ForPatients
by Roche

Spinal Muscular Atrophy (SMA)

A clinical trial of risdiplam for the treatment of very young babies diagnosed with spinal muscular atrophy but are not yet presenting with symptoms

A Study of Risdiplam in Infants With Genetically Diagnosed and Presymptomatic Spinal Muscular Atrophy

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	7 Countries	NCT03779334 2018-002087-12 2023-506009-20-00 BN40703

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

An Open-Label Study of Risdiplam in Infants With Genetically Diagnosed and Presymptomatic Spinal Muscular Atrophy

Trial Summary:

A global study of oral risdiplam in pre-symptomatic participants with spinal muscular atrophy (SMA).

Hoffmann-La Roche Sponsor	**Phase 2** Phase

NCT03779334 2018-002087-12 2023-506009-20-00 BN40703
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#1 Day & # 6 Weeks	No

1. Why is the BN40703 clinical trial needed?

Spinal muscular atrophy (SMA) is a rare genetic disorder that causes progressive weakness and wasting (atrophy) in muscles used for movement (skeletal muscles). It is caused by the loss of certain specialized nerve cells (motor neurons) in the brain and

spinal cord that control muscle movement. If untreated, this results in loss of movement and even death. Early treatment has been associated with better outcomes. Risdiplam (also known as RO7034067) is the first drug to be given by mouth (orally) for treatment of SMA. Risdiplam is approved (also known as Evrysdi) for use in participants with SMA in approximately 81 countries. However, it is considered as an experimental drug (referred to as study medication) for the purpose of this study.

This clinical trial aims to understand the effects, good or bad, of risdiplam in very young babies (infants) with SMA.

2. How does the BN40703 clinical trial work?

This clinical trial has recruited infants with a health condition called spinal muscular atrophy (SMA). Infants who take part in this clinical trial will be given risdiplam once a day for up to 5 years. The trial doctor will see the infants together with parents/caregiver 15 times in the clinic for the first two years, followed by 2 visits per year for each additional year. These visits will include administration of the daily dose of risdiplam, collecting blood samples, conducting study specific tests such as muscle function tests, electrocardiogram (ECG) measurements, eye and vision tests. Total time of participation in the clinical trial will be at least 5 years, the participant may continue treatment till the end of study if risdiplam is not commercially available in the country of the site. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the BN40703 clinical trial?

The main clinical trial endpoint (the main results measured in the trial to see if the drug has worked) is to determine the percentage of participants that can sit without support after 12 months of treatment. This will be assessed in a limited set of infants. The other clinical trial endpoints are:

- Percentage of participants developing clinical features of SMA.
- Time to death and/or permanent ventilation.
- Percentage of participants alive and alive without permanent ventilation.
- Percentage of participants who are sitting without support for 5 seconds and for 30 seconds, and who are standing alone for at least 3 seconds and walking alone at least 3 steps. This will be assessed in all participants.
- Percentage of participants who can swallow and feed by mouth.

Additionally, the safety of the study medication will be determined along with its effects on the human body.

4. Who can take part in this clinical trial?

Infants could take part in this clinical trial if they were no older than 42 days of age at the time of first dose (Day 1); a minimum age of 7 days at first dose was required for the first

infant to be enrolled and were diagnosed with SMA and did not show any symptoms at the time of screening. Infants were not able to take part in this trial if they had any significant existing disease conditions or inadequate access to blood via their veins. Participants also were not able to take part if they have received any treatment such as *SMN2*-targeting antisense oligonucleotide, *SMN2*-splicing modifier, or gene therapy in the past.

5. What treatment will participants be given in this clinical trial?

Every infant who joins this clinical trial will receive once daily a dose of risdiplam in the morning. The participants who can swallow will receive it via a syringe inserted between gum and cheek of the participant. Participants who are unable to swallow the study medication and who have a feeding tube in situ should receive the study medication by bolus via the tube.

