JUNE 2024

SAVOIR & COMPRENDRE
AVANCÉES DE LA RECHERCHE

Advances 2024 in *SMN1*-related proximal spinal muscular atrophy

© Jean-Yves Seguy/ AFM-Téléthon

This document, published for the AFM-Téléthon 2024 General Assembly, presents research news from the past 12 months regarding *SMN1*-related proximal spinal muscular atrophy: ongoing clinical trials and studies, clinical/scientific publications...

AFMTÉLÉTHON
INNOVER POUR GUÉRIR

Table of Contents

Drafted by
- Lisa Cukierman - Myoinfo, Neuromuscular Disease Information Department, AFM-Téléthon, Évry

Validation
- Dr Suzie Lefebvre
T3S – UMR 1124 INSERM
University of Paris, Paris
- Carole André
Department of Scientific Operations and Innovations, AFM-Téléthon, Évry

English translation
Master TST students, UHA Mulhouse :
- Marion Dujardin
- Fiona Bregu
- Brunella Adami
- Kim Klinger

And english translation review
- Anakin Petit
- Lucile Chaure
- Léna Turenne
- Améline Dillig
- Louisa Garriga
- Lara Hollander
- Ozlem Yayla

Acknowledgments
- We would like to thank all the individuals affected by this disease who have taken the time to review and amend all or part of this document.

*

**

SMN1-related proximal spinal muscular SMA

Also called "**5q SMA**", due to the gene responsible for the disease being on the fifth chromosome, it's a **degenerative disease of the motor Neuron**, the neural cell that sends the order to contract the muscle from the spinal cord.

Main symptoms

Weakness and degradation of the so-called "proximal" muscles (atrophy), meaning those closest to the torso: shoulder and arm muscles for the upper limbs and hip and thigh muscles for the lower limbs.

Very variable depending on the type of SMA, which depends on the age of onset and the severity of the symptoms.

Multiple types

Standard clinical classification without treatment.

Type 0
Prenatal
Decreased movements of the fetus

Type I
0 – 6 months
Unable to sit up

Type II
6 – 18 months
Able to sit up. Unable to walk

Type III
18 months – end of adolescence
Able to walk. Symptoms before the age of 6 years

Type IV
Adult
Acquired ability to walk. Symptoms in adulthood

Now that **the treatments are available**, this classification is bound to change, specifically for the patients treated before the onset of symptoms (presymptomatic or asymptomatic).

3 available treatments in France

Spinraza®
Antisense oligonucleotide
presymptomatic SMA, SMA type I, II and III

Zolgensma®
Product of gene therapy
presymptomatic SMA, SMA type I and II

Evrysdi®
Product of splicing modifiers
presymptomatic SMA, SMA type I, II and III

* EMA approved but waiting to be commercialized in France

In numbers

3 out of 100,000 patients with SMA

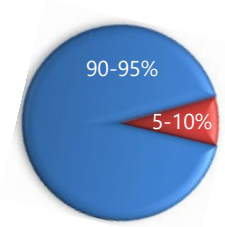
675 scientific articles published between May 2023 and May 2024 *(PubMed)*

93 clinical trials
20 of them in France
(ClinicalTrials.gov 31/05/24)

What causes it?

☑ Anomalies in the ***SMN1* gene** (on the fifth chromosome) lead to the halt of the **SMN** survival protein production (*Survival Motor Neuron*).

☑ Autosomal recessive transmission: two specimens of the *SMN1* gene, each present on a chromosome 5, must contain a genetic anomaly.

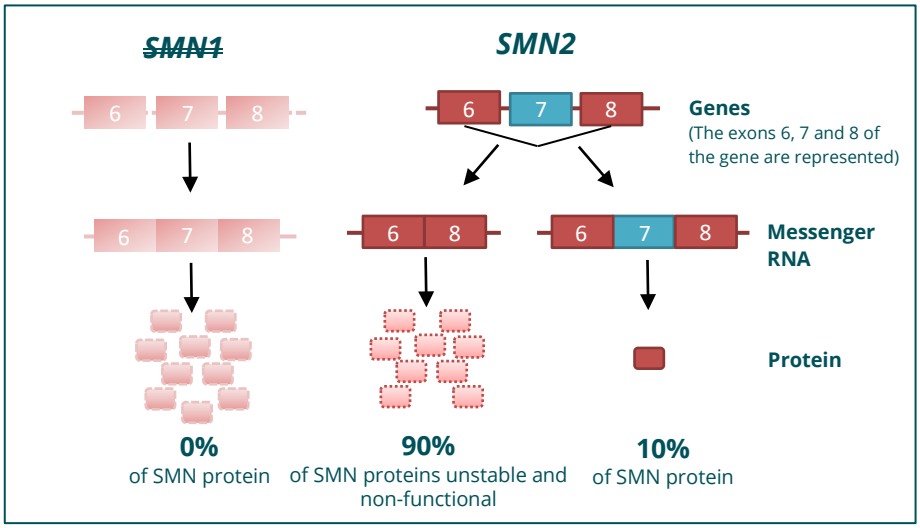


Two types of genetic anomalies

- No copy of the *SMN1* gene on the chromosome 5 pair (homozygous loss of the *SMN1* gene).
- No copy of the *SMN1* gene present on one of the chromosome 5 and anomaly of the *SMN1* gene on the other chromosome 5 (heterozygous loss of the *SMN1* gene).

☑ **An *SMN2*** gene present on the fifth chromosome in one or multiple copies: its sequence is practically identical to that of the *SMN1* gene, with the exception of a nucleotide in **exon 7**.

☑ The *SMN2* gene mostly produces a shortened, **barely functional and easily destroyed SMN protein**, which is lower in quality than a normal SMN protein, identical to that produced by the *SMN1* gene.



☑ The higher the number of *SMN2* copies (between 1 and 6), the more the severity of the disease seems to decrease.

Number of copies of the *SMN2* gene	Clinical signs		
	SMA I	SMA II	SMA III/IV
1	7%	<1%	0%
2	73%	16%	5%
3	20%	78%	49%
4 to 6	<1%	5%	46%

To learn more about SMA
www.afm-telethon.fr/fr/fiches-maladies/amyotrophie-spinale-proximale-liee-smn1

3 Important facts from the past 12 months

A growing interest in **anti-myostatins**

They block myostatin, a natural muscle growth inhibitor, in order **to increase muscle mass**.

Used in **addition to the three authorized treatments** to reinforce their effects by targeting the muscle.

Multiple ongoing clinical trials, including
one in France, the SAPPHIRE trial.

The neonatal screening is unfolding in more and more countries to treat patients faster

In the **United States**, 100% of all babies are tested.

In **Europe**, 65% of all babies are tested.

In **France**, the DEPISMA project

- Prefiguration program
- Over the span of 2 years
- Grand Est and Nouvelle Aquitaine regions
- 81 maternity hospitals
- 7 babies screened out of 81,000 tested
- 5 of them treated

The SMA Registry France, the collection of data continues

Number of patients

- 1,285 patients
- Including 610 children

Number of copies *SMN2*

- 1% 1 copy
- 18% 2 copies
- 50% 3 copies
- 16% 4 copies
- 0% 5 copies
- 15% unavailable information

Types of SMA

- 23% SMA I
- 38% SMA II
- 36% SMA III
- 2% SMA IV
- 1% presymptomatic

Treatment

- 44% on Spinraza®
- 26% on Evrysdi®
- 8% on Zolgensma®
- 22% untreated

Clinical trials

Clinical trials are used to evaluate a potential treatment (a drug candidate, a medical device...), to make sure it is well tolerated and effective in fighting a disease. It is then tested throughout multiple consecutive trials representing different phases (I, II, III, IV) that will answer specific questions about the product: is it well tolerated? What is the optimal dose? Is it effective and on what criteria (walking, motor function, breathing...)? After being put on the market, the product now used in the real world will still be observed to improve the knowledge and identify any unexpected or severe side effects that might occur.

www.afm-telethon.fr/fr/vivre-avec-la-maladie/mon-parcours-de-soins/les-essais-cliniques-en-pratique

Clinical trials of drugs in France

TRIAL TITLE Participants	THERAPEUTIC APPROACH	PRECLINICAL RESEARCH	CLINICAL DEVELOPMENT			REGULATORY ASPECT
			PHASE I	PHASE II	PHASE III	
DEVOTE trial and extension phase	**Gene therapy:** **Oligonucleotide** targeting *SMN2*					

Spinraza® (nusinersen)

Worldwide

- More than 14,000 patients treated as of Dec. 31, 2023
- In more than 71 countries

© AFM-Téléthon

In France

- Prescribed during a consultation for neuromuscular diseases after a multidisciplinary consultation meeting
- Reimbursed for SMA I, II and III

Method of administration

- Regular intrathecal injections between two lumbar vertebrae at the hospital.

