Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine(s) Studied: Zimlovisertib (PF-06650833)

Protocol Number: B7921026

Dates of Study: 08 October 2021 to 16 December 2021

Title of this Study: A Study to Estimate the Effect of PF-06650833 on the Pharmacokinetics (PK) of Oral Contraceptive (OC)

[A Phase 1, Open Label, Fixed Sequence Study to Estimate the Effect of Multiple Dose PF-06650833 on the Pharmacokinetics of Single Dose Oral Contraceptive Steroids in Healthy Female Participants]

Date(s) of this Report: 30 August 2022

– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is rheumatoid arthritis (RA) and hidradenitis suppurativa (HS)?

Rheumatoid arthritis (RA) is a disease that causes swelling, pain, and stiffness in the joints. RA is an "autoimmune disease", which means that patients with RA have an overactive immune system that mistakenly attacks healthy parts of the body, such as the joints.

Hidradenitis suppurativa (HS), also known as acne inversa, is a skin condition that causes painful lumps to form under the skin.

Both RA and HS are inflammatory conditions, which means they cause responses in the body that may include pain, swelling, redness, and destruction of tissues. The study medication, zimlovisertib, is a potential treatment for inflammation.

What are ethinyl estradiol (EE), levonorgestrel (LN) and zimlovisertib?

Ethinyl estradiol (EE) and levonorgestrel (LN) are hormones which are used together as an oral contraceptive (OC), also known as oral birth control. These medicines are combined in 1 pill and taken daily to prevent a woman, who is able to have children, from becoming pregnant.

Zimlovisertib is a new drug being developed as a possible way to treat inflammation; it has not yet been approved for the treatment of any disease. Zimlovisertib acts by stopping a specific type of enzyme from working. This enzyme is called interleukin-1 receptor-associated kinase 4 (IRAK4). Enzymes are proteins that speed things up in our cells or break down substances such as other proteins, carbohydrates (e.g., starch), and sugars. This is either to be used as fuel for bodily functions or as a way for the body to get rid of (metabolize) substances such as drugs. However, zimlovisertib may also impact other enzymes that affect how an OC is broken down that could lead either to an increase or a decrease in the amount of hormones (EE + LN) in the

blood. Lower levels of hormones could potentially make the OC less effective, while higher levels of hormones might cause undesirable (negative) effects. Zimlovisertib comes in a tablet form that is swallowed.

What was the purpose of this study?

The purpose of this study was to estimate the effect of multiple doses of zimlovisertib on the levels of hormones in the blood after a dose of OC in healthy, female adult participants.

All participants received 2 single doses of OC during the study. The first dose was taken alone in the beginning of the study, and the second dose was taken together with zimlovisertib after multiple doses of zimlovisertib taken alone (single dose once daily for 9 days).

After the OC tablet was swallowed, the hormones (EE + LN) entered the blood and organs (for example, stomach, liver, and kidneys) as it moved through the body. Afterwards, the OC was removed from the body through urine and feces. The effect of multiple doses of zimlovisertib on this movement of OC over time through the body was measured.

The study did not evaluate the effectiveness of the drug for the treatment of any condition.

Researchers wanted to know:

- **How did multiple doses of zimlovisertib affect how a single dose of combination oral contraceptive moved in the body?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

The study consisted of 2 periods:

- **Period 1:** One dose of OC (EE 0.03 mg and LN 0.15 mg) was given on the morning of Day 1.
- **Period 2:** Zimlovisertib (400 mg) was given once a day for 11 days. One dose of OC was given on the morning of Day 10.

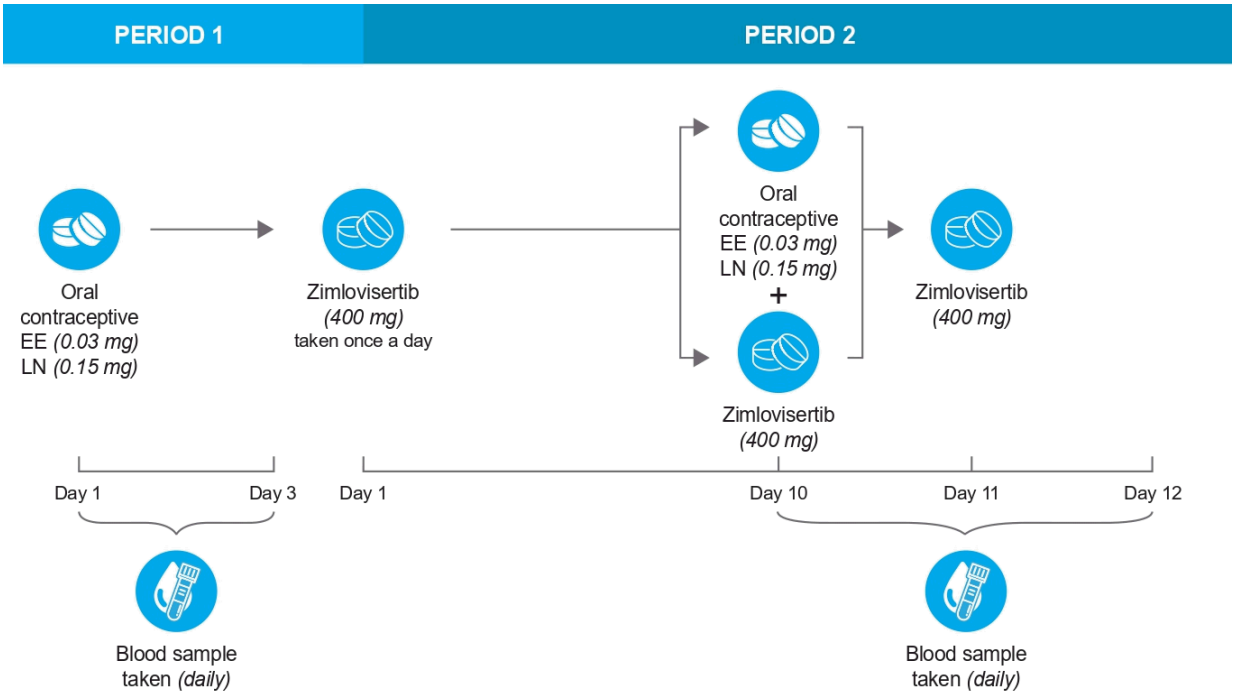
There was no washout period between the study periods. A washout is when a participant is not given any other treatment and it gives the body time to work the drug out of their system.

