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:	Binimetinib (MEK162)/PF-06811462
Protocol Number:	C4211003 (ARRAY-162-311, MILO)
Dates of Study:	27 June 2013 to 23 August 2022
Title of this Study:	A Study of MEK162 vs. Physician's Choice Chemotherapy in Patients With Low-Grade Serous Ovarian, Fallopian Tube, or Peritoneal Cancer [The MILO Study (MEK Inhibitor in Low-grade Serous Ovarian Cancer): A Multinational, Randomized, Open-Label Phase 3 Study of MEK162 vs. Physician's Choice Chemotherapy in Patients with Recurrent or Persistent Low-grade Serous Carcinomas of the Ovary, Fallopian Tube or Primary Peritoneum]
Date(s) of this Report:	02 March 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 low-grade serous ovarian, fallopian tube, or peritoneal cancer?

Ovarian, fallopian tube, and peritoneal cancers are 3 closely related types of cancer. Serous ovarian cancer begins in the tissue that lines the ovary, the female reproductive organ that produces an egg. Fallopian tube cancer begins in the fallopian tube, which is the tube that carries the egg from the ovary to the uterus (womb). Peritoneal cancer begins in the primary peritoneum, the tissue that covers and protects the abdominal organs.

"Low-grade" means that the cancer cells appear almost normal when looked at under a microscope, and tend to grow and spread slowly.

What is binimetinib?

Binimetinib is a cancer growth blocker known as a "MEK inhibitor". It works by targeting certain proteins that help cancer cells grow. By blocking these proteins, binimetinib may help to stop or slow down the growth of cancer cells. Binimetinib is given in a tablet and is taken by mouth.

What was the purpose of this study?

The main purposes of this study were to learn more about the safety and about the possible efficacy of binimetinib in women with low-grade serous ovarian, fallopian tube, and peritoneal cancers.

Researchers wanted to know:

How long did participants who received binimetinib live without their cancer getting worse, compared to participants who received chemotherapy?

What medical problems did participants have during the study?

What happened during the study?

How was the study done?

Researchers studied a group of participants to learn more about the safety and the possible efficacy of binimetinib in women with low-grade serous ovarian, fallopian tube, and peritoneal cancers.

Participants included in the study:

- Were examined by a study doctor and determined to be appropriate to participate
- Were adult women
- Had low-grade serous ovarian, fallopian tube, or peritoneal cancer that either reoccurred or persisted despite treatment
- Had previously been treated with at least 1 platinum-based chemotherapy treatment and no more than 3 lines of chemotherapy treatment (platinum is a metal that is used in some chemotherapy treatments)

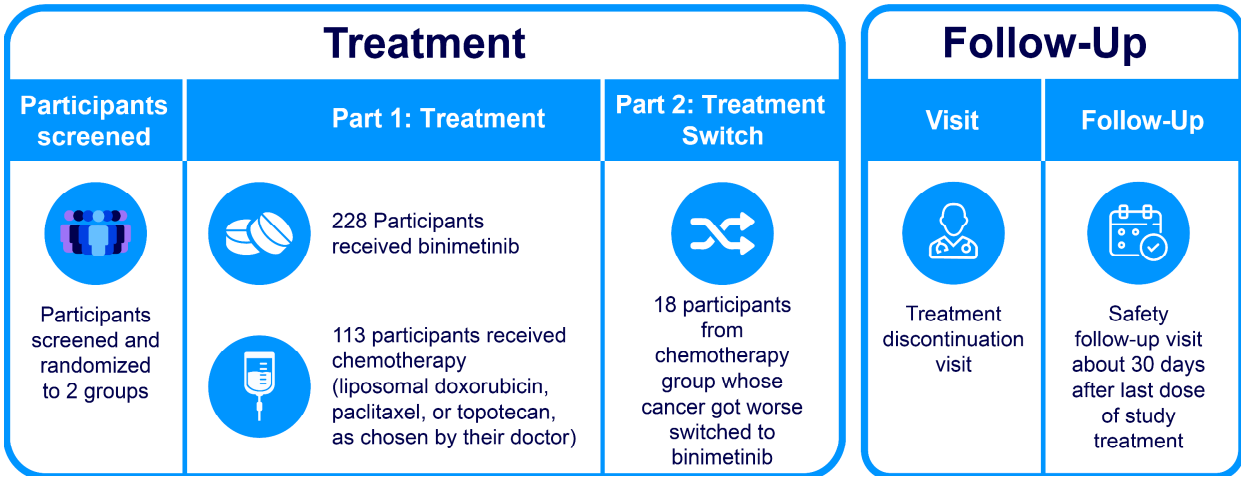
First, a study doctor checked each potential participant to make sure they were appropriate to join the study. This is known as the screening period. This study was done in 2 parts. During Part 1, participants were randomized (assigned by chance) to receive either binimetinib 45 milligrams (mg) twice per day or a chemotherapy

