



CLINICAL STUDY RESULTS

A study to assess the effects of fidrisertib on the amount of caffeine and a combined oral contraceptive in the blood of healthy adults

Overall, the results suggest that the amount of caffeine in blood was similar with or without fidrisertib, while the amount of the combined oral contraceptive in blood changed in healthy adults.

The results shown in this summary represent one clinical study in healthy adults. Other clinical studies may produce different results.

What was the study about?

Fidrisertib (also known as IPN60130) is being developed as a treatment for fibrodysplasia ossificans progressiva (FOP).

FOP is a very rare condition in which bone grows in places where it does not normally exist, such as muscles and tissues that hold muscles and bones together (tendons and ligaments). This new bone can cause loss of movement.

Palovarotene is an approved drug for patients with FOP above 8 to 10 years of age. However, as FOP starts to affect the body from early childhood, there is a need for new treatments.

Fidrisertib is expected to act on the abnormal protein that causes extra bone growth in patients with FOP.

Researchers wanted to know how fidrisertib affects the amount of caffeine and a combined oral contraceptive in the blood of healthy adults.

Caffeine is broken down by a protein called CYP1A2. CYP1A2 helps break down many other substances and drugs in the body. By assessing the amount of caffeine in blood, researchers wanted to learn if fidrisertib affects the activity of CYP1A2.

An increase in the amount of caffeine in blood means the activity of CYP1A2 is lowered, and thus less caffeine is broken down. Similarly, a decrease in the amount of caffeine in blood means the activity of CYP1A2 is increased, and thus more caffeine is broken down.

Fidrisertib may also cause birth defects, thus a reliable birth control is needed during treatment. By assessing the amount of combined oral contraceptives in the blood, researchers wanted to learn if fidrisertib could affect the activity of the oral contraceptives. An oral contraceptive, also called 'the pill', helps to prevent unwanted pregnancy. A decrease in the amount of oral contraceptive in the blood means that the female is at risk of becoming pregnant.

So, the researchers wanted to know how fidrisertib affects the amount of caffeine and a combined oral contraceptive in the blood of healthy adults. A once daily dose of 120 milligrams (mg) fidrisertib was chosen for this study because it represents the highest amount that might be used in patients.

The aim of this study was to learn how fidrisertib affects the amount of

1. caffeine in the blood of healthy men and women, and
2. a combined oral contraceptive in the blood of healthy women.

This study did not test if fidrisertib helps improve FOP.

The study took place between May 2024 and October 2024 at a single study site in the United States.

Who took part in this study?



45

PARTICIPANTS



7

MEN



38

WOMEN



40 YEARS

AVERAGE AGE

To take part in the study, participants had to:



- be aged between 18 and 55 years,
- be female for the group that received combined oral contraceptive, and either male or female for the group that received caffeine,
- be healthy, as assessed by the study doctors,
- weigh at least 50 kg, and
- have a body mass index (BMI), a measure of body fat based on height and weight, between 18 and 30 kilograms per square metre (kg/m²).



Participants could not take part in the study if:

- they had a health condition or had received treatments that could affect the result of the study.

What treatments were used in this study?

Study drug		Drugs to check interaction with fidrisertib	
	Fidrisertib		Caffeine
Taken by mouth at a dose of 120 mg once a day as 4 capsules, 2 capsules of 50 mg and 10 mg each.		Taken by mouth as 1 tablet of 100 mg.	
From Day 3 to Day 18 (when given with caffeine), and		Taken by mouth as 1 tablet.	
From Day 5 to Day 22 (when given with combined oral contraceptive).		This was a combination of two drugs, called levonorgestrel (LN) and ethinyl estradiol (EE). 1 tablet had 0.02 mg of EE and 0.15 mg LN.	
		A single dose on Day 1 and Day 17.	
		A single dose on Day 1 and Day 19.	

This study had three parts:

Screening: The study doctor checked whether participants could take part in this study within 28 days before they started the study treatment.

Treatment:

A total of 45 participants were enrolled to 2 treatment groups. The treatment was done in two parts.

Group 1 had 17 participants. In Part 1, they received a single dose of caffeine alone on Day 1. In Part 2, they took fidrisertib daily and took a single dose of caffeine on Day 17.

