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 study participants. The results of this study might be different than the results of other studies that the researchers review.

Sponsor:	Pfizer Inc.
Medicine(s) Studied:	Encorafenib + Binimetinib
Protocol Number:	C4221008
Dates of Study:	04 June 2019 to 22 September 2022 (Primary completion; Study Ongoing)
Title of this Study:	A Study of Encorafenib + Binimetinib in Patients With *BRAF* V600-mutant Non-Small Cell Lung Cancer [Phase 2, Open-label Study of Encorafenib + Binimetinib in Patients With *BRAF* V600-mutant Non-Small Cell Lung Cancer]
Date(s) of this Report:	31 March 2023

– Thank You –

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

Since the study is still ongoing, this summary will describe the study primary 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 Non-Small Cell Lung Cancer (NSCLC)?

NSCLC is the most common type of lung cancer accounting for 80% to 85% of all lung cancer diagnoses. NSCLC patients can have changes (mutations) in a variety of molecules. This study included NSCLC patients with a change in a gene called *BRAF* V600.

What is encorafenib and binimetinib?

This study tested 2 treatments: Encorafenib (en-koe-raf-e-nib) and binimetinib (bin-i-me-ti-nib). These treatments were given together so the study medication is referred to as "encorafenib + binimetinib combination treatment".

Encorafenib and binimetinib are both cancer growth blockers. They work by targeting certain proteins that help cancer cells grow. By blocking these proteins, this combination treatment may help to stop or slow down the growth of cancer cells. Both medications were given orally to the participants.

What was the purpose of this study?

The purpose of this study was to learn whether encorafenib + binimetinib combination treatment had positive effects on the lung cancer of participants with *BRAF* V600 mutation and who have cancer spread to other sites in the body (metastatic). The participants included both those that had no prior cancer treatment as well as those that had taken other cancer treatments previously. Researchers measured the effect of the medications by comparing images of the tumors before, during and after treatment. Using this information, researchers determined how many participants benefitted by the treatment. Investigators looked at a type of measure called the "Objective Response Rate" (ORR). ORR is the percentage of participants in whom all signs of cancer disappeared, called complete response, or got smaller during treatment (decrease in size or extent of cancer), called partial response. The extent of response is determined by an independent review.

Researchers wanted to know:

1. Did the participants taking encorafenib and binimetinib have positive effects on their tumors?

2. What medical problems did the participants have during the study?

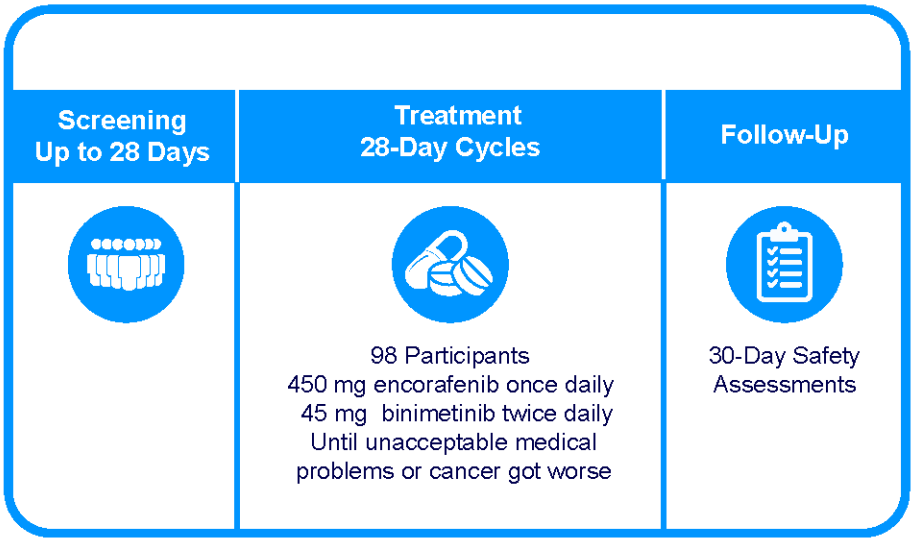
What happened during the study?

How was the study done?

In this study participants took 450 milligrams (mg) of encorafenib once daily and 45 mg of binimetinib twice daily, for 28 days in each cycle until, their cancer got worse, they experienced unacceptable medical problems, they left the study, they started new anticancer treatment, or the participant died. Encorafenib and binimetinib are both taken by mouth. The study design is shown in Figure 1. This was an "open-label" study. That means participants and the researchers knew which study drug they were taking for treatment.

Researchers evaluated a group of study participants to find out if taking encorafenib and binimetinib had positive effects on the NSCLC.

Figure 1. How Was the Study Done?



Where did this study take place?

The Sponsor ran this study at 56 locations in 5 countries (The United States of America, Italy, Republic of Korea, Netherlands, and Spain).

When did this study take place?

It began 04 June 2019 and is ongoing.

The information collected until 22 September 2022 is reported here.

Who participated in this study?

The study included participants who were at least 18 years old. They must have been diagnosed with metastatic NSCLC with a *BRAF* V600 mutation.

- A total of 46 men participated
- A total of 52 women participated
- All participants were between the ages of 47 and 86 years.

Of the 98 participants who started the study, 33 are still undergoing treatment.

38 stopped participating in the study because of death, unwillingness to participate or were unavailable for follow-up. Of whom 7 participants left the study by their choice.

How long did the study last?

Study participants received study treatment for an average of 12 months until primary analysis. The study is still ongoing.

