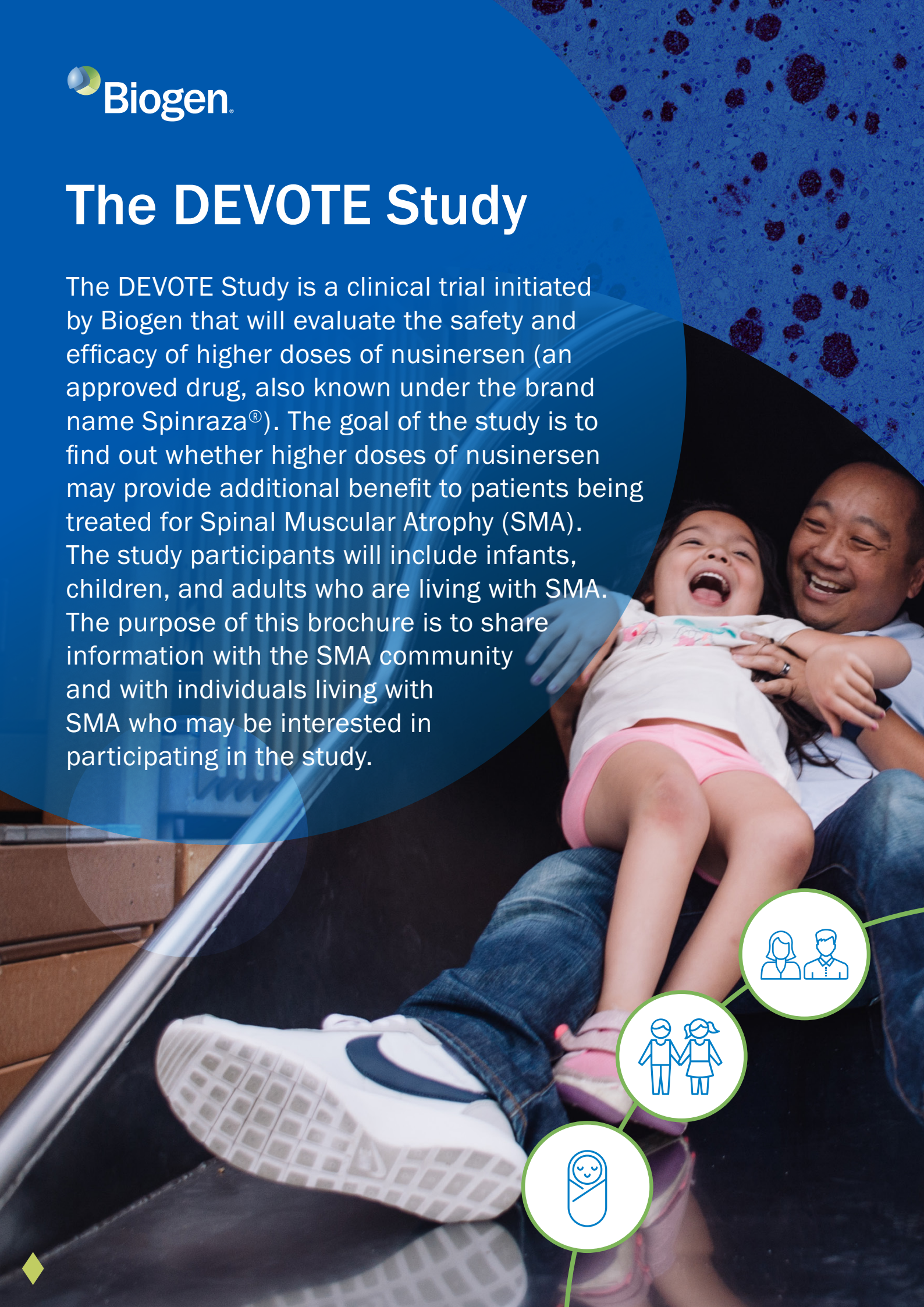
Biogen

The DEVOTE Study

The DEVOTE Study is a clinical trial initiated by Biogen that will evaluate the safety and efficacy of higher doses of nusinersen (an approved drug, also known under the brand name Spinraza®). The goal of the study is to find out whether higher doses of nusinersen may provide additional benefit to patients being treated for Spinal Muscular Atrophy (SMA). The study participants will include infants, children, and adults who are living with SMA. The purpose of this brochure is to share information with the SMA community and with individuals living with SMA who may be interested in participating in the study.

