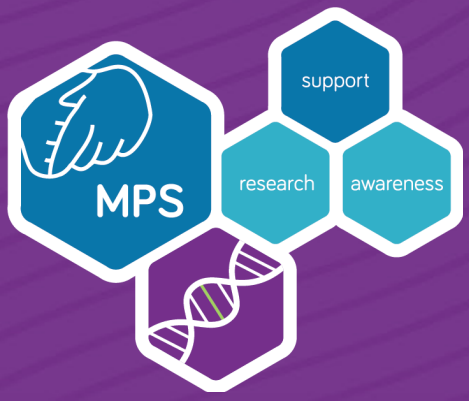
FOCUS ON **FABRY**

Fabry treatment update



Fabry treatment update

On 22nd September 2020, the MPS Society hosted a webinar where current research into new treatments for Fabry were discussed.

This document provides information on these new treatments and details of the ongoing research studies and clinical trials underway in the UK for Fabry.

For those who would like to find out more or are interested in taking part in one of the studies, contact information has been included.

Contents

Disclaimer

This document is intended as a guide only.
Please check with your Fabry consultant or on www.clinicaltrials.gov for the latest information regarding the clinical trials listed.
This document does not provide medical advice, always seek the advice of your doctor with any questions you may have regarding your medical condition.

Clinical trials

Clinical trials are an essential step in the development of new medicines. They are used to test the safety of new therapies, to see how well they work and to determine if they are better than existing treatments.

When you take part in a clinical trial, you may be one of the first people to benefit from a new therapy. However, there is also a chance that the new treatment is no better than current treatments, or sometimes it can be worse.

If you are considering taking part in a clinical trial your Fabry consultant will be able to discuss with you what the clinical trial will involve and whether the clinical trial and treatment being tested are suitable for you. You can also use the links in this document to find out more about the individual trials listed.

Being accepted onto a clinical trial

Each clinical trial has its own set of rules on who can and can't take part, the main ones have been included in this document, but for full details of who can and cannot take part please refer to the sources of additional information indicated or speak to your Fabry consultant.

- In general, you must have a confirmed diagnosis of Fabry – some clinical trials may also require the presence of specific symptoms
- Some trials are accepting men and women, whereas others are accepting men only
- Those with certain additional health conditions may not be able to take part

Pegunigalsidase alfa (PRX-102)

Enzyme replacement therapy: Pegunigalsidase alfa (PRX-102)

A new investigational enzyme replacement therapy, pegunigalsidase alfa (PRX-102), is designed to last longer in the blood stream following infusion. This may reduce the number of required enzyme infusions to once a month, compared to existing enzyme replacement therapies that need to be administered every two weeks.

Extensions of the BALANCE, BRIDGE & BRIGHT clinical trials

BALANCE & BRIDGE extension

This study is evaluating the long-term safety and effectiveness of PRX-102 given at a dose of 1mg/kg every 2 weeks.

BRIGHT extension

This study will determine the long-term safety and effectiveness of PRX-102 given at a dose of 2mg/kg every 4 weeks.

These extension studies are running in two centres in the UK and are open to those who have completed the BALANCE, BRIDGE or BRIGHT trials.

What's involved?

- Everyone on the trial will receive PRX-102
- The BALANCE & BRIDGE extension will run for between 2—4 years
- The BRIGHT extension will run for up to 3 years
- Patients will receive regular follow-up

Access to these trials is by invitation only

Would I be able to take part?

- Access to these trials is by invitation only
- You must have completed either the BALANCE, BRIDGE or BRIGHT clinical trial
- These clinical trials accept males and females
- You need to be aged 18 years or over

Lucerastat

Substrate reduction therapy: Lucerastat

Lucerastat is a substrate reduction therapy. It works by reducing the amount of Gb3 made in the body. Gb3 is a type of fat. People with Fabry lack the enzyme activity needed to break down these fat molecules and so Gb3 accumulates in body tissues and organs, causing the symptoms of Fabry.

Lucerastat is an oral therapy, that may be suitable for people with all Fabry mutations.

