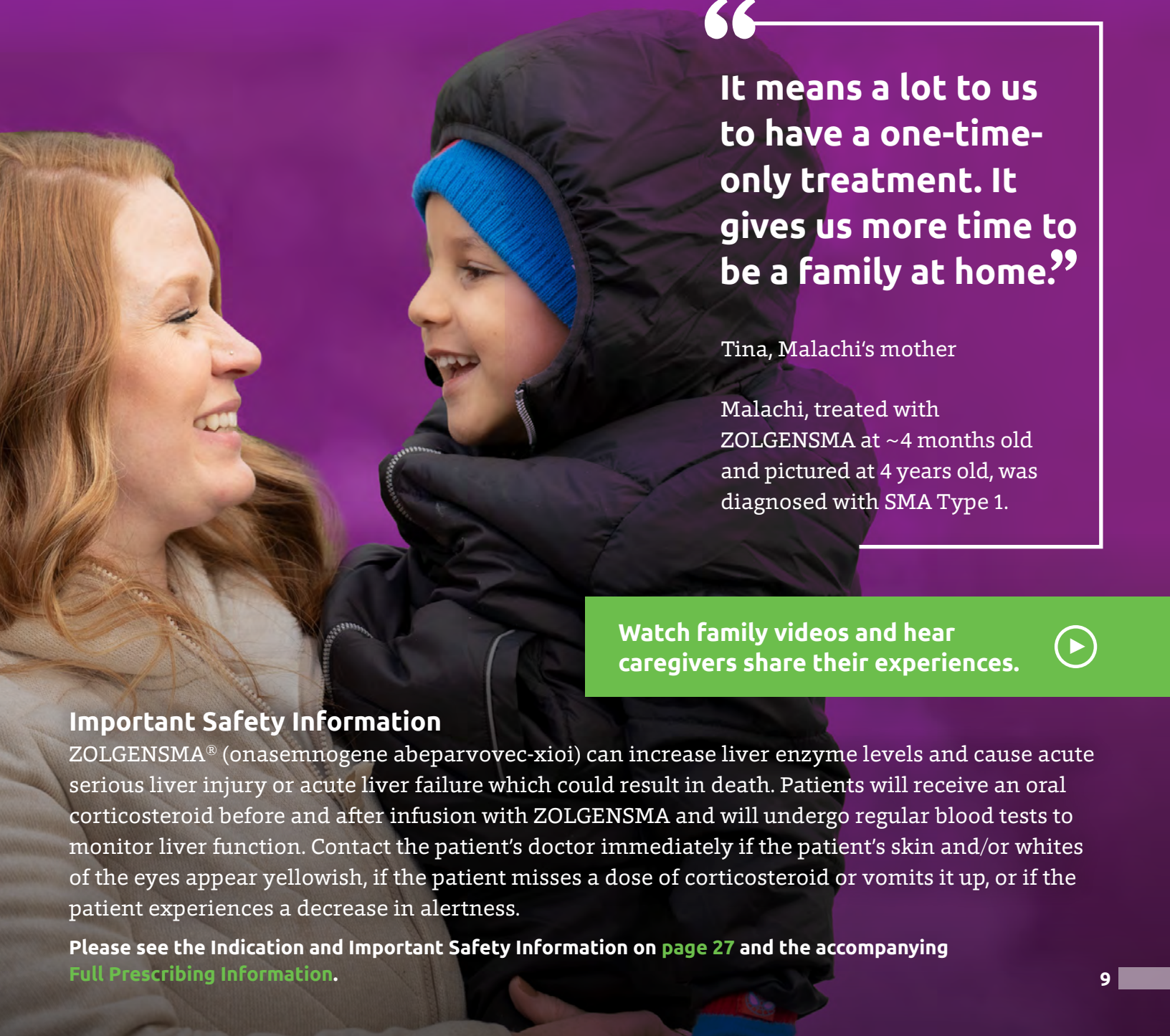
TREATMENT WITH ZOLGENSMA



“It means a lot to us to have a one-time-only treatment. It gives us more time to be a family at home.”

Tina, Malachi’s mother

Malachi, treated with ZOLGENSMA at ~4 months old and pictured at 4 years old, was diagnosed with SMA Type 1.

Watch family videos and hear caregivers share their experiences.

