Clinical Trial Results

Drug Studied: BPS-314*d*-MR, also known as esuberaprost

A trial to learn how esuberaprost worked and how safe it was in people with pulmonary arterial hypertension

Sponsor: Lung Biotechnology PBC

LUNG BIOTECHNOLOGY

Thank you!

Thank you to the participants who took part in this clinical trial, called the BEAT trial, to study esuberaprost. You and all of the participants helped researchers learn more about how esuberaprost works in people with pulmonary arterial hypertension.

Lung Biotechnology PBC sponsored this trial and thinks it is important to share the results with you as a trial participant or patient caregiver and the general public.

It is important to note that this summary only shows the results of a single trial. Other trials could have different results. Researchers and health authorities look at the results of many trials to determine which drugs work and how safe they are. It takes many participants like you in multiple trials around the world to help answer these questions.

Topics

If you are reading this on a computer, you can click on any of the topics below to go to that section.

Why was the research needed?

Pulmonary arterial hypertension, also known as PAH, is a type of high blood pressure that makes it difficult for blood to flow through the lungs. There is no known cure for PAH. Over time, this type of high blood pressure can damage the heart and lungs.

Treatments for PAH include medicines that lower blood pressure in the lungs. People with PAH may need blood thinners, which are medicines that help prevent blood clots from forming. They may also need supplemental oxygen therapy to get enough oxygen to the body.

Common symptoms people with PAH may have are:

- dizziness • feeling tired or worn out • shortness of breath • chest pain or discomfort
- rapid, hard, or irregular heartbeat • swelling in the abdomen, arms, legs, or ankles

Esuberaprost is a drug that is thought to lower blood pressure and prevent blood clots from forming. Researchers wanted to learn how esuberaprost would work with inhaled treprostinil, which is another medicine that lowers blood pressure in the lungs.

These were the main questions the researchers wanted to answer:

- Did esuberaprost help the participants manage their PAH?
- What medical problems did the participants have during the trial?

What kind of trial was this?

This was a “Phase 3” trial. In a Phase 3 trial, a drug is tested in a large number of participants with a specific disease or condition. Drugs tested in Phase 3 trials have already been studied in smaller Phase 1 and 2 trials. Phase 3 trial participants help researchers understand more about how a drug works and how safe it is.

This was also a “double-blind” trial. This means that none of the participants, doctors, or other staff knew during the trial which treatment each participant was taking. Some trials are done this way because knowing what treatment each participant is taking can affect the results. When the trial ended, the sponsor found out which treatment each participant took so they could report the trial’s results.

The researchers used a computer program to randomly choose the treatment each participant would take. This helped make sure the treatments were chosen fairly and the treatment groups were evenly balanced.

Who took part in the trial?

The trial included 271 participants with PAH who received a trial drug from 70 trial sites in the United States and Israel.

There were 197 women and 74 men. Everyone in this trial was 19 to 80 years old when they joined.

What happened during the trial?

Before starting the trial treatment, people who wanted to join the trial met with a trial doctor. The doctors made sure that everyone who joined the trial had PAH. They gave the participants a full check-up.

If participants were not already taking inhaled treprostinil when they met with the trial doctor, they started taking it before they received their trial treatment.

At the start of treatment, the participants made a 2-day visit to the trial site. **During treatment,** the participants took their trial medication 4 times per day.

The participants in this trial took one of the following treatments:

- One esuberaprost 15 microgram tablet 4 times per day for the first 2 weeks, and then two esuberaprost 30 microgram tablets 4 times per day

OR

- One placebo tablet 4 times per day for the first 2 weeks, and then two placebo tablets 4 times per day

A **placebo** looks like the trial drug tablet but does not have any real medicine in it. When participants take a placebo, they follow the same steps in a trial as someone who takes the trial drug. The only difference is whether or not the participant gets the trial drug. This helps researchers better understand the actual effects of the drug.

Esuberaprost or a placebo was taken as a tablet by mouth. All of the participants in this trial also took inhaled treprostinil. They took treprostinil with a nebulizer.

The participants visited the trial site once a month for the first 3 months and then once every 3 months after that.