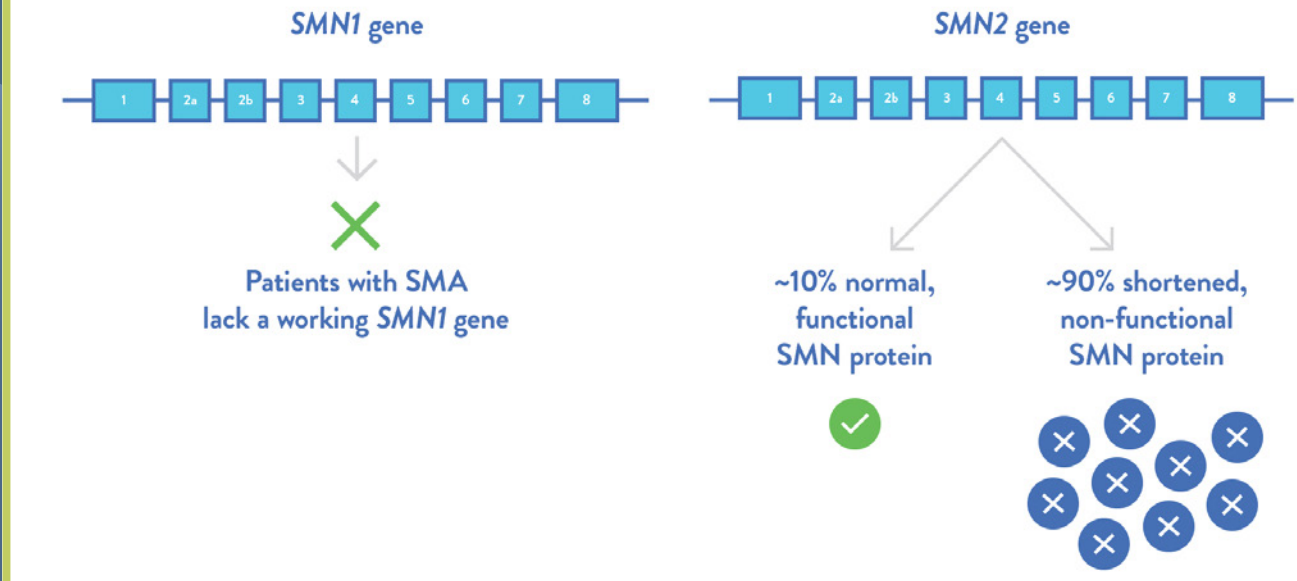


What is SMA?

SMA is a rare, genetic disease which can lead to muscle weakness, problems with movement, and reduced life expectancy for patients most severely affected. It is caused by a mutation or change, in a gene called survival motor neuron 1 (SMN1). This gene produces a protein called survival motor neuron (SMN) that is important for nerve and muscle function. Individuals living with SMA do not produce enough of this protein. However, there is a "back-up" gene called SMN2 that mostly produces a shortened version of the SMN protein, which does not work as well as the full-length protein.

There are a number of different treatments available which can help people living with SMA. Nusinersen – a medicine approved for use in SMA patients – works by increasing the amount of full-length SMN protein coming from the SMN2 gene. By replacing this missing protein, nerves and muscles are helped to function properly.

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



Study design

Despite the treatment options available, there is still no cure for SMA. To learn more about the disease and to improve the health and wellbeing of people living with SMA, clinical studies, like DEVOTE, are developed. The goal of the DEVOTE study is to find out whether increasing the dose of nusinersen has additional clinical benefit, while continuing to have a favourable safety profile.

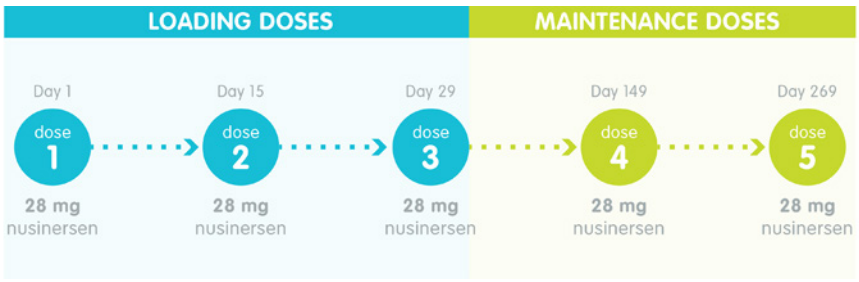
The study has been designed with three parts, each lasting approximately 11–13 months. A participant in the DEVOTE study will only participate in Part A, B or C.

Part A

Children aged 2 to 15 whose symptoms appeared *after* they were 6 months old*

To test the safety and tolerability of nusinersen at higher doses, in later-onset SMA

Open-label design meaning participants will know the dose they are receiving.



Part B

Infants aged >1 week to 7 months who had symptoms appear at 6 months old or younger*

OR

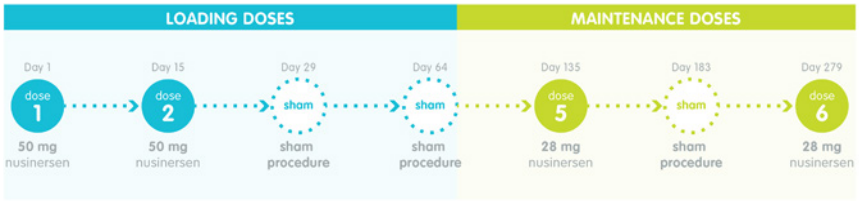
Children aged 2 to <10 years who had symptoms appear after they were 6 months of age, providing they can sit independently but have never been able to walk independently*

To test the clinical efficacy of nusinersen at higher doses, in both infantile-onset and later-onset SMA

Randomised, double-blind design meaning participants will be randomised to receive one of two different doses; they will not know which dose they are receiving:

- 1 in 3 participants will receive the current approved dosing schedule

- 2 in 3 participants will receive the investigational dosing schedule



sham procedure = needle prick in the lower back but no injection of treatment

Study design

The study has been designed with three parts, each lasting approximately 11–13 months. A participant in the DEVOTE study will only participate in Part A, B or C.

