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:	Bosutinib /PF-05208763
Protocol Number:	B1871062
Dates of Study:	19 January 2022 to 25 June 2022
Title of this Study:	Bioavailability of Bosutinib Capsules and the Effect of Food on Bosutinib Capsule [A Phase 1, Randomized, Open-Label, 3 Period, 4-Sequence, Crossover, Single-Dose Study to Compare the Bioavailability of Orally Administered Bosutinib Capsules and to Estimate the Effect of Food on Bosutinib Capsule]
Date(s) of this Report:	18 May 2023

– 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 bosutinib?

Bosutinib (pronounced as (boe sue' ti nib**)** is a medicine approved to treat chronic myeloid leukemia (CML).

What is CML?

CML is a cancer that begins in cells within the bone marrow, the spongy inner portion of bones where blood cells are made.

What was the purpose of this study?

Bosutinib is a medicine that is taken by mouth (oral) as a capsule or tablet and is then absorbed (enters the blood) and distributed throughout the body to cancer cells. Bosutinib is available as 25, 50 and 100 milligram (mg) capsules and 100, 400, and 500 mg tablets. The purpose of this study was to determine if the amount of bosutinib that becomes available (enters the blood—known as "bioavailability") when one 100 mg capsule is taken by the participants is similar to when four 25 mg capsules are taken and to determine if a high-fat, high-calorie meal has any effect on the bioavailability of bosutinib.

Relative bioavailability (comparison of the amount of bosutinib that becomes available when administered as different drug products [i.e. capsules or tablets] or conditions) is assessed through 2 parameters: (1) the highest amount of bosutinib in the blood and (2) the total amount of bosutinib in the blood from when it is administered until it is no longer present in the body.

This study did not test if bosutinib helps to treat CML.

Researchers wanted to know:

- **How did the highest amount of bosutinib in the blood compare when bosutinib was taken in these ways: (1) four 25 mg capsules (2) one 100 mg capsule in the fed state and one 100 mg capsule in the fasted state? (3) one 100 mg capsule in the fasted state?**
- **How did the estimated total amount of bosutinib in the blood compare when bosutinib was taken in these ways: (1) four 25 mg capsules (2) one 100 mg capsule in the fed state and (3) one 100 mg capsule in the fasted state?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

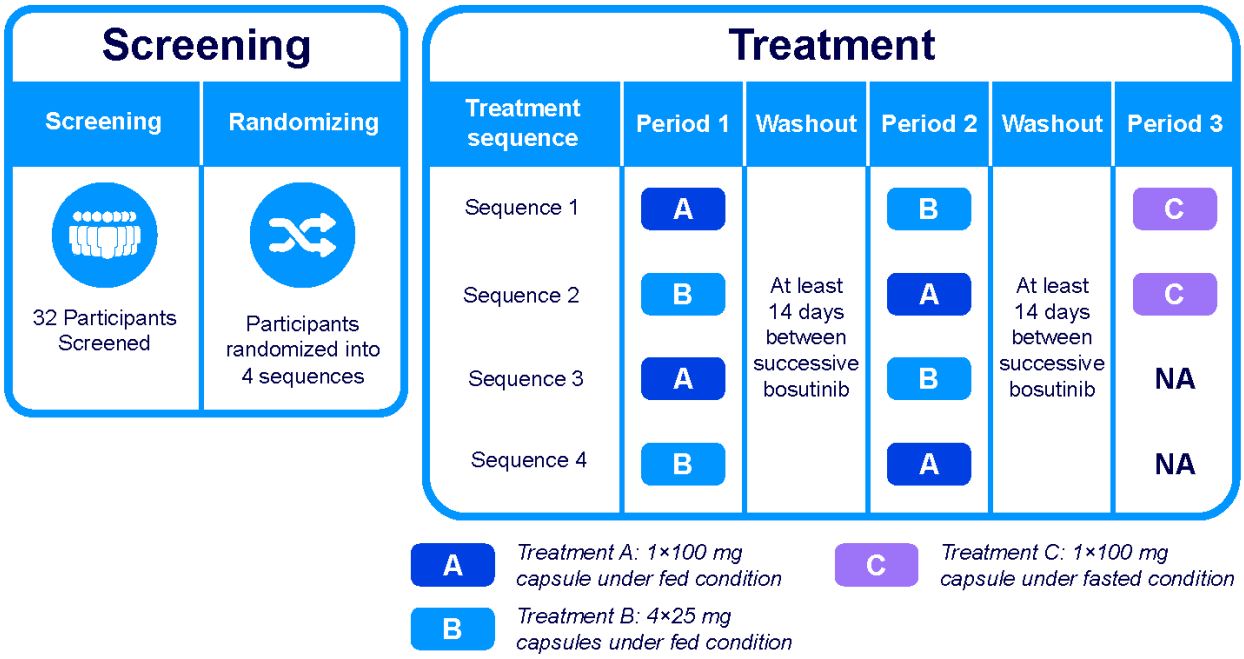
Researchers tested bosutinib on 32 healthy adult participants to determine the amount of bosutinib that entered the blood when participants took bosutinib as either one 100 mg capsule or four 25 mg capsules with or without a high-fat, high-calorie meal.

