Clinical Trial Results

Drug Studied: APL-130277

A trial to learn how APL-130277 works and how safe it is in people with Parkinson's disease

Sponsor: Sunovion Pharmaceuticals Inc.

Thank you!

Thank you to the participants who took part in this clinical trial to study APL-130277. You and all of the participants helped researchers learn more about how APL-130277 works in people with Parkinson's disease.

Sunovion Pharmaceuticals sponsored this trial and thinks it is important to share the results with you and the general public.

If you participated in the trial and have questions about the results, please speak to a doctor or a staff member at your trial site or talk to your doctor.

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.

What has happened since the trial ended?

The participants were in this trial for about 5 months, but the entire trial took about 2 years and 6 months to finish. The trial started in June 2015 and ended in December 2017. The trial included 141 participants from 33 trial sites in the United States and Canada.

Sunovion Pharmaceuticals reviewed the data when the trial ended and created a report of the results. This is a summary of that report.

Why was the research needed?

Parkinson's disease is a disease that affects the nervous system. People with Parkinson's disease have problems with movement that get worse with time. The movement symptoms, or **motor symptoms**, of Parkinson's disease include:

- shaking, also called tremor, which often starts in the hands
- slowed movement
- rigid muscles
- problems with posture and balance

There are treatments to help control these symptoms. One of these treatments is a medication called levodopa. People with Parkinson's disease may take levodopa and other medications several times a day to help control their symptoms.

Even with these medications, people with Parkinson's disease often have periods of time during the day when these symptoms happen anyway, such as when their medication wears off. These periods are known as **"off" episodes**.

A medication called apomorphine is used to treat "off" episodes when they happen. It is given as an injection under the skin.

In this trial, researchers tested a new form of apomorphine called APL-130277. APL-130277 is made as a thin film that dissolves when placed under the tongue.

The main questions the researchers wanted to answer were:

- Did APL-130277 improve motor symptoms when taken during "off" episodes?
- What side effects did the participants have?

Who took part in the trial?

To answer these questions, the researchers asked for the help of men and women with Parkinson's disease whose symptoms improved with levodopa, but who still had "off" episodes. There were 89 men and 52 women in the trial. Everyone was 43 to 86 years old when they joined.

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 trials. Phase 3 trial participants help researchers understand more about how a drug works and how safe it is.

What treatments did the participants take?

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

- APL-130277 (trial drug)
- A placebo

A **placebo** looks like the trial drug 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 medicine. The only difference is whether or not the participant gets the trial treatment. This helps researchers better understand the actual effects of the treatment.

What happened during the trial?

Before the trial started, people with Parkinson's disease who wanted to join the trial met with trial doctors. The trial doctors gave everyone a full check-up and collected blood and urine samples.

Once the trial started, the participants kept taking their regular Parkinson's disease medications. But they took APL-130277 or a placebo to treat "off" episodes. The participants also took a medication that would help manage nausea and vomiting that can happen when people take apomorphine.

During Part 1 of the trial, the participants worked with trial doctors to find the dose of APL-130277 that would help them move from an "off" state to an "on" state within 45 minutes of taking APL-130277.

Participants were considered to be "on" if their motor symptoms improved and they could perform daily activities at least as well as when their regular Parkinson's disease medications were working well for them.

All of the participants started with 10 milligrams of APL-130277 at their first visit. If they did not reach an "on" state with this dose, they came back to the trial site within the next few days to try the next highest dose.

These were the doses of APL-130277 used in the trial:

- 10 milligrams
- 15 milligrams
- 20 milligrams
- 25 milligrams
- 30 milligrams
- 35 milligrams

If the participants moved to an "on" state with one of these doses of APL-130277, they could move to Part 2 of the trial.

During Part 2 of the trial, the participants were assigned to take APL-130277 or a placebo at home to treat "off" episodes for 3 months. The researchers used a computer program to randomly choose the treatment each participant would take. This helped make sure the treatments were chosen fairly. The participants who were assigned to take APL-130277 took the same dose that helped them move from an "off" state to an "on" state in Part 1 of the trial.

