

Summary of Clinical Trial Results

MORPHEUS Pancreatic Cancer Study: data from a subgroup of previously treated people who received atezolizumab with BL-8040 compared to those who were treated with chemotherapy

See the end of the summary for the full title of the study.

About This Summary

This is a summary of the results from a small group of people (called a 'subgroup' in this document) who were part of a large clinical trial (called a 'study' in this document) called the MORPHEUS Pancreatic Cancer Study.

This summary has been written for:

- People who were part of this subgroup
- People who are part of the MORPHEUS Pancreatic Cancer Study, and
- Members of the public.

This summary is based on information known at the time that it was written in April 2021.

While the larger MORPHEUS study is still ongoing, the patients in this subgroup started their treatment in July 2017 and ended in July 2019. This summary includes the complete results that were analysed in July 2019.

Key Questions

1. What has happened since this study ended?
2. Why was this research needed?
3. General information about the study
4. Who was part of this subgroup?
5. What medicines were given to people in this subgroup?
6. What were the results for this subgroup?
7. What side effects did people in this subgroup experience?
8. What do these results mean for patients and researchers?
9. Are there plans to add other people to this subgroup or to carry out other studies with these medicines?
10. Where can I find more information?

Thank you to our study participants!

As a clinical study participant, you belong to a large community of people around the world who have made it possible for researchers to answer important health questions and discover new medicines.

Thank you for taking part in this clinical study of atezolizumab with BL-8040. The part of the study for this subgroup began in July 2017 and finished in July 2019. You and 29 other patients helped researchers find out how safe atezolizumab is and how well it works when used in combination with BL-8040 compared to chemotherapy for people with pancreatic cancer.

As the company that organized and funded this study (Sponsor), we believe it is important for you to know the results of this study. We hope this summary helps you understand and feel proud of the

critical role you have played in medical research. If you have questions about the results outlined in this document, please speak with the study researcher, research nurse, or other team member at your study site.

It is important to remember that one study can't tell us everything about the possible side effects of a drug and how well it may work. It takes a lot of people in many studies to learn as much as we can about medicines like atezolizumab and BL-8040. The results of this study may be different from the results of other studies of these medicines. **This means that you should not make medical decisions based on this one summary. Always talk to your study researcher before making any decisions about your treatment.**

1. What has happened since this study ended?

The larger MORPHEUS study is still ongoing. However, the part of the study that you participated in – which looked at a subgroup of people who were given either atezolizumab with BL-8040 or chemotherapy – took 24 months (2 years) to complete and included people from 3 countries. A total of 15 patients with pancreatic cancer received 1200 mg of atezolizumab by injection into a vein every 3 weeks plus 1.25 mg/kg of BL-8040 by injection just under the skin (in the thigh, arm, or abdomen) for the first 5 days and then 3 times a week. Fifteen (15) additional patients with pancreatic cancer had chemotherapy by injection into a vein. This is a summary of the results from these patients. The Sponsor presented early results from this study at the Gastrointestinal Cancers Symposium (ASCO-GI) in January 2020, and the final results were presented to health authorities, like the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA), in March 2020.

2. Why was this research needed?

People who have cancer of the pancreas (pancreatic cancer) that worsens and spreads to other parts of the body do not live for very long.

Current treatments for pancreatic cancer include chemotherapy, which kills cancer cells and stops the cancer from growing. People with pancreatic cancer take a combination of different chemotherapies to treat their cancer. However, these medicines may work for only a short time and then the cancer gets worse again. Also, in some people, the cancer still grows even with treatment.

Therefore, new medicines are needed to treat this type of cancer (shrink the tumour). If the tumour shrinks, even by a little bit, people may be able to manage their cancer better.

One medicine that has helped people with cancer live longer is a cancer 'immunotherapy' medicine called atezolizumab. Cancer immunotherapy medicines work by stimulating your body's immune system to find and fight cancer. Researchers think that these types of medicines might work better to shrink tumours if they are combined with other medicines.

