From Clinical Trials to Clinical Practice: What Have We Learnt About Zolgensma▼ (onasemnogene abeparvovec) Treatment in SMA?

SAVE THE DATE!
November 30th, 2023 | 3:15–4:15 PM CET

Join a virtual Novartis-sponsored symposium at ICNMDigital 2023, where a panel of Medical Experts will discuss the experiences of children and their families affected by SMA and explore learnings from Zolgensma in clinical trials and the real world.

Hear from SMA experts from around the world

Dr Sean Wallace
Department of Clinical Neurosciences for Children, Oslo University Hospital
(Norway)

Prof. Eugenio Mercuri
Gemelli University Hospital
(Italy)

Dr Hugh McMillan
Children's Hospital of Eastern Ontario
(Canada)

Agenda

SMA: From Diagnosis to Long-Term Care
Dr Sean Wallace

Long-Term Outcomes of Patients Treated With Zolgensma
Prof. Eugenio Mercuri

What Does RWE Tell Us About Zolgensma Treatment for Children With SMA?
Prof. Eugenio Mercuri

Zolgensma Treatment Benefit:Risk in a Broader Patient Population
Dr Hugh McMillan

We invite you to watch the symposium here!
Click HERE to add this meeting to your calendar

ICNMD, International Congress on Neuromuscular Diseases; RWE, real-world evidence; SMA, spinal muscular atrophy.

Please see below for adverse event reporting information and the Summary of Product Characteristics for ZOLGENSMA.

This promotional symposium is organised and sponsored by Novartis Gene Therapies and is intended for healthcare professionals only.

This presentation was approved by the Program Committee as an independent activity held in conjunction with ICNMDigital 2023. This presentation is not sponsored or endorsed by ICNMDigital 2023.

Abbreviated Summary of Product Characteristics

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See the Summary of Product Characteristics on how to report adverse reactions and contact the local representative of the Marketing Authorisation Holder for country specific information.

ZOLGENSMA® (ONASEMNOGENE ABEPARVOVEC)
2×10^{13} VECTOR GENOMES/ML SOLUTION FOR INFUSION

Important note: Before prescribing, consult the full Summary of Product Characteristics.

Presentation:
Onasemnogene abeparvovec. Solution for infusion 2×10^{13} vector genomes/mL.
Each mL contains onasemnogene abeparvovec with a nominal concentration of 2×10^{13} vector genomes (vg). Vials will contain an extractable volume of not less than either 5.5 mL or 8.3 mL. The total number of vials and combination of fill volumes in each finished pack will be customised to meet dosing requirements for individual patients depending on their weight.

Indications:
Zolgensma is indicated for the treatment of:
- patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or
- patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.

Dosage and administration:
Treatment should be initiated and administered in clinical centres and supervised by a physician experienced in the management of patients with SMA.
Patients will receive a dose of nominal 1.1×10^{14} vg/kg onasemnogene abeparvovec. The total volume is determined by patient body weight.
In case of acute or chronic uncontrolled active infections, treatment should be postponed until the infection has resolved and the patient is clinically stable.
Before administration of onasemnogene abeparvovec, baseline laboratory testing is required, including, but not limited to: AAV9 antibody testing using an appropriately validated assay, liver function (alanine aminotransferase [ALT], aspartate aminotransferase [AST], total bilirubin, albumin, prothrombin time, partial thromboplastin time [PTT], and international normalised ratio [INR]); creatinine; complete blood count (including haemoglobin and platelet count), and troponin-I.
The need for close monitoring of liver function, platelet count and troponin-I after administration and the need for corticosteroid treatment are to be considered when establishing the timing of onasemnogene abeparvovec treatment.
Liver function (ALT, AST, total bilirubin) should be monitored at regular intervals for at least 3 months following onasemnogene abeparvovec infusion (weekly in the first month and during the entire corticosteroid taper period, followed by every two weeks for another month), and at other times as clinically indicated.
For complete instructions, refer to the full Summary of Product Characteristics.

Special populations:
Renal impairment: The safety and efficacy of onasemnogene abeparvovec have not been established in patients with renal impairment. A dose adjustment should not be considered.
Hepatic impairment: Onasemnogene abeparvovec therapy should be carefully considered in patients with hepatic impairment. A dose adjustment should not be considered.
Pediatric patients: The safety and efficacy of onasemnogene abeparvovec in premature neonates before reaching full-term gestational age have not been established. No data are available. Administration of onasemnogene abeparvovec should be carefully considered because concomitant treatment with corticosteroids may adversely affect neurological development. There is limited experience in patients 2 years of age and older or with body weight above 13.5 kg. The safety and efficacy of Zolgensma in these patients have not been established.
0SMN1/SMN2 genotype: No dose adjustment should be considered in patients with a bi-allelic mutation of the *SMN1* gene and only one copy of *SMN2*.
Anti-AAV9 antibodies: No dose adjustment should be considered in patients with baseline anti-AAV9 antibody titres above 1:50.

Method of administration: For single-dose intravenous infusion only.
Intravenous infusion instructions: Administer onasemnogene abeparvovec with a syringe pump as a single intravenous infusion with a slow infusion of approximately 60 minutes. It must not be administered as an intravenous push or bolus.
For complete preparation and intravenous infusion instructions, refer to the full Summary of Product Characteristics.

Contraindications:
Hypersensitivity to the active substance or to any of the excipients.