Antisense oligonucleotide

*An **antisense oligonucleotide (OAS)** is a DNA fragment, generally synthesized in a laboratory that specifically links itself to a natural messenger RNA (the sequence of the antisense oligonucleotide is complimentary to that of the messenger RNA). It can therefore modify the messenger RNA in specific places (skipping or incorporating exons by intervening in the maturation phase (splicing).*

First authorized SMA treatment since 2017 in France, Spinraza® (nusinersen) is an antisense oligonucleotide developed by Biogen that has an effect on **the maturation (splicing) of the *SMN2* gene.** It allows the expression of the SMN protein in the motor neurons with a real clinical benefit but of varying significance depending on SMA type and age at the start of treatment.

It is directly injected into the cerebrospinal fluid between two lumbar vertebrae, via intrathecal administration (like a spinal puncture) to reach the spinal cord and the brain.

In France, a reimbursed treatment for SMA type I, II and III

In France, Spinraza® is prescribed in special consultations for neuromuscular diseases after a multidisciplinary consultation meeting (RCP), during which multiple healthcare experts specialized in SMA share their points of view to pick the best care for the patient. It is reimbursed for patients with SMA type I, II and III.

www.afm-telethon.fr/fr/vivre-avec-la-maladie/mon-parcours-de-soins/les-medicaments/le-spinrazar-dans-la-sma

Trials in progress

Multiple clinical trials that had Biogen as a sponsor continue to evaluate the effects of Spinraza® depending on the age at the start of treatment, with higher doses than those currently used...

Main Spinraza® trials in progress

NURTURE
SMA presymptomatic
25 participants (< than 6 weeks)
Abroad
8 years follow-up
May 2015 – Dec. 2024
NCT02386553

DEVOTE
SMA High doses
145 participants
France and abroad
1 year follow-up
Mar. 2020 – Jun. 2024
NCT04089566

Extension DEVOTE
5 years follow-up
Apr. 2021 – Jul. 2026
NCT04729907

© AFM-Téléthon

New results with Spinraza®

Multiple studies have evaluated the effects of Spinraza® (nusinersen) on a long- or short-term basis and on different functions, in the context of clinical trials or by collecting "real life" data of patients undergoing treatment.

*Complementary to clinical trials, observational studies, also called "**real world studies**" are conducted without changing the patient care. They focus on data that can come from different sources: medical records, reimbursement of medical care, medical smart devices... These studies reflect the "real life" of the patients even more. Another advantage is that they can include a high number of participants.*

Before the onset of symptoms

New top-line results from the **NURTURE trial** confirm that the benefits of Spinraza® over time in presymptomatic SMA, meaning before the first onset of the disease's symptoms, are that the child participants, aged on average 4.9 years, are alive and none of them need permanent assisted ventilation.
Crawford TO et al. Muscle Nerve. 2023

With a higher dose

Made of three parts, the **DEVOTE trial** evaluates the tolerability end efficiency of Spinraza® in higher doses than those currently used (12 mg) with a triple objective: improve the efficiency of the treatment, space out the injections and adapting the dose to the weight of the patient, when it currently is identical for infants, children and adults.
After 10 months of treatment, the six participants from the first round of the trial, aged 6 to 12 years, have tolerated the 28 mg dose Spinraza® well. Furthermore, even if it was not planned to evaluate the product's efficiency in this round of the study, the motor function of those participants has improved or stabilized.
This trial, which notably takes place in France, in Garches and in Toulouse, continues to evaluate higher doses of Spinraza® throughout the other two planned rounds.
Finkel RS et al. J Neuromuscul Dis. 2023

In children, the French experience

Doctors from the French reference centers for neuromuscular diseases did a follow-up study of three years on 37 children with SMA, treated with Spinraza® before the age of 3. The vast majority (93%) of them noticed their motor functions improve. However, only the patients with three copies of the *SMN2* gene were capable of standing up and walking with an aid by the end of the study, none of those with two copies were able to do so. The cerebral, respiratory and orthopedic improvements are also more important if the child presents three copies rather than two. All patients with two copies and two thirds of those with three have developed scoliosis.
Audic F et al. Arch Pediatr. 2024

In adults

- The follow-up study by Spinraza® of 237 adults aged 16 to 17 years with SMA, over the course of three years showed a stabilization or an improvement in the scores evaluating their motor functions. To this day, it was the longest follow-up study of Spinraza® on a large group of affected adults.
Günther R et al. Lancet Reg Health Eur. 2024

- The treatment of 105 adults (with a median age of 32 years) and 15 "older" children (with a median age of 9.3 years) with SMA type I, II and III lead to a functional improvement over the course of a follow-up lasting up to 2.5 years.
Łusakowska A et al. Orphanet J Rare Dis. 2023

Diaphragmatic weakness

The study of the diaphragm of the 24 adults with SMA type I, II or III shows that it can be weakened for 20 to 30% of them without treatment. However, after more than 2 years of treatment, the diaphragmatic function has improved.

Freigang M et al. Muscle Nerve. 2023

With scoliosis

An analysis of Spinraza® treatment during 2.5 years on 95 children with late onset SMA shows it stabilizes or improves their motor functions, regardless of the severity of the scoliosis at the beginning of treatment (moderate, mild or absent).

Dunaway Young S et al. J Clin Med. 2023

In the long term

In Japan, a real-world study led on a large group of 524 patients with SMA confirms the efficiency of Spinraza® on the motor functions over a median period of two years.

Tachibana Y et al. Int J Neurosci. 2023

Quantitative muscle imaging

Researchers from the Netherlands have tested magnetic resonance imaging (MRI) of the muscle as a possible measuring tool for the efficiency of Spinraza® in eight children with SMA, aged 9 years on average. The analysis of the images over a year of observation shows that the microstructure of the muscle seems to have improved, in the thighs in particular, but the progression of fatty tissue persists in the other muscles.

Otto LAM et al. J Neuromuscul Dis. 2024

In France, ongoing observational studies

- A study follows the evolution of the measuring of the 32-item motor function in adults with SMA type II treated with Spinraza®. It takes place in seven French investigation centers (in Lille, Lyon, Marseilles, Nice, Paris and Toulouse).

Study of the motor function in SMA type II

In France	20 (over the age of 18)	Recruitment completed	Feb. 2020 – Aug. 2025 27-month follow-up

NCT04159987

- A French study, REALITY, evaluates the benefits of using a "virtual reality" headset, in order to decrease the anxiety and pain that can be linked to the intrathecal injections of Spinraza®, between two lumbar vertebrae. This study takes place in Angers, Brest, Clermont-Ferrand, Garches, Lille, Nancy, Nice, Paris, Strasbourg and Toulouse.

REALITY trial

In France	62 (over the age of 7)	Ongoing recruitment	May 2022 – Oct. 2024 1-year follow-up

NCT05354414

- The effects of Spinraza® on the motor function capacities are under ongoing evaluation in SMA type II and type III in the teaching hospital of Amiens.

NUSI-AD-5qSM trial

In France	24 (over the age of 18)	Ongoing recruitment	Jan. 2023 – Jun. 2025 1-year follow-up

NCT04576494

- To evaluate the role of non-invasive ventilation in the occurrence of respiratory bacterial infection or superinfections, an ongoing trial is recruiting children with SMA, younger than 12 years old under Spinraza® treatment and non-invasive ventilation. It takes place in the teaching hospital of Amiens.

AVNIR trial

In France	8 (under the age of 12)	Ongoing recruitment	Jan. 2023 – Sept. 2024 1-year follow-up

NCT05712330

A new device to administer Spinraza® under study

A pivotal trial of the first implantable device called *ThecaFlex,* shaped like a box placed under the skin and attached by a very thin tube (catheter), to the space that surrounds the spinal cord, into the cerebrospinal fluid, has been administered to its first patient in January 2024. This device allows the repeated administration of Spinraza® as an alternative to the current intrathecal injection, administered via spinal puncture between two lumbar vertebrae. This PIERRE trial happens in collaboration with the *Biogen* Laboratory that produces Spinraza® and should include 90 participants in the United States and Europe.