For the subgroup participants, researchers wanted to see if giving people a medicine called BL-8040 with a cancer immunotherapy medicine at the same time would work better than only chemotherapy to shrink their tumours. BL-8040 is a type of medicine called a CXCR4 inhibitor (a drug that blocks the protein CXCR4 and affects the ability of immune cells to the tumour and attack it). Specifically, researchers wanted to know if treating people who have pancreatic cancer with atezolizumab together with BL-8040 would help them live longer and/or lengthen the amount of time before their cancer got worse, compared to people who were treated with only chemotherapy.

They also wanted to find out how safe the drug combinations are by counting the number of people who had side effects, and seeing how severe these side effects were.

The results for this subgroup of people helped answer the following important questions:

- How many people had smaller or no tumours after taking their medicine?
- How safe is the combination of atezolizumab plus BL-8040?
- How many people had side effects and how severe were these side effects?

3. General information about this study

What medicines were used to treat people in this subgroup?

People with pancreatic cancer who were part of this subgroup were split into 2 smaller groups – Group A and Group B.

People in **Group A** were treated with a medicine called atezolizumab (known by its brand name, TECENTRIQ®) taken together with another medicine called BL-8040.

- Atezolizumab (you say this as ‘a – teh – zo – liz – oo – mab’)
 - This medicine is a type of immunotherapy.
 - The body’s immune system fights diseases like cancer. But cancer cells can block (stop) the immune system from attacking the cancer. Atezolizumab releases this blockage – meaning that the immune system again becomes able to fight the cancer cells.
 - When people take atezolizumab, their tumour (cancer) may get smaller.
- BL-8040 (you say this as ‘bee – el – 80 – 40’)
 - This medicine is a CXCR4 inhibitor.
 - The body’s immune system fights diseases like cancer. But cancer cells can block (stop) the immune system from attacking the cancer. BL-8040 blocks a protein called CXCR4 and helps immune cells to surround the tumour so they can attack the cancer.
 - BL-8040 might help atezolizumab work better so people’s tumours (cancer) may get smaller.
- People in **Group B** were treated either with (1) a medicine that has already been approved for use called gemcitabine (known by its brand name Gemzar®) plus a commonly used chemotherapy drug called *nab*-paclitaxel (known by its brand name Abraxane®) or (2) a combination of 3 medicines – 5-fluorouracil, leucovorin, and oxaliplatin (also called mFOLFOX6). These are available treatments for people with pancreatic cancer:
 - Gemcitabine (you say this as ‘jem – sai – tuh – been’)
 - This medicine is a chemotherapy medicine.
 - Chemotherapy works by stopping cancer cells from separating into new cells, so it blocks the growth of the tumour.
 - *nab*-paclitaxel (you say this as ‘nab – pac – lee – tax – el’)
 - This medicine is a chemotherapy medicine.
 - Chemotherapy works by stopping cancer cells from separating into new cells, so it blocks the growth of the tumour.
 - mFOLFOX6 (you say this as ‘em – foal – fox – 6’)
 - This medicine is a chemotherapy medicine.
 - Chemotherapy works by stopping cancer cells from separating into new cells, so it blocks the growth of the tumour.

What kind of study was this?

This subgroup is part of a larger study called the MORPHEUS Pancreatic Cancer Study. MORPHEUS is a 'Phase 1b/2' study (also known as an early research study) that looks at how well a new combination of cancer medicines works, and how safe the medicines are. A small number of people in this subgroup took atezolizumab together with BL-8040, and researchers did medical tests on these people to find out if these 2 medicines taken together had any effect on treating their cancer.

The people in this subgroup were 'randomised,' meaning that they were randomly put into two smaller groups – **Group A** or **Group B** – by chance. Randomly putting people into these groups makes it more likely that the characteristics of the people in both groups (for example, age, race, how sick they are) will be similar at the start of the study.

This part of the study used an 'open label' design, which means that both the study researchers and the people in this subgroup knew which medicines people were taking. Apart from the different medicines being tested in **Group A** and **Group B**, all other aspects of care were the same between the 2 groups.

When and where did the study of this subgroup take place?

