The effects and safety of BAF312 for people with intracerebral hemorrhage

Thank you!

Thank you to the participants who took part in the clinical trial for the trial drug **BAF312**, also called siponimod. Every participant helped the researchers learn more about BAF312.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public.

We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CBAF312X2207
Drug studied: BAF312
Sponsor: Novartis

What was the main purpose of this trial?

The main purpose of this trial was to learn if BAF312 could reduce brain swelling in people with intracerebral hemorrhage, also called ICH. It was also to learn more about the safety of BAF312. To find this out, researchers compared the effects of BAF312 to a placebo.

ICH is bleeding inside the brain from a burst blood vessel. It almost always leads to brain damage and **brain swelling**, which is a build-up of fluid in the brain. Currently, there are no drugs approved to prevent brain swelling and damage from ICH.

BAF312 – a trial drug that researchers thought may help prevent brain swelling.

Placebo – looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

The main questions this trial was designed to answer:

- Did the participants who received BAF312 have less brain swelling?
- What medical problems did the participants have during this trial?
  Keeping track of the medical problems helped to learn about the safety of BAF312.

Main results: The participants who received BAF312 had about the same amount of brain swelling as those who received the placebo after 2 weeks. The clinical trial team found no new safety concerns with BAF312.

How long was this trial?

The trial began in December 2017 and ended in May 2020. It was planned for the participants to be in the trial for about 3 months.

The sponsor paused recruitment for this trial in 2020 because of COVID-19. After the first group of participants participated in the trial, early data showed that BAF312 did not reduce brain swelling. Because of this, the sponsor decided to end this trial early. The decision to end the trial was not related to safety concerns with BAF312.

Who was in this trial?

29 participants were in this trial – 16 women and 13 men. The participants were 40 to 84 years old. Their average age was 61.

19 participants reported their race as White, 5 participants as Black or African American, 4 participants as Other, and 1 participant as Asian.

Every participant had ICH that:

- Could not be treated with surgery
- Was located in certain parts of the brain
- Happened within 24 hours of joining the trial

They were also in good health before their ICH.

This trial took place in the United States.

Visit **novctrd.com** for more information about:

- Who could and could not be in this trial
- Reasons why the participants did not complete the trial

Use trial number **CBAF312X2207** to find the scientific summary.

What trial treatments did the participants receive?

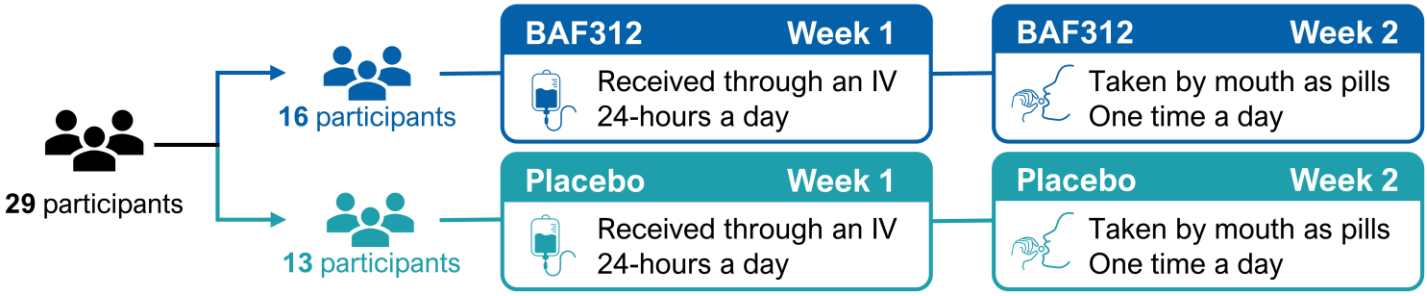
A computer program was used to randomly assign each participant to one of these treatments:

- **BAF312** –1.75 up to 10 milligrams (mg) for 14 days
- **Placebo** – looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

Using a computer program to assign the treatments helped make sure the team compared the results as fairly as possible.

The participants and trial staff did not know what treatment each participant received during the trial. Some trials are done this way because knowing what treatment participants receive can influence the results. Not knowing what treatment participants receive helps make sure the results are looked at fairly.

