FAQ for the ASPro-PD trial of ambroxol

What are the main effects seen with ambroxol in previous studies?

Ambroxol boosts the activity of an enzyme called glucocerebrosidase (GCase), which is known to help clear away waste products in cells. In Parkinson's, a build up of a troublesome protein called alpha-synuclein is often seen in brain cells called neurons. It's thought that ambroxol may help improve the body's ability to clear away these clumps of alpha-synuclein and prevent damage to brain cells. Previous studies have suggested that ambroxol may improve lysosomal function, which is important for clearing cellular waste in neurons.

Results from a trial of the drug which were published in 2020, funded and supported by Cure Parkinson's and its strategic partners, showed that ambroxol was safe for people with Parkinson's to take. It also showed that the drug could reach the brain and boost levels of GCase.

The ASPro-PD trial will test the drug in a larger group of people with Parkinson's. It will compare it to a dummy drug to see if it can slow the progression of the condition.

Why do participants need to undergo genetic testing through PD Frontline first?

Genes are segments of DNA that help direct cell activity. One of their most important roles is in providing the cell with instructions for building proteins. Small changes or variations in our genes can therefore lead to issues with their associated proteins.

There's some evidence to show that people that have a change in a gene called GBA1, which is associated with Parkinson's, might benefit from treatment with ambroxol. This is because the GBA1 gene contains the instructions to make an enzyme involved in dealing with cellular waste, called GCase. Variations in the gene mean that the enzyme may not function properly, which can increase the risk of developing Parkinson's. Ambroxol is thought to increase GCase activity.

The ASPro-PD study team wants to know if there's any difference in how ambroxol works for people with and without the GBA1 mutation. They'd like to include a fair

balance of people with and without the mutation in the study. To do this, they need to establish whether someone has the mutation before they start in the trial.

The PD Frontline study is an online genetic testing platform involving taking saliva and blood samples at home. The samples are then analysed by the team to look for mutations in genes associated with Parkinson's, including GBA1. All recruitment to ASPro-PD will come from people who have taken part in the PD Frontline study, regardless of whether they have a GBA1 variation or not.

If ambroxol works, how long will it take to become mainstream?
This depends on the outcome of the trial and regulatory approval processes, which can take several years. The study will be recruiting until 2027, and each participant will be part of the study for 2.5 years.

Parkinson's UK and Cure Parkinson's are working with regulators and pharmaceutical companies to try and speed up the approval process. You can read more about this on our website.

If ambroxol is successful, will participants have to stop taking it at the end of the trial while it awaits potential NICE approval?
Yes, participants will have to stop taking ambroxol after the trial.

Taking part and eligibility

Where is the ASPro-PD study based?
The ASPro-PD trial of ambroxol is a multi-centre study that will take place across approximately 15 NHS research sites in the UK, with UCLH (University College London Hospitals) as a key centre. The specific locations of the sites will be announced on the **ASPro-PD website** as sites open.

How do I register for the ASPro-PD trial? How can I take part in the ambroxol trial?
The ASPro-PD research team is reaching out to people who are eligible to take part and who have taken part in the **PD Frontline study**. This is a study where

people are asked to supply a saliva swab and a blood sample, which are then studied to look for changes in certain genes.

People who meet the criteria for ASPro-PD, and have already taken part in PD Frontline, will be invited to visit one of 15 study sites across England, Scotland and Wales. You will be contacted directly by the ASPro-PD team if you fit these criteria. We encourage people to contact the ASPro-PD team at **cctu.aspro-pd@ucl.ac.uk** if they have any questions.

If you haven't already registered and taken part in PD Frontline, you may not be able to join the ASPro-PD study. Currently, for those who haven't already registered and taken part in PD Frontline, you may only be invited to take part in the ASPro-PD study if you are found to have the GBA1 mutation after genetic testing.

You can still **register to get genetically tested by PD Frontline** and explore other research opportunities through the **Parkinson's UK Take Part Hub** or **Cure Parkinson's Get Involved with Research** page.

Who is eligible to take part in ASPro-PD?

