Operetta2

A clinical research study for children and teenagers living with multiple sclerosis (MS)

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Defining MS

Multiple sclerosis (MS) is an unpredictable, at times disabling, **autoimmune** disease that affects the nervous system.

In individuals living with MS, the body's immune system attacks and damages a fatty substance that surrounds and protects the nerves, called myelin. As a result, nerve impulses (or messages) that travel to and from the brain are unclear or interrupted, like a frayed electrical cord that does not work properly.

Autoimmune:
when someone's immune system attacks its own body causing inflammation

Children and teenagers get MS too!

- Most children and teenagers living with MS have a type of MS called *Relapsing-Remitting MS (RRMS)*
- RRMS is the most common type of MS and is known for periods where new or existing symptoms get worse (relapse) followed by a period of recovery where few or no symptoms are present (remission)
- During RRMS relapses, the immune system attacks the nerve fibres and causes inflammation (or swelling) which leads to MS symptoms

How is MS treated?

- There is no cure for MS. The goal of current treatments is to reduce the number of relapses and help keep symptoms under control
- Some treatments can be prescribed for children and teenagers living with MS, but more options are needed to help better control relapses and allow children and teenagers to fully take part in daily activities
- Clinical research studies are a part of the process to identify and make new treatment options available to children and teenagers

Common symptoms

Feeling tired or weak

Tingling feeling

Dizziness

Difficulty walking or balancing

Numbness

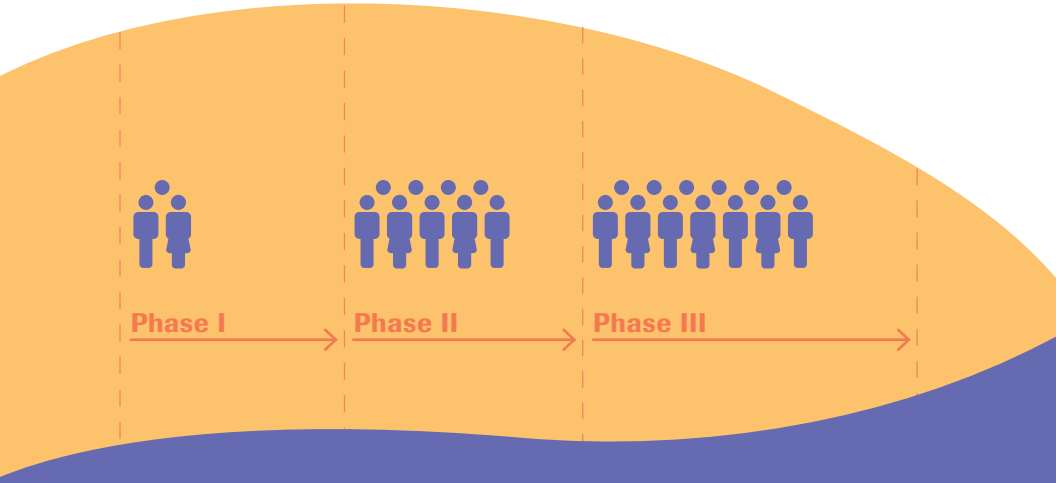
Problems with thinking or memory

Feeling angry or sad without a reason

Blurry vision

What is a research study?

- Before a new medicine can be given to children or teenagers, a team of doctors and researchers have to make sure the medicine is safe and that it works. To make sure of that they do ‘research studies’ or ‘studies’
- Research studies on a new medicine (also known as a ‘study medication’) are done in **three phases**:



In **Phase I,** the study medication is given to healthy adult volunteers to make sure that it is safe

In **Phase II,** the study medication is given to volunteers who have the condition (for example, MS) that the study medication is made for

In **Phase III**, the study medication is given to even more people in different countries who are living with the condition to see how well it works to treat it, and compare it to other medicines for this condition

All research studies must follow strict rules to keep volunteers safe and a group of experts make sure all rules are being followed.

What is the Operetta2 study?

Operetta2 is a phase III study conducted in countries all around the world. The purpose of this study is to compare the good or bad effects of the study medication, ocrelizumab versus fingolimod in the treatment of RRMS in children and teenagers.

