Treated with ZOLGENSMA at 14 months old[1]

Pictured here at ~2 years old

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suspension for intravenous infusion

Meet Brady

HE HAS SMA TYPE 2 AND THIS IS HIS STORY

Brady was diagnosed with spinal muscular atrophy (SMA) Type 2 at 13 months old. See his journey from being diagnosed to treated in 1 month.[1]

SCROLL DOWN

Indication and Important Safety Information

Indication

ZOLGENSMA is an adeno-associated virus vector-based gene therapy indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron 1* (*SMN1*) gene.

Limitations of Use

The safety and effectiveness of repeat administration or the use in patients with advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence) has not been evaluated with ZOLGENSMA.

Important Safety Information

BOXED WARNING: Acute Serious Liver Injury and Acute Liver Failure

Acute serious liver injury, acute liver failure, and elevated aminotransferases can occur with ZOLGENSMA. Patients with preexisting liver impairment may be at higher risk. Prior to infusion, assess liver function of all patients by clinical examination and laboratory testing (e.g., hepatic aminotransferases [aspartate aminotransferase (AST) and alanine aminotransferase (ALT)], total bilirubin, and prothrombin time). Administer a systemic corticosteroid to all patients before and after ZOLGENSMA infusion. Continue to monitor liver function for at least 3 months after infusion.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.

~13 MONTHS OLD

Brady's DIAGNOSIS

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Brady was first diagnosed with SMA Type 2 at 13 months old[1]

- Patients with SMA Type 2 typically have 2–3 copies of the *SMN2* backup gene[2]

Brady's parents met with a genetic specialist and pediatric neurologists to learn about SMA and discuss different treatment options[1]

- At the time of treatment, ZOLGENSMA was one of 2 FDA-approved treatments available[1]

> ***"We chose ZOLGENSMA because it was a one-time treatment that treats the genetic root cause."[1]***
>
> **– Tyler, father of Brady**

ZOLGENSMA is:

- **Designed to treat the genetic cause of SMA**, a deletion or mutation of the *survival motor neuron 1* (*SMN1*) gene, by providing a working copy of the human *SMN* gene[3]
  - ZOLGENSMA is designed not to integrate into the patient's genome[4]
- **Designed for continuous SMN protein expression** with self-complementary DNA and a continuous promoter, which provide rapid activation and expression of the *SMN* transgene[3,5]
- **Designed for targeted delivery** with a non-replicating, adeno-associated virus (AAV9) capsid that can cross the blood-brain barrier into non-dividing motor neurons[3,4]
  - AAV9 vectors are not known to cause disease in humans[4]

Important Safety Information

WARNINGS AND PRECAUTIONS

Thrombocytopenia

Transient decreases in platelet counts, some of which met the criteria for thrombocytopenia, were typically observed within the first two weeks after ZOLGENSMA infusion. Monitor platelet counts before ZOLGENSMA infusion and on a regular basis for at least 3 months afterwards.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.

~14 MONTHS OLD

Brady

RECEIVED TREATMENT WITH ZOLGENSMA ~1 MONTH AFTER DIAGNOSIS[1]

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Brady was treated with one-time-only ZOLGENSMA at ~14 months old[1]

> *"From the day of our diagnosis, our journey went really fast, and our doctor was prepared."*[1]
>
> – Nicole, mother of Brady

At the time of treatment, Brady had already lost mobility in his legs[1]

- He struggled to crawl and to hold toys[1]
- SMA causes progressive and irreversible motor neuron loss[2]

Baseline testing is required for all patients before ZOLGENSMA treatment[3]

- Anti-AAV9 antibody titers ≤1:50[3]
- Liver function, creatinine, complete blood count (including hemoglobin and platelet count), and troponin-I[3]

One day before ZOLGENSMA treatment, Brady started a corticosteroid regimen that continued after treatment[1]

Per the regimen detailed in the **Full Prescribing Information,** treatment with systemic corticosteroids before and after ZOLGENSMA infusion is required. Due to increased risk of serious systemic immune response, treatment in patients with concurrent infections should be postponed until resolved.[3]

AFTER ZOLGENSMA TREATMENT: 14 MONTHS OLD

After treatment with ZOLGENSMA, Brady had elevated liver enzymes[1]

- Brady's doctor monitored his lab results until results were unremarkable

Important Safety Information

WARNINGS AND PRECAUTIONS

Thrombotic Microangiopathy

Cases of thrombotic microangiopathy (TMA) were reported approximately 1 week after ZOLGENSMA infusion. Obtain baseline creatinine and complete blood count before ZOLGENSMA infusion. Following infusion, monitor for thrombocytopenia as well as other signs and symptoms of TMA. Consult a pediatric hematologist and/or pediatric nephrologist immediately to manage if clinically indicated.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.

~2 YEARS OLD

Brady

~1 YEAR AFTER ZOLGENSMA TREATMENT

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Brady has gained motor function[1]

- He is able to crawl up the stairs and can get into his walker independently[1]
- Brady uses a walker to travel short distances on his own[1]

Brady has achieved independent oral feeding[1]

- He receives all of his nutrition orally and eats solid foods[1]
- He eats independently using utensils and finger foods[1]

"He amazes me every day with the new things he's doing."[1]

– Tyler, father of Brady

Results and outcomes vary among children based on several factors, including how far their SMA symptoms had progressed prior to receiving treatment.

