SMA Community Update from Novartis Gene Therapies:
September 2022

Dear SMA Community:

Thank you for the joy of being together in person for the first time in two years at the Cure SMA Annual SMA Conference and SMA Research & Clinical Care Meeting, and we look forward to seeing several of you at the Cure SMA Chapter and Leadership Meeting. We greatly appreciate your insights and partnership. We're here to provide you with an update on our clinical trials, long-term studies, and some recent publications.

We join you in your commitment to improving care for patients with SMA.

With gratitude,
YOUR NOVARTIS GENE THERAPIES TEAM

Access Snapshot for ZOLGENSMA® (onasemnogene abeparvovec-xioi) suspension, for intravenous infusion

APPROVED IN OVER 40 COUNTRIES

98%[1] **OF US PATIENTS APPROVED FOR ACCESS***

OVER 2,300+[2] **PATIENTS TREATED GLOBALLY****

*Insurance approval rate based on data from 24May2019-31Oct2020, all patients <2 years of age for whom a payer decision was known
**As of June 2022, including clinical trials, commercially, and through the managed access programs

SMA Clinical Trial Program

Completed Clinical Studies

START

Phase 1 study that evaluated safety and efficacy of ZOLGENSMA® in symptomatic patients

STR1VE

Phase 3 study that evaluated safety and efficacy of ZOLGENSMA® in symptomatic patients

SPR1NT

Phase 3 study that evaluated safety and efficacy of ZOLGENSMA® in presymptomatic patients

STRONG

Phase 1 study that evaluated safety and tolerability of investigational intrathecal gene therapy (OAV101)

Please keep reading for Indication and Important Safety Information, and please see accompanying **Full Prescribing Information**, including Boxed Warning

SMA Clinical Trial Program

Investigational Studies

SMART

SMART is a Phase 3b clinical study to further evaluate safety, tolerability, and efficacy of intravenous ZOLGENSMA® in patients with SMA weighing ≥8.5 kg and ≤21 kg. The global study has completed enrollment of 24 symptomatic children at SMA sites in Europe, North America, Australia and Taiwan, and will follow patients for a period of 12 months. For the latest information, please visit clinicaltrials.gov.

STRENGTH

STRENGTH is a global, Phase 3b, open-label study to evaluate safety and tolerability of our investigational intrathecal gene therapy (OAV101) in patients aged 2-12 years with SMA after discontinuing treatment with nusinersen or risdiplam. The study is not yet recruiting. For the latest information, please visit clinicaltrials.gov.

STEER

STEER is a global Phase 3 clinical study of our investigational intrathecal gene therapy (OAV101) in patients with type 2 SMA. The STEER trial will include treatment naive patients aged 2 to <18 years, able to sit, but who have never walked. Recruitment has begun. For the latest information, please visit clinicaltrials.gov.

Long-Term Follow-Up Studies

Three long-term follow-up studies to monitor safety and efficacy in participants from Phase 1 and 3 OAV101 IV and IT clinical trials

LT-001
for participants from START

LT-002
for participants from IV and IT clinical trials

A12308
for participants from IV and IT clinical trials

New Webpage for the STEER Clinical Trial

Information on the study, including study design, endpoints and eligibility criteria, can be found on **Novartis.com**.

Recently Published Data

Nature Medicine
Published the SPR1NT trial of ZOLGENSMA in presymptomatic infants with two copies of *SMN2*.[3]

Nature Medicine
Published the SPR1NT trial of ZOLGENSMA in presymptomatic infants with three copies of *SMN2*.[4]

Pediatric Neurology
Published a paper about safety of onasemnogene abeparvovec for patients with SMA who were 8.5 kg or heavier in a global managed access program.[5]

Indication and Important Safety Information for ZOLGENSMA® (onasemnogene abeparvovec-xioi)

What is ZOLGENSMA?
ZOLGENSMA 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.
- 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. Contact the patient's doctor immediately if you see 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 occur approximately one week after ZOLGENSMA infusion. Caregivers should 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.

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 respiratory syncytial virus (RSV) is recommended.

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 bodily waste for 1 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 833-828-3947.
Please see the Full Prescribing Information.

References

1. Data on file. Novartis Gene Therapies, Inc. 2020. **2.** Data on file. Novartis Gene Therapies, Inc. 2022. **3.** Strauss KA, Farrar MA, Muntoni F, et al. Onasemnogene abeparvovec for presymptomatic infants with two copies of *SMN2* at risk for spinal muscular atrophy type 1: the Phase III SPR1NT trial. *Nat Med.* 2022;28:1381-1389. **4.** Strauss KA, Farrar MA, Muntoni F, et al. Onasemnogene abeparvovec for presymptomatic infants with three copies of *SMN2* at risk for spinal muscular atrophy: the Phase III SPR1NT trial. *Nat Med.* 2022;28:1390-1397. **5.** Chand DH, Mitchell S, Sun R, LaMarca N, Reyna SP, Sutter T. Safety of onasemnogene abeparvovec for patients with spinal muscular atrophy 8.5 kg or heavier in a global managed access program. *Pediatr Neurol.* 2022;132:27–32.

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