Who will take part in the study?

- **171 children and teenagers** from around the world living with RRMS
- 10-17 years of age

What are the study medication and how do they work?

Ocrelizumab and fingolimod are medicines that temporarily reduce the inflammation caused by the immune system and are intended to reduce how often relapses are experienced.

Study medication

Ocrelizumab

can be prescribed for the treatment of MS in **adults only**

Fingolimod

can be prescribed for the treatment of RRMS in children **10 years of age or older**

What study treatment will I receive?

In this study you will be given two study medicines:

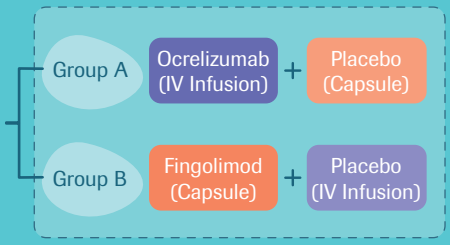
- one 'real' (ocrelizumab or fingolimod)

  AND

- one 'fake' that looks real but does not have an active medicine, this is called a **placebo**

A placebo is a dummy medicine that does not contain any active ingredient

If the study doctor confirms that you can safely take part in the study, you will be placed in one of the two treatment groups (Group A or B) 'at random' or 'by chance'.



How would I take the study medication?

No matter what treatment group (A or B) you are in, you will be given the study medicine in two ways:

- **Ocrelizumab (or placebo): IV infusion** during a study visit at the clinic about once every 6 months
- **Fingolimod (or placebo): Capsules** (like tablets) taken daily at home

No matter what group you are in, you will receive active treatment

Ocrelizumab or placebo (IV Infusion)

First dose

- **Given in two parts** (1st half dose on Day 1 and 2nd half dose 2 weeks later)

Subsequent doses

- Full dose given once every **6 months**

Fingolimod or placebo (capsules)

First dose

- Taken by mouth at the clinic (one capsule)

Subsequent doses

- Taken at home by mouth **daily** (one capsule)

Intravenous (IV) infusion:
when a medicine is given slowly into your arm

What happens during the Operetta2 study?

The Operetta2 study has four parts:

Screening to see if you can safely take part in the study

Treatment Part 1 you will be enrolled in the study and placed in one of two treatment groups (Group A or Group B) and you will receive ocrelizumab or fingolimod

Treatment Part 2 is an optional part of the Operetta2 study where you will **only be given ocrelizumab** if it is the best choice for you

Follow-Up is used to check on your health condition once your study treatment is completed

During Treatment Part 1, neither you, your parent/carer, nor the study doctor will know which treatment group you are placed in. The study doctor can find out which treatment group you were placed in if there is concern for your safety

Before you can take part in the study, you and your parents/carers will be asked to read and sign the **Informed Consent Form (ICF)**. This is an important document!

Informed consent process

The ICF must be signed before any study procedures take place.

This process will ensure that:

- you and your parents/carers understand all the information about participating in the study
- the opportunity is given to ask questions before you make a decision to take part

Taking part in a research study is a big decision for any family and is **your choice**.

Please take all the time you need to decide if this study is right for you and your family.

You can decide to stop being in the study at any time and for any reason!

Screening

This process starts once the ICF is signed and can last up to **10 weeks**.

The study doctor will check to make sure the study is right for you. You will have some tests and procedures done to make sure you can take part in the study and to check if it is safe for you.

Key criteria to take part

- Signed ICF
- 10-17 years of age
- Confirmed diagnosis of RRMS
- Able to have MRI

Tests and procedures

- Medical history
- Physical exam
- Questions about disease
- Brain MRI scan
- Eye exam
- Test of how well your brain processes information
- Blood tests
- Urine tests
- Wrist/Hand X-ray (optional)

