ASOs: understanding this treatment approach

Antisense oligonucleotides (ASOs) are one of the treatment approaches being studied for MYT1L syndrome. This document explains how ASOs work, what can be expected from ASOs, and what an ASO treatment would ask of the person with MYT1L syndrome, their family or their carers.

Key points

1. In MYT1L syndrome, about **half of the working MYT1L protein** is missing.
2. An ASO could help the working copy of the gene **make more MYT1L protein**.
3. There is **not yet an ASO ready** to be given to people with MYT1L syndrome. ASOs are being tested in the laboratory. The research will take several years.

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This document is for information only. It does not replace the advice of your medical team. Version: November 2026. Translated from the French original.

- Les Extra-Vaillants MYT1L, “Comprendre la recherche sur le syndrome MYT1L” (Understanding research on MYT1L syndrome), June 2026.
- Presentation “Antisense oligonucleotides (ASO)”, family meeting, July 2025.

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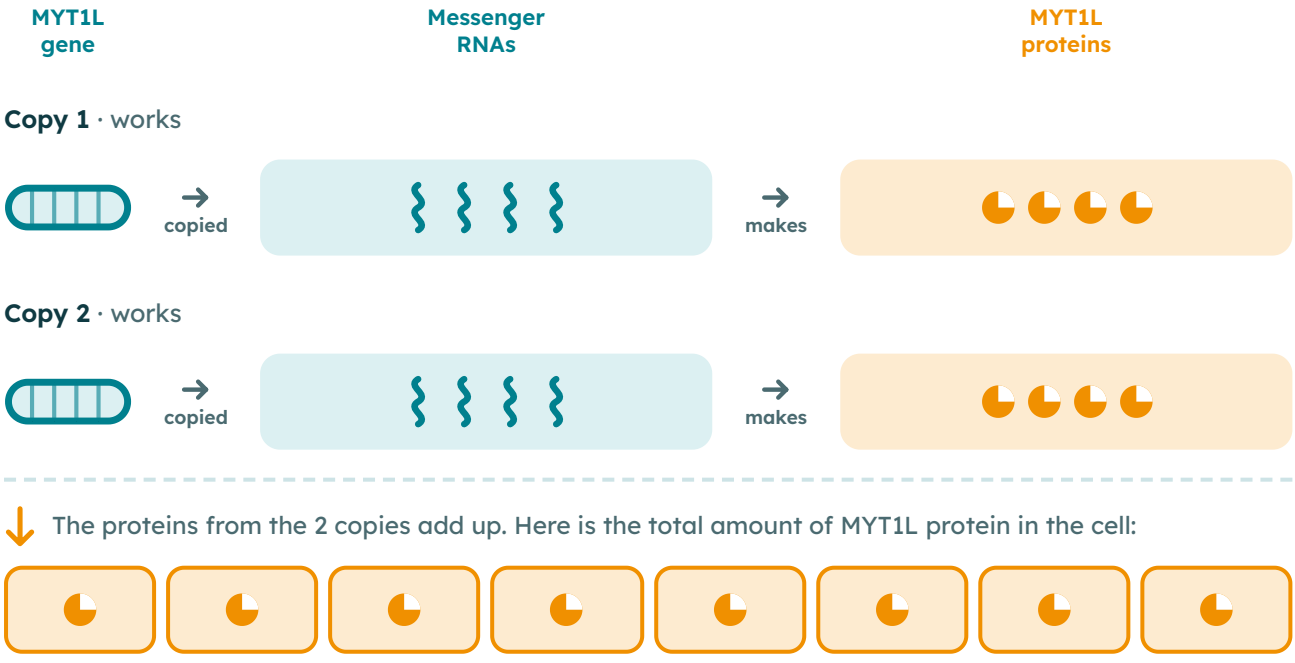
1 How the MYT1L gene works

The **MYT1L gene** is an instruction written in our DNA. Every person has **2 copies of the MYT1L gene**: one copy inherited from the mother, one copy inherited from the father.

To use the MYT1L gene, the cell makes **working copies** of the gene. These working copies are called **messenger RNAs**. Messenger RNAs are temporary: the cell quickly breaks down the messenger RNAs and makes new ones.

From the messenger RNAs, the cell makes the **MYT1L protein**. The MYT1L protein guides the development of neurons.

In a person without the syndrome



8 of 8: normal amount

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2 What happens in MYT1L syndrome

One of the 2 copies of the MYT1L gene carries a **genetic change**. The other copy of the MYT1L gene works normally.

↓

The genetic change can be of 3 types. The genetic test report states the type of genetic change.



A variant

The MYT1L gene is complete, but one or a few “letters” of the gene are changed, like a spelling mistake.



A deletion

A piece of the chromosome is missing. Part of the MYT1L gene, or the whole MYT1L gene, is missing.