During site visits, the participants:Had a full check-up

- Had their heart health checked with a test called an “electrocardiogram”
- Gave blood and urine samples
- Told the trial staff how they were feeling and what medications they were taking

At all trial site visits, the participants took a test called a “6-minute walk test”. This test measures how far a person can walk in 6 minutes. It also measures whether the person is getting enough oxygen while they exercise. This test helps doctors understand how severe a person’s PAH might be.

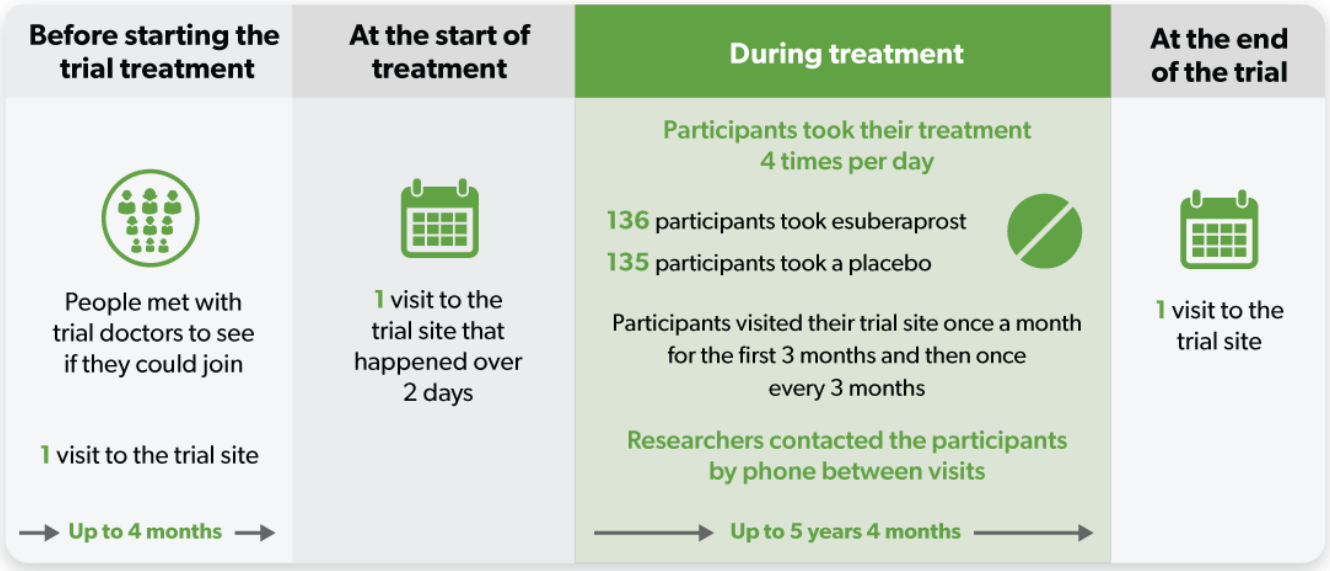
Between visits, the trial site staff contacted the participants by phone to ask about how they were feeling and what medications they were taking.

At the end of the trial, the participants visited the trial site 1 more time as part of the trial.

The participants could stay in the trial until:

- They decided to leave the trial
- Their trial doctor thought they needed different treatment for their PAH outside of the trial
- The trial ended

The figure below shows how the trial was done.



Did esuberaprost help the participants manage their PAH?

This is a summary of the main results of the trial. This summary looks at data for all the participants. Results for individual participants are not provided.

You can find more information about this trial – including other questions the researchers wanted to answer – in the website listed at the end of this summary.

Researchers look at the results of many trials to decide which treatments work best and are safest. Other trials could have different results. Always talk to a doctor before making any treatment changes.

