

# Intra-cerebral gene therapy for Sanfilippo type B syndrome

<b>Submission date</b> 30/09/2010	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 03/08/2011	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 30/09/2021	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Sanfilippo syndrome, also known as mucopolysaccharidosis type III (MPS III), is a rare genetic disorder. There are four types (A to D). Sanfilippo syndrome subtype B, or mucopolysaccharidosis type IIIB (MPSIIIB), is caused by a genetic defect of the enzyme  $\alpha$ -N-acetylglucosaminidase (NAGLU). This enzyme is involved in breaking down long chains of sugar molecules. In its absence, these molecules build up. This causes brain damage starting most often during the first 5 years of life. Affected children require specific care and death occurs at the average age of 15, although some patients are still alive after the age of 20. MPSIIIB could be treated by delivering the correct gene for the missing enzyme using a virus (gene therapy). The aim of this study is to test this gene therapy approach in patients with MPSIIIB.

### Who can participate?

Patients age 18 months to 5 years with MPSIIIB

### What does the study involve?

Participants receive gene therapy combined with immunosuppressant drugs (to suppress the strength of the body's immune system). The virus is injected into the brain at 6 injection sites in a single session. Clinical and x-ray examinations are carried out and blood and cerebrospinal fluid samples are taken before and after treatment, with daily follow-up during 1 week after the injections, then 14 and 21 days, 1, 3, 6 and 12 months after treatment.

### What are the possible benefits and risks of participating?

Not provided at time of registration

### Where is the study run from?

Hôpital Bicêtre (France)

### When is the study starting and how long is it expected to run for?

September 2013 to November 2015

Who is funding the study?

1. French Patient Association (France)
2. Private donations (France)

Who is the main contact?

Prof. Marc Tardieu

## Contact information

### Type(s)

Scientific

### Contact name

Prof Marc Tardieu

### Contact details

Service de Neurologie Pédiatrique  
Hôpital Bicêtre  
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78, rue du Général Leclerc  
Le Bicêtre-Bicêtre  
France  
94275

## Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

### Secondary identifying numbers

MPS3-IP-01

## Study information

### Scientific Title

A phase I/II, open-label, study of intracerebral administration of adeno-associated viral vectors carrying human NaGlu cDNA for the treatment of Sanfilippo type B syndrome

### Acronym

MPS3B

### Study objectives

There is currently no available treatment for Sanfilippo syndrome. The rationale for therapeutic approaches in mucopolysaccharidoses (MPS) is based on the observation that delivery of the missing enzyme reverses phenotypic abnormalities in genetically deficient cells. Although enzyme replacement therapy (ERT) is being explored, there is still not currently available for MPSIIIB.

On the other hand, MPS have long been recognized as prime candidate diseases for gene therapy as it was shown that the missing enzyme may be produced and distributed to the organism by a group of genetically modified cells.

Indeed, numerous studies in animal models of MPS have described the effects of genetic modification of tissues including bone marrow, skin, muscle, liver and brain, resulting in the production of a therapeutically active enzyme.

However, when vectors are administered in the periphery, the produced enzymes do not cross the blood-brain barrier. Only very high doses of enzyme in the circulation may result in detectable transport into the brain.

In MPSIII, a direct administration into the brain would be required, since most lesions take place in this organ.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

CCP Il-de-France II, 17/04/2013, ref: 2013-03-17

### **Study design**

Phase I/II single-arm open-label study

### **Primary study design**

Interventional

### **Secondary study design**

Non randomised study

### **Study setting(s)**

Hospital

### **Study type(s)**

Treatment

### **Participant information sheet**

Not available in web format, please use the contact details to request a patient information sheet

### **Health condition(s) or problem(s) studied**

Mucopolysaccharidose - neurodegenerative disease

### **Interventions**

Patients will receive gene therapy combined with immunosuppressant regimen. The vector is a serotype 2 AAV genome encoding the human  $\alpha$ -N-acetylglucosaminidase cDNA packaged in a serotype 5 capsid called AAV-NAGLU. Vector suspensions will be simultaneously injected into the brain parenchyma at 6 injections sites in a single neurosurgical session. Combined

immunosuppression (Tacrolimus, Cell-Cept) is justified by previous studies in children receiving recombinant enzyme infusions and investigations of AAV-mediated gene therapy in Sanfilippo and Hurler dogs.