Alcyone Therapeutics. Press release of 3 January 2024

PIERRE trial of a Spinraza® administration device

Europe and abroad	90 (over the age of 3)	Ongoing recruitment	Nov. 2023 – Mar. 2027 1-year follow-up

NCT05866419

Zolgensma® (onasemnogene abeparvovec)

Worldwide

- More than 3,700 patients treated as of December 12, 2023
- In more than 51 countries

In France

- Post-ATU mechanism
- Favourable opinion regarding reimbursement: SMA types I and II, or presymptomatic with up to 3 copies of *SMN2*

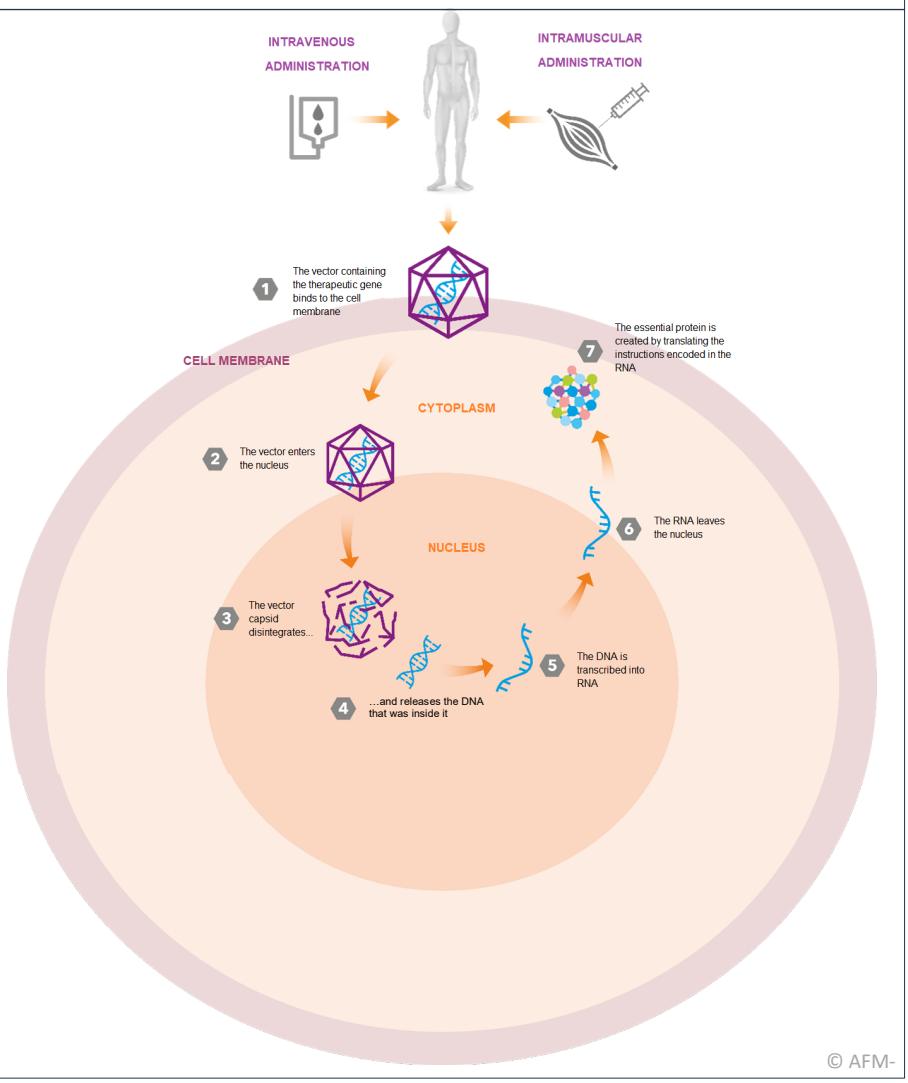
Method of administration

- A single injection by intravenous infusion (at hospital)

A gene therapy product

Zolgensma® or onasemnogene abeparvovec (AVXS-101) is a gene therapy treatment for *SMN1* gene-related proximal spinal muscular atrophy (SMA). This treatment consists in **introducing the functional *SMN1* gene** using a transportation method, or vector (an adeno-associated virus AAV) to replace the defective *SMN1* gene.

What is gene therapy?



By allowing SMN protein production, it showed quick and lasting benefits: improvement of motor performances, autonomous breathing, increased life expectancy... However, these benefits vary depending on patients, SMA type, age at the start of the treatment, symptoms they were presenting when the treatment started...

Trailblazing work conducted by AFM-Téléthon laboratories

The efficacy of this gene therapy was demonstrated for the first time in mice models with SMA, thanks to researchers at Généthon and the Institute of Myology. Généthon then granted a license to AveXis to use the patents relating to the AAV9-SMN products, and its administration in vivo into the central nervous system, by intrathecal or intravenous route.

In Europe, a "conditional" marketing authorization

In 2020, Zolgensma® obtained a European "conditional" Marketing Authorization which only concerns babies and young children weighing less than 21 kg, presenting SMA type I or carriers of a bi-allelic mutation of the *SMN1* gene and of a maximum of 3 copies of the *SMN2* gene.

The health authorities in each European country will now assess the therapeutic and economic benefit of the treatment, in order to finalize its marketing status in their country.

www.ema.europa.eu/en/medicines/human/EPAR/zolgensma

In France, a post-ATU mechanism

In France, Zolgensma® is prescribed in the context of a **post-ATU mechanism** for children weighing less than 21 kg "*with a clinical diagnosis of SMN1-related proximal spinal muscular atrophy (SMA) type I or with SMA with a bi-allelic mutation of the SMN1 gene and up to 3 copies of the SMN2 gene.*"

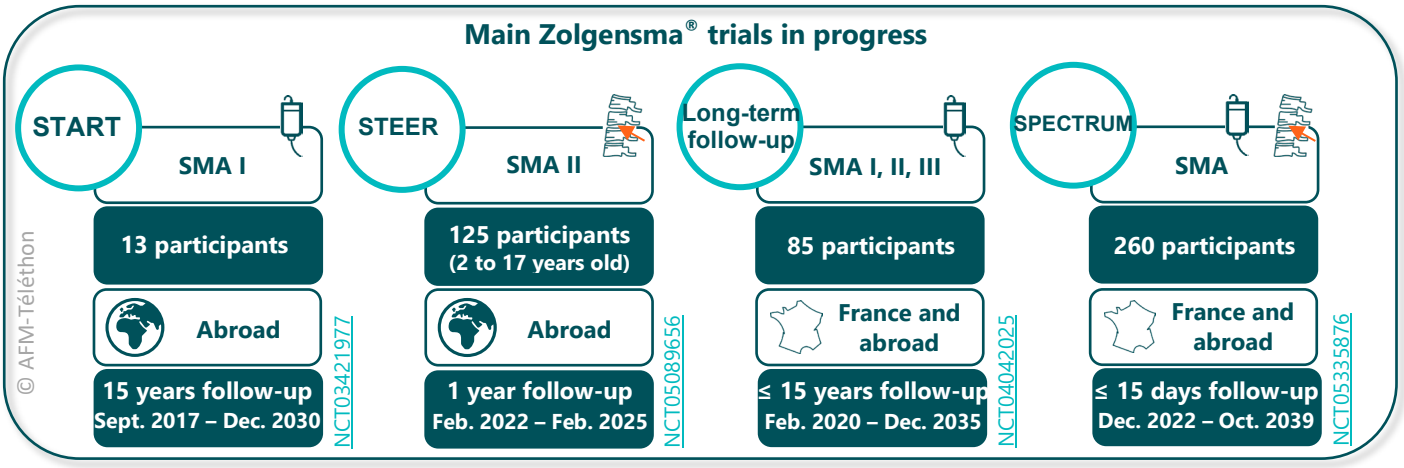
Since most data currently available only concerns children weighing less than 13.5 kg, MDT (multidisciplinary team) consultation meeting decisions are made according to specific criteria and depending on each patient's medical situation.

www.afm-telethon.fr/fr/vivre-avec-la-maladie/mon-parcours-de-soins/les-medicaments/le-zolgensmar-dans-la-sma (in French)

Temporary Authorization for Use (ATU) *is a regulatory mechanism which allows the use of a medicine before it is brought to market for a specific indication (a specific disease).*

Trials in progress

Other clinical trials conducted by Novartis Gene Therapies continue to assess the more or less long-term effects of Zolgensma® worldwide in different SMA-types, with different injection routes (intravenously or intrathecally).