The study team will work with people with Parkinson's who:

- Supply a saliva and blood sample as part of the PD Frontline study, which looks at whether they have changes in the GBA and LRRK2 genes status
- Are between 35-75 years old
- Diagnosed within the last 7 years
- Have **not** had Deep Brain Stimulation (DBS) surgery
- Have **not** taken exenatide or any other investigational drug for Parkinson's in the last 12 months

You **won't** be able to take part, even if you meet the above criteria, if you have:

- participated in a clinical trial of a new or repurposed drug or treatment within 90 days prior to the first dose of trial treatment.
- used a new or repurposed drug or treatment that is under investigation for treating Parkinson's within 90 days prior to the first dose of trial treatment.

- participated in another clinical trial of an investigational new drug being tested for its ability to slow down Parkinson's progression within 12 months prior to the first dose of trial treatment.

Specific eligibility questions should be directed to the ASPro-PD team at **cctu.aspro-pd@ucl.ac.uk .**

How do I find out if I am registered/eligible for the ambroxol study?
First, if you haven't already, you will need to **register to get genetically tested by the PD Frontline study**.

Once your genetic testing results are ready, you will be contacted by the PD Frontline team if you are eligible. The PD Frontline team will ask you for consent to share your details with participating ASPro-PD trial sites.

If you sent your sample over 8 months ago and have not received your results in the predicted timeframe, and you are concerned, you can contact the PD Frontline mailbox for an update (**pdfrontline@ucl.ac.uk**). Please note that the research team releases results as soon as they are available.

Are there any risks to taking ambroxol?
The risks of ambroxol are still being studied, and like any medication, there may be side effects. In the pilot study of ambroxol, the reported side effects were generally mild. The ASPro-PD trial will be longer, however, as it is designed to assess both efficacy and safety. The longer treatment period will highlight any possible negative consequences of taking ambroxol.

I've heard that the trial has started, but I haven't been invited to participate, despite meeting all the eligibility criteria. When will I hear?
The ASPro-PD trial will be taking place at 15 sites across England, Scotland and Wales. While the trial has started with the first participant taking part in London, not all of the 15 sites are ready to start seeing participants.

The ASPro-PD team is working with local sites to train and prepare staff at all local sites. Some sites will be more ready, while others will take more time. The study team hopes that all sites will be open and ready by the end of 2025. Recruitment into the trial is planned over the next 2 years.

If you have been made aware that you are eligible from the PD Frontline team, but have not yet been introduced to your local ASPro-PD study team, it's likely that your local site is not yet open.

I meet the criteria and would like to take part in ASPro-PD but I do not live in the UK. Is this possible?
Unfortunately no. The ASPro-PD trial is a multi-centre study that will take place across approximately 15 NHS research sites in the UK, with UCLH (University College London Hospitals) as a key centre.

If I have the GBA1 variant and I'm approaching seven years post-diagnosis, am I excluded? Are people diagnosed over seven years ago excluded?
The eligibility criteria require a Parkinson's diagnosis within the last seven years, sites have been asked to prioritise those with approaching exclusion criteria for enrolment if they are deemed eligible.

People diagnosed more than seven years ago are not eligible for this trial. But you can explore other research opportunities through the **Parkinson's UK Take Part Hub** or **Cure Parkinson's Get Involved with Research** page.

Will the ASPro-PD trial include participants who don't have a change in GBA1?
Yes, the trial will recruit participants both with and without the GBA1 variant.

If I am not eligible for ASPro-PD, what other trials can I take part in?
You can find many opportunities to take part in research by searching the Parkinson's UK **Take Part Hub** or the Cure Parkinson's **Get involved with research page**.

