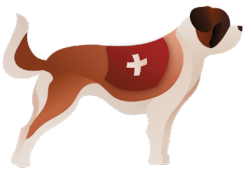
Biogen



The RESPOND Study

A clinical study in young children with Spinal Muscular Atrophy (SMA)

The RESPOND study is an ongoing clinical study initiated by Biogen to find out if patients could benefit from treatment with nusinersen (an approved drug, also known as Spinraza®), *after* they have been treated with gene therapy (onasemnogene abeparvovec-xioi).

The study will look at the benefits of this treatment approach to children's health and development, as well as the side effects.

The people taking part in the study will include babies and children up to the age of 3 years who have unmet clinical needs following treatment with gene therapy.

The purpose of this brochure is to share information on the study with the SMA community.

Biogen

RESPOND

What is SMA?

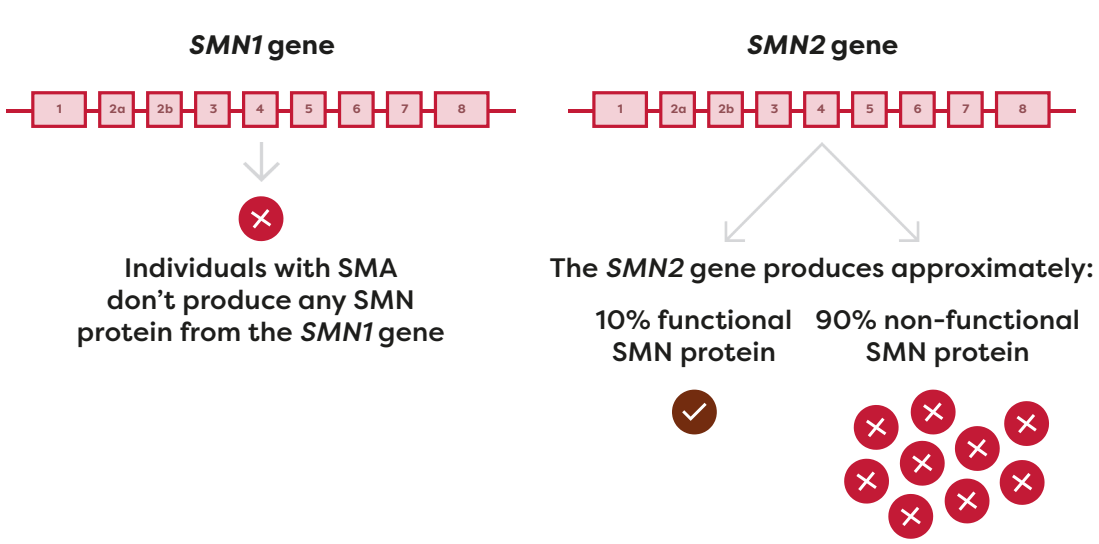
SMA is a rare, genetic disease which can lead to muscle weakness, problems with movement, and reduced life expectancy for people most severely affected.

Those affected by the most severe form of SMA (Type 1) can begin to show symptoms in the first 6 months of their life. The most common symptoms include limited arm and leg movement, swallowing and feeding difficulties, and breathing problems. It is possible to be diagnosed with SMA before symptoms begin, either via a test carried out by a healthcare professional during pregnancy (called 'prenatal genetic testing'), or once the baby is born.

SMA is caused by a change in a gene called 'survival motor neuron 1 gene' (*SMN1*). A gene is a set of instructions for making a specific protein in the body. The *SMN1* gene produces a protein called 'survival motor neuron' (SMN) protein that is important for nerve and muscle function.

Individuals living with SMA do not produce enough SMN protein. There is a 'back-up' gene called *SMN2* that produces a small amount of SMN protein. Nusinersen – a medicine approved in Europe in 2017 – works by increasing the amount of functional SMN protein coming from the *SMN2* gene. By increasing SMN protein, nerves and muscles are helped to survive and function properly.

EXAMPLE SMN PRODUCTION FROM SMN1 AND SMN2 GENES IN AN INDIVIDUAL WITH SMA



Biogen

RESPOND

What is the aim of the RESPOND study?

Clinical studies like the RESPOND study are set up to learn more about SMA, to find better treatment options, and to improve the health and wellbeing of people living with SMA. There are different treatment options available but there is still no cure for SMA.

The goal of the RESPOND study is to find out if treatment with nusinersen is tolerated and could benefit SMA patients who have already received treatment with onasemnogene abeparvovec-xioi (a one-time gene therapy treatment approved in the EU in 2020 to treat children with SMA under 2 years old).