A duplication inside the gene

A piece of the MYT1L gene is doubled, inside the gene. This duplication can disrupt the MYT1L gene. The geneticist checks whether this is the case.

Other duplications leave a complete copy of the MYT1L gene. In general, these other duplications do not cause MYT1L syndrome, but their effects are not yet well understood. Talk to your geneticist.

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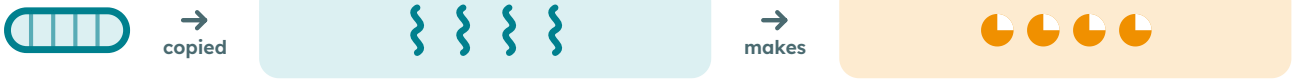
↓ **in all 3 cases, the result is usually the same**

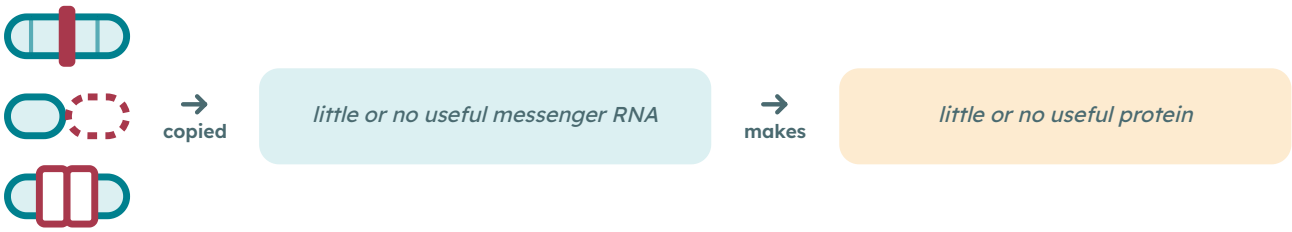
In MYT1L syndrome

MYT1L gene	Messenger RNAs	MYT1L proteins

Copy 1 · works



Copy 2 · **with the genetic change (one of the 3 types)**



↓ The proteins from the 2 copies add up. Here is the total amount of MYT1L protein in the cell:



4 of 8: about half

↓ **so**

The copy with the genetic change makes **little or no useful MYT1L protein**. So the cell has only about **half** of the usual amount of MYT1L protein.

Doctors call this lack of protein haploinsufficiency.

↓ **so**

With half of the MYT1L protein, the brain develops **differently**. This different development explains the difficulties, which vary a lot from one person to another: language, motor skills, behaviour, learning, sleep, weight and appetite…

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3 What an ASO would do

With an ASO (what we hope for)

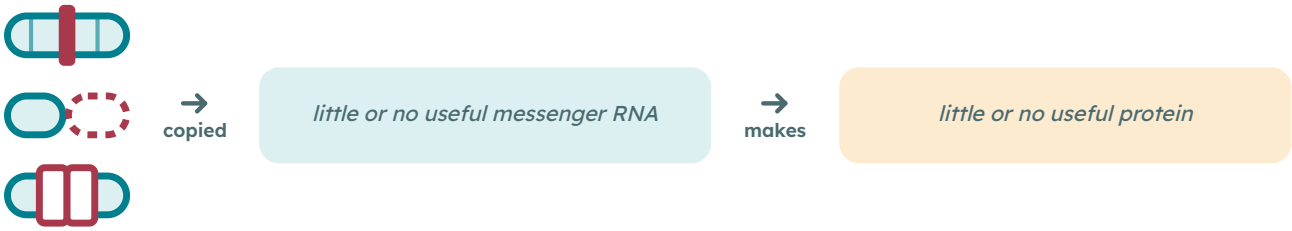
ASO attached to the MYT1L messenger RNAs

MYT1L gene	Messenger RNAs	MYT1L proteins

Copy 1 · works



Copy 2 · **with the genetic change (one of the 3 types)**



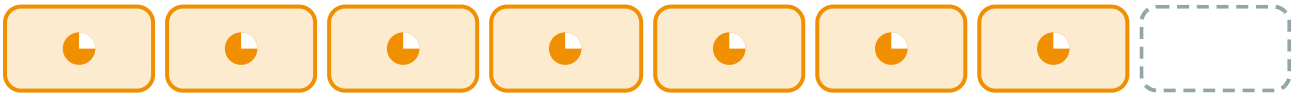
The proteins from the 2 copies add up. Here is the total amount of MYT1L protein in the cell:

Without an ASO



4 of 8: about half

With an ASO



7 of 8: close to normal (what we hope for)

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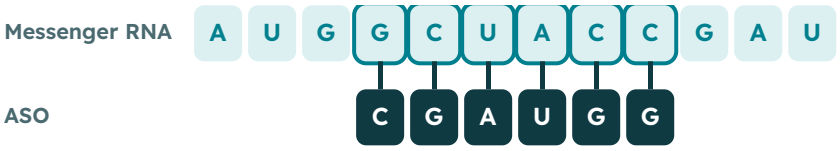
how the ASO works

An ASO is a **short molecule made in a laboratory**, about twenty genetic “letters” long.

