Clinical trials: Current opportunities in Fabry

Clinical trials are an essential step to make new medicines, so they help improve the health and quality of life of people with Fabry. Clinical trials test that new therapies are safe, how well they work and 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.

Deciding to take part in a clinical trial

You may consider taking part in a trial because you wish to contribute to making a new treatment that may benefit you or those living with Fabry in the future. You might be looking for a better or more convenient treatment or one that does not have particular side-effects.

Choosing to take part in a clinical trial is a personal decision. 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 use the links in this document to help you find out more.

Will I be accepted on a clinical trial?

Each clinical trial has its own set of rules on who can and can't take part. Some general rules apply to the clinical trials listed in this booklet:

- You must have a confirmed diagnosis of Fabry – some clinical trials may also require the presence of specific symptoms
- Pregnancy must be avoided, so both women and men with a partner who could become pregnant, must use contraception
- Women who are pregnant, planning to become pregnant during the clinical trial, or are breast feeding cannot take part

What clinical trials are available now?

Enzyme replacement therapy: Pegunigalsidase alfa (PRX-102)

Current enzyme replacement therapy (ERT) is administered by regular infusions, usually every two weeks. A new investigational ERT, pegunigalsidase alfa (PRX-102), developed by Protalix Biotherapeutics, is designed to last longer in the blood stream, which might help protect the body's organs from the effects of Fabry disease and reduce symptoms.[1] This new ERT is currently being investigated as a therapy at two different doses and schedules including the option for infusions once a month. The treatment is suitable for all Fabry mutations.

Chaperone therapy: Migalastat (Galafold®)

Galafold® (migalastat), developed by Amicus Therapeutics has been approved for use in adults in many countries. This oral therapy is taken every other day on an empty stomach.[2] It is suitable for those with certain Fabry mutations, and acts by restoring enzyme activity.[3] This clinical trial will determine its use in younger people with Fabry.

Substrate reduction therapy: Lucerastat

Lucerastat is another oral therapy, in development by Idorsia Pharmaceuticals. People with Fabry lack the enzyme activity needed to break down the fat molecules known as Gb3. Lucerastat works by reducing the amount of Gb3 made in the body and thereby lessens its build-up. It may have the potential to treat Fabry, regardless of the specific mutation.[4]

Gene therapy: AVR-RD-01

This therapy offers the potential to be a single dose treatment.[5] It is currently undergoing safety and effectiveness testing in two trials in a small number of men with Fabry. These early clinical trials will build understanding of this new approach to treatment.

Disclaimer

This document is intended as a guide. All source material was accessed on 7th February 2019. Please check with your 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.

Enzyme replacement therapy: Pegunigalsidase alfa (PRX-102)

How does it work?

Current enzyme replacement therapy (ERT) is administered by regular infusions, usually every two weeks. A new investigational ERT, pegunigalsidase alfa (PRX-102), developed by Protalix Biotherapeutics, is designed to last longer in the blood stream, which might help protect the body's organs from the effects of Fabry disease and reduce symptoms.[1]

This new ERT is currently being investigated as a therapy at two different doses and schedules including the option for infusions once a month. The treatment is suitable for all Fabry mutations.

The BALANCE study: Safety and effectiveness of pegunigalsidase alfa compared to Fabrazyme® (agalsidase beta) in those individuals with impaired kidney function

This clinical trial aims to determine how effective pegunigalsidase alfa will be compared to existing treatment in those with declining kidney function.[6]

What's involved?

- Participants will either continue with their current Fabrazyme® (agalsidase beta) therapy or be switched to pegunigalsidase alfa. Both ERTs will be provided by the clinical trial
- The clinical trial is double-blind which means that you and the research staff will not know which treatment you are receiving during the clinical trial
- Infusions at a dose of 1mg/kg for either ERT will be given every two weeks for two years
- When appropriate, infusions will be provided under home care setup
- You may have the option to enrol in the long-term follow up study after completing this clinical trial

Is the clinical trial suitable for you?

- The clinical trial accepts males and females
- 18+ You need to be aged between 18 and 60 years
- The clinical trial is taking place in Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, Finland, France, Hungary, Italy, The Netherlands, Norway, Slovenia, Spain, Sweden, Switzerland, Turkey, UK and USA
- ✓ You must have been on treatment with Fabrazyme® (agalsidase beta) for at least one year
- ✓ You will be examined for your kidney function to assess whether it is deteriorating as a result of your Fabry disease

Find out more **here** or **here**

The BRIGHT study: Safety and effectiveness of pegunigalsidase alfa in those currently treated with Fabrazyme® (agalsidase beta) or Replagal™ (agalsidase alfa)

This clinical trial aims to evaluate a more convenient infusion schedule (2 mg/kg every four weeks).[6]

What's involved?

- Participants will be switched from their current ERT to receive intravenous infusions of pegunigalsidase alfa
- Infusions will be every four weeks for one year
- First infusions will be administered at the clinical trial site
- When appropriate, infusions will be provided under home care setup
- You may have the option to enrol in the long-term follow up study after completing this clinical trial

Is the clinical trial suitable for you?

- The clinical trial accepts males and females
- 18+ You need to be aged between 18 and 60 years
- The clinical trial is taking place in Australia, Belgium, Canada, Czech Republic, Denmark, Italy, Norway, Spain, Taiwan, Turkey, UK and USA
- ✓ You must have been on treatment with Fabrazyme® (agalsidase beta) or Replagal™ (agalsidase alfa) for at least three years and on a stable dose for at least the last six months

Find out more **here**

Chaperone therapy: Migalastat

How does it work?