The MODIFY clinical trial

The MODIFY clinical trial is testing lucerastat's potential to reduce hand and foot pain (neuropathic pain). The investigators are also assessing the effects of this treatment on gastrointestinal symptoms and Gb3 levels.

The trial is running in five centres across the UK.

What's involved?

- You will receive either lucerastat or a placebo, as capsules, twice a day
- The clinical trial is double-blind which means that both you and the research staff will not know which capsule you are receiving (lucerastat or placebo), during the clinical trial
- The clinical trial will last for six months
- You will be asked to complete an electronic diary every day to track your symptoms
- You may have the option to enrol in the long-term follow up study after completing this clinical trial

Find out more on the MODIFY website

Would I be able to take part?

- The clinical trial accepts males and females
- You need to be aged 18 years or over
- You must have moderate or severe neuropathic pain
- The trial is open to those willing to switch from ERT therapy and those who are not on ERT

Arrhythmia in Fabry disease

The Role of Implantable Loop Recorders in Fabry Disease

This study is investigating how Fabry affects the heart and causes heart rhythm disorders (arrhythmias). While many patients will experience heart palpitations, not much is known about the frequency of abnormal heart rhythms or the risk factors for developing these.

An implantable loop recorder (ILR), is a small device (smaller than a AAA battery) that monitors your heart. It is inserted under the skin on the front of the chest. The ILR captures a continuous measure of your heart activity, which allows doctors to detect any abnormal heart rhythms as they occur.

The RaILRoAD trial

The RaILRoAD study will assess the frequency of abnormal heart rhythms, determine whether the ILR improves outcomes for patients through earlier detection of these arrhythmias and increase understanding of the risk factors.

The trial is running in five centres across the UK.

What's involved?

- You will be assigned to a group that receives an ILR and standard care or standard care only
- The clinical trial will last for 3 years
- You will undergo a number of assessments at 6—12 monthly intervals
- The ILR will be removed at the end of the study

Would I be able to take part?

- The clinical trial accepts males and females
- You need to be aged 18 years or over
- There must be evidence that Fabry is affecting your heart

To find out more contact:

Lead research fellow
Dr Ravi Vijapurapu
ravi.vijapurapu@uhb.nhs.uk

Lead research nurse
Ms Heather Small
heather.small@uhb.nhs.uk

- You must not have a heart device fitted already e.g. a pacemaker
- You must not have coronary artery disease
- You must not have a mutation that causes disease of the heart muscle (cardiomyopathy)

Gene therapy with FLT190

Gene therapy: FLT190

Fabry disease is caused by mutations in the GLA gene that provides instructions for the production of an enzyme called alpha-galactosidase A (alpha-GAL A). These mutations affect the function of the enzyme and lead to the accumulation of a type of fat called Gb3 in several tissues and organs such as the heart, kidney, or liver, which can result in organ damage.

FLT190 is a gene therapy that uses a harmless virus (that does not cause disease or infection) as a vehicle to deliver a healthy copy of the GLA gene in the hope that it will induce the production of normal alpha-GAL A enzyme.

The MARVEL1 clinical trial

This study aims to investigate the safety of FLT190 and its potential to treat the signs and symptoms of Fabry disease following a single dose of FLT190.

The trial is running in one centre in the UK.

What's involved?

- FLT190 will be administered as a single dose, slow intravenous infusion
- Monitoring visits will take place for a period of 9 months
- After this, patients will enter a period of long-term follow-up

Would I be able to take part?

- The clinical trial accepts males only
- You need to be aged 18 years or over
- You must have classical Fabry disease

- You must not have been treated with any other gene therapy

To find out more e-mail:

contact@freeline.life

Gene therapy with ST-920

Gene therapy: ST-920

Fabry disease is caused by mutations in the gene that provides instructions for the production of an enzyme called alpha-galactosidase A. This enzyme is responsible for breaking down a type of fat called Gb3. The mutations mean that the enzyme cannot function properly, resulting in a buildup of Gb3 in cells and tissues. That buildup interferes with their function and causes the symptoms of the disease.

Gene therapy involves supplying a healthy copy of the faulty gene to patients' cells so that they can produce the enzyme necessary to break down Gb3. In order to introduce genetic material into cells, a vehicle or gene carrier is necessary. ST-920 contains a modified virus (that researchers have modified so that it cannot cause disease) as the vehicle to deliver the healthy gene.