Warnings and precautions:
- **Traceability:** In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded
- **Pre-existing immunity against AAV9:** Patients should be tested for the presence of AAV9 antibodies prior to infusion with onasemnogene abeparvovec. Re-testing may be performed if AAV9 antibody titres are reported as above 1:50.
- **Advanced SMA:** The benefit/risk profile of onasemnogene abeparvovec in patients with advanced SMA, kept alive through permanent ventilation and without the ability to thrive, is not established.
- **Immunogenicity:** An immune response to the AAV9 capsid will occur after infusion of onasemnogene abeparvovec, including antibody formation against the AAV9 capsid and T cell mediated immune response, despite the immunomodulatory regimen recommended.
- **Hepatotoxicity:** Administration of AAV vector often results in aminotransferase elevations. Acute serious liver injury and acute liver failure, including fatal cases, have been reported with onasemnogene abeparvovec use, typically within 2 months after infusion and despite receiving corticosteroids before and after infusion. Immune mediated hepatotoxicity may require adjustment of the immunomodulatory regimen including longer duration, increased dose, or prolongation of the corticosteroid taper. The risks and benefits of onasemnogene abeparvovec therapy should be carefully considered in patients with pre existing hepatic impairment. Patients with pre existing hepatic impairment or acute hepatic viral infection may be at higher risk of acute serious liver injury. Prior to infusion, liver function of all patients should be assessed by clinical examination and laboratory testing. In order to mitigate potential aminotransferase elevations, a systemic corticosteroid should be administered to all patients before and after onasemnogene abeparvovec infusion. Liver function should be monitored at regular intervals for at least 3 months after infusion, and at other times as clinically indicated.Patients with worsening liver function test results and/or signs or symptoms of acute illness should be promptly clinically assessed and monitored closely.In case hepatic injury is suspected, prompt consultation with a paediatric gastroenterologist or hepatologist, adjustment of the recommended immunomodulatory regimen and further testing is recommended (e.g. albumin, prothrombin time, PTT, and INR).
- **Thrombocytopenia:** Platelet counts should be obtained before onasemnogene abeparvovec infusion and should be closely monitored within the first two weeks following infusion and on a regular basis afterwards, at least weekly for the first month and every other week for the second and third months until platelet counts return to baseline.
- **Thrombotic microangiopathy:** If patients show clinical signs, symptoms or laboratory findings consistent with TMA, a specialist should be consulted immediately to manage TMA as clinically indicated. Cases of thrombotic microangiopathy (TMA) have been reported with onasemnogene abeparvovec. Cases generally occurred within the first two weeks after onasemnogene abeparvovec infusion. Fatal outcomes have been reported.
- **Elevated troponin-I:** Troponin I levels should be obtained before onasemnogene abeparvovec infusion and monitored for at least 3 months following onasemnogene abeparvovec infusion or until levels return to within normal reference range for SMA patients. Consider consultation with a cardiac expert as needed.
- **Systemic immune response:** It is recommended that patients are clinically stable in their overall health status (e.g. hydration and nutritional status, absence of infection) prior to onasemnogene abeparvovec infusion. Treatment should not be initiated concurrently to active infections, either acute (such as acute respiratory infections or acute hepatitis) or uncontrolled chronic (such as chronic active hepatitis B), until the infection has resolved and the patient is clinically stable. Increased vigilance in the prevention, monitoring, and management of infection is recommended before and after onasemnogene abeparvovec infusion. Seasonal prophylactic treatments, that prevent respiratory syncytial virus (RSV) infections, are recommended and should be up to date.
- **Risk of tumourigenicity as a result of vector integration:** There is a theoretical risk of tumourigenicity due to integration of AAV vector DNA into the genome. Rare instances of random vector integration into human DNA are possible with recombinant AAV. Individual integration events could potentially contribute to a risk of tumourigenicity. So far, no cases of malignancies associated with onasemnogene abeparvovec treatment have been reported. In the event of a tumour, the marketing authorisation holder should be contacted for guidance on collecting patient samples for testing.
- **Shedding:** Temporary onasemnogene abeparvovec shedding occurs, primarily through bodily waste. Caregivers and patient families should be advised on following instructions for the proper handling of patient stools. For complete instructions, refer to the full Summary of Product Characteristics.
- **Blood, organ, tissue and cell donation:** Patients treated with Zolgensma should not donate blood, organs, tissues or cells for transplantation.
- **Sodium content:** This medicinal product contains 4.6 mg sodium per mL, equivalent to 0.23% of the WHO recommended maximum daily intake of 2 g sodium for an adult. Each 5.5 mL vial contains 25.3 mg sodium, and each 8.3 mL vial contains 38.2 mg sodium.

Fertility, pregnancy and lactation
Human data on use during pregnancy or lactation are not available and animal fertility or reproduction studies have not been performed.

Adverse drug reactions:
Very common (≥10%): Hepatic enzyme increased
Common (≥1 to <10%): Thrombocytopenia, vomiting, hepatotoxicity, pyrexia, troponin increased.
Frequency not known: Thrombotic microangiopathy (including fatal cases), acute liver failure (including fatal cases), acute liver injury

Interactions:
No interaction studies have been performed. Experience with use of onasemnogene abeparvovec in patients receiving hepatotoxic medicinal products or using hepatotoxic substances is limited. Safety of onasemnogene abeparvovec in these patients have not been established. Experience with use of concomitant 5q SMA targeting agents is limited. Where feasible, the patient's vaccination schedule should be adjusted to accommodate concomitant corticosteroid administration prior to and following onasemnogene abeparvovec infusion.

Packs and prices: Country-specific.
Legal classification: Country-specific.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

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