New results with Zolgensma®

Before the manifestation of symptoms

A *post-hoc* analysis of the results of the **SPR1NT trial** showed positive effects of the gene therapy product Zolgensma® on bulbar function in presymptomatic SMA, meaning before the manifestation of initial symptoms: the 29 participants were able to swallow normally, to eat orally, while maintaining respiratory stability.

Shell RD et al.Neuromuscul Disord. 2023

In older and heavier children

▪ Though mainly assessed in children weighing less than 13.5 kg and under two years old, the gene therapy product also showed results in a British study on slightly older (up to 7 years old) and heavier (up to 20 kg) children with SMA type I: it is well tolerated and improves their motor function. However, as weight increases, so does the duration of corticosteroids use that must complement the Zolgensma® treatment, as well as temporary liver damage risk, hence the importance of a careful follow-up before and after treatment.

Gowda V et al. Lancet Reg Health Eur. 2023

▪ In the context of the year-long **SMART trial**, Zolgensma® was administered intravenously to 24 symptomatic children aged between 1.5 and 9 years, weighing 8.5 to 21 kg, some of whom (87.5% of participants) had benefited from another innovative therapy (Spinraza® or Evrysdi®). New results of this trial, published in March 2024 by a Novartis press release and presented during the annual Muscular Dystrophy Association (MDA) conference, showed the good tolerability and efficacy of the product in this pediatric population after one year of treatment. The motor functions of most participants remained stable or improved. Three participants gained the ability to stand up with assistance, and another, to walk with assistance. The six participants who were able to walk at the start of the trial maintained this ability until the end of the study.

Novartis. Press release of March 4, 2024

On bulbar function

An American team conducted *post-hoc* analyses on the results of the START (phase I), STR1VE-EU and STR1VE-US (phase III) trials of Zolgensma®. They concerned a total of 65 infants with SMA type I who were followed up from the age of 18 to 24 months. The results showed additional benefit of treatment on bulbar muscles (throat, tongue, cheeks, lips…), with improvement of the ability to feed sufficiently, swallow and communicate. They also regained stabilization in respiratory function.

McGrattan KE et al. J Neuromuscul Dis. 2023

Depending on antibody levels against AAVs

A study conducted on 882 children aged 6.5 months on average showed high levels of antibodies against AAV9 (the viral vector used in Zolgensma®) in 13% of them. However, these important levels concerned only 1.1% of children over 21 months old, suggesting maternal antibodies transfer through the placenta. A new AAV9-antibodies test could be considered for children whose levels were high at a very young age so that they may benefit from the treatment.

Day JW et al. Mol Ther Methods Clin Dev. 2023

From a survey by the Cure SMA association

The results of a survey conducted by the *Cure SMA* American association, which were published in 2023, concerned 614 of its members, 64 of whom had received Zolgensma® treatment between the ages of 6 and 23 months. All of the latter were able to sit up without assistance, and over half of them (58.8%) were able to walk with assistance. The hospitalization or surgery rates were lower and deglutition disorders were less frequent than in patients who had not received treatment. None of them required tracheotomy with a ventilator. The patients' quality of life was also improved.

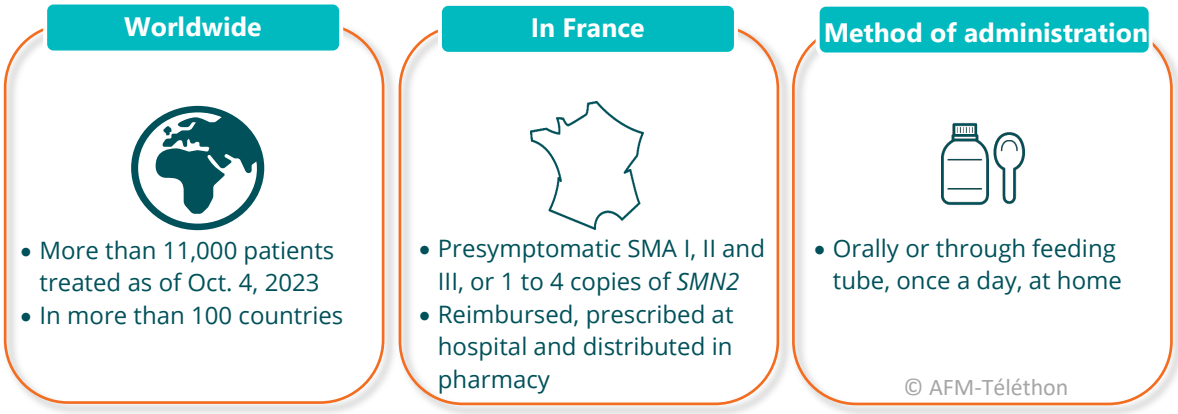
Toro W et al. Adv Ther. 2023

From the RESTORE registry

The analysis of the data of 168 patients treated with Zolgensma® from the RESTORE registry (a SMA patients data repository) provided new results showing effectiveness in a real-life setting. All of the children who were treated between the ages of one and 10 months improved or maintained their motor performances over the course of a 14-month follow-up on average. Over half of them (58.3%) could be identified before showing symptoms of SMA thanks to neonatal screening and obtained a better motor function score (CHOP INTEND) than those who were identified when clinical signs of the disease appeared.

Servais L et al. J Neuromuscul Dis. 2024

Evrysdi® (risdiplam)



*Genes are structured as alternating coding sequences, the **exons**, and non-coding sequences, the introns. The exons are the parts of the gene that are used by the cell machinery as an assembly guide for protein production.*

A small drug molecule administered orally

Developed by Hoffmann-La Roche, Evrysdi® (risdipalm) is an ***SMN2* gene splicing modifier**. It induces the reintegration of exon 7 in order to increase SMN protein synthesis.

This treatment improves or stabilizes the motor function, with effects that may however vary depending on SMA type and age at the start of the treatment.

www.afm-telethon.fr/fr/vivre-avec-la-maladie/mon-parcours-de-soins/les-medicaments/le-zolgensmar-dans-la-sma (in French)

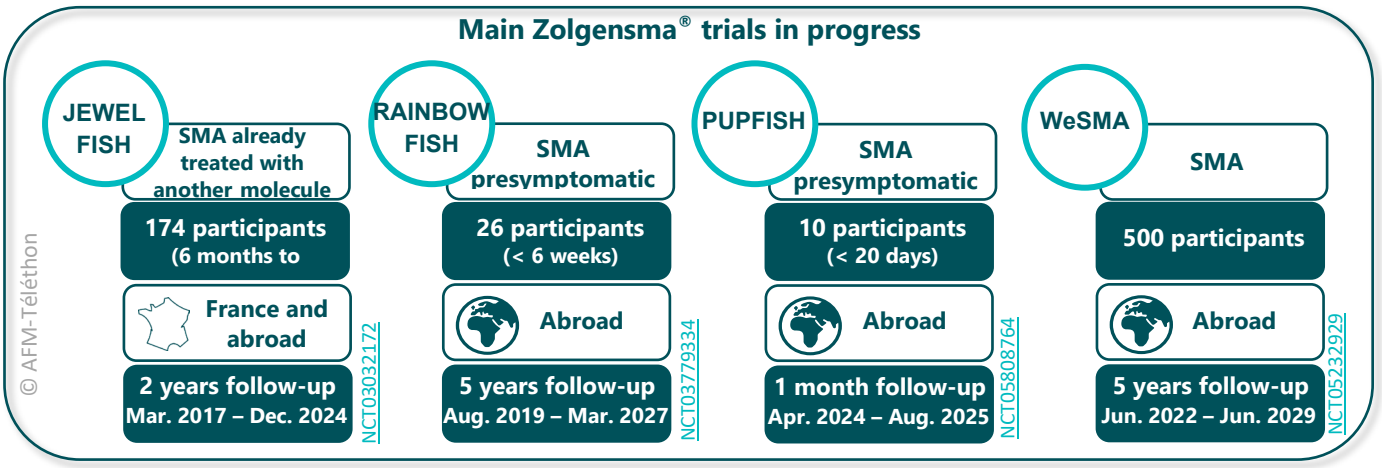
In France, a treatment reimbursed and available in pharmacy

- In France, prescription of Evrysdi® is restricted to neurologists or pediatric neurologists at reference centers or centers of expertise for neuromuscular diseases after a favourable opinion is provided by a multidisciplinary team (MDT) consultation. It is prescribed at hospital but available in retail pharmacies.
- Evrisdy® is currently marketed and reimbursed for patients with SMA type I, II and III.
- In August 2023, the European Commission approved administration of Evrysdi® at birth (in presymptomatic cases) rather than from two months of age onwards, as was the case earlier. However, it will take more time for this new indication to be effective in France.

