# 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:** Avelumab (MSB0010718C), Binimetinib (MEK162), Talazoparib (PF-06944076)

**Protocol Number:** B9991033

**Dates of Study:** 15 August 2018 to 02 February 2021

**Title of this Study:** Study to Evaluate the Safety of Combinations of Avelumab, Binimetinib and Talazoparib in Patients With Advanced Cancer

[A Phase 1B/2 Study to Evaluate Safety and Clinical Activity of Combinations of Avelumab, Binimetinib and Talazoparib in Patients With Locally Advanced or Metastatic RAS-Mutant Solid Tumors]

**Date(s) of this Report:** 29 November 2021

## – 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 advanced cancer?

This study looked at participants with different types of advanced cancer, including metastatic pancreatic ductal adenocarcinoma (mPDAC). Pancreatic ductal adenocarcinoma is the most common type of pancreatic cancer. The pancreas is an organ located near the stomach that plays a role in the breakdown of food and helps to regulate blood sugar levels. Cancer occurs when cells in the body divide without control, sometimes these cells form masses called "tumours". Cancer is called "metastatic" when it spreads to other parts of the body. Metastatic cancer is extremely difficult to be cured or controlled with treatment.

## What are avelumab, binimetinib, and talazoparib?

Avelumab, binimetinib, and talazoparib are all medications made to help patients fight cancer in different ways. All three medications have been approved in the United States and Europe for treating different types of cancer. Avelumab is an intravenous (IV) cancer treatment, received at a clinic. Binimetinib and talazoparib are both taken by mouth. Researchers think that using combinations of these medications may help stop cancers from growing.

## What was the purpose of this study?

The purpose of this study was to learn if combinations of avelumab, binimetinib, and talazoparib were safe for study participants with advanced cancer. All three drugs together had never been given before as a combination treatment. If the medications were safe, the researchers would then ask if participants with advanced cancer taking only 2 of the study medications or participants taking all 3 study medications saw their cancer get better.

**Researchers wanted to know:**

- **Was there a combination of doses of avelumab and binimetinib or binimetinib and talazoparib that could be given safely for more studies in the future?**

# What happened during the study?

## How was the study done?

This study had 2 phases: a dose-finding and anti-tumour phase. The dose-finding phase also had two parts: different dose combinations of two pairs of the medications and different dose combinations of all 3 medications.

The combinations of medications for each of the parts of the study were:

- Dose-finding phase:
  - 2 medications
    - 800 mg avelumab (1 time every other week) and 45 mg binimetinib (2 times every day, every other week)
    - 800 mg avelumab (1 time every other week) and 30 mg binimetinib (2 times every day, every other week)
    - 45 mg binimetinib (2 times every day, every other week) and 0.75 mg talazoparib (1 time every day, every other week)
    - 30 mg binimetinib (2 times every day, every other week) and 0.75 mg talazoparib (1 time every day, every other week)
  - 3 medications (planned, but not done)
- Anti-tumour phase (planned, but not done)