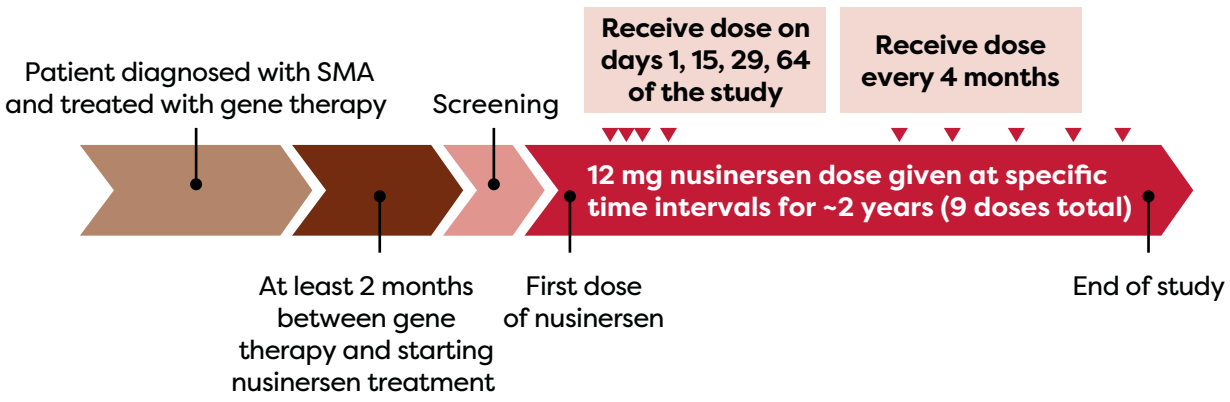
RESPOND is a phase 4, open-label study which means:

- the study medicine, nusinersen, has already been approved for use based on earlier studies.
- both the patient's caregiver and their doctor are made aware that this is the medicine being given to the child in the study.

Study design

Before patients can join the study, there is a screening process where tests and checks are carried out to find out if the study is suitable for them.

Those in the study will receive the study treatment for approximately 2 years. During this time their health and development will be closely monitored and assessed by a team of healthcare professionals.



Biogen

RESPOND

Patient characteristics

The study plans to include 60 children who have unmet clinical needs after receiving gene therapy (as identified by a doctor).

The children in the study will join one of the two groups below and meet the following criteria:

All participants

Around 60 in total will all have:

- **Unmet clinical needs following treatment with onasemnogene abeparvovec**
- **Never received the study medicine nusinersen**

Younger age group

Around 40 participants who all:

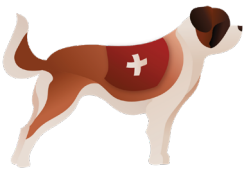
- Have two copies of the *SMN2* gene
- Showed SMA symptoms by 4 months old
- Received gene therapy (onasemnogene abeparvovec) by 6 months old
- Will start to receive the study medicine after symptoms appear and by 9 months old

Broader age group

Around 20 participants who all:

- Have one or two copies of the *SMN2* gene
- Will start to receive the study medicine by 3 years old

Biogen



RESPOND

What is being measured in the study?

During the study, healthcare professionals will assess the participants using a list of childhood development targets called 'motor milestones'. These are physical movements such as kicking, sitting, rolling and head control. The tool that will be used to assess and measure these milestones is the 'HINE Section 2 motor milestone score'. These will be the key measurements that are used to see if the treatment is providing additional benefit to the children in the study. Additional measures will also be used to evaluate the children's development.

THE HINE SECTION 2 MOTOR MILESTONE SCORE:

- Voluntary grasp
- Sitting
- Head control
- Standing
- Ability to kick
- Crawling
- Rolling
- Walking

The study team will also assess the children's overall health, including:

- Monitoring heart rhythms
- Measuring body weight
- Checking feeding routines
- Taking blood and urine samples

The study team will also closely monitor the children during the study to identify any side effects to the treatment.

Biogen

RESPOND

Study timing and locations

The RESPOND study began in January 2021, when the first child joined the study and started their course of treatment. The study aims to include up to 60 children with SMA by 2024.

The study is a global study and will take place in approximately 30 different clinics worldwide. The list of locations can be found on clinicaltrials.gov (NCT04488133).

Further information

For the most up-to-date information and to learn more about the RESPOND study, visit clinicaltrials.gov and search using the trial code NCT04488133.

If you are interested in taking part in the study, or have specific questions about SMA symptoms and treatment options, please speak with your doctor.

Contact details for the sponsor of this study:

Biogen International GmbH
Neuhofstrasse 30, 6340 Baar, Switzerland
ClinicalTrials@biogen.com

Biogen

www.biogen.com

Veeva number: Biogen-136621, September 2021