Roche.Press release of August 29, 2023

Trials in progress

Several more or less long-term Evrysdi® trials in SMA conducted by the sponsor Hoffmann-La Roche are in progress worldwide, on different types of SMA.



New results with Zolgensma®

Before the manifestation of symptoms

After a year of treatment, a large majority (80%) of the young children in the **RAINBOWFISH trial** treated with Evrysdi® before the disease's initial symptoms appeared (presymptomatic SMA) were able to sit up on their own for at least 30 seconds. Furthermore, the 26 infant participants in this trial can swallow and eat orally; none of them need permanent ventilation.

Roche. Press release of October 4, 2023

In SMA type I

New results after four years of treatment with Evrysdi® on SMA type I from the **FIREFISH trial** confirm the product's long-term efficacy: 91% of the children who were treated between the ages of one and seven months are alive, with their motor function maintained or improved. The vast majority are able to eat orally.

Roche. Press release of June 30, 2023

In adults

Two studies conducted on adults with SMA type II and III, mainly non-mobile, showed that the product was well tolerated. Furthermore, it improved or stabilized the motor function of half of the patients and improved their ability to swallow.

Bjelica B et al. BMC Neurol. 2024
Brakemeier S et al.J Neurol. 2024

From a literature review

A systemic review combined with a meta-analysis on 11 studies showed the efficacy of Evrysdi® on motor function after a year of treatment in 57% of patients with SMA type I. Over half of them were able to eat orally and control their head. The motor function scores also improved in patients with SMA type II and III. However, the product does not seem to have a significant effect on respiratory function.

Pascual-Morena C et al. Pharmacotherapy. 2024

Trials combining two treatments

There are **two main types of trials** combining several treatments. In some trials, the medicine available on the market (Spinraza®, Zolgensma®, Evrysdi®), which directly target the production of SMN protein, are assessed together. Other trials combine them with treatments developed to target the muscle, such as anti-myostatins, which increase muscle mass by blocking myostatin, a natural muscle growth inhibitor. Together, they could improve muscle function and strength.

Trial	Spinraza®	Zolgensma®	Evrysdi®	Anti-myostatin
RESPOND	X	X		
ASCEND	X		X	
RISE	X		X	
FORCE	X	X	X	
HINALEA 1		X	X	
HINALEA 2		X	X	
MANATEE			X	X
RESILIENT	X	X	X	X
TOPAZ	X			X
SAPPHIRE	X		X	X
ONYX	X		X	X

RESPOND study

The RESPOND study, which started in January 2021 with Biogen as its sponsor, assesses the effects of **Spinraza® (nusinersen)** over a period of two years on very young children with SMA who were already treated with **Zolgensma®** with insufficiently satisfactory effects. Together, both treatments may target all of the body's motor neurons more effectively to increase SMN protein production.

- Results at six months in 29 participants showed that the motor function of most participants was improved. These data suggest that Spinraza® may provide additional benefits after gene therapy. These will need to be confirmed in the long run in all participants.

Biogen. Press release of June 30, 2023

Phase IV
Pharmacovigilance

RESPOND study

Abroad (outside France)	46 (2 to 36 months)	Recruitment completed	Jan. 2021 – Oct. 2025 2 years follow-up

NCT04488133

ASCEND trial

A phase III trial is in the process of recruiting 45 participants, to assess the effects of a **higher dose of Spinraza® (nusinersen)** than the one currently being used (dose assessed in the DEVOTE trial) in patients with a late-onset form of SMA being treated with **Evrysdi® (risdiplam)**.

This trial led by Biogen is being conducted in several countries around the world, but not in France.

ASCEND trial

Phase III
Efficacy

Abroad (outside France)	45 (15 to 50 years old)	Ongoing recruitment	Jan. 2022 – Jun. 2027 2.5 years follow-up

NCT05067790

RISE trial

An ongoing American study is assessing the effects of a change in treatment in 10 participants with 3 or 4 copies of SMN2 over a period of three years: they will receive **Evrysdi®** after being treated with **Spinraza®** for at least two years.

RISE trial

Phase IV
Pharmacovigilance

Abroad (outside France)	10 (2 to 35 years old)	Recruitment completed	Nov. 2022 – Jun. 2026 3 years follow-up

NCT05522361

STRENGTH trial

Novartis recently started a phase III trial to assess the effects of **intrathecally injected Zolgensma®** in patients who interrupted their **Spinraza® or Evrysdi®** treatment. This trial includes two groups of participants, aged 2 to 5 years and 6 to 12 years. It is also being conducted in France, in Bron and Toulouse.

STRENGTH trial

Phase III
Efficacy

France and abroad	27 (2 to 12 years old)	Recruitment completed	Jan. 2023 – Dec. 2024 1 year follow-up

NCT05386680

HINALEA 1 and HINALEA 2 trials

These two open-label studies assess the safety and efficacy of **Evrysdi®** in children under two years old with 2 copies of the *SMN2* gene who are already treated with **Zolgensma®**. Both are conducted in the United States with Hoffmann-La Roche as their sponsor.

*An **open-label trial** is a therapeutic trial in which doctors and participants are aware of the treatment being tested.*

- The former will include 28 children who received the Zolgensma® injection between 3 and 7 months before being included in this study.

Phase IV
Pharmacovigilance

HINALEA 1 trial

Abroad (outside France)	28 (under the age of 2)	Ongoing recruitment	Apr. 2024 – Mar. 2028 2.5 years follow-up

NCT05861986

- The latter will concern 28 children who received the Zolgensma® injection at the earliest 3 months before being included in this study and who experienced functional decline or stagnation after the injection.

Phase IV
Pharmacovigilance

HINALEA 2 trial

Abroad (outside France)	28 (under the age of 2)	Ongoing recruitment	May 2024 – Mar. 2028 2.5 years follow-up

NCT05861999

MANATEE trial

The clinical trial called MANATEE, which aims to test the effects of **anti-myostatin GYM329 (RO7204239)** combined with **Evrysdi®** in SMA, is in progress. The sponsor is Hoffmann-La Roche.

Phase II
Effect/dose

Phase III
Efficacy

MANATEE trial

Abroad (outside France)	259 (2 to 25 years old)	Ongoing recruitment	Jun. 2022 – Jun. 2026 4.5 years follow-up

NCT05115110

RESILIENT trial

A phase III trial with another **anti-myostatin, taldefgrobep alfa**, conducted by Biohaven Pharmaceuticals, which started in July 2022 with 269 patients with SMA already treated with **Spinraza®, Zolgensma® or Evrysdi®**.

Phase III
Efficacy

RESILIENT trial

Abroad (outside France)	269 (4 to 21 years old)	Recruitment completed	Jul. 2022 – Jan. 2025 1 year follow-up

NCT05337553

*The designation "**orphan medicine**" applies to candidate medicines (whose efficacy has not been proven yet) in rare diseases, in order to facilitate the different stage of their development.*

TOPAZ, SAPPIRE and ONYX trials with apitegromab

- Developed by Scholar Rock, **Apitegromab (SRK-015)** is also **an anti-myostatin**. It has received the orphan medicine designation from the American health authorities (the FDA or Food and Drug Administration).