Galafold® (migalastat), developed by Amicus Therapeutics has been approved for use in adults in many countries. This oral therapy is taken every other day on an empty stomach.[2] It is suitable for those with certain Fabry mutations, and acts by restoring enzyme activity.[3] This clinical trial will determine its use in younger people with Fabry.

Paediatric study: Safety and effectiveness of migalastat in 12–17 year olds

What's involved?

- Migalastat is taken by mouth as a capsule, once every two days
- You will be given migalastat treatment for 12 months
- At the end of 12 months there will be a 30 day follow up period during which you will receive no treatment
- You may have the option to enrol in the long-term study after completing this clinical trial

Is the clinical trial suitable for you?

- The clinical trial accepts males and females
- 12+ You need to be aged between 12 and 17 years
- The clinical trial is taking place in the USA
- ✓ You must have a Fabry mutation that is suitable for treatment with migalastat
- ✓ You must weigh at least 45 kg (99 pounds)
- ✗ You must have never been treated with ERT or have not received ERT in the last 14 days before starting the screening phase of the clinical trial
- ✗ You must not have received gene therapy and must not start gene therapy during the clinical trial period

Find out more **here**

Substrate reduction therapy: Lucerastat

How does it work?

Lucerastat is another oral therapy, in development by Idorsia Pharmaceuticals. People with Fabry lack the enzyme activity needed to break down the fat molecules known as Gb3. Lucerastat works by reducing the amount of Gb3 made in the body and thereby lessens its build-up. It may have the potential to treat Fabry, regardless of the specific mutation.[4]

The MODIFY study: Safety and effectiveness of lucerastat

The main goal of the clinical trial is to demonstrate lucerastat's potential to reduce hand and foot pain (neuropathic pain). The investigators will also assess the effects on gastrointestinal symptoms.[7]

What's involved?

- You will be given either lucerastat or a placebo, taken by mouth as capsules, twice a day
- The clinical trial is double-blind which means that both you and the research staff will not know which 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 to track your symptoms
- You may have the option to enrol in the long-term follow up study after completing this clinical trial

Is the clinical trial suitable for you?

- The clinical trial accepts males and females
- 18+ You need to be aged 18 years or over
- The clinical trial is taking place in Australia, Austria, Canada, Germany, Netherlands, Poland, UK and USA
- ✓ You must have moderate or severe neuropathic pain
- ✗ You must have never been treated with ERT or have not received ERT in the last six months

Find out more **here** and in the Fabry International Network newsletter **here**

Gene therapy: AVR-RD-01

How does it work?

This therapy offers the potential to be a single dose treatment.[5] It is currently undergoing safety and effectiveness testing in two trials in a small number of men with Fabry. These early clinical trials will build understanding of this new approach to treatment.

Fabry disease is caused by a mutation in the GLA gene, which results in the lack of the enzyme alpha-galactosidase A. Gene therapy is a way of introducing a working GLA gene into the body. AVR-RD-01 is a gene delivery system that uses a harmless virus to insert the GLA gene into stem cells taken from your blood. These modified cells produce alpha-galactosidase A with the potential to raise enzyme levels to normal ranges.[5]

Pilot study: Stem cell transplantation of cells engineered to express alpha-galactosidase A

What's involved?

- Therapy begins with a conditioning agent to stimulate the production of stem cells. Your stem cells are extracted and genetically modified by the virus, adding a new, fully functional copy of the faulty GLA gene[8]
- The modified cells are then delivered back to you via a one-time infusion[8]
- You will be followed for a period of time to determine the effects of treatment

Is the clinical trial suitable for you?

- In this clinical trial the therapy is only being tested in men
- 18+ You need to be aged between 18 and 50 years
- The clinical trial is taking place in Canada
- ✓ This clinical trial accepts those currently receiving ERT
- ✓ You must be willing to use contraception until at least 12 months after the treatment
- ✓ You must also be willing to not donate sperm (sperm banking will be recommended to anyone who would like to father children in the future)

Find out more **here**

The FAB-201 study: Effectiveness and safety of AVR-RD-01

What's involved?

- Therapy begins with a conditioning agent to stimulate the production of stem cells. Your stem cells are extracted and genetically modified by the virus, adding a new, fully functional copy of the faulty GLA gene[8]
- The modified cells are then delivered back to you via a one-time infusion[8]
- You will be followed for a period of time to determine the effects of treatment

Is the clinical trial suitable for you?

- This clinical trial accepts males only
- 16+ You need to be aged between 16 and 40 years, and past puberty
- The clinical trial is taking place in Australia
- ✓ You must have a history of gastro-intestinal symptoms including abdominal pain and diarrhoea due to your Fabry
- ✗ You must not have received ERT and/or chaperone therapy at any time for treatment of your Fabry
- ✗ You must not have previously received treatment with AVR-RD-01 or any other gene therapy

Find out more **here** or see **trial update here**

Reference links

1. http://www.fabrynext.com/
2. https://www.amicusrx.com/pi/galafold.pdf
3. https://fabrydiseasenews.com/galafold-migalastat/
4. https://fabrydiseasenews.com/2018/07/12/investigative-lucerastat-found-suitable-all-types-fabry-disease-patients/
5. https://fabrydiseasenews.com/avr-rd-101/
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7. https://fabrydiseasenews.com/2018/05/24/idorsia-is-enrolling-adult-fabry-patients-for-phase-3-lucerastat-trial/
8. http://www.avrobio.com/technology/

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