ASO C G A U G G U A … about 20 letters

Each ASO is designed to **attach as precisely as possible to one messenger RNA only**, like a jigsaw puzzle piece.



Each letter of the ASO goes with only one letter of the messenger RNA: A with U, G with C. If too many letters do not match, the ASO does not attach. Researchers check that the ASO does not attach, or only very little, elsewhere.

for MYT1L, the idea is that

The ASO helps **the working copy of the gene** give more usable messenger RNAs, for example by protecting the messenger RNAs from being broken down.

so

With more messenger RNAs, the cell would make **more MYT1L protein**. The amount of MYT1L protein would get closer to normal. Researchers hope that more MYT1L protein would improve some of the difficulties.

ASO medicines already exist for other genetic conditions, for example spinal muscular atrophy (SMA). These medicines show that ASOs can work in some conditions. For MYT1L syndrome, researchers still have to show it.

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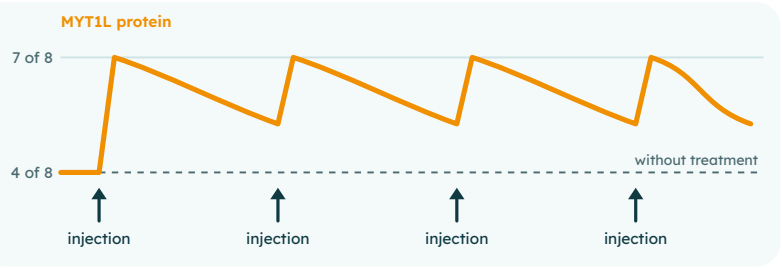
4 The limits of an ASO

An ASO **does not change the DNA**. An ASO does not repair the genetic change. The ASO only acts on the messenger RNAs.



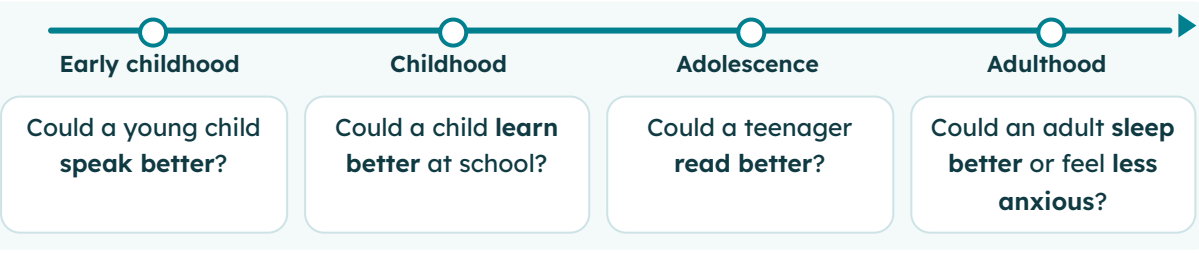
The genetic change is still there. The ASO would increase what the working copy makes. Depending on the type of genetic change, the ASO might also slightly increase what the copy with the genetic change makes: this is one of the questions research needs to study.

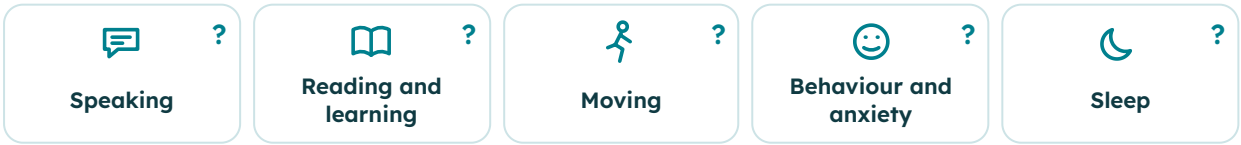
The effect of an ASO is **temporary**. When the body has cleared the ASO, the effect stops. So regular injections are needed.



After each injection, MYT1L protein goes up. Then the effect slowly fades, until the next injection (depending on the medicine, every 1 to 4 months). Simplified diagram.

An ASO is not a cure. Even if an ASO helps, it will not make MYT1L syndrome go away. Researchers do not yet know **which difficulties** could improve. Researchers also do not know whether **the age at the start of treatment** matters.





No one can answer these questions yet. Clinical trials will measure exactly this: what changes, at what age, and for whom.

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5 What a treatment would involve

The brain is protected by a **barrier** that blocks most medicines coming from the blood. An ASO taken as a tablet or by infusion into a vein would not reach the brain in sufficient amounts.