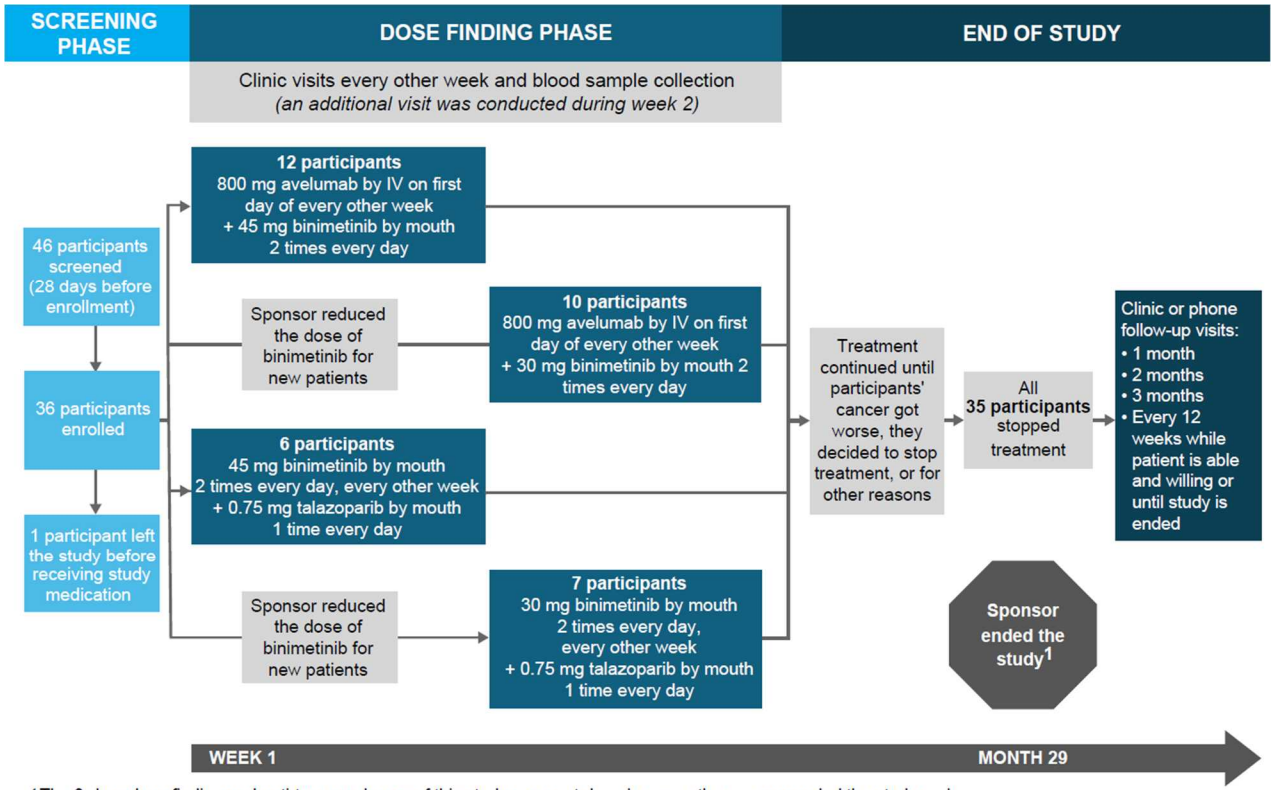
In the dose-finding phase of the study, researchers tested the combination of avelumab and binimetinib or the combination of binimetinib and talazoparib on a

group of study participants to find out if study participants had medical problems that could be the result of taking the medications at the same time.

It was planned that groups of participants would take avelumab and binimetinib or binimetinib and talazoparib. When a safe dose was found, new participants would enter the study and take avelumab, binimetinib, and talazoparib together. However, this study was stopped before any participants joined the dose finding part with all 3 drugs taken together. The anti-tumor phase of the study was also not done.

The study participants and researchers knew who took avelumab and binimetinib and who took talazoparib and binimetinib. This is known as an "open label" study.

The sponsor ended this study during the 2-medication part of the dose-finding phase because it was not likely the dose levels the researchers wanted to use would be reached.




[1] The 3-drug dose finding and anti-tumour phases of this study were not done because the sponsor ended the study early

## Where did this study take place?

The Sponsor ran this study at 10 locations in 3 countries in Asia, Europe, and North America.

## When did this study take place?

It began on 15 August 2018 and ended on 02 February 2021.

## Who participated in this study?

The study included participants who were at least 18 years old, had been diagnosed with mPDAC that had worsened following prior treatment, had at least 1 tumour that could be measured by doctor, and did not have other major health concerns.

- A total of 19 men participated
- A total of 16 women participated
- All participants were between the ages of 42 and 83 years old

Most participants stopped taking the study medications because their disease got worse. All 35 participants stopped being in the study, mostly because they died, by their choice, or they were still in the study when it was ended early by the sponsor.

## How long did the study last?

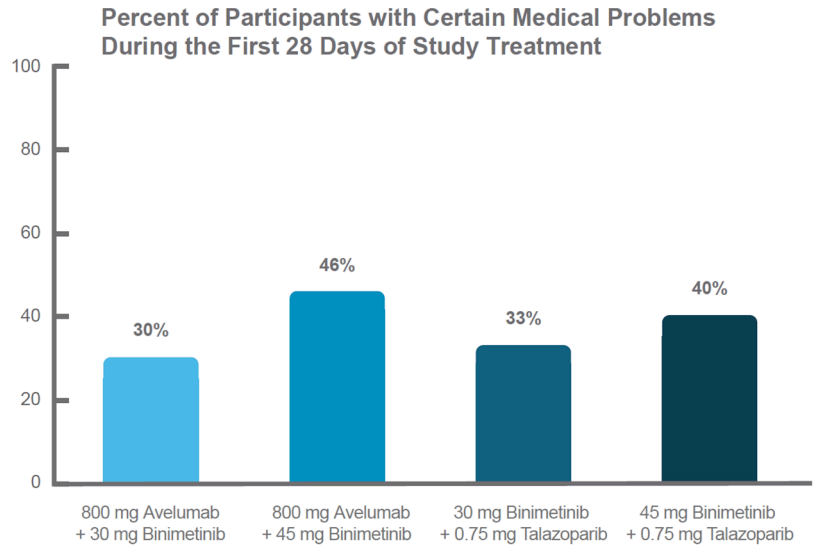
Study participants received study treatment until their cancer got worse, they had serious medical problems that did not allow continued treatment with one or both of the study drugs, or by their choice. The entire study ran over 29 months before it was ended early by the sponsor.