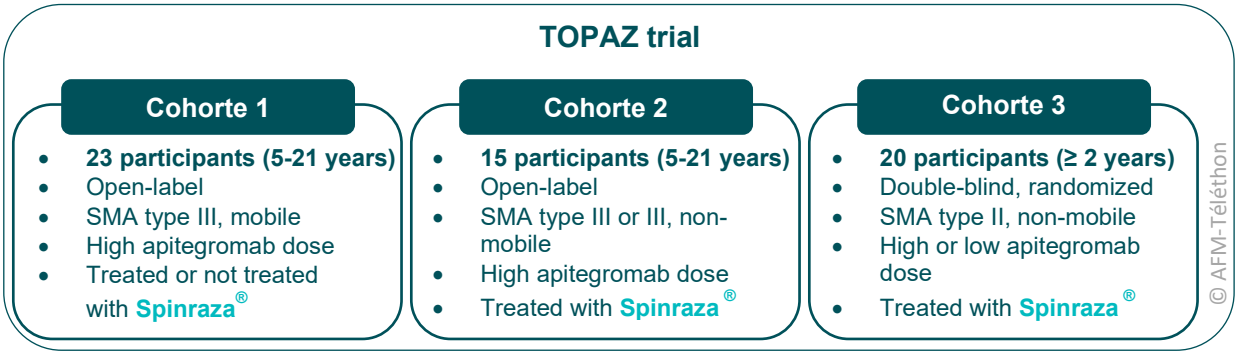
Phase I
Tolerability

▪ Scholar Rock has successfully conducted a phase I trial of SRK-015 in volunteers without the disease. They tolerated the product well, with assessment done at different doses.

TOPAZ trial

Phase II
Effect/dose

▪ The phase II TOPAZ trial was conducted in the United States and Europe (but not in France) among 58 patients with SMA type II or III, aged between 2 and 21 years. They also received a dose of **apitegromab** (either a low dose of 2 mg/kg or a high dose of 20 mg/kg) intravenously every 4 weeks for a year, with or without **Spinraza®**. Its safety and efficacy are being studied using 3 cohorts.



▪ Results at one year of treatment showed positive effects on motor function, particularly in cohort 3, which includes younger participants. Other results communicated by Scholar Rock suggest that these beneficial effects seem to last after three years of treatment as part of an extension phase.

Crawford TO et al. Neurology. 2024

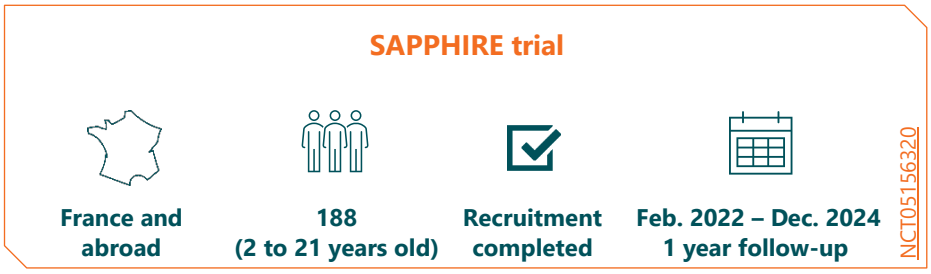
Scholar Rock. Press release of September 19, 2023

SAPPHIRE trial

▪The goal of this trial is to assess the effects of a double treatment combining **apitegromab** with **Spinraza® or Evrysdi®**. This trial, which notably takes place in France, concerns two groups of participants divided by age, who will receive apitegromab or a placebo intravenously every 4 weeks in addition to their Spinraza® or Evrysdi® treatment:

- 156 participants with SMA type II or III aged 2 to 12 years and non-mobile,
- 48 participants with SMA type II or III aged 13 to 21 years and non-mobile.

Phase III
Efficacy



ONYX trial

▪ The ONYX trial is an open-label extension phase conducted for patients who completed the previous TOPAZ and SAPPHIRE trials to assess the long-term effects of **apitegromab**.

ONYX extension phase

France and abroad	260 (2 years old or more)	Recruitment completed	Apr. 2023 – Jan. 2027 Up to 6 years follow

NCT05626855

A clinical trial with a new candidate medicine

The SYNAPSE-SMA phase II trial started recently to determine the safety, the tolerability, and the efficacy of a ClC-1 chloride channel inhibitor, **NMD670**, versus placebo in mobile patients with SMA type III. The product is administered orally twice a day for 21 days.
NMDPharma. Press release of 26 September 2023

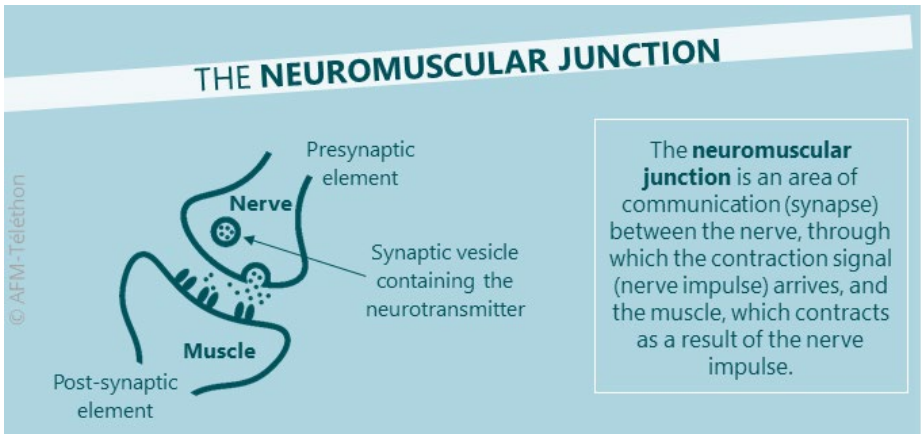
Phase II
Effect/Dose

SYNAPSE-SMA trial

Abroad (outside France)	54 (18 to 75 years old)	Ongoing recruitment	Sept. 2023 – Dec 2024 21 days follow up

NCT05794139

Already assessed in myasthenia gravis, it should target the muscle and improve the neuromuscular transmission.



In France, some clinical trials are currently in progress

Several studies are being conducted in France to assess the quality of life of adults with SMA, identify predictive markers of the disease progression, or quantify the motor function of infants with SMA and treated with innovative therapies.

▪ In Bron (Lyon suburb), an ongoing trial assesses the quality of life of adults with SMA by collecting in an online questionnaire demographic and social data and data on the activities, participation…

QOLSMA trial

In France

175 (18 to 85 years old)

Ongoing recruitment

Oct. 2022 – Oct. 2024 1 visit

NCT05366465

▪ A trial is in progress among adults with SMA type III or type IV in order to identify predictive markers of the disease progression and obtain relevant and sensitive measurement tools to use as assessment criteria in future clinical trials. It is being conducted in Garches, Lille, Lyon, Montpellier, Nantes, Nice, Paris, Saint-Étienne, Saint-Pierre (Reunion Island), Strasbourg, and Toulouse.

SMOB trial

In France

100 (18 to 70 years old)

Ongoing recruitment

Jul. 2021 – Jul. 2025 2 years follow up

NCT04690998

▪ Another study is in progress to quantify the motor function of infants with SMA treated with innovative therapies, whose symptoms appeared before the age of one, and who do not present any acute respiratory failure or bulbar involvement. It is being conducted at the Necker Children's Hospital (Paris).

IMUSMA trial

In France

60 (under the age of 2)

Ongoing recruitment

Mar. 2021 – Mar. 2027 2 years follow up

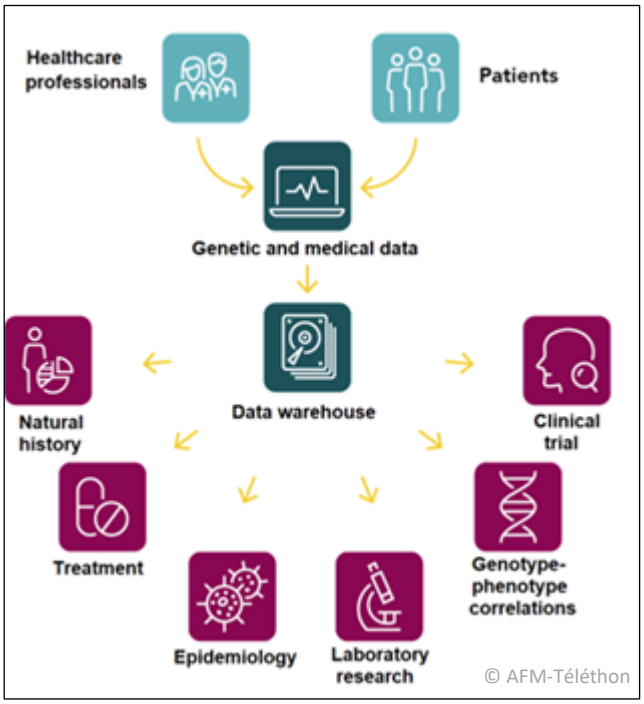
NCT04833348

Databases

Databases and registers consolidate medical and genetic data from patients with the same disease. The analysis of collated data helps to clarify the natural history of the disease, to establish genotype/phenotype correlations, to facilitate the recruitment of participants for clinical trials...