The graphic below shows how many participants were assigned each treatment.



For the first week, the participants received their assigned treatment into their blood through a needle in a vein, called an intravenous infusion (IV). The participants who received BAF312 started with a low dose that slowly went up over 3 days. For the second week, the participants received their treatment by mouth as pills, as long as they could safely swallow them. Those who couldn't safely swallow the pills stopped treatment after the first week. Throughout the trial, each participant also received the usual medical care for ICH.

What were the main results of this trial?

This is a summary of the overall results of this trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results.

Always talk to a doctor before making any changes to your health care.

Did the participants who received BAF312 have less brain swelling?

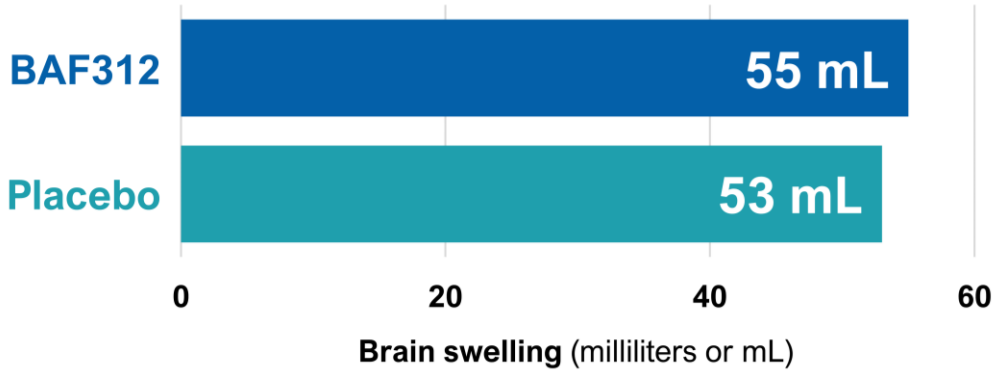
No, the participants who received BAF312 had about the same amount of brain swelling as those who received the placebo after 2 weeks.

To find this out, the trial doctors took images of the participants' brains with a type of X-ray called a **CT** (Computed Tomography) scan. These images show the amount of fluid in the swelling around their ICH, measured in milliliters (mL). The clinical trial team compared the amount of swelling in the participants who received BAF312 to those who received the placebo.

The team found that both groups had about the same amount of brain swelling 2 weeks after starting treatment. The team concluded that BAF312 did not reduce brain swelling after ICH and the sponsor decided to end the trial early.

The participants' brain swelling 2 weeks after starting treatment

The average amount of fluid in the swelling around the participants' ICH 2 weeks after starting treatment. The chart below compares those who received BAF312 to those who received the placebo.



What medical problems did the participants have during this trial?

Medical problems that happen during trials are called “adverse events”. Trial doctors looked for any adverse events during the visits to the trial site. The participants also reported adverse events.

Many trials are needed to know if a drug or treatment causes an adverse event. Trial doctors keep track of all adverse events that happen in trials, even if they think the adverse events are not related to the trial treatments.

An adverse event is:

- Any **unwanted sign or symptom** that the participants have during a trial.
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

The adverse events in this section include any that happened during treatment and up to about 3 months after treatment.

Most of the participants (25 of 29 participants) reported adverse events, some of which were considered serious. A similar number of participants in each group had adverse events. The clinical trial team concluded there were no new safety concerns for BAF312.

What serious adverse events did the participants have?