All 10 participants were included in Period 1 (lasting 3 days) and Period 2 (lasting 12 days).

The researchers assessed the levels of hormones (EE + LN) in all participants before both periods began, as well as for 48 hours after the OC was given on Day 1 (Period 1) and Day 10 (Period 2).

A summary of how the study was done is shown in Figure 1 below:

Figure 1. Overall study design



Researchers took samples of blood from participants during the study and measured the amount of OC (EE + LN). Researchers also checked the participants' health during the study and asked them how they were feeling.

The participants and researchers knew who took the study medications. This is known as an "open-abel" study.

Where did this study take place?

The Sponsor ran this study at 1 location in the United States.

When did this study take place?

It began on 08 October 2021 and ended on 16 December 2021.

Who participated in this study?

The study included healthy female adult participants who met the inclusion/exclusion criteria for things such as age, weight, and lack of any major illness or chronic disease.

- A total of 10 women participated
- All participants were between the ages of 46 and 60

All 10 participants finished the study.

How long did the study last?

Study participants were in the study for 16 days. The entire study took 10 weeks to complete.

When the study ended in December 2021, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

How did multiple doses of zimlovisertib affect how a single dose of combination oral contraceptive moved in the body?

Researchers used different factors to measure how the OC entered and moved through the body and how long it stayed in the body. These factors are shown below.

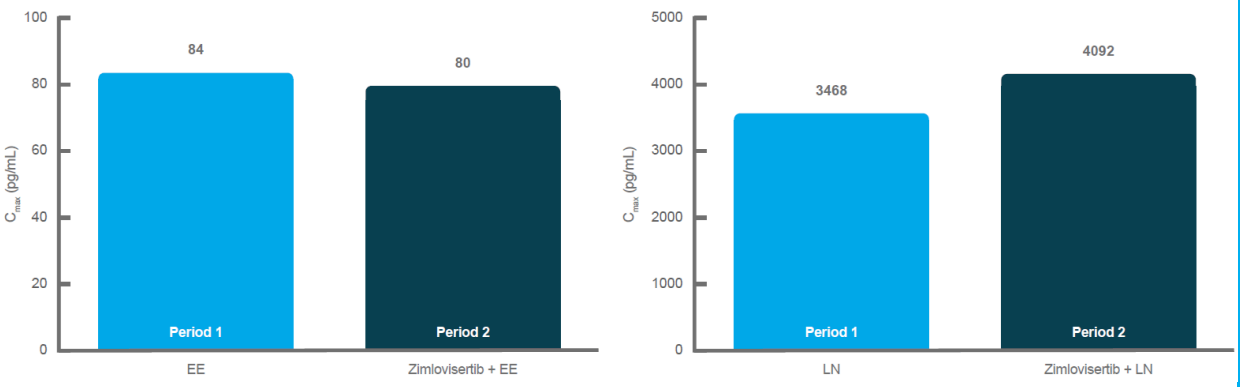
What was the amount of OC (EE + LN) in the blood after participants took a single dose of OC alone, and after participants took multiple doses of zimlovisertib (400 mg) with a single dose of OC?

- The highest amount of OC (EE + LN) in the blood (known as C_{max}) after participants took the OC alone or after multiple doses of zimlovisertib

(400 mg) is shown in Figure 2. The amount of OC (EE + LN) in the blood was measured in picograms per milliliter, also called pg/mL.

- The highest amount of EE and LN in the blood after participants took a single dose of OC was 84 pg/mL and 3468 pg/mL, respectively (Study Period 1).
- The highest amount of EE and LN in the blood after participants took a single dose of OC following multiple doses of zimlovisertib was 80 pg/mL and 4092 pg/mL, respectively (Study Period 2).