Important Safety Information

ZOLGENSMA® (onasemnogene abeparvovec-xioi) can increase liver enzyme levels and cause acute serious liver injury or acute liver failure which could result in death. Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function. Contact the patient’s doctor immediately if the patient’s skin and/or whites of the eyes appear yellowish, if the patient misses a dose of corticosteroid or vomits it up, or if the patient experiences a decrease in alertness.

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STEP 1

Pretreatment testing to determine if your child qualifies for ZOLGENSMA

ZOLGENSMA® (onasemnogene abeparvovec-xioi) is a prescription gene therapy used to treat children less than 2 years old with SMA. It is given as a one-time infusion into a vein. If you and your child's doctor have chosen ZOLGENSMA, there are a few steps that need to be taken to determine if your child qualifies for ZOLGENSMA.

Complete important lab tests

Confirm a diagnosis

While your child may have received their SMA diagnosis from a newborn screening, insurance companies often require an additional SMA genetic test to confirm the diagnosis.

Perform an AAV9 antibody test

ZOLGENSMA travels throughout the body using a delivery vehicle made from a virus called adeno-associated virus 9, or AAV9. This type of virus is not known to make people sick.

An AAV9 antibody test measures the amount of anti-AAV9 antibodies in your child's blood. If your child's existing level of AAV9 antibodies doesn't fall within a certain range you can ask your doctor to monitor and retest. If antibody levels lower, your child may become eligible for treatment.

Perform baseline blood tests

Your child's doctor will need to establish a starting point so they can monitor closely after treatment with ZOLGENSMA, keeping an eye on things like liver function,* creatinine levels, complete blood count (hemoglobin, platelet count, etc.), and troponin-I. These tests may happen while waiting for approval or as you get closer to treatment.

*Liver function assessment includes clinical exam, aspartate aminotransferase [AST], alanine aminotransferase [ALT], total bilirubin, albumin, prothrombin time, partial thromboplastin time [PTT], and international normalized ratio [INR].

Download our complete guide to treatment with ZOLGENSMA.

Important Safety Information

Infections before or after ZOLGENSMA infusion can lead to more serious complications. Caregivers and close contacts with the patient should follow infection prevention procedures. Contact the patient's doctor immediately if the patient experiences any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

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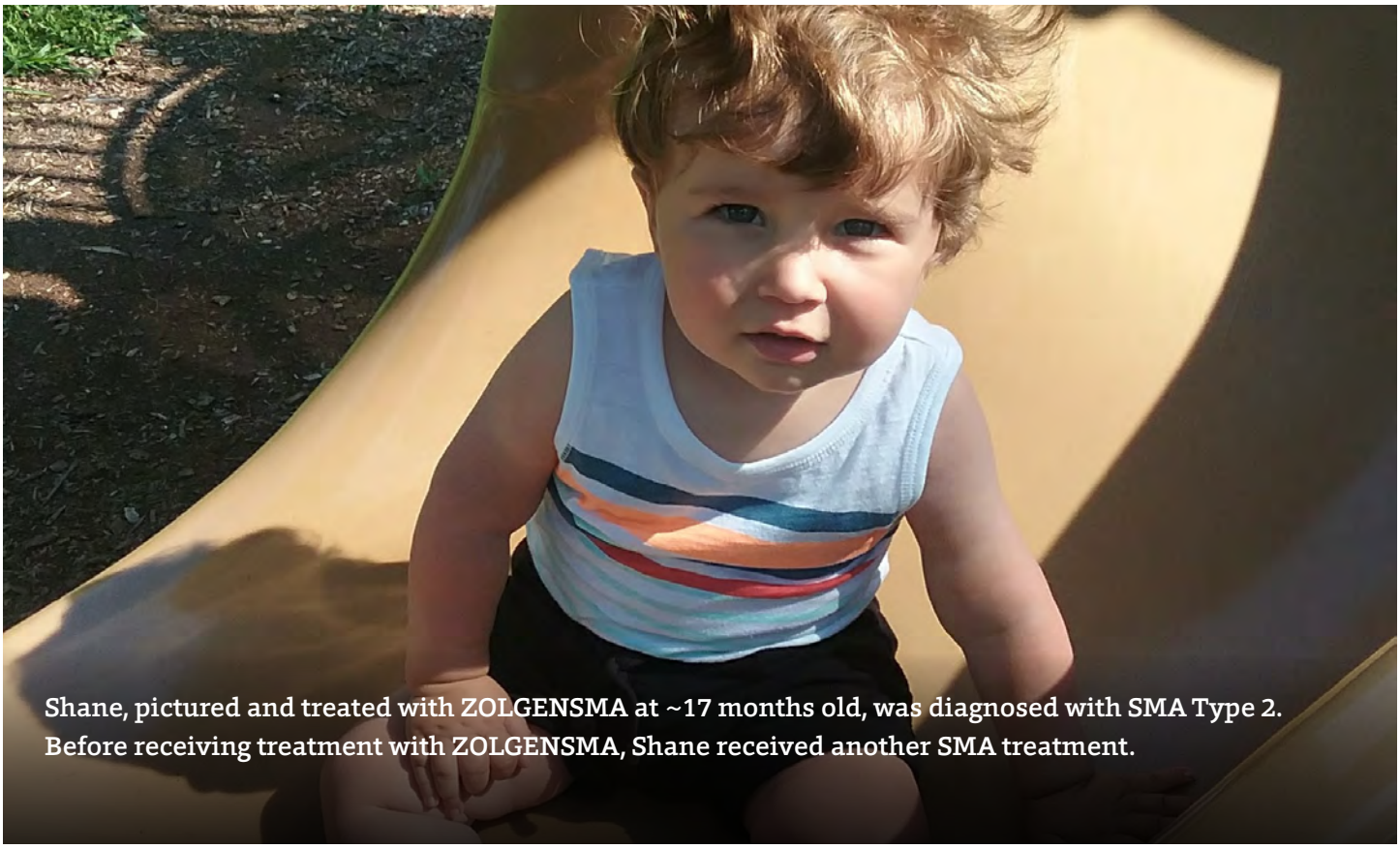