Group 2 had 28 participants. In Part 1, they received a single dose of combined oral contraceptive alone on Day 1. In Part 2, they took fidrisertib daily and took a single dose of combined oral contraceptive on Day 19.

Caffeine and the combined oral contraceptive were given on an empty stomach.

This study was “open-label”. This means that the researchers and the participants knew which treatment was given to each participant.

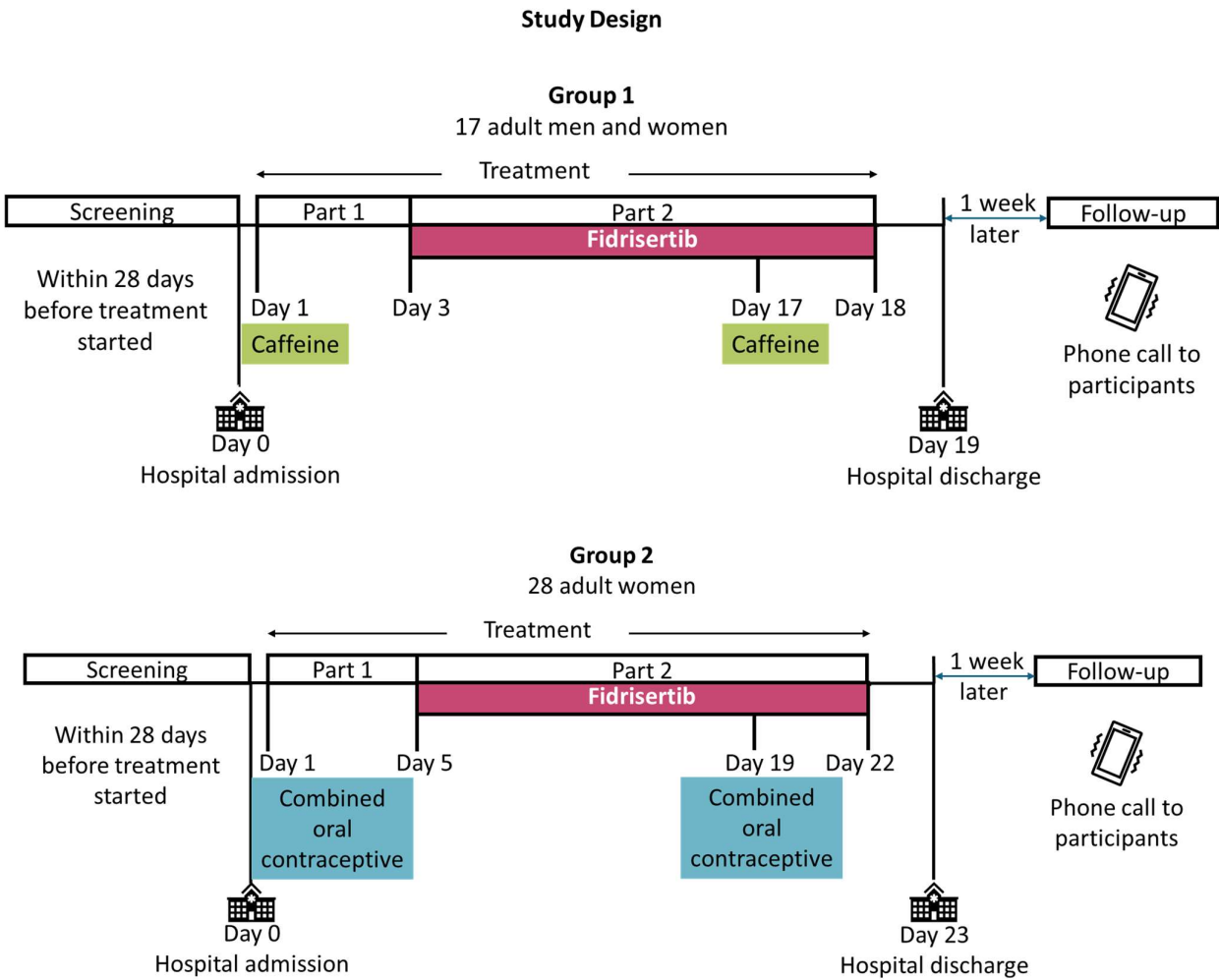
The study doctors collected blood samples at various times from the participants to measure the amount of fidrisertib, caffeine and combined oral contraceptive in the blood.