This is an open-label trial, which means everyone involved, including the participant and the clinical trial doctor, will know the clinical trial treatment the participant has been given.

6. Are there any risks or benefits in taking part in this clinical trial?

There may be risks or side effects related to the study drug or other study procedures that are unknown at this time. Most trials involve some risks to the participant. In all clinical studies so far, risdiplam has been assessed to be well-tolerated. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial drug

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drug used in this clinical trial. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly.

Risdiplam

Participants will be told about the known side effects of risdiplam, and possible side effects based on human and laboratory studies or knowledge of similar drugs. Risdiplam will be given as a solution by mouth or by a feeding tube. Participants will be told about any known side effects of oral administration or administration via a feeding tube.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

- Males and females aged from birth (1 day) to 6 weeks (42 days) of age at the time of first dose (Day 1); a minimum age of 7 days at first dose is required for the first infant to be enrolled
- Gestational age of 37-42 weeks for singleton births; gestational age of 34-42 weeks for twins
- Body weight >= 3rd percentile for age, using appropriate country-specific guidelines
- Genetic diagnosis of 5q-autosomal recessive SMA, including confirmation of homozygous deletion or compound heterozygosity predictive of loss of function of the SMN1 gene
- Absence of clinical signs or symptoms at screening (Day -42 to Day -2) or at baseline (Day -1) that are, in the opinion of the investigator, strongly suggestive of SMA
- Receiving adequate nutrition and hydration at the time of screening, in the opinion of the investigator
- Adequately recovered from any acute illness at baseline and considered well enough to participate in the study, in the opinion of the investigator
- Able and expected to be able to safely travel to the study site for the entire duration of the study and in accordance to the frequency of required study visits, in the opinion of the investigator
- Able to complete all study procedures, measurements, and visits, and the parent (or caregiver), in the opinion of the investigator, has adequately supportive psychosocial circumstances
- Parent (or caregiver) is willing to consider nasogastric, naso-jejunal, or gastrostomy tube placement during the study to maintain safe hydration, nutrition, and treatment delivery, if recommended by the investigator
- Parent (or caregiver) is willing to consider the use of non-invasive ventilation during the study, if recommended by the investigator

Exclusion Criteria:

- Concomitant or previous participation in any investigational drug or device study at any time
- Concomitant or previous administration of an SMN2-targeting antisense oligonucleotide, SMN2-splicing modifier, or gene therapy either in a clinical study or as part of medical care
- Presence of significant concurrent syndromes or diseases
- In the opinion of the investigator, inadequate venous or capillary blood access for the study procedures
- Requiring invasive ventilation, tracheostomy or awake non-invasive ventilation
- Awake hypoxemia (SaO2 < 95%) with or without ventilator support
- Multiple or fixed contractures and/or hip subluxation or dislocation at birth
- Systolic blood pressure or diastolic blood pressure or heart rate considered to be clinically significant by the investigator
- Presence of clinically relevant ECG abnormalities before study drug administration; corrected QT interval using Bazett's method > 460 ms; personal or family history (first degree relatives) of congenital long QT syndrome indicating a safety risk for patients as determined by the investigator. First-degree atrioventricular block or isolated right bundle branch block are allowed
- The infant (and the mother, if breastfeeding the infant) taking any inhibitor of CYP3A4 taken within 2 weeks, any inducer of CYP3A4 taken within 4 weeks, any OCT 2 and MATE substrates within 2 weeks and known FMO1 or FMO3 inhibitors or substrates
- Clinically significant abnormalities in laboratory test results
- Ascertained or presumptive hypersensitivity to risdiplam or to the constituents of its formulation
- Treatment with oral salbutamol or another beta-2 adrenergic agonist taken orally for SMA is not allowed. Use of inhaled beta-2 adrenergic agonists is allowed
- Infants exposed to drugs with known retinal toxicity given to mothers during pregnancy (and lactation) should not be enrolled. Anticipated need for drugs known to cause retinal toxicity during the study.

- Diagnosis of ophthalmic diseases