Shane, pictured and treated with ZOLGENSMA at ~17 months old, was diagnosed with SMA Type 2. Before receiving treatment with ZOLGENSMA, Shane received another SMA treatment.

Have your child's doctor submit a ZOLGENSMA Prescription Form and a Patient Consent Form

While waiting for test results, ask your child's doctor to submit a ZOLGENSMA® (onasemnogene abeparvovec-xioi) Prescription Form and a Patient Consent Form. When you sign the consent form, you'll be enrolled in the **OneGene Program®** and you will meet your Family Ambassador who will be your main, dedicated point of contact. In addition, you will also have the support of the Case Coordinator, who will work closely with your doctor, Family Ambassador, and you to help with the process for your child to receive ZOLGENSMA.

Once the Prescription Form and Patient Consent Form are received, a representative from the OneGene Program will call you to discuss the patient support available to you.

Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

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STEP 2

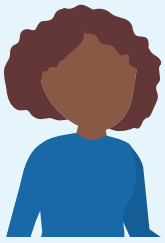
Connect with the OneGene Program®

The **OneGene Program**, a team of highly trained and dedicated people, is a one-on-one support offering for you and your child who has been prescribed the one-time ZOLGENSMA® (onasemnogene abeparvovec-xioi) treatment.

OneGene, OneTeam, OnePurpose:

Call 855-441-GENE (4363), Monday–Friday (8 AM–8 PM ET), to learn more.

Novartis Gene Therapies is there for your family, providing additional assistance throughout the treatment journey.



Family Ambassador

A Family Ambassador will be your main point of contact who can answer questions you have related to SMA, ZOLGENSMA, and health insurance coverage. Your Family Ambassador is there to provide support throughout your child's treatment journey.

Case Coordinator

A Case Coordinator can discuss financial assistance options with you based on your child's eligibility, answer insurance questions and provide appropriate resources to your doctor when needed, and track ZOLGENSMA treatment from the moment the prescription is written until it arrives at the doctor's office.

OneGene Program team members are there for additional support, and do not take the place of the medical expertise your doctor provides. For specific medical questions and guidance, please check with your doctor to receive the most accurate and appropriate information.

Important Safety Information

Thrombotic microangiopathy (TMA) has been reported to generally occur within the first two weeks after ZOLGENSMA infusion. Seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

There is a theoretical risk of tumor development with gene therapies such as ZOLGENSMA. Contact the patient's doctor and Novartis Gene Therapies, Inc. (1-833-828-3947) if a tumor develops.

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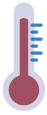
STEP 3

Prepare for treatment day

If your child is approved for treatment with ZOLGENSMA® (onasemnogene abeparvovec-xioi), your child's doctor and care team will help ensure you know exactly what to expect on the day of treatment and how to prepare. Additionally, your Family Ambassador will work with you to understand how he or she can best support your family on treatment day.