The participants could treat up to 5 "off" episodes a day.

During this part of the trial, none of the participants, doctors, or other staff knew whether the participant was taking APL-130277 or a placebo. 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.

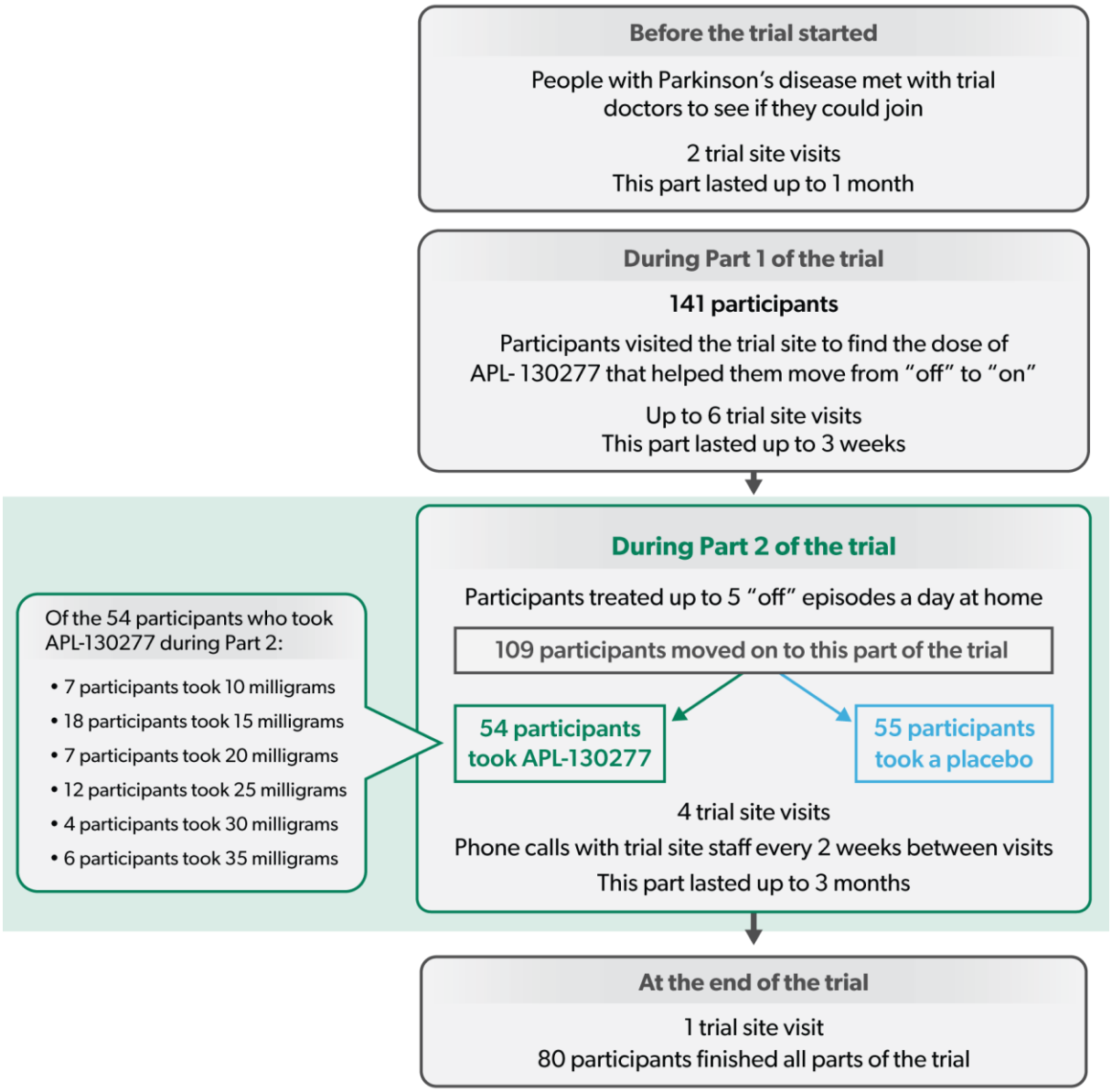
During trial site visits, the trial doctors checked the participants' health. The participants:

- Took their assigned treatment to treat an "off" episode
- Answered questions about their Parkinson's disease symptoms and "off" episodes
- Told the trial doctors about how they were feeling, what medications they were taking, and if they were having any side effects
- Completed questionnaires

Participants could leave the trial at any time, either because of side effects or other reasons.

