

# 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  
inflammationcausing  
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 fibers and causes inflammation (or swelling) which leads to MS symptoms

### Common symptoms



Numbness



Tingling  
feeling



Dizziness



Difficulty  
walking or  
balancing

## 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 participate in daily activities
- Clinical studies are a part of the process to identify and make new treatment options available to children and teenagers



Feeling tired  
or weak



Problems with  
thinking or  
memory



Feeling hungry  
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’
- Research studies of a new medicine (also known as a “study drug”) are done in **three phases**:

## Human Safety

Days or Weeks

Tens



### Phase I

Includes people who don't have the target condition

## Expanded Safety

Weeks or Months

Hundreds



### Phase I/II

Includes people with the target condition

## Efficacy & Safety

Several Years

Thousands



### Phase II/III

Continued monitoring conducted for as long as drug is on market

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

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

In **Phase III**, the study drug 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 effects, good or bad, of the study drug ocrelizumab versus fingolimod in the treatment of RRMS in children and teenagers

## Who will take part in the study?

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



# What are the study drugs 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 drugs

### 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** 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:

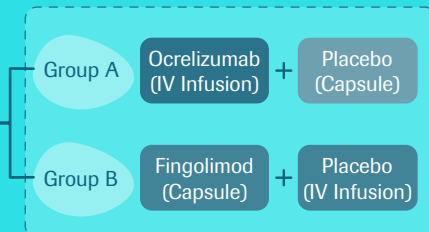
- one “real” (ocrelizumab or fingolimod),
- AND**
- one “fake” that looks real but does not have an active medicine, this is called a **placebo**

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

## Study treatments

**233 children and teenagers (10-17 years of age)**

→ Treatment assignment group





# How would I take the study drugs?

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 pills) taken daily at home

## NOTE:

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

### Ocrelizumab or placebo (IV Infusion)



#### First dose

- Given in two parts (1<sup>st</sup> half dose Day 1 and 2<sup>nd</sup> 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 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/caregiver, nor the study doctor will know which treatment group you are placed in you are placed in**

**NOTE:**

*The study doctor can find out which treatment group you were placed in if there is concern for your safety*

Before you and your parents/caregivers begin participating in the study, you will be asked to read and sign the **Informed Consent Form (ICF) and Assent form**. These are important documents!

## Informed consent/assent process

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

This process will ensure that:

- You and your parents/caregivers understand all the information about participating in the study
- The opportunity is given to ask questions before you make a decision to participate

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

# Screening

This process starts once the ICF/Assent are 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 determine if it is safe for you.

## Screening - Key inclusion criteria



Signed ICF/Assent forms



10-17 years of age



Confirmed diagnosis of RRMS



Able to have MRI during screening

## Screening - 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 2 years but may be longer
- At the end of Part 1, you will be told which study drug you received

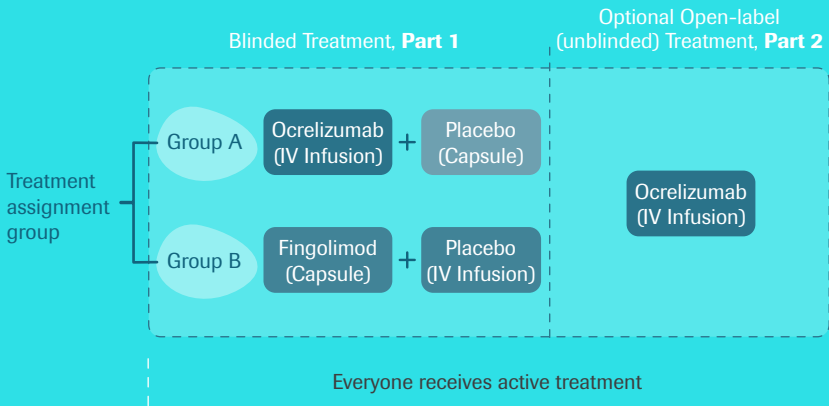
## Treatment Part 2:

- 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

### NOTE:

***Treatment Part 2 is optional***

## Treatment Parts 1 and 2



***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 study 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



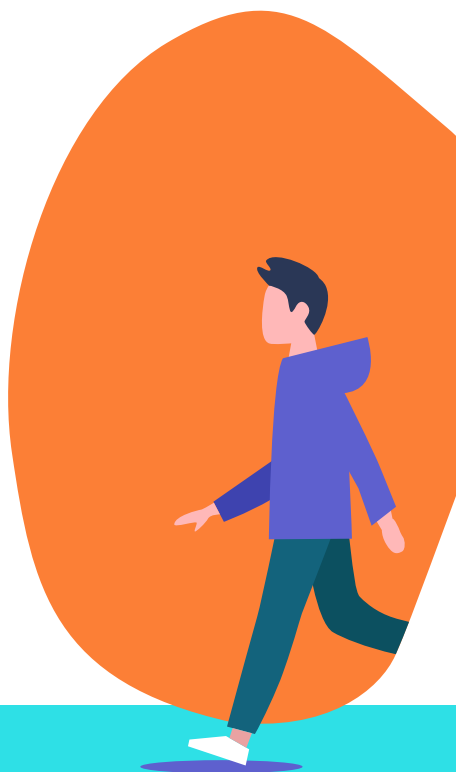
Study visit  
every 3 months  
(3-7 hours)

## 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.

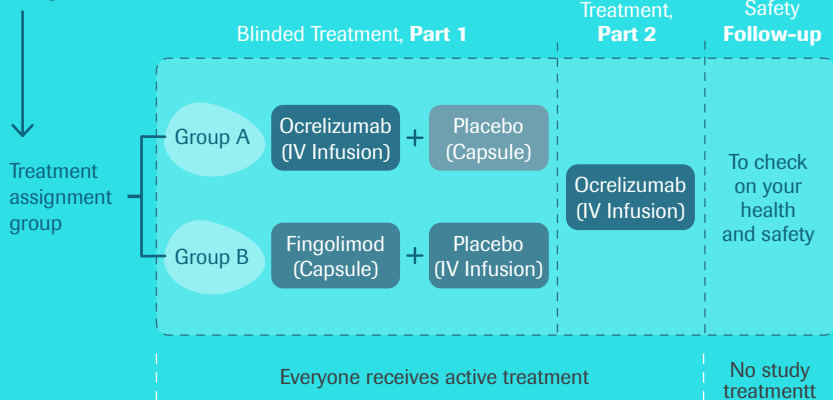
During these visits, you will do similar tests to those done during treatment Parts 1 and 2. Your doctor will talk to you about your treatment choices after stopping ocrelizumab.



# How long does the Operetta2 study last?

You will be in the study for at least 2 years, but it may be longer if you decide to participate in Part 2.

233 children and teenagers (10-17 years of age)



← *Total length of the study is 2-6 years (or longer)* →

## 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/caregiver, 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 participating in Operetta2, and why should I participate?

- Doctors don't know if this study will make participants better. If you participate in the study, you may get better, or you may stay the same or get worse
- 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 drug, 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 caregiver will be told about the risks and benefits before you make a decision about participating
- Before participating, speak to your study doctor and other family members about the possible risks associated with taking part in Operetta2

**NOTE:**

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

# Are there any costs associated with participating in Operetta2?

- You will not be charged for the study drugs while participating 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







# Operetta<sup>2</sup>