If not completed already, your child's doctor should perform blood tests to check their liver function and to establish baseline levels for creatinine, complete blood count (including hemoglobin and platelet count), and troponin-I. And, ask your child's doctor if any additional tests are needed before treatment day. These tests will help your child's doctor and care team monitor your child after dosing. It's best to have the blood tests done as soon as you can so that your child can get treated promptly.



Infections before or after ZOLGENSMA infusion can lead to more serious complications. To reduce the risk of illness, limit contact with others. Practice good hygiene like coughing or sneezing into a tissue, and washing hands with soap and water for at least 20 seconds. If symptoms of infection appear before infusion, you may be asked to postpone treatment until the infection has resolved. Watch for signs of infection and contact your child's doctor immediately if you see any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

A course of an oral corticosteroid should be started the day before infusion with ZOLGENSMA. This helps manage elevated liver enzyme reactions to ZOLGENSMA by the body's immune system. Fill the prescription for the oral corticosteroid as soon as you get it. (Your pharmacy may have to order it). And talk to your doctor about what protocol to follow, and what to do if your child refuses the dose or vomits it up.

Confirm your child's infusion date, time, and location with your child's doctor. Determine your family's transportation plan and get directions to the treatment center, including the address and available parking areas if you're driving. Ask the treatment center about their policy regarding what you can bring and how many family members can be with you and your child on the day of infusion.

Important Safety Information

Talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid. Protection against influenza and respiratory syncytial virus (RSV) is recommended and vaccination status should be up-to-date prior to ZOLGENSMA administration. Please consult the patient's doctor.

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STEP 4

Treatment day

On the day of treatment, your child will be infused with ZOLGENSMA

You should give your child the second dose of the oral corticosteroid on the day of infusion as prescribed by your child's doctor to help manage reactions to ZOLGENSMA® (onasemnogene abeparvovec-xioi) by the body's immune system. Confirm with your doctor whether you should administer this dose before arriving at the hospital. The actual infusion will take 60 minutes. Ask your child's doctor or care team in advance about how long you'll be required to stay at the treatment center after your child's infusion.

Remember to talk to your child's doctor and care team about any family members you would like to have with you on treatment day. If possible, you may have the option of having your Family Ambassador present on the day of treatment to support your family.

You will be given a Post-Treatment Kit on treatment day that details additional medical monitoring and types of specialists that may be part of your child's healthcare team. Ensure you receive the kit from your child's doctor or ask your Family Ambassador for one.

Sienna, pictured and treated with ZOLGENSMA at 17 months old, was diagnosed with SMA Type 1. Before receiving treatment with ZOLGENSMA, Sienna received another SMA treatment.

Important Safety Information

Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with patient body waste for one month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

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What to do and know before you leave the hospital

Talk with your child's doctor about post-treatment follow-up and additional monitoring. You will continue to give your child the corticosteroid as prescribed by the doctor. The specific corticosteroid treatment course for each child will be based on several clinical factors and will be determined by your child's doctor.

The doctor will monitor your child's liver function after ZOLGENSMA® (onasemnogene abeparvovec-xioi) treatment through blood tests and clinical exams and determine when to begin gradually lowering the corticosteroid dose and eventually stop the corticosteroid. The suggested period of lowering the dose (taper period) is no less than 28 days. Your child's doctor will monitor their liver function weekly during the corticosteroid course and taper period (at least 2 months), and then every other week for at least 1 month after your child stops the corticosteroid.

- Contact your child's doctor immediately if your child's skin and/or whites of the eyes appear yellowish, if your child misses a dose of corticosteroid or vomits it up, or if your child experiences a decrease in alertness.
- Talk to your child's doctor about potential side effects that may occur after treatment, especially what to do if vomiting or fever occur.

In addition to liver function,* your child's doctor will perform blood tests to measure platelet counts and troponin-I levels. Use the space below to help you keep track of appointments.

	Date	Time	Location
Week 1			
Week 2			
Week 3			
Week 4			
Week 5			
Week 6			
Week 7			
Week 8			
Week 9			
Week 10			
Week 11			
Week 12†			

*Your child's liver function will be monitored weekly for **two months or longer**, during the corticosteroid treatment and as the dose is reduced. Your child's liver function will continue to be monitored every other week for **another month** after stopping the corticosteroid.