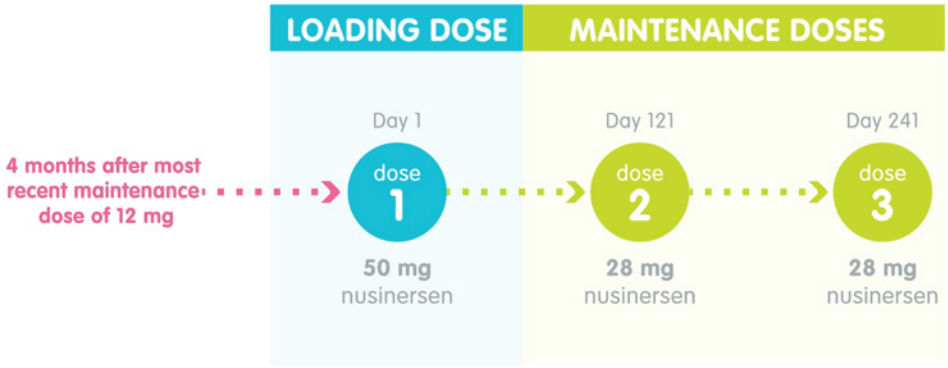
Part C

Participants of any age or SMA status who are currently being treated with nusinersen and received their first dose at least 1 year prior to the study

Those over 18 years old must be able to walk*

To test the safety and tolerability of nusinersen in all SMA types, when transitioning from an approved dose to a high dose regimen

Open-label design meaning participants will know the investigational dose they are receiving.



Patients who meet the eligibility criteria and are interested in participating will be provided will full details of the study. This will include information on the screening process, study logistics and details of how the treatment will be administered.

*Across parts A, B and C, all participants must have been genetically diagnosed with SMA (5q SMA homozygous gene deletion, mutation, or compound heterozygote. Additional eligibility criteria apply for this study and there are a number of factors which may prevent someone from being eligible to participate (also known as 'exclusion criteria'). Please visit clinicaltrials.gov (NCT04089566) for the full eligibility criteria.

What is being measured in the study?

Primary outcome measures are the most important measurements that the researchers will look at to answer the key study question: whether higher levels of nusinersen may provide additional benefit to patients with SMA. In the DEVOTE study, the primary outcome measures include:

Part B: CHOP INTEND

Part A and Part C: Safety and tolerability assessments

Other measures will also be assessed by the researchers, including secondary outcome measures of motor function, motor milestones, and quality of life.

How will the outcome measures be assessed?

The safety and tolerability of the treatment will be assessed with close monitoring of the participants' health during the study (using blood tests, urine tests, heart screening and other measures). Their motor function will also be monitored, such as their ability to control their head and body movements.

The following scales will be used to make these assessments:

- The Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND)
- Hammersmith Functional Motor Scale - Expanded (HFMSE)
- Revised Upper Limb Module (RULM)
- Hammersmith Infant Neurological Examination (HINE) Section 2

An example of one of the measures that will be used in the study:

THE HAMMERSMITH FUNCTIONAL MOTOR SCALE:

See clinicaltrials.gov (NCT04089566) for further details.

Study timing and locations

The study aims to enrol approximately 150 patients from across the globe, with approximately 60 sites in about 26 countries. Travel support may be available in the form of coordination and coverage of expenses in compliance with local country regulations. Neither eligible patients nor their insurance provider will be charged for the costs of any procedures performed as part of the clinical study who enroll in the trial.

All candidate study participants will receive more detailed information on study objectives, benefits, risks and further relevant information on the clinical trials process.

The first patient joined the study in March 2020.

For the most up-to-date information and to learn more about the DEVOTE study, visit **clinicaltrials.gov** (NCT04089566) or contact the Biogen Clinical Trial Center: **clinicaltrials@biogen.com**

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

Glossary

Infantile-onset SMA: when SMA symptoms are present at 6 months of age or younger. Often referred to as SMA Type 1.

Later-onset SMA: symptoms typically appear after 6 months but can be diagnosed throughout childhood and into adulthood. Often referred to as SMA Type 2 or 3.

Primary outcome measures: the most important measurements used to evaluate the effect of an intervention/treatment.

Secondary outcome measures: additional measurements used alongside primary outcome measures to further evaluate the effect of an intervention/treatment.

The photographs used in this brochure are real patients and the required consent to use their pictures/stories has been obtained from the patients and families. Photographs are for illustrative purposes only.

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