Follow-up: 1 week after discharge, a phone call was made to check on the participants’ health.

The participants were admitted to a clinical research hospital 1 day before the first dose of caffeine or the combined oral contraceptive. Participants in both groups were discharged on the day of the last scheduled blood collection.

The longest duration a participant was in the study was for up to 2 months. During this time, researchers regularly monitored participants’ health through safety assessments, including after the last treatment.

The following figure shows what happened during the study.



What did researchers find out in the study?

The researchers found that

- the amount of caffeine in the blood over time was similar with or without fidrisertib.
- fidrisertib 120 mg affected the amount of combined oral contraceptive in the blood. However, this change is not expected to affect how well the pill prevents pregnancy.

To evaluate how fidrisertib affects caffeine and combined oral contraceptive, the researchers measured and compared the amount of caffeine and combined oral contraceptive in blood when taken alone or with fidrisertib.

How did the amount of caffeine in the blood change over 2 days after taking it, alone or with fidrisertib?

Over 2 days after taking caffeine, the researchers found that the amounts of caffeine in the blood were similar, whether taken with or without fidrisertib. This means that fidrisertib did not affect how the body breaks down caffeine.

How did the amount of oral contraceptives in the blood change over 4 days after taking it, alone or with fidrisertib?

Over 4 days, the amount of the two drugs, EE and LN, in the combined oral contraceptive changed differently in the blood. Fidrisertib increased the highest amount of EE by 27% and the total amount of EE up to 39%. Fidrisertib lowered the highest amount of LN by 14% while the total amount of LN remained similar with or without fidrisertib.

These changes are not expected to affect how well the combined oral contraceptive pill prevents pregnancy.

What were the other findings in the study?

How safe and well-tolerated was fidrisertib when given with caffeine or combined oral contraceptive in healthy adults?

The researchers found that fidrisertib at a dose of 120 mg once daily, was safe and well-tolerated when given with either caffeine or the combined oral contraceptive in healthy adults.

How did the treatment make participants feel?

During the study, participants were asked to report any 'adverse events', that is, if they felt unwell, experienced any kind of medical event, or noticed anything different about their bodies. Researchers recorded all adverse events reported by participants, whatever the cause. For example, if some participants caught COVID-19, this was reported as an adverse event, although it was not related to the study treatment.

If the study doctor thinks an adverse event may be related to the study treatments, it is called a 'side effect'.

A side effect is considered 'serious' when it is life-threatening, causes lasting problems, or leads to hospitalisation.

- No participants in this study experienced any serious side effects.
- No participants died during the study.

Overall, 13% (6 out of 45) of participants experienced side effects.

In Group 1, 6% (1 out of 17) of participants experienced headache that was related to fidrisertib. No side effects related to caffeine were reported.

In Group 2, 18% (5 out of 28) of participants reported side effects that were related to fidrisertib. 7% (2 out of 28) of participants reported side effects that were related to the oral contraceptive (EE and LN).

The side effects related to fidrisertib were constipation in 11% (3 out of 28) of participants, and itching and menstrual disorder reported in 4% (1 out of 28) of participants each.

The side effects related to the oral contraceptive (EE and LN) were bleeding between menstrual cycles and menstrual disorder reported in 4% (1 out of 28) of participants each.

No participants stopped taking part in the study because of a side effect.

More information

For more information about current treatments available, please speak to your healthcare provider. If you have any questions about this study, please contact the sponsor, Ipsen at:



clinical.trials@ipson.com

Future research

There are more ongoing studies with fidrisertib.

Study identification and other information

FULL STUDY TITLE: An open-label, two-cohort, Phase I study to investigate the effects of steady-state fidrisertib on the pharmacokinetics of caffeine, a CYP1A2 index substrate, and combined oral contraceptives in healthy adult participants

PROTOCOL: CLIN-60130-455

OTHER INFORMATION: Phase I studies are conducted with small numbers of healthy participants. This helps researchers figure out what dose to use in future studies, to understand what happens to the study drug in the body and how safe it is.



We thank all the volunteers who took part in this study. Without their support, advances in treatments for medical conditions would not be possible.



We would also like to thank the people who took the time to review this document to make it easier for a general audience to read.