†Monitoring beyond 12 weeks may be required.

Your child should be assessed immediately and closely monitored if their liver function tests worsen or if you or the doctor notice signs or symptoms of acute illness, such as vomiting or worsening health.

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STEP 5

After treatment with ZOLGENSMA

Once your child has been treated with ZOLGENSMA® (onasemnogene abeparvovec-xioi), it is important to learn how to continue managing your child's SMA. This includes speaking with a neuromuscular specialist and creating an extended healthcare team.

Continuing your child's SMA care

While ZOLGENSMA stops the progression of SMA by replacing the function of your child's missing or nonworking *SMN1* gene, ZOLGENSMA is not a cure and cannot reverse damage already caused by SMA before treatment. That's why it is important to speak with your child's neuromuscular specialist and healthcare team to review supportive care (like physical and occupational therapy, working with a nutritionist, and meeting with a pulmonologist) to determine what kind of care may be best for your child following treatment. Additional therapies, accommodations, and support may be needed to guide your child's ongoing development. Work with your child's healthcare team to evaluate their progress after treatment.

Your child may continue to show signs of SMA. These may include difficulty swallowing or breathing or muscle weakness. Discuss any signs or symptoms with your child's doctor and healthcare team.

The SMA community is here for you

cure SMA

To connect with other caregivers and discover valuable resources, check out **CureSMA.org**.

Important Safety Information

ZOLGENSMA can increase liver enzyme levels and cause acute serious liver injury or acute liver failure which could result in death. Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function. Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, if the patient misses a dose of corticosteroid or vomits it up, or if the patient experiences a decrease in alertness.

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Pictured left to right: Matthew, Ellie, Montgomery, and Emily. Ellie, treated with ZOLGENSMA at 15 days old and pictured at 9 months old, was diagnosed with SMA *in utero*.

Connect with families to discover more

See what children treated with ZOLGENSMA® (onasemnogene abeparvovec-xioi) are up to, hear from SMA caregivers, and learn more about treatment.

Important Safety Information

Infections before or after ZOLGENSMA infusion can lead to more serious complications. Caregivers and close contacts with the patient should follow infection prevention procedures. Contact the patient's doctor immediately if the patient experiences any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

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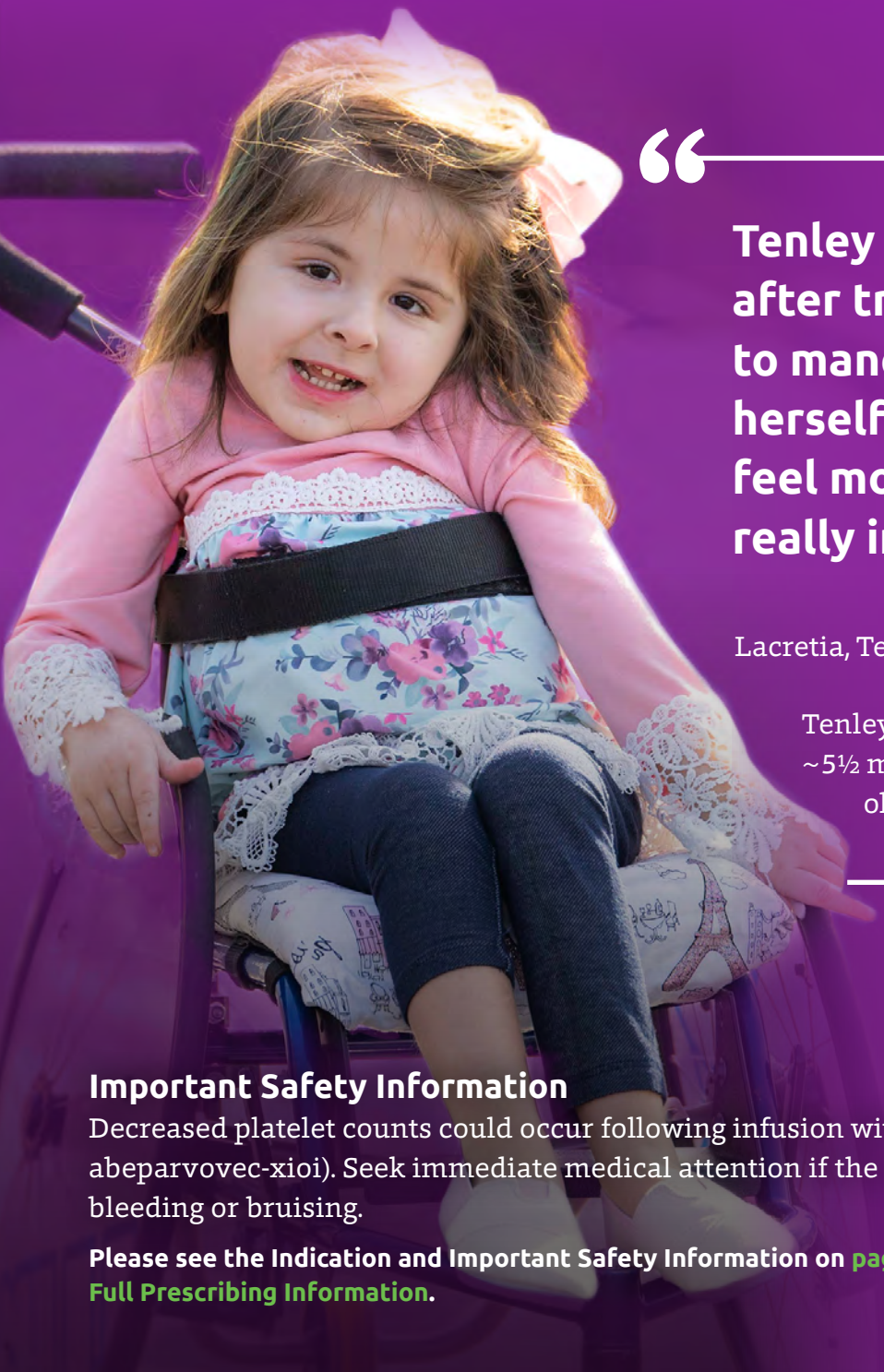