The STAAR clinical trial

The purpose of this study is to evaluate the safety and tolerability of different doses of ST-920.

The trial is running in four centres in the UK.

What's involved?

- ST-920 will be administered as a single infusion
- You will visit the clinic every 2—4 weeks for follow-up for one year

Would I be able to take part?

- The clinical trial accepts males only
- You need to be aged 18 years or over
- You must have classical Fabry disease

- You must not have been treated with any other gene therapy
- You must not be receiving Galafold® (migalastat)

To find out more: clinicaltrials@sangamo.com **or visit** www.staarclinicalstudy.com

Information sources

The information in this guide was obtained from the following sources.

Click on the link to access the original article.

Enzyme replacement therapy: Pegunigalsidase alfa (PRX-102)

News article on PRX-102

PRX-102 (Pegunigalsidase Alfa). Fabry Disease News
[Internet]. Florida: BioNews Services LLC; [cited 2020 Sept 28].
Available from: https://fabrydiseasenews.com/prx-102-pegunigalsidase-alfa/

BALANCE & BRIDGE extension clinical trial

Extension study of 1mg/kg pegunigalsidase alfa in patients with Fabry disease.
ClinicalTrials.gov [Internet]. Bethesda: National Library of Medicine; [updated 2018 Nov 21; cited 2020 Sept 28].
Available from: https://clinicaltrials.gov/ct2/show/NCT03566017?term=prx-102&draw=2&rank=8

BRIGHT extension clinical trial

Open label extension of 2mg/kg pegunigalsidase alfa (PRX-102) every 4 weeks in adult Fabry disease patients.
ClinicalTrials.gov [Internet]. Bethesda: National Library of Medicine; [updated 2019 Oct 01; cited 2020 Sept 28].
Available from: https://clinicaltrials.gov/ct2/show/NCT03614234?term=prx-102&draw=2&rank=6

Substrate reduction therapy: Lucerastat

News article on Lucerastat

Experimental Lucerastat suitable for all types of Fabry disease patients, study shows.
Fabry Disease News [Internet]. Florida: BioNews Services LLC; [updated 2018 Jul 12; cited 2020 Sept 28].
Available from: https://fabrydiseasenews.com/2018/07/12/investigative-lucerastat-found-suitable-all-types-fabry-disease-patients/

MODIFY clinical trial

Efficacy and safety of Lucerastat oral monotherapy in adult subjects with Fabry disease (MODIFY). ClinicalTrials.gov [Internet]. Bethesda: National Library of Medicine; [updated 2020 Sep 24; cited 2020 Sept 28].
Available from: https://clinicaltrials.gov/ct2/show/NCT03425539?erm=modify&cond=Fabry+Disease&draw=2&rank=1

MODIFY website

MODIFY
[Internet]. Switzerland: Idorsia Pharmaceuticals Ltd; [updated 2020 Jul 18, cited 2020 Sept 28].
Available from: www.modifyfabry.com

The Role of Implantable Loop Recorders in Anderson-Fabry Disease

Article published in the scientific journal (Trials) explaning the design and purpose of this trial

Vijapurapu R, Kozor R, Jughes D, et al. A randomised controlled trial evaluating arrhythmia burden, risk of sudden cardiac death and stroke in patients with Fabry disease: the role of implantable loop recorders (RaILRoAD) compared with current standard practice. Trials. [Internet] 2019 [cited 2020 Sept 28]; 20:314.
Available from: https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-019-3425-1

The clinical trial

Arrhythmia burden, risk of sudden cardiac death and stroke in patients with Fabry disease (RaILRoAD).
ClinicalTrials.gov [Internet]. Bethesda: National Library of Medicine; [updated 2020 Mar 20; cited 2020 Sept 28].
Available from: https://clinicaltrials.gov/ct2/show/NCT03305250?term=railroad&draw=2&rank=1