The planned treatments of the study were:

- Treatment A: 1×100 mg capsule under fed condition
- Treatment B: 4×25 mg capsules under fed condition
- Treatment C: 1×100 mg capsule under fasted condition

Participants were randomly assigned to one of the following treatment sequences. Participants received treatments in different sequences as shown in the Figure 1. Participants had a wash out period of 14 days between bosutinib doses as shown in Figure 1.

Figure 1: How was the Study done?



Researchers took samples of blood from participants during the study and measured the amount of bosutinib. Researchers also checked the participants' health during the study and asked them how they were feeling.

Researchers then compared the results of participants taking bosutinib either as one 100 mg capsule or four 25 mg capsules under fed or one 100 mg capsules under fasting conditions.

This was an open-label study, which means that the participants and the researchers knew which treatments the participants received and in what order.

Where did this study take place?

The Sponsor ran this study at 1 location in Belgium.

When did this study take place?

It began 19 January 2022 and ended 25 June 2022.

Who participated in this study?

The study included healthy participants who met the inclusion/exclusion criteria for things such as age, and weight.

- All participants in the study were men and were between the ages of 19 and 54 years

Of the 32 participants who started the study, 25 finished the study. 7 did not finish the study because:

- 3 participants discontinued due to side effects
- 2 participants withdrew from the study
- 2 participants no longer met the criteria to be in the study

How long did the study last?

Study participants were in the study for approximately 1 month. The entire study took 5 months to complete.

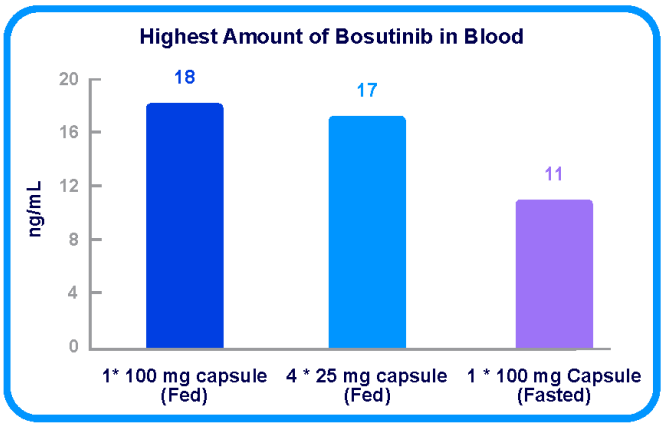
When the study ended in June 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

- **How did the highest amount of bosutinib in the blood compare when bosutinib was taken in these ways: (1) Four 25 mg capsules (2) One 100 mg capsule in the fed state and (3) one 100 mg capsule in the fasted state?**

The highest amount of bosutinib in the blood after participants took either one 100 mg capsule or four 25 mg capsules in the fed state and one 100 mg capsule fasted state is shown in Figure 2. The amount of drug in the blood was measured in nanograms per milliliter, (ng/mL). Researchers considered the difference in the results as minor/no difference between capsule strengths, but the capsule administered under fasted conditions resulted in lower amount of bosutinib in the body.

Figure 2: Estimated Highest Amount of Bosutinib in the Blood

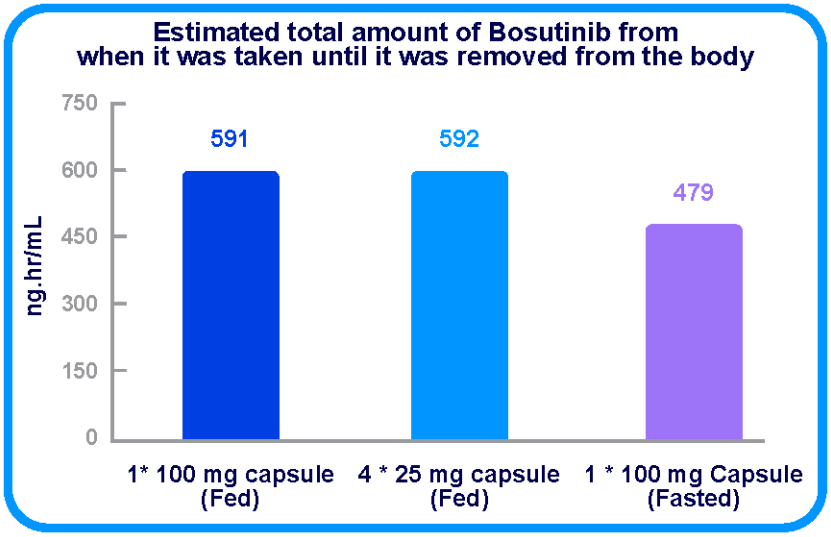


How did the estimated total amount of bosutinib in the blood compare when bosutinib was taken in these ways: (1) Four