PD Frontline: genetic testing, saliva and blood samples

Sample collection

Participants will provide saliva and blood samples at home. Saliva will be collected via a small tube, which you can spit into. The blood is collected with a Tasso+ device, which is an innovative, easy, and painless method for obtaining a small blood sample at home. The device attaches to the upper arm using a vacuum and creates a small prick in the skin, remaining on the arm for less than a minute as approximately 0.5ml (one tenth of a teaspoon) of blood is collected. For more information about Tasso+ devices, please visit their website: **www.tassoinc.com/tasso-plus.**

Existing PD Frontline participants have found the Tasso+ kits to be user-friendly and easy to use. Blood testing provides higher quality DNA, allowing more people to receive results more quickly and reducing the likelihood of needing to resubmit samples. Saliva samples will serve as a backup in the uncommon event that blood testing fails. For more information about the testing process and sample collection kits, please visit **www.pdfrontline.com**. All instructions and components required are enclosed in the kit, which will be posted to participants. After collecting your sample, participants can return it to PD Frontline using the provided Freepost envelope.

Does everyone who registers for PD Frontline get sample collection kits?

People with Parkinson's who live in the UK and are aged between 18 to 90 years old will be sent sample collection kits.

Do I need to wait for my saliva test results before being considered for a trial?

Yes, genetic results are needed for eligibility in certain trials like the ASPro-PD study. But if you are eligible for ASPro-PD, your details will be passed on to the ASPro-PD research team automatically.

How long will it take for my PD Frontline saliva kit to arrive?

Up to 4 weeks. You will be emailed when the kit has been sent and when the research team have received your samples. Please check your spam folder if you haven't heard, as these emails can sometimes be misdirected to spam.

When will the genetic testing of my samples be completed? How long does it take to get results from genetic testing?

There are several stages to sequencing the GBA gene, and the process is complex, so the timeline for receiving results can vary. The team is working as quickly as possible to return results and typically allows between 6 to 8 months for sequencing.

The research team apologises in advance for the delay and will contact you once your results are ready.

I sent my samples over 8 months ago, but haven't received my results. What should I do?

If you have not received your results in the predicted timeframe and you are concerned, you can contact the PD Frontline mailbox for an update (pdfrontline@ucl.ac.uk).

Are samples sent 18 months ago still viable, or do I need to send a new one?

Most samples remain viable, but if needed, participants may be contacted for new samples (eg, in the instance of a sample repeatedly failing testing.) You'll hear directly from the PD Frontline team if this is the case.

I haven't received a response from the PD Frontline team. What can I do?

The PD Frontline team checks the mailbox daily for enquiries and aims to respond to all emails within a week. If you have not received any response to a query, please check the following:

1. You are emailing the correct address. Our email address for enquiries is **pdfrontline@ucl.ac.uk.** Please do not email no_reply@pdfrontline.com, as this does not direct messages to the team.
2. Please check your spam folder. Unfortunately, our emails are sometimes diverted to participants' spam folders, and so information is not delivered to all participants. Please regularly check your spam folders for any communications.

3. All PD Frontline-related enquiries should be directed to the mailbox mentioned above and not any personal email addresses. This helps the team keep track of enquiries.

If genetic testing shows an anomaly, will family members be checked?
If you test positive for a genetic variant, the research team will provide guidance on potential testing for family members. Family members can participate in other studies through PD Frontline, such as Rapsodi, without a diagnosis of Parkinson's.

You can find more FAQs on the PD Frontline website:
https://pdfrontline.com/en/faqs

Staying up-to-date

I am not personally eligible to take part in the trial, but as someone with Parkinson's, I am very interested in its progress. How do I keep updated?
Parkinson's UK and Cure Parkinson's are committed to keeping the wider community up to date as the ASPro-PD trial progresses. Sign up for the Research Support Network for regular updates about research news and opportunities.

You can also watch a recording of an update about ASPro-PD and PD Frontline from the Cure Parkinson's **Spring Research Update Meeting**.

Delays

As funders of the trial, can Parkinson's UK or Cure Parkinson's share information regarding the cause of the delays to this trial? When will the trial start?

The delay in recruitment is mainly due to difficulties in manufacturing the study drug. In an earlier clinical study, participants had to take 22 pills of ambroxol per day. The research team has managed to reduce this to just 3 pills per day for the phase 3 ASPro-PD study. Additionally, because the trial is a collaboration between multiple companies, it has added further logistical challenges.