Gene therapy: FLT190

News article on FLT190

Patients being recruited in Europe to test gene therapy candidate FLT190 after promising preclinical results.
Fabry Disease News [Internet]. Florida: BioNews Services LLC; [updated 2019 Jun 05; cited 2020 Sept 28].
Available from: https://fabrydiseasenews.com/2019/06/05/gene-therapy-flt190-phase-1-trial-recruiting-patients-promising-preclinical-data/

The MARVEL1 clinical trial

A Fabry disease gene therapy study (MARVEL1).
ClinicalTrials.gov [Internet]. Bethesda: National Library of Medicine; [updated 2020 Feb 06; cited 2020 Sept 28].
Available from: https://clinicaltrials.gov/ct2/show/record/NCT04040049?term=marvel1&draw=2&rank=1

Gene therapy: ST-920

News article on ST-920

ST-920.
Fabry Disease News [Internet]. Florida: BioNews Services LLC; [updated 2020 Aug 24; cited 2020 Sept 28].
Available from: https://fabrydiseasenews.com/st-920-experimental-gene-therapy-for-treating-fabry-disease/

The STAAR clinical trial

Dose-ranging study of ST-920, a rAAV2/6 human alpha galactosidase A gene therapy in subjects with Fabry disease.
ClinicalTrials.gov [Internet]. Bethesda: National Library of Medicine; [updated 2020 Apr 06; cited 2020 Sept 28].
Available from: https://clinicaltrials.gov/ct2/show/study/NCT04046224?term=st-920&draw=2&rank=1

The STAAR website

STAAR.
[Internet]. Sangamo Therapeutics; [cited 2020 Sept 28] .
Available from: https://staarclinicalstudy.com/study-overview/

Hospital contact list

Addenbrooks Hospital

Cambridge University Hospital NHS Foundation
Department of Medicine
Hills Road
Cambridge
CB2 0QQ

Tel: 0122 324 5151

National Hospital of Neurology & Neurosurgery

National Hospital for Neurology & Neurosurgery
Charles Dent Metabolic Unit
Queens Square, London
WC1N 3BG

Tel: 0207 829 8778

Royal Free, London

Royal Free Hampstead NHS Trust
Pond Street
London
NW3 2QG

Tel: 0207 794 0500

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Herries Rd
Sheffield
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University Hospital Wales

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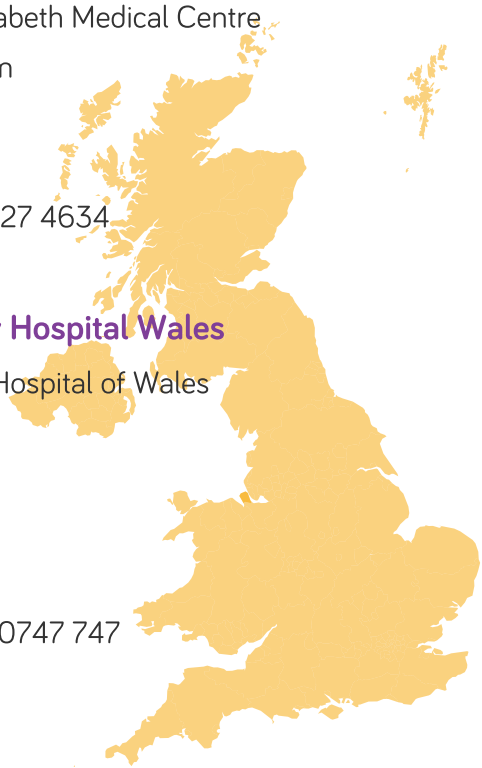

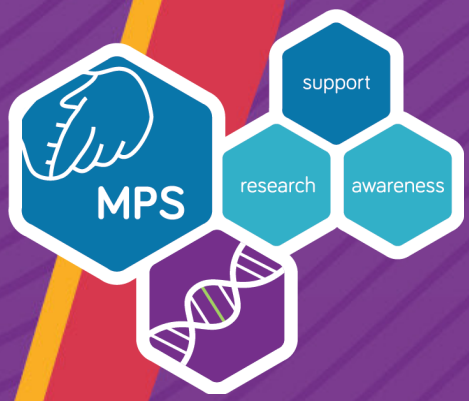

This document was prepared by Rare Disease Research Partners* for the MPS Society in October 2020.

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