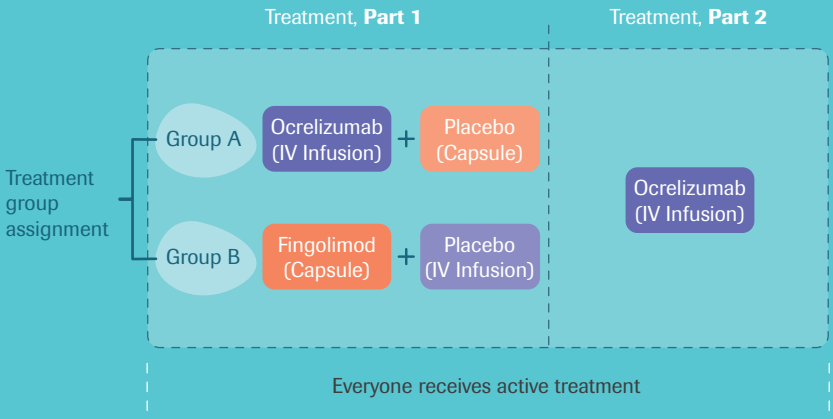
Treatment Part 1:

- You will be placed in a treatment group and receive either ocrelizumab or fingolimod
- Whichever group you are in, you will also take a **placebo**
- Part 1 of the study will last at least 6 months but may be longer
- At the end of Part 1, you will be told which study medication you received

Treatment Part 2:

- In this part of the study, you will only be given ocrelizumab
- Every 6 months (twice a year) you will visit the study clinic to receive an ocrelizumab infusion
- Part 2 of the study will last ~ 3 years but may be longer

Treatment Part 2 is optional



During Treatment Parts 1 and 2, you will have to visit the study clinic at least 6 times each year. At each visit, you will have some tests and procedures similar to those you did during screening.

Expected visits during treatment Parts 1 and 2

Study visit
2 weeks before IV infusion (1-2 hours)

IV infusion
study visit (3-7 hours)

Phone call
1 day after IV infusion and monthly

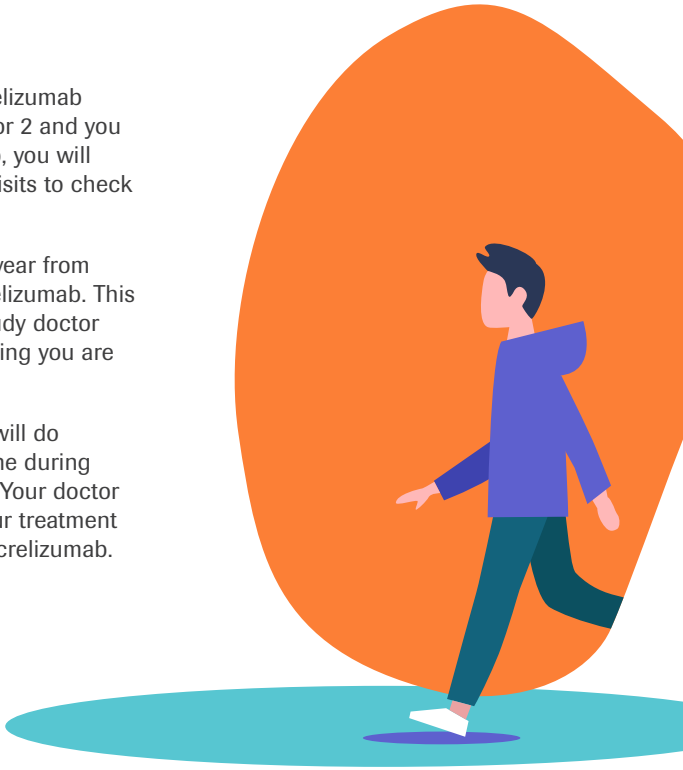
Study visit
every 3 months (3-7 hours)

Follow-Up

If you have received ocrelizumab during treatment Part 1 or 2 and you stop getting ocrelizumab, you will continue to have study visits to check on how you are doing.