Figure 2. Peak Level of OC (EE + LN) in the Blood

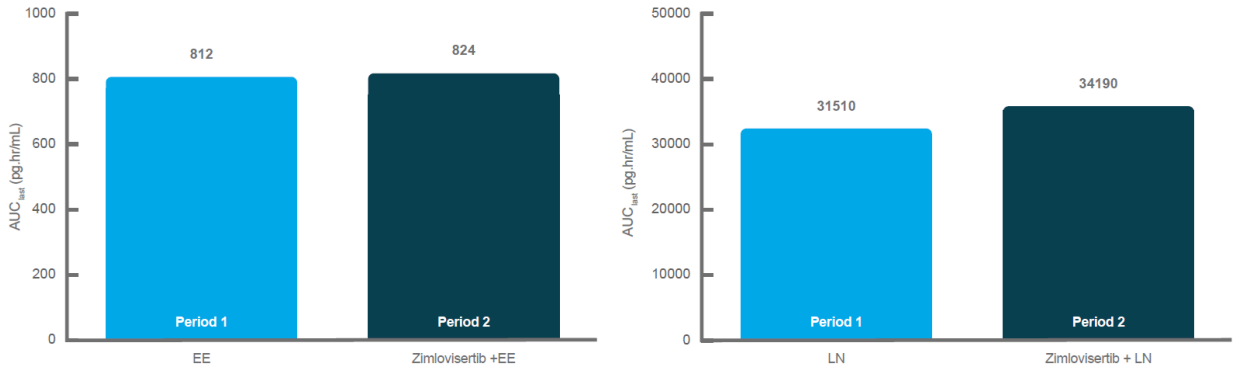


The estimated total amount of OC in the blood, from when the OC was taken until it was removed from the body (known as AUC_{last}) is shown in Figure 3 below for each study period. This was measured in picogram-hours per milliliter, also called pg.hr/mL. The pg.hr/mL is a unit used to measure total amount of drug over time in the blood.

- The AUC_{last} for EE and LN after participants took a single dose of OC was 812 pg.hr/mL and 31510 pg.hr/mL respectively.

- The AUC_{last} for EE and LN after participants took a single dose of OC following multiple doses of zimlovisertib was 824 pg.hr/mL and 34190 pg.hr/mL respectively.

Figure 3. Cumulative level of OC (EE + LN) over time



To summarize the above results, the concentration of OC in the blood was very similar when participants took a single dose of OC in the absence of zimlovisertib (Period 1) compared to when participants took a single dose of OC following multiple doses of zimlovisertib (Period 2).

The OC (EE + LN) levels and cumulative levels over time are similar with or without zimlovisertib. The combined OC (EE + LN) does not act differently in the body following multiple doses of zimlovisertib.

This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

Three out of 10 (30%) participants in this study had at least 1 medical problem. None of these medical problems were considered by the study doctor to be caused by the study medication. No participants left the study because of medical problems. All the medical problems are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were reported during the study. All medical problems reported are listed.
- The **2nd** column tells how many of the 10 participants reported each medical problem after taking the single dose of OC. Below this number is the percentage of the 10 participants taking the OC who reported the medical problem.
- The **3rd** column tells how many of the 10 participants reported each medical problem after taking multiple doses of zimlovisertib. Below this number is the percentage of the 10 participants taking multiple doses of zimlovisertib who reported the medical problem.

- The **4th** column tells how many of the 10 participants reported each medical problem after taking the OC and zimlovisertib together on the same day. Below this number is the percentage of the 10 participants taking the OC and zimlovisertib together who reported the medical problem.
- Using these instructions, you can see that 2 out of the 10 (20%) participants taking multiple doses of zimlovisertib reported itchy skin. None of the participants taking the single dose of OC reported itchy skin, and no participants taking the OC and zimlovisertib on the same day reported itchy skin.

Table 1. Medical problems reported by study participants

Medical Problem	Single dose OC (10 Participants)	Multiple dose Zimlovisertib (10 Participants)	OC and Zimlovisertib taken together (10 Participants)
Nausea (feeling sick)	0 out of 10 participants (0%)	1 out of 10 participants (10%)	0 out of 10 participants (0%)
Toothache	0 out of 10 participants (0%)	0 out of 10 participants (0%)	1 out of 10 participants (10%)
Headache	0 out of 10 participants (0%)	1 out of 10 participants (10%)	0 out of 10 participants (0%)
Itchy skin	0 out of 10 participants (0%)	2 out of 10 participants (20%)	0 out of 10 participants (0%)

Did study participants have any serious medical problems?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.

No participants had serious medical problems.

Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

The full scientific report of this study is available online at:

www.clinicaltrials.gov
Use the study identifier **NCT05064332**

www.pfizer.com/research/research_clinical_trials/trial_results
Use the protocol number B7921026

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study,
thank you for volunteering.
We do research to try to find the
best ways to help patients, and you helped
us to do that!