treatment chosen by their study doctor (either liposomal doxorubicin 40 mg/m^2 IV (40 milligrams per square meter of body surface area, into the vein) on Day 1 of every 28-day treatment cycle, paclitaxel 80 mg/m^2 IV on Days 1, 8, and 15 of every 28-day treatment cycle, or topotecan 1.25 mg/m^2 IV on Days 1 through 5 of every 21-day treatment cycle). This was an open-label study, which means that the participants, researchers, and study doctors knew which treatment the participants received. During Part 2, participants who received chemotherapy (liposomal doxorubicin, paclitaxel, or topotecan) during Part 1 and did not have adequate results (their cancer got worse) could switch to binimetinib treatment.

Participants could continue receiving study treatment as long they continued to benefit from it (their cancer improved or did not get worse, they were able to tolerate the study treatment, and they did not have unacceptable medical problems) and the study was ongoing. Participants were expected to attend a treatment discontinuation visit when they stopped study treatment, as well as a safety follow-up visit about 30 days after their last dose of study treatment.

Figure 1 below shows what happened during the study.

Figure 1. What Happened During This Study?



Where did this study take place?

Participants were recruited from 123 study centers in Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, the Netherlands, Norway, Poland, Spain, Sweden, the United Kingdom, and the United States.

When did this study take place?

This study began in June 2013. The study results showed no difference between binimetinib and chemotherapy treatment, and therefore the study was ended in August 2022. The Sponsor reviewed the information collected and created a report of the results. This is a summary of that report.

Who participated in this study?

A total of 341 women joined this study; 228 (67%) were assigned to the binimetinib group and 113 (33%) were assigned to the chemotherapy group. At the time the study ended, 18 out of 113 (16%) participants were in Part 2 of the study (receiving binimetinib after their cancer got worse with liposomal doxorubicin, paclitaxel, or topotecan treatment during Part 1). All participants were between the ages of 22 and 79 years.

Overall, all participants (100%) in this study discontinued the study and study treatment. The most common reasons for discontinuing the study were that the study was ended by the Sponsor or the participant died for reasons not related to the study treatment. The most common reasons for discontinuing study treatment were worsening cancer, medical problems or unable to tolerate the study treatment, and study doctor's decision.

How long did the study last?

The amount of time that participants were in the study varied, depending on how they responded to study treatment. This study began in June 2013 and ended in August 2022. The entire study lasted about 9 years.

What were the results of the study?

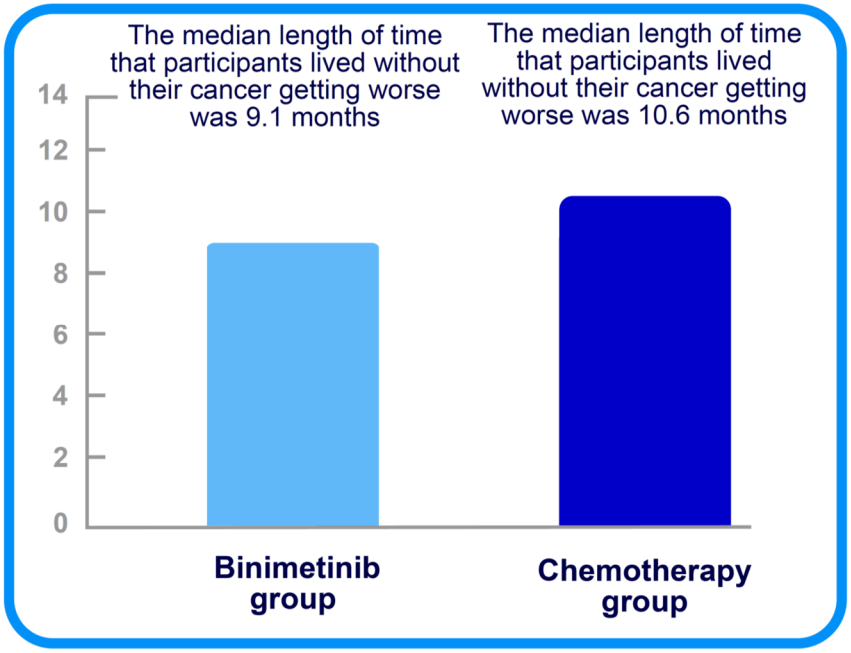
How long did participants who received binimetinib live without their cancer getting worse, compared to participants who received chemotherapy?

To answer this question, the researchers looked at data collected through 20 January 2016. They looked at the median length of time that participants lived without their cancer getting worse. The median is the time by which half of the participants are expected to live without their cancer getting worse. So, participants would have the same chance of living without their cancer getting worse a longer time or a shorter time than this number.