25 mg capsules (2) One 100 mg capsule in the fed state and (3) one 100 mg capsule in the fasted state

Figure 3 below shows the estimated total amount of bosutinib measured in the blood from when bosutinib was taken until bosutinib was removed from the body. The estimated total amount of bosutinib in the blood was measured in nanogram hours per milliliter (ng•hr/mL).

Figure 3: Estimated Total Amount of Bosutinib in the Blood



Based on these results, the researchers have decided that the results are not likely the result of chance. The study medication may not act differently in the body whether taken as one 100 mg capsule or four 25 mg capsules. However, the total amount and total exposure of bosutinib under fed conditions was higher than in the fasted condition.

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 unknown 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.

13 out of 30 (43.3%) in the 1*100 mg group; 20 out of 31 (64.5%) in the 4*25 mg group; 5 out of 12 (41.7%) in the 1*100 mg fasted group reported at least 1 medical problem. A total of 3 participants left the study because of medical problems. The most common medical problems – those reported by at least 5% of participants – 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 commonly reported during the study. All medical problems reported by more than ⩾5% of participants are listed.
- The **2nd** column tells how many of the 30 participants taking bosutinib 100 mg capsule under fed conditions reported each

medical problem. Next to this number is the percentage of the 30 participants who reported the medical problem.

- The **3rd** column tells how many of the 31 participants taking 4 * 25 mg capsules of bosutinib under fed conditions reported each medical problem. Next to this number is the percentage of the 31 participants who reported the medical problem.
- The **4th** column tells how many of the 12 participants taking one 100 mg capsule of bosutinib under fasted conditions reported each medical problem. Next to this number is the percentage of the 12 participants who reported the medical problem.
- Using these instructions, you can see that 4 out of the 31 (12.9%) participants taking bosutinib 4 * 25 mg capsule under fed conditions reported diarrhoea. A total of 1 out of the 12 (8.3%) participants taking bosutinib 100 mg capsule under fasted condition reported diarrhoea. Zero out of 30 participants (0%) in 1*100 mg bosutinib in fed state reported diarrhoea.

Table 1. Medical problems reported by ≥5% study participants			
Medical Problem	**1 * 100 mg bosutinib (30 Participants) Fed**	**4 * 25 mg bosutinib (31 Participants) Fed**	**1 * 100 mg bosutinib (12 Participants) Fasted**
Diarrhoea	0 out of 30 participants (0%)	4 out of 31 participants (12.9%)	1 out of 12 participants (8.3%)
Tiredness	2 out of 30 participants (6.7%)	2 out of 31 participants (6.5%)	1 out of 12 participants (8.3%)
Fever	1 out of 30 participants (3.3%)	2 out of 31 participants (6.5%)	0 out of 12 participants (0%)
SARS-CoV-2 test positive	1 out of 30 participants (3.3%)	2 out of 31 participants (6.5%)	1 out of 12 participants (8.3%)
Back pain	1 out of 30 participants (3.3%)	3 out of 31 participants (9.7%)	0 out of 12 participants (0%)
Headache	4 out of 30 participants (13.3%)	6 out of 31 participants (19.4%)	0 out of 12 participants (0%)

Table 1. Medical problems reported by ≥5% study participants			
Medical Problem	1 * 100 mg bosutinib (30 Participants) Fed	4 * 25 mg bosutinib (31 Participants) Fed	1 * 100 mg bosutinib (12 Participants) Fasted
Cough	0 out of 30 participants (0%)	2 out of 31 participants (6.5%)	0 out of 12 participants (0%)
Bleeding outside of blood vessel	0 out of 30 participants (0%)	2 out of 31 participants (6.5%)	2 out of 12 participants (16.7%)
Bleeding at the vessel puncture site	0 out of 30 participants (0%)	0 out of 31 participants (0%)	1 out of 12 participants (8.3%)

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 in the study had serious medical problems.

No participants died during the study.

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:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number B1871062

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

www.clinicaltrials.gov	Use the study identifier **NCT05032690**

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!