When the study was ended early by the sponsor in February 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?

## Was there a combination of doses of avelumab and binimetinib or binimetinib and talazoparib that could be given safely for more studies in the future?

To learn more about the safety of taking 2 types of medications together, the study doctors looked at the number of certain medical problems possibly caused by the study drugs during the first 28 days of the study treatment. The percentage of participants who had such medical problems in each group are shown in the graph below.




The sponsor decided to end the study early because giving all 3 drugs at the same time did not appear to be practical.

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.

All of the participants in this study had at least 1 medical problem. A total of 3 participants stopped all the study treatment because of medical problems. The most common medical problems – those reported by more than 30% 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 30% of participants are listed.
- The **2nd** column tells how many of the 22 participants taking binimetinib and avelumab reported each medical problem. Next to this number is the percentage of the 22 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 13 participants taking binimetinib and talazoparib reported each medical problem. Next to this number is the percentage of the 13 participants taking binimetinib and talazoparib who reported the medical problem.

- Using these instructions, you can see that 12 out of the 22 (55%) participants taking binimetinib and avelumab reported rash. A total of 3 out of the 13 (23%) participants taking binimetinib and talazoparib reported rash.

**Table 1. Commonly reported medical problems by study participants**

| Medical Problem | Binimetinib and Avelumab (22 Participants) | Binimetinib and Talazoparib (13 Participants) |
|---|---|---|
| **Rash** | 12 out of 22 participants (55%) | 3 out of 13 participants (23%) |
| **Liver test levels increased** | 8 out of 22 participants (36%) | 1 out of 13 participants (8%) |
| **Muscle protein (creatine phosphokinase) increased in the blood** | 7 out of 22 participants (32%) | 3 out of 13 participants (23%) |
| **Acne-like skin infection** | 7 out of 22 participants (32%) | 5 out of 13 participants (39%) |

| | | |
|---|---|---|
| **Feeling very tired** | 7 out of 22 participants (32%) | 5 out of 13 participants (39%) |
| **Vomiting** | 7 out of 22 participants (32%) | 7 out of 13 participants (54%) |
| **Diarrhoea** | 6 out of 22 participants (27%) | 5 out of 13 participants (39%) |
| **Nausea** | 6 out of 22 participants (27%) | 7 out of 13 participants (54%) |
| **Dehydration** | 4 out of 22 participants (18%) | 4 out of 13 participants (31%) |
| **Low red blood cell count** | 3 out of 22 participants (14%) | 4 out of 13 participants (31%) |
| **Low blood potassium** | 2 out of 22 participants (9%) | 4 out of 13 participants (31%) |
| **Low levels of platelets** | 0 out of 22 participants (0%) | 4 out of 13 participants (31%) |

## 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.

Twenty-one (21) participants (60%, or 3 out of 5 participants) had serious medical problems. Most serious medical problems only happened in 1 participant; those which happened in 2 or more participants are listed below.

- 3 participants in the binimetinib and avelumab group and 2 participants in the binimetinib and talazoparib group had their cancer get worse and they died from their advanced cancer before the end of the 90-day follow-up period.
- 2 participants in the avelumab and binimetinib group had a serious fever.
- 3 participants in the avelumab and binimetinib group had a serious complication from an infection.
- 2 participants in the binimetinib and talazoparib group had serious vomiting.

Researchers believe that 5 participants had serious medical problems related to at least 1 of the study medications.

- In the avelumab and binimetinib group:
    - 1 participant had swelling of mucus producing tissues and lungs
    - 1 participant had increased ALT levels in their liver test
    - 1 participant had increased AST levels in their liver test
- In the binimetinib and talazoparib group:
    - 1 participant had serious diarrhoea and vomiting
    - 1 participant had blood clots in the lung

Twenty-six (26) participants (81%, or 13 out of 16 participants) died during the study, most of these deaths were from the participants' advanced cancer. Researchers do not believe any of the deaths were related to the study medications.

## 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 **NCT03637491** |
| www.clinicaltrialsregister.eu | Use the study identifier **2018-000124-34** |

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 study participants, and you
helped us to do that!