To answer this question, the trial doctors looked at how many participants had PAH that got worse during the trial. One of the ways trial doctors measure PAH worsening is by looking at whether a person with PAH experiences one of these 5 events:

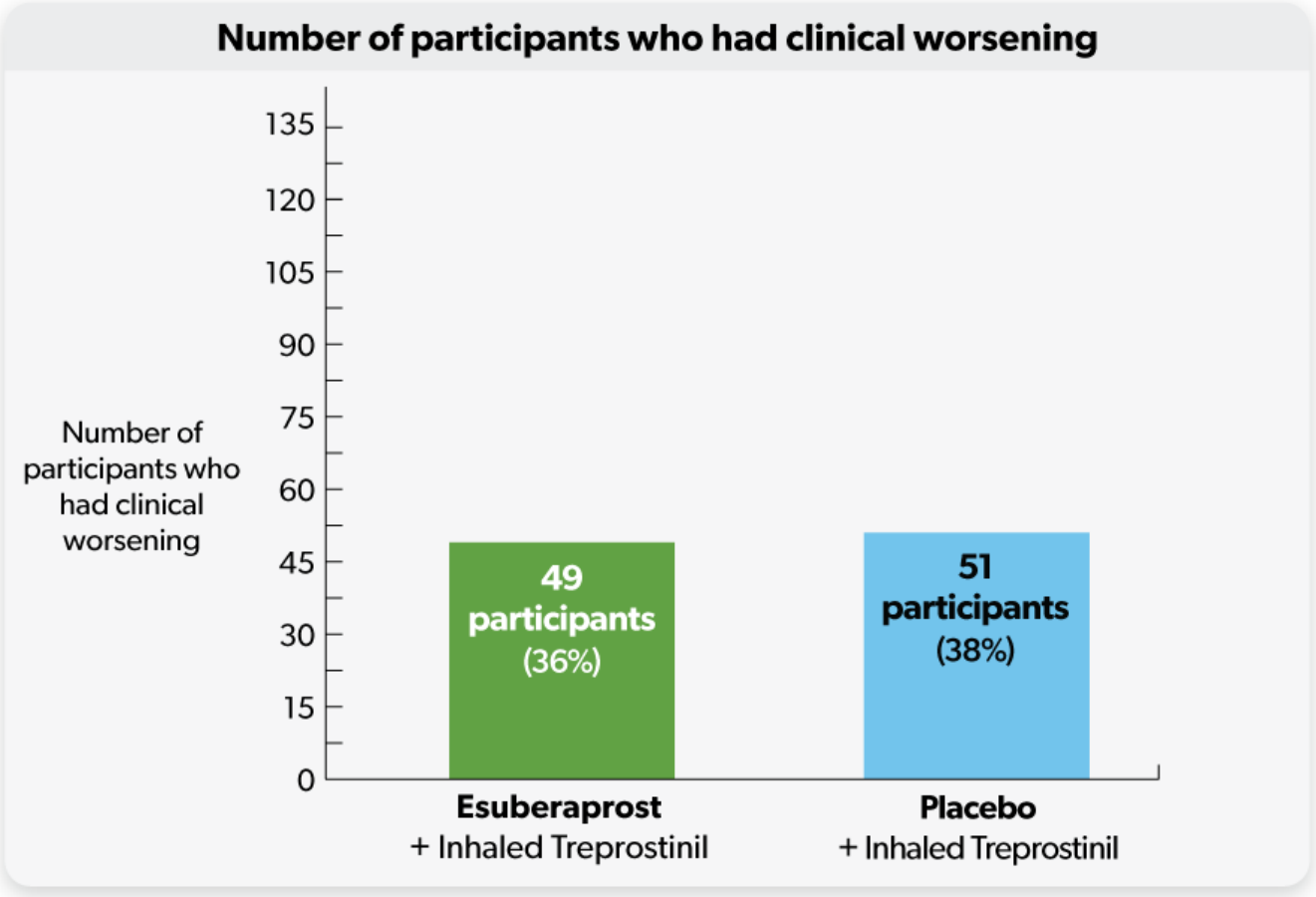
- Worsening of PAH symptoms
- Needing to change their treatment for their PAH to a different PAH medicine
- Needing to be hospitalized for their PAH
- Having symptoms that did not get better with their assigned trial treatment
- Death

If someone with PAH experienced any of these events, they were considered to have had what is called **clinical worsening**, or feeling worse compared to when they started the trial. When trial doctors test new PAH treatments, they often want to know whether a new treatment can prevent or delay clinical worsening.

In this trial, doctors looked at the number of participants who had clinical worsening while taking esuberaprost and compared it with the number of participants who had clinical worsening while taking a placebo.

In this trial, esuberaprost did not help prevent clinical worsening any better than a placebo did.

The figure below shows how many participants had clinical worsening during the trial.