*What doctors call the **natural history** of a disease is the description of the different manifestations of a disease and how they develop over time in the absence of treatment.*

*Studies of **genotype/phenotype correlations** explore potential links between the genetic characteristics (genotype) and the visible characteristics (phenotype: size, color and shape of the eyes, hair color, sign of a disease...). This way, one can identify a link between a genetic abnormality and the signs of a genetic*



The SMA registry France

The goal of the French registry of patients with SMA is to collect and analyze data from any individual with SMA (of all types, I to IV), whether living or deceased, whether the individual is or has been taking an innovative treatment or not, who has been seen and/or followed up in a reference center, a center of expertise or a neuromuscular disease specialized consultation, since September 2016.

- The SMA Registry France is intended to last 10 years. It was set up at the beginning of 2020 and is being led by Prof. Susana Quijano-Roy at the Raymond-Poincaré Hospital in Garches in conjunction with the clinical research unit of the Ambroise-Paré Hospital (part of the AP-HP, the Paris Network of Public Hospitals).

Results in April 2024

- A total of **1,285 patients** were included in this registry: 610 children and 675 adults.
- The distribution by **types of SMA** corresponds to 23% of SMA type I, 38% of SMA type II, 36% of SMA type III, 2% of SMA type IV, and 1% of presymptomatic SMA.
- Regarding of the **number of copies of the *SMN2***, the distribution is 1 copy for 1% of the participants, 2 copies for 18%, 3 copies for 50%, 4 copies for 16%, and 5 copies for 0% (15% of the data are not available).
- In terms of **treatment**, it corresponds to 44% of the patients on Spinraza® (nusinersen), 26% on Evrysdi® (risdiplam), 8% on Zolgensma® (onasemnogene abeparvovec), and 22% without any treatment.
- Altogether, **64 centers** take part in this registry: 32 pediatric centers, 29 centers for adults, and 3 mixed centers.

French registry of patients with spinal muscular atrophy (SMA registry France) Newsletter April 2024

French registry of patients with SMA

In France

Objective 1,000 patients

Ongoing recruitment

Created in January 2020

NCT04177134

The SMArtCARE German observational study

SMArtCARE is an observational study of German-speaking patients with *SMN1*-related proximal spinal muscular atrophy, residing in Germany, Austria or Switzerland. The objective is to learn more about the progression of the disease and its daily impact.

▪ This database, which was constructed to take into account data in a real-life setting regarding both the impact of innovative therapies and aspects of traditional care, aims to be a prospective longitudinal follow-up tool, for doctors themselves (whether they are prescribers or not), researchers, health authorities and patient associations. Healthcare companies are linked to the setting up of SMArtCARE, but not with the analysis of its data.

***SMArtCARE* databases**

Abroad (outside France)

Ongoing recruitment

Created in August 2018

www.smartcare.de/en/index.html

Neonatal screening

The neonatal screening of a disease consists of systematically testing all the newborns for this disease at birth.
In France, screening of this type has been first established for six diseases: phenylketonuria (since 1972), congenital hypothyroidism (1978), congenital adrenal hyperplasia (1995), sickle-cell disease (1989 in the French overseas territories and 1995 in mainland France), cystic fibrosis (2002) and, more recently, medium-chain acyl-CoA dehydrogenase (MCAD) deficiency (2020).
Since January 1, 2023, the screening of 7 inborn errors of metabolism was added.

A treatment as early as possible

In SMA, this subject has become central since the recent marketing authorization of the three disease-modifying treatments, Spinraza®, Zolgensma®, and Evrysdi®. They have shown a better efficacy (in particular faster and more significant motor improvements), and even an absence of symptoms, if they are initiated before the first disease symptoms (pre-symptomatically) rather than afterwards (symptomatic phase). This shows the importance of initiating these treatments as early as possible, which supposes an early diagnosis of the disease. Neonatal screening makes this possible.

How is the genetic diagnosis of SMA performed?
In 90 to 95% of cases, *SMN1*-related proximal spinal muscular atrophy (SMA) is caused by a complete loss of the *SMN1* gene (homozygous loss with no copies of the *SMN1* gene). Using a blood draw, the most commonly used diagnostic technique in SMA consists of highlighting the absence of copies of the *SMN1* gene. Other techniques determine genetic abnormalities in the *SMN1* gene or the number of copies of the *SMN2* gene.

The neonatal screening keeps unfolding worldwide

The feasibility and efficacy of the neonatal screening of SMA have been demonstrated for several years by different pilot programs in various regions or countries around the world. Such program is now conducted on a national basis in an increasing number of countries.

- To this day, in the United States, **100% of newborns** are screened at birth for all types of SMA.
www.curesma.org/wp-content/uploads/2024/01/NBS_Maps_Screening_States_2024.pdf

- In Europe, including the three South Caucasus countries as well as all of Russia and Turkey, **65% of newborns** are screened for SMA at birth.
www.sma-screening-alliance.org/map

- More and more countries are gradually unfolding a pilot program in some regions to screen *SMN1*-related proximal spinal muscular atrophy, like in Japan, Brazil, Italy, Bulgaria…

Sonehara S et al. Genes (Basel). 2023 *Oliveira Netto AB. Genet Mol Biol. 2023*
Gagliardi DAnn Clin Transl Neurol. 2024 *Iskrov G et al. Int J Neonatal Screen. 2023*

In France, the DEPISMA project

Initiated by AFM-Téléthon, the FILNEMUS network, Strasbourg University Hospital and Bordeaux University Hospital, a forerunner pilot project started in the end of December 2022 in the Grand Est region and in the beginning of January 2023 in the region of New Aquitaine.
Their objective is to show the feasibility of neonatal screening of the SMA in these two regions over a period of 2 years. If this experience proves to be successful, a deployment all over the country can be proposed.

Interim results in 16 months
Preliminary data are presented in the *International Myology Congress 2024*, organized by the AFM-Téléthon in Paris from 21st until 24th of April:
- approximately 81,000 children tested;
- 7 infants tested "positive" for SMA;
- 5 could benefit of a treatment (Zolgensma®) between 20 up to 27 days old;
- the frequency of the disease is 1/11,000 in total.

First studies of comparison with or without neonatal screening

▪ A first study has compared the data of 234 children (all of them presenting up to 3 copies of *SMN2*) from the registry SMArtCare: 44 diagnosed diseases during neonatal screening (tested group) compared with those of 190 identified patients during the manifestation of the first symptoms of disease (non-tested group).
The average age in the beginning of the treatment is from 1,3 months for the tested group at birth and 10,7 for the other group. At clinical level, 91% of infants of the tested group are able to sit by themselves against 74% for the non-tested group. In the tested group, 64% are able to walk without assistance, meanwhile in the other group they represent 15%.
Schwartz O et al. JAMA Pediatr. 2024

▪ Researchers have carried out a study on the cost and the profit of neonatal screening in SMA, established in Belgium for several years. They were studying, over a period of 30 months, a small number of children treated either after they had been tested (12 children), or during a manifestation of the symptoms (43 children).
If the costs (direct and indirect) remain comparable in these two populations, the gain in terms of quality of life is much higher in children treated as a result of screening.
Dangouloff T et al.Neuromuscul Disord. 2024

Other clinical/scientific advances

Other therapeutic avenues under investigation

Different therapeutic avenues are evaluated, both for improving one of the authorized treatments and for acting in synergy with them. They are firstly tested in preclinical trials, in cell or animal models.

Preclinical research, an unavoidable step
The preclinical research corresponds to the study of the candidate medicines inside of cells (*in vitro)* culture and animal models *(in vivo).* It is the necessary preliminary for the administration of a candidate medicine to humans.
During the preclinical phase of the development of a candidate medicine, researchers study the pharmacology, the pharmacokinetics and the toxicology of the molecule: mechanisms of action, physicochemical properties, becoming of a compound in the organism, targeted organs, toxicity... The preclinical research allows thereby to determine a first estimation of the dose, without toxic effects, that can be administered to humans.
This data is essential for compiling the marketing authorisation application for marketing authorisation (MA) for the future drug from the regulatory regulatory agencies.