↓ so

The ASO is injected directly into the fluid around the spinal cord and the brain, through a **lumbar puncture** in the lower back.

↓

The injection takes place **in hospital**, often with sedation, especially for children or in case of anxiety. The injection itself takes a few minutes. With preparation and monitoring afterwards, expect to spend half a day in hospital, sometimes more.

↓ and because the effect is temporary

The injection is **repeated over the long term**. At the start, injections are often closer together (every 2 weeks). After that, depending on the medicine, the injection is given every 1 to 4 months. For a MYT1L ASO, the schedule is not yet known.

Known risks

These risks are known from ASOs already used in other conditions.

⚠ **Linked to the lumbar puncture**: headaches, vomiting, pain in the back or legs. Scoliosis can make the procedure more difficult.

⚠ **Linked to the medicine**, in particular: a drop in blood platelets, effects on the kidneys, inflammation of the spinal cord or nerve roots, and more rarely a build-up of fluid in the brain. A MYT1L ASO could have other risks. Trials will also look for them.

✓ These risks are **monitored** with regular tests: blood and urine tests.

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6 What it would mean in daily life

One day, an ASO trial may be offered. Taking part in a trial is a **big commitment**, for the person with MYT1L syndrome as well as for their family or carers. It is best to know about this commitment well in advance.

For the person with MYT1L syndrome

Child, teenager or adult.

Repeated injections by lumbar puncture, in hospital, often with sedation.

Many assessments: language, behaviour, sleep, medical tests. These assessments can be long or tiring.

Changes to routines: travel, unfamiliar places, new people. These changes can be hard to cope with, especially with the anxiety or sensory differences that are common in MYT1L syndrome.

These steps can be **prepared for**: visual supports, visiting the places beforehand, having a familiar person there.

The person concerned has a say. The medical team explains the trial with words and supports adapted to the person's abilities, and seeks their agreement. If the person refuses, their refusal is respected. For a child, the parents (or the people with parental authority) give authorisation. For an adult under a legal protection measure (such as guardianship), the person responsible for that measure gives authorisation or assists the person, depending on the measure.

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For the family, relatives and carers

⚠ **Time and organisation**: many appointments, sometimes far from home. Work, school, brothers' and sisters' lives, or the link with the service that supports the person all need to be organised.

⚠ A **long commitment**: injections take place regularly, over several years.

⚠ **Uncertainty**: no one knows in advance whether the treatment will work. In some trials, some participants receive, for a time, a product with no active medicine (placebo) or a simulated injection. Participants and their families do not know whether they are receiving the real treatment or not. Hope and worry often go together.

⚠ **Not everyone will be able to take part.** Each trial chooses its participants according to precise criteria, for example age or type of genetic change.

Taking part in a trial asks a lot of the person with MYT1L syndrome, their family or their carers.

↓ **that is why**

Taking part is **always voluntary**. You can say no, or stop at any time, without any change to usual care. In France, the trial's medical costs are covered by the trial sponsor, and travel costs are reimbursed on proof of expense. In other countries, ask the trial team.

Before deciding, some questions to ask yourselves together:

- How does the person cope today with care, hospitals and blood tests?
- Can we often travel to the hospital, sometimes far away?
- Who can help us day to day during the trial?
- What do we expect from the treatment, and what would we do if it does not work?

You are not alone: the trial team, the association and other families can support you.

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7 What the person with MYT1L syndrome and their family, or carers, can do now

The ASOs being studied for MYT1L target **the working copy of the gene**. In principle, such an ASO could therefore be relevant for many people, especially people whose copy with the genetic change makes no protein (deletions, and most variants that stop the protein from being made in full). For other genetic changes, such as some "missense" variants (one changed letter that alters the protein without stopping it), this is less certain.

↓ **but**

Each genetic change is different, and some situations are special. **Nothing has been proven yet.**

↓ **so**

The best thing is to talk about it with **your geneticist**, bringing the genetic test report of the person concerned.

A question to ask:

> **"Can you explain the genetic change involved? Could an ASO treatment one day be relevant for our relative?"**

In the meantime: keep up the **medical follow-up and therapies**, and take part in **studies** when possible. Studies prepare the way for future trials.

Be wary of announcements that promise a **cure** or a medicine **within five years**, and of **paid treatments** offered outside an authorised trial.

A question? The association can help you:

extravaillants@gmail.com

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8 The timeline

2026 — **Today**: researchers are testing ASOs in the laboratory to find the most effective ASO.

around 2030 — **First trial** in a few patients, to check that the treatment is safe.

2035 to 2040 — **Medicine available**, if trials show that it is safe and useful.

Developing a medicine often takes 10 to 15 years. These dates are **estimates**, presented at the July 2025 family meeting. These dates may change. When a team announces “the start of trials”, the medicine is not ready yet.

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