CLINICAL TRIAL RESULTS SUMMARY

A First-in-Human Single and Multiple Ascending Dose Study With A2342

THANK YOU!

Thank you to those who participated in this research study for A2342. Without trial participants, drug development would not be possible. Participation in this trial has helped the researchers learn how A2342 works and if it is safe to use.

The trial information given in this summary is from one trial only and must not be used to make medical decisions. This drug is not yet approved and the outcomes of this trial may not apply to all patients as this trial was conducted in healthy volunteers. Do not change your current medical treatment without consulting your doctor.

WHAT WAS THE PURPOSE OF THIS CLINICAL TRIAL?

The purpose of this trial was to learn about any potential side effects of A2342 treatment, if A2342 should be given with food or not, and if it is okay to take A2342 at the same time as tenofovir alafenamide (TAF), and to gain information about which dose of A2342 can be used in future clinical trials.

HOW WAS THIS TRIAL DONE?

Who took part in this trial?

This trial included 37 healthy men and 39 healthy women volunteers between the ages of 20 and 60 years.

Where did this trial take place?

This trial took place in the United Kingdom.

When did this trial take place?

This trial started in February 2023 and ended in September 2023.

What treatments were tested in this trial?

This trial studied A2342 capsules compared to a placebo taken by mouth. A placebo is an identical-looking capsule that does not have any active medical ingredients in it. A2342 is being

researched for the possible treatment of Hepatitis D virus, which only occurs in people who are infected with Hepatitis B virus.

This trial also studied TAF tablets given alone or alongside A2342. TAF is an approved medication most commonly used for the treatment of Hepatitis B infection in adults and often given in combination with other medications. Since it is likely in the future that A2342, if approved, would need to be given with other medications, it was tested in this study with TAF to see if there were any possible interactions between the 2 drugs.

What has been completed?

Before treatment, the trial doctor checked the health of every person to ensure they could be in the trial.

This trial was done in 3 parts. In all of these parts, people were split to receive one of the treatments (A2342 or placebo). Around 3 in every 4 people took A2342 and around 1 in every 4 people took placebo. The treatment (A2342 or placebo) a person was given was determined by chance (randomised) to reduce any possible differences between the people who were receiving the treatments. Reducing differences between the treatments makes the comparison between the treatments fairer. In the third part, everyone also took TAF.

This trial was also "double-blinded." This means that neither the people taking part in the trial nor the trial doctors knew who was given which medicine (A2342 or placebo). This was done to make sure that the trial results were not influenced in any way.

The first part of the trial had 4 groups that were given their treatment once. A different dose of trial medicine (A2342) was tested in the 4 groups, starting at the lowest strength in the first group. A2342 was given to these people after they fasted overnight. Each group started with 1 person getting A2342 and 1 person getting placebo. At least 24 hours later, the trial doctor reviewed their medical tests and what side effects, if any, these people had. If there were no safety concerns in these 2 people, the rest of the people in that group were treated. People stayed in the clinic for 4 days, from the day before treatment until 2 days after treatment. The third group of people returned to the clinic for a second time and were given A2342 again, but this time it was given after eating a meal. This was done to check if food changed how A2342 works. People in all groups returned to the clinic 7 days later for an additional check-up.

The second part of the trial had 4 groups that were given their treatment for 7 days. A different dose of trial medicine was tested in each group, with the lowest strength given once a day in the first group after they fasted overnight and twice a day in the second group after they had eaten meals. The highest strength was given twice a day in the third group after they had eaten meals and a dose in between the lowest and highest strengths was given twice a day in the fourth group after they had eaten meals. People stayed in the clinic for 10 days, from the day before treatment started until 2 days after treatment ended. They returned to the clinic 7 days later for an additional check-up.

The third part of the trial had 1 group that was given TAF once a day for 20 days. For the first 10 days, TAF was the only medicine given. For the second 10 days, TAF was given to people once a day on the same days as they were given their treatment (A2342 or placebo twice a day) after they had eaten meals. People stayed in the clinic for 22 days, from the day before treatment started until 1 day after treatment ended. They returned to the clinic 7 days later for an additional check-up.

Blood tests were done to see how much medicine was in the blood. The trial doctor checked for any side effects from the medicines. After each group completed, researchers reviewed the amount of medicine in people's blood, blood tests, vital signs, the electrical activity of their heart, and what side effects they had to decide if the next planned group could be treated and what strength of trial medicine to give to the next group.