What medical problems did the participants have during the trial?

This section is a summary of the medical problems the participants had during this trial. These medical problems are called **adverse events**. An adverse event is considered "serious" when it is life threatening, causes long-term problems, or the participant needs hospital care to treat it.

These adverse events may or may not have been caused by the trial drug. A lot of research is needed to know whether a treatment causes an adverse event. .

The website listed at the end of this summary may have more information about the adverse events that happened in this trial.

How many participants had serious adverse events or died during the trial?

	Esuberaprost + Inhaled Treprostinil	**Placebo + Inhaled Treprostinil**
How many participants had serious adverse events?	75 out of 137 (55%)	78 out of 134 (58%)
How many participants died during the trial?	26 out of 137 (19%)	22 out of 134 (16%)

What serious adverse events did the participants have?

The most common serious adverse event was PAH that got worse during the trial. This happened to:

- 23 out of 137 participants who took esuberaprost, which was 17% of this group.
- 30 out of 134 participants who took a placebo, which was 22% of this group

This was the only serious adverse event that happened in at least 10% of the participants in either group. There were other serious adverse events, but these happened in fewer participants.

Of the participants who died during the trial, most of the deaths were due to PAH that got worse.

How many participants had any adverse events and what were they?

The table below shows how many participants in each group had adverse events and how many participants stopped their trial treatment because of adverse events.

	Esuberaprost + Inhaled Treprostinil	Placebo + Inhaled Treprostinil
How many participants had at least 1 adverse event?	135 out of 137 (99%)	132 out of 134 (99%)
How many participants stopped taking their trial treatment because of an adverse event?	43 out of 137 (31%)	44 out of 134 (33%)

The table below shows the most common adverse events that happened in at least 15% of participants in any treatment group. There were other adverse events, but they happened in fewer participants.

The most common adverse events in this trial

	Esuberaprost + Inhaled Treprostinil (Out of 137 participants)	Placebo + Inhaled Treprostinil (Out of 134 participants)
Headache	61 (45%)	39 (29%)
Nausea	41 (30%)	33 (25%)
Shortness of breath	36 (26%)	44 (33%)
Worsening of PAH	33 (24%)	32 (24%)
Diarrhea	32 (23%)	24 (18%)
Cough	27 (20%)	26 (19%)
Upper respiratory infection	26 (19%)	44 (33%)
Dizziness	24 (18%)	36 (27%)
Fatigue	22 (16%)	28 (21%)
Swelling in arms or legs	22 (16%)	17 (13%)
Common cold	21 (15%)	19 (14%)
Sinus infection	21 (15%)	19 (14%)
Urinary tract infection	15 (11%)	21 (16%)

How has this trial helped?

The results of this trial helped the researchers learn more about how esuberaprost works in people with PAH.

In this trial, taking esuberaprost with inhaled treprostinil did not help the participants manage their PAH better than taking a placebo with inhaled treprostinil.

Clinical trials like this are important to help researchers understand which treatments work best and are safest for patients.

Researchers and health authorities look at the results of many trials to understand how a drug works. This summary only shows the main results from this trial. Other trials might provide different results.

Lung Biotechnology does not have plans for other clinical trials with esuberaprost at this time.

What has happened since the trial ended?

The participants were in this trial for up to 5 years and 4 months. The entire trial took about 5 years and 8 months to finish. The trial started in June 2013 and ended in February 2019.

Lung Biotechnology PBC reviewed the data when the trial ended and created a report of the results. This is a summary of that report.

Where can I learn more about this trial?

You can find more information about this trial on the website listed below. If a full report of the results is available, it can also be found there.

http://www.clinicaltrials.gov – On this website, type **NCT01908699** into one of the search boxes and click "Search".

Trial title: A multicenter, double-blind, randomized, placebo-controlled, Phase 3 study to assess the efficacy and safety of oral BPS-314*d*-MR added on to treprostinil, inhaled (Tyvaso®) in subjects with pulmonary arterial hypertension

Protocol number: BPS-314*d*-MR-PAH-302

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Thank you!

Lung Biotechnology thanks you again for your time and interest in this clinical trial. Clinical trial participants like you help researchers and health authorities find answers to important health questions and discover new treatments.