Improving gene therapy

To increase the efficacy of gene therapy and limit its side effects, two teams of researchers are determined to improve the construction of the product. With the optimization of the human transgene *SMN1*, the promoter for a better targeting and the viral vector for the transport, the production of the SMN protein is increased in mice models with SMA.
Nafchi NAM et al. Gene Ther. 2023 *Xie Q et al. EMBO Mol Med. 2024*

In addition to current treatments

▪ French researchers are interested in the potential role of oxidative stress in the loss of motor neurons.

The oxidative stress
When the function of mitochondria is disturbed, this will result in an excessive production of the toxic molecules, "free radicals," which damage the compounds of the cell (DNA, proteins....). The oxidative stress corresponds to a situation where the cell does not control anymore the excessive presence of these free radicals.

In the mice models of SMA, the researchers have observed an overexpression of NOX4, a molecule which favors the production of free radicals. The inhibition of this molecule **by setanaxib**, a medicine in development, protects the motor neurons from the degeneration. Furthermore, the motor function and the lifespan of mice are improved. Moreover, setanaxib seems to act in synergy with Spinraza® to lessen the symptoms of the disease in mice.
El Khoury M et al. Front Cell Neurosci. 2023

▪ According to a British study, the screening of molecules acting on epigenetics in mouse models of SMA have helped identifying a compound, **the MS023**, which increases the production of the SMN protein. MS023 is an inhibitor of arginine methyltransferase proteins, a therapeutic family in

which certain products are already tested in clinical trials. It also increases the effects of Spinraza® when they are administered together.
Nafchi AJ et al.EMBO Mol Med. 2023

The role of SMN protein in studies

▪ When a cell of our organism goes through a stress situation, one part of her nucleus called nucleolus, the one that fabricates the manufacture components of the protein-producing machinery of the cell, can be disorganized.
A French team, supported by AFM-Téléthon, demonstrated the implication of SMN protein in restoring the organization of this nucleolus. And it is when it changes compartment in the nucleus (moving from Cajal body to nucleolus) that the SMN protein will be involved and will allow the cell to resume its biological activities.
Musawi S et al. Nat Commun. 2023

▪ Another team has developed mice presenting a decrease of SMN protein in the mesenchymal progenitor cells, that means the ones that are going to give birth to bones, cartilage...They have observed that this would alter the development of bones and neuromuscular junction suggesting a role of SMN, beyond motor neurons.
Hann SH et al. Elife. 2024

A model for evaluating the passage of the blood-brain barrier

English researchers have perfected lines of the induced pluripotent stem cells in order to test the permeability of the blood-brain barrier to two therapeutic agents.

The blood-brain barrier
The blood-brain barrier separates the central nervous system (brain and spinal cord) from the rest of the body. It is composed, essentially, of cells that line the inside of the small blood vessels (or capillaries) in the brain, closely connected to each other. The brain capillaries themselves are wrapped in nerve cell extensions (astrocytes) that participate in the blood-brain barrier.
This barrier plays a protective role with respect to the central nervous system. It allows certain useful compounds, such as glucose, to pass into the brain and the spinal cord. On the contrary, it limits or prevents the passage of microorganisms, toxic substances and numerous medicines.

Three iPSC cell lines are later differentiated in the endothelial cells involved in the vascularization of the brain. The researchers have observed that the adeno-associated virus type 9 (AAV-9) crosses the blood-brain barrier better than the AAV-8 while antisense oligonucleotides do not cross it at all.
Selvakumaran J et al. Biomedicines. 2023

***Stem cells** are undifferentiated cells able to self-renew and to differentiate in order to give birth to any specialized cell of our organism (blood cells, muscle cells, neurons...).
Unlike the embryonic stem cells which originate from a surplus embryo not used after the in vitro fertilization, **the induced pluripotent stem cells IPSC** are the result of taken cells in an adult which are "rejuvenated" in order to restore their capacity to transform in any kind of cell.*

Studies in function of the number of copies of the *SMN2*

With 2 copies of *SMN2*

A first longitudinal observational study over one year evaluated motor and neurocognitive changes in 12 patients with type I SMA with 2 copies of *SMN2*, treated by Zolgensma® between the age of 1,7 et 52,6 months.

There are two types of existing **clinical observational studies**:
- **longitudinal studies**, which describe the progression of the disease over time (for example, a natural history protocol).
- **cross-sectional studies**, which describe the way the disease manifests in a group/population of patients at a specific moment in time.

After a year, their motor performance had been significantly improved. The patients have also shown improvements of their cognitive, verbal and communication skills. These results suggest that the neurocognitive aspects could also be taken into account in the evaluation of patients with SMA type I.
Bitetti I et al. Front Neurol. 2024

With 3 copies of *SMN2*

A review of literature relating specifically to patients presenting 3 copies of *SMN2* evidenced clinical signs more variable than with 1, 2, 4 or 5 copies.
Regarding the presymptomatic children or patients with SMA type I, those who have 3 copies have symptoms which appear later on, a motor function which declines more slowly and a longer lifespan than those with 2 copies. In patients with type II or III with 3 copies, the beginning of symptoms happens earlier, in particular for the loss of the ability to walk and the dependence on a ventilator, than with 4 copies. An early initiation of a treatment in presymptomatic patients with 3 copies turns out to be very efficient to delay the beginning of the manifestation of the symptoms and stabilize the motor function.
Dosi C et al. Front Neurol. 2024

With 4 copies of *SMN2*

Two studies describe symptoms that can be severe or the early manifestation in this form of SMA, important findings to take into account, in particular in the context of neonatal screening.

- In the first study, the data of 268 patients with SMA with 4 copies of *SMN2*, aged 3 up to 75 years old and coming from German-speaking registry SMArtCARE, were analyzed. The results highlight the manifestation of first symptoms at a young age: 6,4 years in average, but before the age of 3 for more than the half of the participants. At 18 years old, the majority (approximately 95% of them) shows symptoms.
In this registry nearly one third of patients have lost the capacity of walking by themselves and 42% have scoliosis (against 2 and 4% for the general population). Nevertheless, it has to be noted that the data of the patients that have little or not at all symptoms are not integrated in this registry.
Vill K et al.J Neurol. 2024

- In this second study, the Italian network ITASMAC dedicated to SMA, has studied the files of 169 people, child or adult, having a homozygous deletion of *SMN1* gene and 4 copies of *SMN2* gene, and non-treated for an innovative therapy. The patients were mainly males (102/169). Six patients were presymptomatic children, 8 had a SMA type II, 145 had a SMA type III and 8 hand a type IV. Two patients, identified in the context of a family survey, were totally asymptomatic adults. More than a third of type III patients and a quarter of type IV patients had lost the ability to walk.
Ricci M et al. Ann Neurol. 2023

Very early symptoms could impact motor development

In Italy, the follow-up of 18 infants over the course of two years identified as having spinal muscular atrophy during neonatal screening shows that the very early manifestation of symptoms can predict their motor development. Among them, 14 patients have been treated; four others had at least 4 *SMN2* copies of the gene and they were not treated.
In the first days of life of infants, the clinical examination showed to be normal for 11 of them (including the four non-treated who then later on gained the ability to walk before the age of 18 months. Four have had very early symptoms (between the age of 3 and 13 days) and they did not gain the capacity to walk and three presented a few early symptoms (asymptomatic) and they could walk at the age of 13 months or between 22 and 24 months.
Pane M et al. Eur J Pediatr. 2024

The link between fatigue and severity?

During a survey on fatigue in SMA conducted by the American association Cure SMA 253 adults were invited to use three instruments in order to measure these symptoms, randomly chosen among five proposed ones. Surprisingly, these devices did not evidence the correlation between the fatigue and the severity of the disease. Nevertheless, a significant difference of the scores of fatigues had been observed among the patients and the volunteers without the disease. Therefore, the setting of the measure scale of fatigue which would be specific to SMA seems recommended.
Belter L et al. Neurol Ther. 2023

A new tool for the evaluation of swallowing difficulties

A new tool called "DySMA" was tested in order to evaluate the swallowing difficulties in the young children with SMA aged from 0 up to 24 months. Based on the questionnaire and the examination, and comprising ten categories and 36 items, it was found to be feasible and useful after being evaluated in eight volunteers without the disease, six presymptomatic people and six symptomatic treated people.
Zang J et al. J Neuromuscul Dis. 2024

*
**

Throughout the year, follow the latest research in proximal spinal muscular atrophy related to the *SMN1* gene in the AFM-Téléthon site:
www.afm-telethon.fr > actualités dans l'amyotrophie spinale proximale liée au gène SMN1
(In French)