“Tenley has gained strength after treatment. She is able to maneuver a wheelchair by herself and get around and feel more like a kid. So that’s really important for us.”

Lacretia, Tenley’s mother

Tenley, treated with ZOLGENSMA at ~5½ months old and pictured at 4½ years old, was diagnosed with SMA Type 1.

Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA® (onasemnogene abeparvovec-xioi). Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

ZOLGENSMA increased achievements for symptomatic children across all measures studied

The purpose of the STR1VE study was to review the efficacy and safety of ZOLGENSMA® (onasemnogene abeparvovec-xioi). The STR1VE study enrolled 22 symptomatic children,* which means they displayed symptoms of SMA before receiving treatment. All children were diagnosed with SMA Type 1, had 2 copies of the *SMN2* backup gene, and were 6 months of age or younger at the time of intravenous (IV) infusion.

- The average age at dosing was 3.7 months (range 0.5-5.9 months)
- All children received the therapeutic dose of ZOLGENSMA (dose approved by the FDA)
- Children were followed through their 18 months of age study visit

*One child was initially classified as presymptomatic but was later confirmed to be symptomatic and was included in the final clinical study findings.

The STR1VE study looked at 5 key measurements

- Event-free survival
- Sitting without assistance (for at least 30 seconds)
- Ability to thrive
- Independence from respiratory and feeding support
- Motor function

See full results from the STR1VE clinical study.

Important Safety Information

Thrombotic microangiopathy (TMA) has been reported to generally occur within the first two weeks after ZOLGENSMA infusion. Seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

There is a theoretical risk of tumor development with gene therapies such as ZOLGENSMA. Contact the patient's doctor and Novartis Gene Therapies, Inc. (1-833-828-3947) if a tumor develops.

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Children survived without breathing support

At the 14 months of age study visit,

(20/22)* of **children were alive and did not need permanent breathing support**

Typically, about 25% of children with SMA Type 1 who have not received treatment are alive without permanent breathing support at 14 months of age.

- 1 child passed away at 7.8 months of age from causes deemed unrelated to treatment
- 1 child withdrew from the study at 11.9 months of age and required permanent ventilation at 11 months of age prior to leaving the study

*One child was initially not part of the data set but is included in the final data analysis.

Children could sit without help

(13/22) of **children could sit without support for at least 30 seconds at the 18 months of age study visit**

Children with SMA Type 1 who do not receive treatment are never able to sit independently.

Important Safety Information

Talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid. Protection against influenza and respiratory syncytial virus (RSV) is recommended and vaccination status should be up-to-date prior to ZOLGENSMA administration. Please consult the patient's doctor.