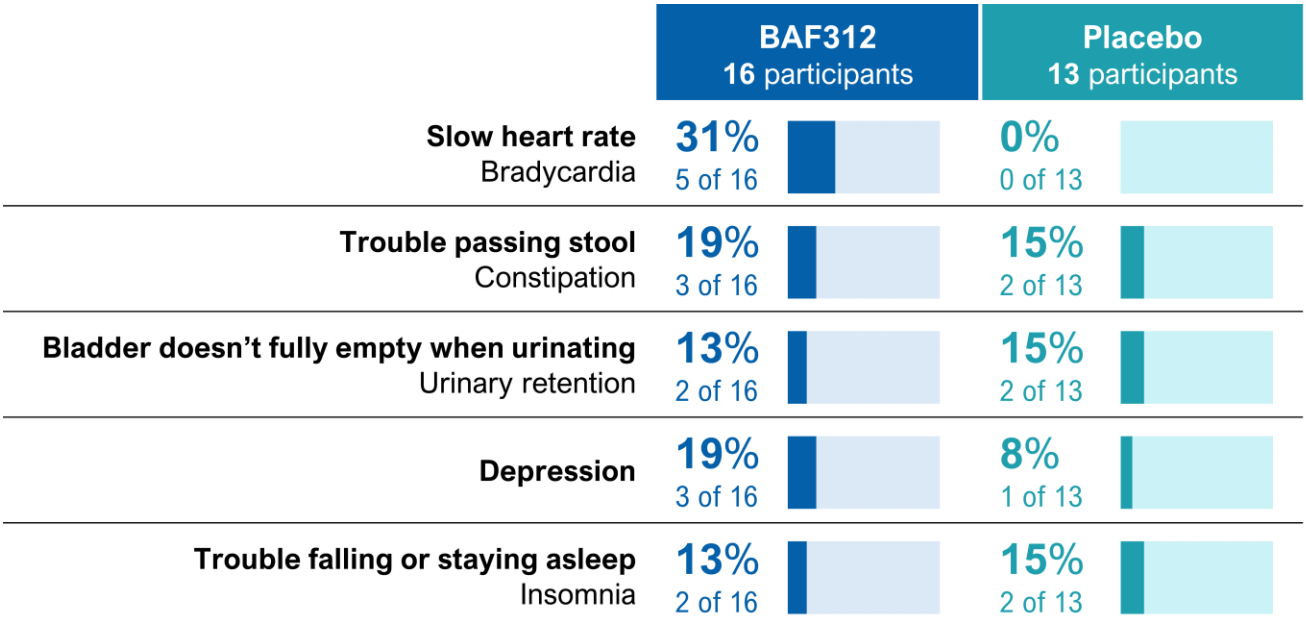
9 of 29 participants, or 31%, reported serious adverse events. Many of these were from problems related to ICH. The table below shows these adverse events that happened in **2 or more participants**. Other serious adverse events were reported by fewer participants.

	BAF312 **16** participants	Placebo **13** participants
Kidneys stop working Renal failure	6% 1 of 16	15% 2 of 13
Breathing food or liquids into the lungs Pneumonia aspiration	6% 1 of 16	8% 1 of 13
Heavy bleeding in the esophagus, stomach, or small intestine Upper gastrointestinal hemorrhage	6% 1 of 16	8% 1 of 13
Lungs can’t get enough oxygen into the blood Respiratory failure	6% 1 of 16	8% 1 of 13

No participants died during this trial.

What other adverse events did the participants have?

25 of 29 participants, or 86%, had adverse events that were not considered serious. The table below shows these adverse events that happened in **4 or more participants**. Other adverse events were reported by fewer participants.



What was learned from this trial?

This was the first trial to learn about the effects and safety of BAF312 in participants with ICH. The sponsor concluded that BAF312 was not likely to meaningfully reduce the participants' brain swelling. Because of this, the trial ended early. The clinical trial team concluded there were no new safety concerns for BAF312.

These are the results of a single trial. Other trials may have different results. This was one of many trials a drug goes through. This type of trial learned about the safety of a trial drug in a small number of participants.

Where can I learn more about this and future trials?

For more information about this trial go to any of the following websites:

- **novctrd.com** – search using the study number **CBAF312X2207**
- **clinicaltrials.gov** – search using the number **NCT03338998**

If more trials are planned, they will appear on the public websites above. When there, search for **BAF312, siponimod, or intracerebral hemorrhage.**

Full trial title:
A phase II, patient- and investigator-blinded, randomized, placebo-controlled study to evaluate efficacy, safety and tolerability of BAF312 (siponimod) in patients with stroke due to intracerebral hemorrhage (ICH)

If you participated in the trial and have **questions** about the results, please speak with the trial doctors or staff at your trial site.

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