Clinical and radiological examination, collection of biological products including blood, peripheral blood mononucleated cells and cerebrospinal fluid (CSF) > 6 weeks prior to treatment, at inclusion, baseline, 14 days prior to treatment, observation and -2 and -1 days, daily follow-up during 1 week post-injection, then 14 and 21 days, 1, 3, 6 and 12 months post-treatment.

The total duration of follow up is 1 year.

Added 02/08/2013:

Vectors will be delivered through 8 small burr holes. Two in the posterior fossa to target the white matter of the cerebellar hemispheres and six supratentorially, to target the white matter adjacent to the putamen. Two deposits will be done on each track, one deep and one superficial, in a single neurosurgical session.

### **Intervention Type**

Drug

### **Phase**

Phase I/II

### **Drug/device/biological/vaccine name(s)**

Intra-cerebral gene therapy

### **Primary outcome measure**

Clinical, radiological, biological tolerance associated to the proposed treatment

### **Secondary outcome measures**

Collection of data to define exploratory tests that will become evaluation criteria for further clinical phase III efficacy studies (brain MRI; neurological and biological markers)

### **Overall study start date**

01/09/2013

### **Completion date**

01/11/2015

## **Eligibility**

### **Key inclusion criteria**

1. Age: 18 months to the end of the 5th year
2. Onset of clinical manifestations related to MPSIIIB during the first 5 years of life
3. NaGlu activity in peripheral blood cell and/or cultured fibroblast extracts of less than 10% of controls
4. Patient affiliated to a social security regimen
5. Family understanding the procedure and the informed consent
6. Vital laboratory parameters within normal range

Sanfilippo disease is a rare disease and so the countries of recruitment will depend on the availabilities of the patient at the time of recruitment. There will be one study centre in France.

**Participant type(s)**

Patient

**Age group**

Child

**Lower age limit**

18 Months

**Upper age limit**

5 Years

**Sex**

Both

**Target number of participants**

4 children from Europe

**Total final enrolment**

4

**Key exclusion criteria**

1. Presence of brain atrophy on pre-inclusion MRI judged on a cortico-dural distance of more than 1 cm
2. Any condition that would contraindicate permanently anaesthesia
3. Any other permanent medical condition not related to MPSIIIB
4. No independent walking (Ability to walk without help)
5. Any vaccination 1 month before vector injection
6. Receipt of aspirin within one month
7. Any medication aiming at modifying the natural course of MPSIIIB given during the 6 months before vector injection

**Date of first enrolment**

01/09/2013

**Date of final enrolment**

01/11/2015

**Locations****Countries of recruitment**

France

**Study participating centre**

Hôpital Bicêtre

Le Bicêtre-Bicêtre

France  
94275

## Sponsor information

### Organisation

Institut Pasteur (France)

### Sponsor details

25-28 Rue du Dr Roux  
Paris  
France  
75015

### Sponsor type

Industry

### Website

<http://www.pasteur.fr/ip/index.jsp>

### ROR

<https://ror.org/0495fxg12>

## Funder(s)

### Funder type

Charity

### Funder Name

French Patient Association (France)

### Funder Name

Private donations (France)

## Results and Publications

### Publication and dissemination plan

Not provided at time of registration

### Intention to publish date

## Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Not provided at time of registration

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/09/2017	18/12/2020	Yes	No
<a href="#">Results article</a>	results	10/05/2021	30/09/2021	Yes	No