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Children maintained milestones for over 5 years after treatment with ZOLGENSMA

The START clinical study was the first study of ZOLGENSMA® (onasemnogene abeparvovec-xioi) and is completed. This study enrolled 15 symptomatic children diagnosed with SMA Type 1 who were 8 months of age or younger at the time of infusion. Children were split into 2 groups. Three children in group 1 received a low dose and 12 children in group 2 received a high dose (~therapeutic dose).

The primary purpose of the study was to evaluate the safety of ZOLGENSMA. Other endpoints measured were event-free survival (defined as being alive without the need for permanent ventilatory support, such as tracheostomy, or the need for respiratory assistance*) and the change from baseline in CHOP INTEND (or the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders). CHOP INTEND measures the motor development of children with SMA Type 1. At the end of the START clinical study, all 12 children in the high-dose group were alive and free of permanent breathing support 24 months after treatment.

92% (11/12) of **children could sit without support for at least 5 seconds**

75% (9/12) of **children could sit without support for at least 30 seconds**

92% (11/12) of **children achieved or maintained CHOP INTEND scores higher than 40 points**

The START long-term follow-up (LTFU) study is designed to monitor the safety of ZOLGENSMA over 15 years. Ongoing study results show the safety and efficacy of ZOLGENSMA up to 5 years after treatment and 5 years of age or older. The study enrolled 13 children from the START study—3 children from group 1 (low dose) and 10 children from group 2 (high dose).

Study results for START LTFU group 2

(10/10) of **children were alive and did not need permanent breathing support (as of May 2022)**

(10/10) have **maintained motor milestones achieved at the end of the START study**

*≥16 hours of respiratory assistance each day continuously for ≥14 days.

Important Safety Information

Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with patient body waste for one month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

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Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA® (onasemnogene abeparvovec-xioi). Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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ZOLGENSMA helped presymptomatic children reach age-appropriate milestones and survive without permanent breathing support

The purpose of the SPR1NT study was to evaluate the efficacy and safety of ZOLGENSMA® (onasemnogene abeparvovec-xioi) in children younger than 6 weeks of age and showing no symptoms (presymptomatic) of SMA. The study enrolled 29 presymptomatic children diagnosed with SMA who had 2 or 3 copies of the *SMN2* backup gene.

The average age at treatment:

- 2 copies of *SMN2* (14 children): 20.6 days
- 3 copies of *SMN2* (15 children): 28.7 days
- Children received the therapeutic dose of ZOLGENSMA (dose approved by the FDA)

Alive and free of permanent ventilation

(29/29) of **children were alive and free of permanent breathing support**

See full results from the SPR1NT clinical study.

Important Safety Information

The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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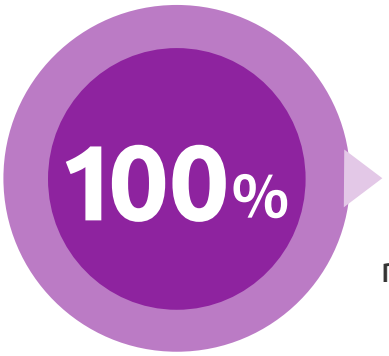
Children could sit without help

Children reached age-appropriate milestones

In the SPR1NT study, the Bayley-III was used to determine children's motor skills compared to what is expected for unaffected developing children. The WHO-MGRS (World Health Organization Multicentre Growth Reference Study) was used to provide a timeline for motor milestone development in unaffected children.



(14/14) of **children with 2 copies of *SMN2* backup gene could sit without assistance** (30 seconds or more) as measured by Bayley-III at any visit up to 18 months of age

In the natural history (untreated) of SMA Type 1, children are not able to sit.

79% (11/14) of children achieved sitting without support within an age-appropriate time period.

Children could stand by themselves

(15/15) of **children with 3 copies of *SMN2* backup gene could stand without assistance** (3 seconds or more) as measured by Bayley-III at any visit up to 24 months of age

93% (14/15) of children achieved this milestone within an age-appropriate time period.

Important Safety Information

Infections before or after ZOLGENSMA infusion can lead to more serious complications. Caregivers and close contacts with the patient should follow infection prevention procedures. Contact the patient's doctor immediately if the patient experiences any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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SAFETY PROFILE OF ZOLGENSMA

“I expected ZOLGENSMA to stop the progression of the disease. Just halt it. And now she’s hitting milestones that were once a dream. I think my little girl’s going to do things that I never even pictured.”

