SMA Community Update from Novartis Gene Therapies:
May 2022

Dear SMA Community:

We are reaching out in appreciation for the milestones that together we have made possible. From launching new clinical trials, to advocating for policies to increase SMA newborn screening, together we have achieved so much.

In this community update, we look ahead to gathering in person, share some of the latest educational resources and provide clinical updates.

As always, thank you for your continuous partnership in improving care and treatment for patients with SMA. Your participation in our clinical trials, your trust and your support helps us deliver on the potencial of gene therapy for those impacted by rare genetic disease.

With gratitude,
YOUR NOVARTIS GENE THERAPIES TEAM

Connecting with the Community

We are proud to be a presenting sponsor of the Cure SMA 2022 Annual SMA Conference in June and are so excited to be gathering again in person. We invite you to stop by the Novartis Gene Therapies booth and say hello to our team!

Gene Therapy Education Resources

Several new resources are available on our Explore Gene Therapy website to help you better understand cell and gene therapy including a fact sheet; information about gene addition, inhibition and editing; and details about the next era of medicine with cell and gene therapies. Take a look and share with your communities to encourage meaningful conversations about the potential of gene therapy.

Recently Published Data

Drug Safety published a paper that described the safety data for ZOLGENSMA®.[1]

Nature Medicine published a paper on the biodistribution of ZOLGENSMA®.[2]

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

APPROVED IN OVER **40** COUNTRIES

98%[3] OF US PATIENTS APPROVED FOR ACCESS*

OVER **2,000+**[4] 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 March 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)

Long-Term Follow-Up Studies

LT-001
Monitoring ongoing safety in START study patients

LT-002
Evaluating long-term safety and efficacy in patients from clinical trials for SMA who were treated with onasemnogene abeparvovec

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

SMA Clinical Trial Program

Ongoing/Upcoming Studies

SMART

SMART is a Phase 3b clinical study to further evaluate the safety, tolerability, and efficacy of intravenous ZOLGENSMA® in patients with SMA weighing ≥8.5 kg and ≤21 kg. The global study has completed recruitment and is expected to enroll 24 symptomatic children with SMA across 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.

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.

STRENGTH

STRENGTH is a global, Phase 3b, open-label study to evaluate the safety and tolerability of our investigational intrathecal gene therapy (OAV101) in patients aged 2-12 years with SMA after discontinuing treatment with nusinersen and/or risdiplam. The study is early in development and specific details including the study protocol are still ongoing.

Intravenous (IV) is a method of administering medicines directly into the vein. **Intrathecal administration (IT)** is a method of administering medicines into the spinal canal so that it reaches the **cerebrospinal fluid (CSF)**.

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 the 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. Day JW, Mendell JR, Mercuri E, et al. Clinical Trial and Postmarketing Safety of Onasemnogene Abeparvovec Therapy. *Drug Saf.* 2021;44:1109–1119. doi: 10.1007/s40264-021-01107-6.
2. Thomsen G, Burghes AHM, Hsieh C, et al. Biodistribution of onasemnogene abeparvovec DNA, mRNA and SMN protein in human tissue. *Nat Med.* 2021;27:1701-1711.
3. Data on file. Novartis Gene Therapies, Inc. 2020.
4. Data on file. Novartis Gene Therapies, Inc. 2022.

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