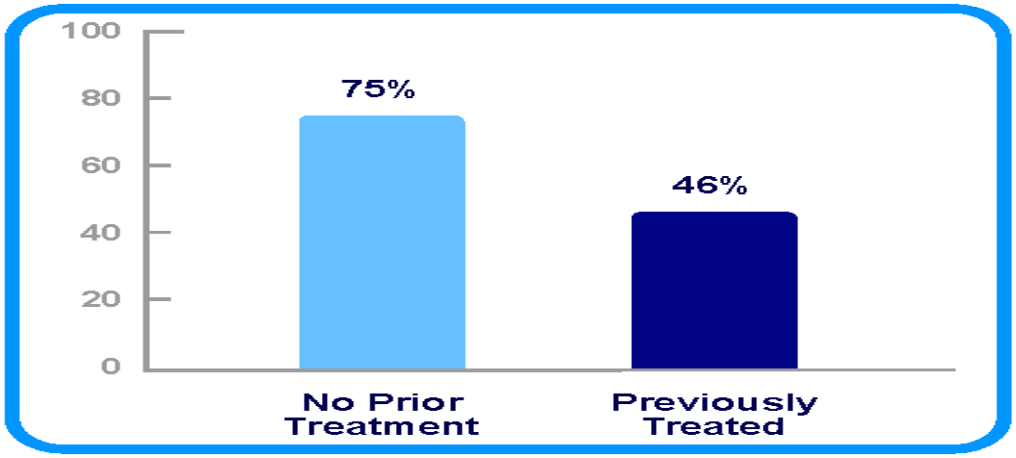
In September 2022, when the primary objective was met, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

Did the study medications have positive effects on the participants tumors as measured by ORR?

44 out of 59 (75%) of the participants who had no prior cancer treatment, met the criteria for Objective Response and 18 out of 39 (46%) of participants who took prior cancer treatments met the criteria for Objective Response as shown in Figure 2.

Figure 2: Percentage of Participants Achieving Objective Response



Based on these results, the researchers have decided that treatment with the combination of encorafenib and binimetinib may offer a new standard of care for patients with *BRAF* V600E-mutant metastatic NSCLC.

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.

97 out of 98 (99%) participants in this study had at least 1 medical problem. 18 (18%) participants discontinued treatment because of medical problems. The most common medical problems – those reported by at least 15% 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 at least 15% of participants are listed.
- The **2nd** column tells how many of the 98 participants taking the study medication reported each medical problem. This problem may be due to any cause not related to study treatment. Next to this number is the percentage of the 98 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 98 participants taking the study medication reported each medical problem. These problems are considered to be related to the treatment. Next to this number is the percentage of the 98 participants who reported the medical problem.
- Using these instructions, you can see that 57 out of the 98 (58%) participants reported nausea which could be due to any cause and 49 out of the 98 (50%) participants reported nausea which was considered to be treatment related.

Table 1. Commonly reported medical problems by study participants		
Medical Problem	All-Causality (98 Participants)	Treatment Related (98 Participants)
Nausea	57 out of 98 participants (58%)	49 out of 98 participants (50%)
Diarrhoea	50 out of 98 participants (51%)	42 out of 98 participants (43%)
Tiredness	45 out of 98 participants (46%)	31 out of 98 participants (32%)
Vomiting	36 out of 98 participants (37%)	28 out of 98 participants (29%)
Low red blood cell count	30 out of 98 participants (31%)	18 out of 98 participants (18%)
Constipation	26 out of 98 participants (27%)	13 out of 98 participants (13%)
Difficulty breathing	25 out of 98 participants (26%)	1 out of 98 participants (1%)
Fever	22 out of 98 participants (22%)	8 out of 98 participants (8%)
Limb swelling	21 out of 98 participants (21%)	11 out of 98 participants (11%)
Stomach pain	20 out of 98 participants (20%)	10 out of 98 participants (10%)
Back pain	20 out of 98 participants (20%)	1 out of 98 participants (1%)
Blurred vision	20 out of 98 participants (20%)	17 out of 98 participants (17%)

Cough	17 out of 98 participants (17%)	0 out of 98 participants (0%)
Loss of strength or energy	16 out of 98 participants (16%)	10 out of 98 participants (10%)
Blood creatinine increased	16 out of 98 participants (16%)	7 out of 98 participants (7%)
Dizziness	16 out of 98 participants (16%)	9 out of 98 participants (9%)
Joint pain	15 out of 98 participants (15%)	6 out of 98 participants (6%)
Liver test levels increased	15 out of 98 participants (15%)	12 out of 98 participants (12%)
Muscle protein (creatine phosphokinase) increased in the blood	15 out of 98 participants (15%)	11 out of 98 participants (11%)
Fat digestive enzyme increased	15 out of 98 participants (15%)	7 out of 98 participants (7%)
Itching	15 out of 98 participants (15%)	12 out of 98 participants (12%)

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.

- 42 (43%) participants had serious medical problems due to any cause.
- 14 (14%) participants had serious medical problems that were related to the study treatment.

30 (31%) participants died during the study. Most of the participants died during the study because their lung condition worsened.

Lung disease getting worse and diarrhoea/colon inflammation were the most common serious medical problems reported by the participants.

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.

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

www.clinicaltrials.gov	Use the study identifier **NCT03915951**
www.clinicaltrialsregister.eu	Use the study identifier 2019-000417-37
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number C4221008

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

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!