Ciji, Maisie’s mother

Maisie, treated with ZOLGENSMA at ~20 months old and pictured at 2 years old, was diagnosed with SMA Type 1. Before receiving treatment with ZOLGENSMA, Maisie received another SMA treatment.

Watch family videos and hear caregivers share their experiences.

Important Safety Information

ZOLGENSMA® (onasemnogene abeparvovec-xioi) can increase liver enzyme levels and cause acute serious liver injury or acute liver failure which could result in death. Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function. Contact the patient’s doctor immediately if the patient’s skin and/or whites of the eyes appear yellowish, if the patient misses a dose of corticosteroid or vomits it up, or if the patient experiences a decrease in alertness.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

Safety profile

ZOLGENSMA® (onasemnogene abeparvovec-xioi) has an established safety profile demonstrated in 3 clinical studies and 1 observational long-term follow-up study.

- **44 children were treated with ZOLGENSMA and ranged in age from 0.3 to 7.9 months at the time of infusion**
- **The most common side effects (5% or more) that occurred in children treated with ZOLGENSMA were elevated liver enzymes and vomiting**
- **Reports of pyrexia (or fever), thrombotic microangiopathy (TMA), thrombocytopenia, acute liver failure (fatal and non-fatal), acute liver injury, and increased troponin were identified during postmarketing experience**

Safety data update

As of June 2020, 102 children have been treated with ZOLGENSMA intravenously (IV) in clinical studies.*

- The most common side effects (5% or more) that occurred in children treated with ZOLGENSMA were elevated liver enzymes and vomiting
- Safety data continue to be collected

*Children from 5 open-label studies, including 2 finished and 3 ongoing studies at the time of the analysis: START (completed, N = 15), STR1VE (completed, N = 22), STR1VE-EU (ongoing, N = 33), STR1VE-AP (ongoing, N = 2), SPR1NT (ongoing, N = 30). Three children in the START study received a lower dose.

Important Safety Information

Infections before or after ZOLGENSMA infusion can lead to more serious complications. Caregivers and close contacts with the patient should follow infection prevention procedures. Contact the patient's doctor immediately if the patient experiences any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

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Indication and Important Safety Information

What is ZOLGENSMA?

ZOLGENSMA® (onasemnogene abeparvovec-xioi) is a prescription gene therapy used to treat children less than 2 years old with spinal muscular atrophy (SMA). ZOLGENSMA is given as a one-time infusion into a vein. ZOLGENSMA was not evaluated in patients with advanced SMA.

What is the most important information I should know about ZOLGENSMA?

- ZOLGENSMA can increase liver enzyme levels and cause acute serious liver injury or acute liver failure which could result in death.
- Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function.
- Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, if the patient misses a dose of corticosteroid or vomits it up, or if the patient experiences a decrease in alertness.

What should I watch for before and after infusion with ZOLGENSMA?

- Infections before or after ZOLGENSMA infusion can lead to more serious complications. Caregivers and close contacts with the patient should follow infection prevention procedures. Contact the patient's doctor immediately if the patient experiences any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.
- Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.
- Thrombotic microangiopathy (TMA) has been reported to generally occur within the first two weeks after ZOLGENSMA infusion. Seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.
- There is a theoretical risk of tumor development with gene therapies such as ZOLGENSMA. Contact the patient's doctor and Novartis Gene Therapies, Inc. (1-833-828-3947) if a tumor develops.

What do I need to know about vaccinations and ZOLGENSMA?

- Talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid.
- Protection against influenza and respiratory syncytial virus (RSV) is recommended and vaccination status should be up-to-date prior to ZOLGENSMA administration. Please consult the patient's doctor.

Do I need to take precautions with the patient's bodily waste?

Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with patient body waste for one month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

What are the possible or likely side effects of ZOLGENSMA?

The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

The safety information provided here is not comprehensive. Talk to the patient's doctor about any side effects that bother the patient or that don't go away.

You are encouraged to report suspected side effects by contacting the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch, or Novartis Gene Therapies, Inc. at 1-833-828-3947.

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“Our Family Ambassador was really vital in helping us address questions we had before, during, and after treatment. It was comforting to be able to speak to someone throughout the process.”

Annie, Quinn’s mother

Quinn, treated with ZOLGENSMA at ~15 months old and pictured at 2½ **years old**, was diagnosed with SMA Type 2.

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