WHAT ARE THE MAIN RESULTS OF THIS TRIAL?

A2342 was well tolerated when administered as one and multiple doses. There were no serious side effects during the study. There were some nonserious side effects as described below.

WHAT WERE THE SIDE EFFECTS?

In this trial, some people experienced side effects. Side effects are unwanted medical events that happen during the trial. Treatment-related side effects are side effects that the trial doctor (investigator) thinks could have been caused by the treatments in the trial. Not all the people in this trial had side effects. All of the side effects that happened in this trial were mild or moderate. There were no reports of serious side effects.

In the first part of the trial when people were treated once, the number of people with side effects was similar for all groups who took A2342 and also for the people who took placebo. In these groups:

- 2 to 3 out of 6 people (33.3% to 50.0%) in each group had side effects after A2342
- 3 out of 8 people (37.5%) had side effects after placebo
- After the third group had A2342 after eating a meal, there were no side effects

The most common side effect in people treated with A2342 once was COVID-19 in 2 out of 30 people (6.7%). All other side effects affected only 1 person each.

One person who received A2342 had a side effect of increased appetite in the lowest dose group, which the investigator thought was possibly related to the treatment. The investigator thought all the other side effects in this part of the trial were not related to the treatment.

In the second part of the trial when people were treated for 7 days, more people who were given higher dose strengths had side effects than people who had lower dose strengths. In these groups:

- 2 to 5 out of 6 people (33.3% to 83.3%) in each group had side effects after A2342
- 5 out of 8 people (62.5%) had side effects after placebo

The most common side effects in people treated with A2342 for 7 days were:

- 3 out of 24 people (12.5%) had dizziness
- 3 out of 24 people (12.5%) had headache
- 3 out of 24 people (12.5%) had back pain
- 3 out of 24 people (12.5%) had myalgia (muscle pain)
- 2 out of 24 people (8.3%) had constipation
- 2 out of 24 people (8.3%) had diarrhoea

Of these side effects, headache and dizziness were also side effects for 1 person each treated with placebo.

One person had a side effect of liver enzymes increased, which was considered by the investigator to be possibly related to A2342 treatment and which got better after the last planned

day of the trial. The investigator thought all the other side effects in this part of the trial were not related to the treatment.

In the third part of the trial when people were treated with TAF for 20 days and with A2342 for 10 days, about the same number of people had side effects in the first 10 days with only TAF as in the second 10 days with TAF plus A2342. In these groups:

- 7 out of 9 people (77.8%) had side effects after TAF plus A2342
- 8 out of 12 people (66.7%) had side effects after TAF alone
- 2 out of 3 people (66.7%) had side effects after TAF plus placebo

The most common side effects in people treated with TAF plus A2342 were:

- 2 out of 9 people (22.2%) had constipation
- 2 out of 9 people (22.2%) had headache

The most common side effects in people treated with only TAF or TAF plus placebo were:

- 2 out of 12 people (16.7%) after TAF only and 2 out of 3 people (66.7%) after TAF plus placebo had constipation
- 2 out of 12 people (16.7%) after TAF only had back pain

All other side effects affected only 1 person each.

One person had a side effect of liver enzymes increased, which was considered by the investigator to be possibly related to A2342 treatment and which got better by the end of the trial. The investigator thought all the other side effects in this part of the trial were not related to A2342 treatment.

WHAT WAS LEARNED FROM THIS TRIAL?

The side effects that happened in this study were mild enough that A2342 can be studied further. Important information was found about the dose of A2342 and how A2342 should be given that can be used in any possible future clinical trials.

WHERE CAN I FIND MORE INFORMATION ABOUT THIS TRIAL?

Trial Title	A Phase 1, Double-blind, Placebo-controlled, Single and Multiple Ascending Dose Study in Healthy Adult Subjects to Investigate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, Food Effect, and Effect on Tenofovir Pharmacokinetics of an Oral Formulation of the NTCP Inhibitor A2342
Public Trial Title	A First-in-Human Single and Multiple Ascending Dose Study With A2342
Protocol Number	A2342-001
Study Sponsor	Albireo AB, an Ipsen company www.ipsen.com

Please email any questions to clinical.trials@ipsen.com
This study is also registered on www.isrctn.com

ARE THERE PLANS FOR FURTHER TRIALS?

There are currently no ongoing trials with A2342, but additional trials with A2342 may be planned.