Currently, Brady receives physical and hippotherapy—the therapeutic use of horseback riding—to help manage his SMA[1]

- Brady does not receive respiratory or feeding support[1]

CONSIDER ZOLGENSMA

The one-time-only dose to stop SMA progression[3]

The safety and efficacy of ZOLGENSMA has been evaluated in completed trials and continues to be evaluated in ongoing trials, including a long-term follow-up.[6-9]

To learn more about the ZOLGENSMA clinical trials, go to ZOLGENSMA-hcp.com.

Important Safety Information

WARNINGS AND PRECAUTIONS

Elevated Troponin-I

Increases in cardiac troponin-I levels were observed following ZOLGENSMA infusion. Monitor troponin-I before ZOLGENSMA infusion and on a regular basis for at least 3 months afterwards.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.

STR1VE PHASE 3 CLINICAL TRIAL

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The efficacy of ZOLGENSMA was evaluated in STR1VE, a completed, open-label, single-arm, multicenter, Phase 3 clinical trial of patients with SMA Type 1 (N=22; genetically confirmed bi-allelic *SMN1* deletion, 1–2 copies of *SMN2*, and <6 months of age at symptom onset and treatment)[7]

Survival: 91% (20/22) of patients were alive and free of permanent ventilation at the 14-months-of-age study visit, a **primary endpoint**, and at 18 months of age[10,a-c]

Sitting independently: 59% (13/22) of patients were sitting without support for ≥30 seconds at the 18-months-of-age study visit, a **primary endpoint**[10,a]

- Patients with SMA Type 1 in historical controls do not typically achieve or maintain motor milestones[11]

Ability to thrive: 41% (9/22) of patients met criteria for ability to thrive at 18 months of age, a secondary endpoint[10,d]

Respiratory support: 68% (15/22) of patients did not require noninvasive respiratory support at any point during the study[10]

- 4/22 patients required ventilatory support as assessed by Trilogy BiPAP data alone at 18 months of age, a secondary endpoint[10]

Motor function improvements: The mean CHOP INTEND score increased from 32 points (range 18–52) at baseline to **53.5** (range 42–60) at 14 months (n=11)[10]

- Mean CHOP INTEND scores increased as early as month 1, and scores were maintained or improved through the end of the study[10]

Results and outcomes vary among children based on several factors, including how far their SMA symptoms had progressed prior to receiving treatment.

[a]One patient was initially classified as presymptomatic and removed from the intent-to-treat (ITT) population. The patient was later confirmed to be symptomatic at the time of treatment and was included in the final ITT analysis.[10]

[b]One patient died at 7.8 months from respiratory failure which was deemed unrelated to treatment. One patient withdrew consent at 11.9 months; this patient required permanent ventilation at 11 months prior to withdrawing consent.[10]

[c]One patient discontinued participation at the age of 18.0 months before the month 18 end-of-study visit due to an adverse event of respiratory distress deemed unrelated to treatment. The patient was alive and without permanent ventilation at 18 months of age and was included in the final analysis.[10]

[d]Ability to thrive was defined as ability to tolerate thin liquids as demonstrated through a formal swallowing test, maintenance of weight (≥3rd percentile for age and gender, as defined by WHO guidelines), and independence from mechanical or non-oral nutritional support.[10]

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Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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ADVERSE REACTIONS

The most commonly observed adverse reactions (incidence ≥5%) in clinical studies were elevated aminotransferases and vomiting.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.

References: 1. Data on file. Novartis Gene Therapies, Inc. 2021. **2.** Anderton RS, Mastaglia FL. Advances and challenges in developing a therapy for spinal muscular atrophy. *Expert Rev Neurother.* 2015;15(8):895-908. **3.** ZOLGENSMA [prescribing information]. Bannockburn, IL: Novartis Gene Therapies, Inc; 2021. **4.** Brommel CM, Cooney AL, Sinn PL. Adeno-associated virus-based gene therapy for lifelong correction of genetic disease. *Hum Gene Ther.* 2020;31(17-18):985-995. doi:10.1089/hum.2020.138. **5.** Mendell JR, Al-Zaidy S, Shell R, et al. Single-dose gene-replacement therapy for spinal muscular atrophy. *N Engl J Med.* 2017;377(18):1713-1722. **6.** Novartis Gene Therapies, Inc. Gene transfer clinical trial for spinal muscular atrophy type 1. https://clinicaltrials.gov/ct2/show/NCT02122952. ClinicalTrials.gov identifier: NCT02122952. Updated June 14, 2021. Accessed October 26, 2021. **7.** Novartis Gene Therapies, Inc. Gene replacement therapy clinical trial for participants with spinal muscular atrophy type 1 (STR1VE). https://clinicaltrials.gov/ct2/show/NCT03306277. ClinicalTrials.gov identifier: NCT03306277. Updated June 14, 2021. Accessed October 26, 2021. **8.** Novartis Gene Therapies, Inc. Pre-symptomatic study of intravenous onasemnogene abeparvovec-xioi in spinal muscular atrophy (SMA) for patients with multiple copies of *SMN2* (SPR1NT). https://clinicaltrials.gov/ct2/show/NCT03505099. ClinicalTrials.gov identifier: NCT03505099. Updated July 29, 2021. Accessed October 26, 2021. **9.** Novartis Gene Therapies, Inc. Long-term follow-up study for patients from AVXS-101-CL-101 (START). https://clinicaltrials.gov/ct2/show/NCT03421977. ClinicalTrials.gov identifier: NCT03421977. Updated June 9, 2021. Accessed October 26, 2021. **10.** Data on file. AveXis, Inc. 2020. **11.** De Sanctis R, Coratti G, Pasternak A, et al. Developmental milestones in type I spinal muscular atrophy. *Neuromuscul Disord.* 2016;26(11):754-759.

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