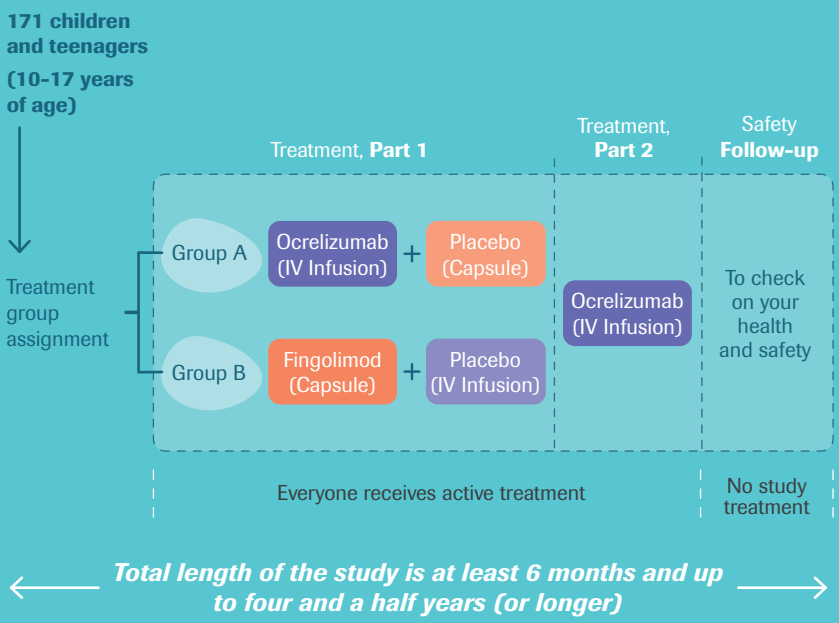
Follow-up will last for 1 year from your last infusion of ocrelizumab. This may be longer if your study doctor wants to continue checking you are doing well.

During these visits, you will do similar tests to those done during treatment Parts 1 and 2. Your doctor will talk to you about your treatment choices after stopping ocrelizumab.



How long does the Operetta2 study last?

You will be in the study for **at least 6 months,** but it may be longer if you decide to take part in Part 2.



What happens if I turn 18 during the study?

If you turn 18 while in the Operetta2 study, you can complete all parts of the study.

As a parent/carer, what are my obligations during the Operetta2 study?

- During this study, if you provided your consent, you will be asked to come to the study clinic with your child about once every 6 months, during Parts 1 and 2, to complete some questionnaires
- You should let the study doctor know if your child has any changes in health, care or medication. Such as:
  - New symptoms or symptoms that get worse
  - Changes in medication
  - Visits to another doctor or hospital
- Ensure your child does not take part in any other research study

What are the risks associated with taking part in Operetta2 and why should I take part?

- Doctors don't know if this study will make you better. If you take part in the study, you may get better or you may stay the same or get worse

You will be monitored closely throughout the study by the study doctor for any side effects

- The information from this study will help children and teenagers living with MS in the future and will help medical professionals learn more about the study medication, and the treatment of RRMS in children and teenagers (10-17 years old)
- There may be risks or side effects involved with taking part in this study. You and your parents or carer will be told about the risks and benefits before you make a decision about taking part

Are there any costs associated with taking part in Operetta2?

- You will not be charged for the study medication while taking part in Operetta2
- Additionally, all procedures that are necessary for participation in the study and are not a part of your regular medical care will be provided at no cost

I’m interested, who do I contact?

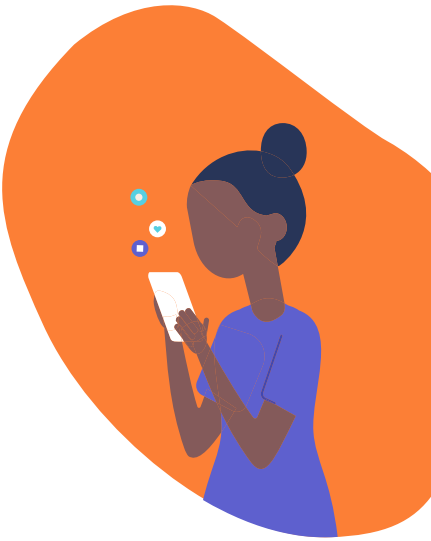
If you are interested in learning more or if you or someone you know might want to consider taking part in the Operetta2 study, please contact the study team.

Operetta2 study team contact information

Name:

Location:

Phone number:



Notes

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