In the binimetinib group, the median length of time that participants lived without their cancer getting worse was 9.1 months. In the chemotherapy group, the median length of time that participants lived without their cancer getting worse was 10.6 months.

Figure 2 below shows this result.

Figure 2. How Long Did Participants Live Without Their Cancer Getting Worse?



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.

To learn more about the safety of binimetinib, the researchers looked at data from 227 participants in the binimetinib group and 106 participants in the chemotherapy

group. 227 (100%) participants in the binimetinib group reported at least 1 medical problem during the study, and 107 (47%) participants in this group stopped taking study treatment because of medical problems. 105 out of 106 (99%) participants in the chemotherapy group reported at least 1 medical problem during the study, and 22 (21%) participants in this group stopped taking study treatment because of medical problems. The table below shows the most common medical problems—those occurring in at least 30% of participants—that happened during the study.

Below are instructions on how to read Tables 1 and 2.

Instructions for Understanding Tables 1 and 2.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by at least 30% of participants are listed.
- The **2nd** column tells how many of the 227 participants in the binimetinib group reported each medical problem. Next to this number is the percentage of the 227 participants in the binimetinib group who reported the medical problem.
- The **3rd** column tells how many of the 106 participants in the chemotherapy group reported each medical problem. Next to this number is the percentage of the 106 participants in the chemotherapy group who reported the medical problem.
- Using these instructions, you can see that 163 out of 227 (72%) participants in the binimetinib group and 39 out of 106 (37%) participants in the chemotherapy group had diarrhea.

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Binimetinib Group (227 Participants)**	**Chemotherapy Group (106 Participants)**
Diarrhea	163 out of 227 participants (72%)	39 out of 106 participants (37%)
Nausea	137 out of 227 participants (60%)	55 out of 106 participants (52%)
Vomiting	132 out of 227 participants (58%)	32 out of 106 participants (30%)
Muscle protein (creatine phosphokinase) increased in blood	121 out of 227 participants (53%)	2 out of 106 participants (2%)
Feeling tired	120 out of 227 participants (53%)	54 out of 106 participants (51%)
Limb swelling	120 out of 227 participants (53%)	16 out of 106 participants (15%)
Acne-like skin infection	110 out of 227 participants (48%)	6 out of 106 participants (6%)
Abdominal pain	80 out of 227 participants (35%)	27 out of 106 participants (25%)
Dry skin	77 out of 227 participants (34%)	14 out of 106 participants (13%)
Constipation	67 out of 227 participants (30%)	32 out of 106 participants (30%)

Mouth pain and sores	54 out of 227 participants (24%)	35 out of 106 participants (33%)
Swelling and blistering on hands and feet	11 out of 227 participants (5%)	36 out of 106 participants (34%)

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. A total of 157 out of 333 (47%) participants reported at least 1 serious medical problem during their treatment in the study, and 68 out of 333 (20%) participants reported at least 1 serious medical problem during their treatment in the study that was considered to be related to study treatment. The table below shows the most common serious medical problems—those occurring in at least 3% of participants—that happened during the study.

Table 2. Commonly reported serious medical problems by study participants		
Serious Medical Problem	**Binimetinib Group (227 Participants)**	**Chemotherapy Group (106 Participants)**
Vomiting	16 out of 227 participants (7%)	2 out of 106 participants (2%)
Blockage of intestine	15 out of 227 participants (7%)	4 out of 106 participants (4%)
Blockage of small intestine	12 out of 227 participants (5%)	8 out of 106 participants (8%)
Diarrhea	10 out of 227 participants (4%)	0 out of 106 participants (0%)
Blood stream infection (sepsis)	9 out of 227 participants (4%)	1 out of 106 participants (1%)
Low red blood cell count	9 out of 227 participants (4%)	2 out of 106 participants (2%)
Abdominal pain	8 out of 227 participants (4%)	2 out of 106 participants (2%)
Urinary tract infection	8 out of 227 participants (4%)	1 out of 106 participants (1%)

Swelling caused by fluid in abdomen	7 out of 227 participants (3%)	4 out of 106 participants (4%)
Nausea	7 out of 227 participants (3%)	1 out of 106 participants (1%)
Partial blockage of the intestine	7 out of 227 participants (3%)	2 out of 106 participants (2%)

15 out of 227 (7%) participants in the binimetinib group and 2 out of 106 (2%) participants in the chemotherapy group died while receiving study treatment or within 30 days of stopping study treatment. Most of the deaths were due to worsening of the participants' cancer and were not considered to be related to the study treatment.

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.clinicaltrials.gov	Use the study identifier **NCT01849874**
www.clinicaltrialsregister.eu	Use the study identifier **2013-000277-72**

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!