At the end of the trial, the participants returned to the trial site for 1 more visit 1 week after their last dose. They got a full check-up and gave blood and urine samples.

The figure below shows how the trial was done.



What were the results of the trial?

This is a summary of the main results of the trial. Results for each participant may have been different and are not in this summary.

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

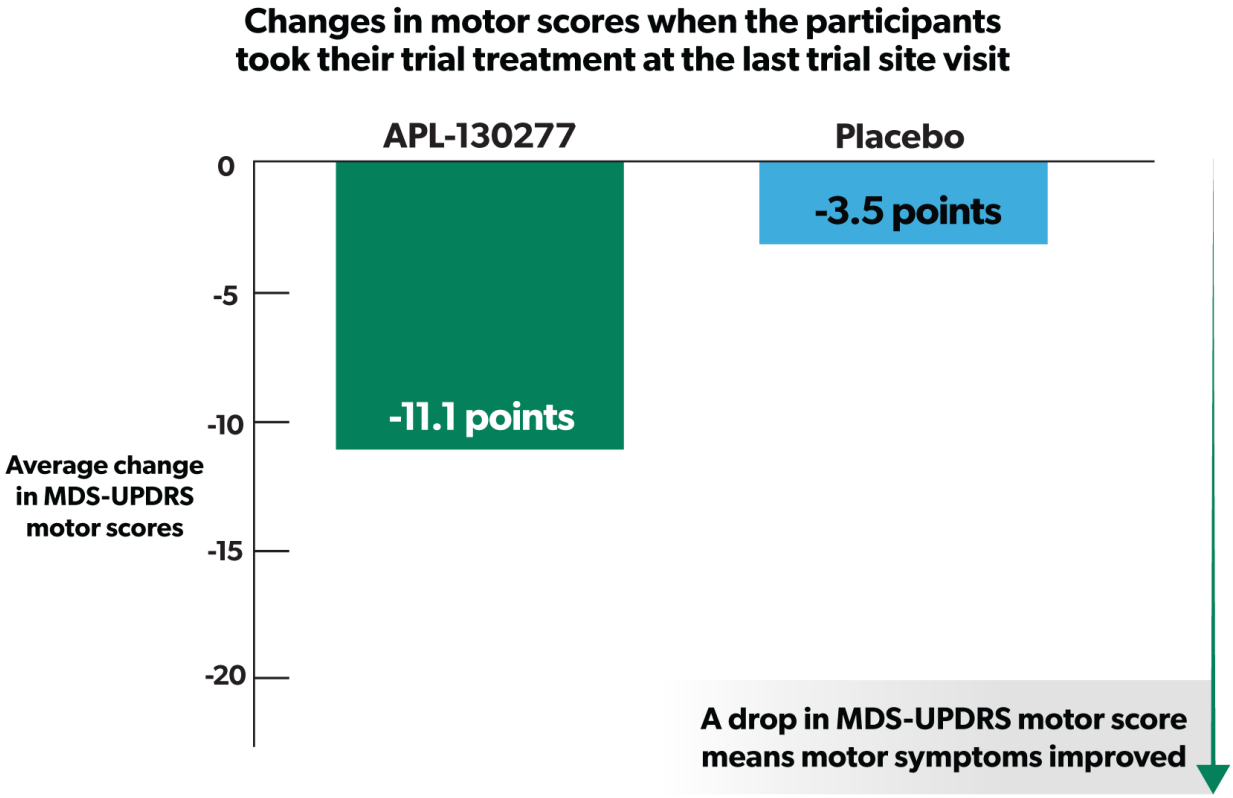
Researchers look at the results of many trials to decide which treatments work best and are safest. Other trials could have different results. Always talk to a doctor before making any treatment changes.

Did APL-130277 improve motor symptoms when taken during "off" episodes?

To answer this question, the researchers measured the participants' motor symptoms with a scale called the **Movement Disorders Society Unified Parkinson's Disease Rating Scale**, also called the **MDS-UPDRS**.

The researchers looked at how MDS-UPDRS motor scores changed from before the participants took their assigned trial treatment to 30 minutes afterward. They measured this change at every trial site visit. But the main goal of the trial was to measure this change at the last visit after the participants had been taking APL-130277 or a placebo for 3 months.

On average, MDS-UPDRS scores improved more for the participants who took APL-130277 than for the participants who took a placebo.



What side effects did the participants have during the trial?

This section is a summary of the side effects the participants had during this trial. Side effects, which are also known as "adverse events", are unwanted or unexpected medical problems that can happen when someone takes a medication. An adverse event is considered "serious" when it is life threatening, causes lasting problems, or requires hospital care.

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 websites 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?

	During Part 1 of the trial	During Part 2 of the trial	
	All 141 participants took APL-130277	54 participants took APL-130277	55 participants took a placebo
How many participants had at least 1 serious adverse event?	1 (0.7%)	2 (3.7%)	1 (1.8%)
How many participants died from a serious adverse event?	0	1 (1.9%)	0

What serious adverse events did the participants have?

During Part 1 of the trial, when all of the participants took APL-130277:

- 1 participant had a serious adverse event that was a type of bacterial infection.

During Part 2 of the trial:

- 1 participant who took APL-130277 had a sudden loss of heart function. This participant died because of this serious adverse event.
- 1 participant who took APL-130277 had 2 serious adverse events. This participant had heart failure and low levels of potassium in the blood.
- 1 participant who took a placebo had 2 serious adverse events. This participant had "encephalopathy", which is a general term that describes any disease or brain damage that affects the way the brain works, and a sudden change in kidney function.

How many participants had any adverse events?

	During Part 1 of the trial	During Part 2 of the trial	
	All 141 participants took APL-130277	54 participants took APL-130277	55 participants took a placebo
How many participants had at least 1 adverse event?	82 (58%)	48 (89%)	25 (46%)
How many participants stopped taking their trial treatment because of an adverse event?	13 (9%)	15 (28%)	4 (7%)

During Part 2 of the trial, more participants who took APL-130277 had adverse events compared with participants who took a placebo. More participants who took APL-130277 stopped taking their trial treatment because of an adverse event compared with participants who took a placebo.

What adverse events did the participants have?

The tables below show the adverse events that happened to at least 10% of the participants in Part 1 of the trial and to at least 10% of the participants in either treatment group in Part 2 of the trial. There were other adverse events, but they happened in fewer participants.

These were the most common adverse events			
During Part 1 of the trial		During Part 2 of the trial	
	All 141 participants took APL-130277	54 participants took APL-130277	55 participants took a placebo
Nausea	29 (21%)	**Nausea**	15 (28%)	2 (4%)
Yawning	17 (12%)	**Feeling sleepy**	7 (13%)	1 (2%)
Feeling sleepy	16 (11%)			
Dizziness	16 (11%)			

During Part 2 of the trial, more participants who took APL-130277 had nausea and reported feeling sleepy compared with the participants who took a placebo.

How has this trial helped?

The results of this trial helped the researchers learn more about how APL-130277 works in people with Parkinson's disease. 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.

Clinical trials with APL-130277 in patients with Parkinson's disease are ongoing. Other clinical trials with APL-130277 are not planned at this time.

Where can I learn more about this trial?

You can find more information about this trial on the websites 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 **NCT02469090** into one of the search boxes and click "Search".

Trial title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Examine the Efficacy, Safety and Tolerability of APL-130277 in Levodopa Responsive Patients with Parkinson's Disease Complicated by Motor Fluctuations ("OFF" Episodes)

Protocol number: CTH-300

Sponsor: Sunovion Pharmaceuticals Inc.

Thank you!

Sunovion 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.