This subgroup is part of a larger study called the MORPHEUS Pancreatic Cancer Study. While the larger study is still continuing, the people in this subgroup started their treatment in July 2017 and ended in July 2019. This summary includes the results up until July 2019.

The study took place at 10 study centres in 3 countries in Asia, Europe, and North America.

4. Who was part of this subgroup?

This subgroup included 30 people with pancreatic cancer: 47% were men and 53% were women between the ages of 44 and 77 years. Each person had cancer that had spread to other parts of the body, and they had already been given treatments that had not worked or had stopped working.

5. What medicines were given to people in this subgroup?

People in this subgroup were randomly placed in either **Group A** or **Group B** by a computer and were given specific treatments. This table shows the 2 groups in the study, what medicines were used to treat each group, and when and how the medicines were taken.

People with pancreatic cancer			
	Group A		Group B
	Atezolizumab	BL-8040	Chemotherapy
Number of people taking this medicine	15		15
When and how the medicines were taken	Injected into a vein on day 1 of	Injected just under the skin initially on days 1, 2, 3, 4 and	Gemcitabine and nab-paclitaxel: injected into a vein on days 1, 8, and 15

	every 21-day cycle	5 before other treatments started, and then on days 1, 3, 5, 8, 10, 12, 15, 17 and 19 of every 21-day cycle	of every 28-day cycle or 5-fluorouracil: injected into a vein on days 1 and 2 and days 15 and 16 of every 28-day cycle Leucovorin and oxaliplatin: injected into a vein on days 1 and 15 of every 28-day cycle
How long treatment was expected to last	Until their disease got worse		
Target end date of treatment	No target end date. People received treatment until their disease got worse		

6. What were the results for this subgroup?

After 18 weeks of treatment, researchers found that tumours had not gotten smaller in the people who were treated with atezolizumab together with BL-8040 or the people treated with chemotherapy. This means that both people in **Group A** and **Group B** of the study did not see their tumours shrink as a result of their treatment.

7. What side effects did people in this subgroup experience?

Side effects are unwanted medical problems (such as fever, headache) that happen during the study.

- They are described in the summary because the study researchers believe the side effects may be related to the treatments in the study.
- Not all of the people in this study had all the side effects.
- Side effects may be mild to very serious and can be different from person to person.

It is important to know that the side effects reported in this summary are from the people involved in this study only. This means that the side effects listed here may be different from those seen in other people, other groups, and/or other studies of the same medicines. The side effects listed here may also be different from what is included in the patient leaflets, brochures, or websites for any of the medicines that are used in this study.

Information about common and serious side effects seen in this study are listed below. It is important to note that researchers did not see any new or unusual side effects in this study other than those that have already been found in other studies of each of the medicines that were used.

Most common side effects

Here are the most common side effects seen in the 15 patients treated in Group A:

- Injection site reaction (for example, pain at the needle injection site, redness at the injection site, swelling at the injection site, etc.): 11 out of 15 people (73%)
- Fatigue (tiredness): 10 out of 15 people (67%)
- Injection-related reaction (for example, nausea, constipation, abdominal (stomach) pain): 8 out of 15 people (53%)

- Abdominal pain: 5 out of 15 people (33%)
- Constipation: 5 out of 15 people (33%)
- Nausea: 5 out of 15 people (33%)

Here are the most common side effects seen in the 15 patients treated in Group B:

- Nausea: 8 out of 15 people (53%)
- Physical weakness or lack of energy: 5 out of 15 people (33%)
- Poor appetite: 5 out of 15 people (33%)
- Abnormally low level of white blood cells: 5 out of 15 people (33%)
- Vomiting: 5 out of 15 people (33%)

People taking the medicine combinations in this study (in either group) did not experience any new or unexpected side effects, compared to people in other studies of each individual medicine.

Some side effects were thought to be caused by the drugs tested in the 2 groups:

During this study, about 28 out of 30 people (93%) had a side effect that the researchers thought was caused by the study medicines they were taking. This is called a ‘treatment-related’ side effect.

- 15 out of 15 people (100%) in **Group A** had a treatment-related side effect.
- 13 out of 15 people (87%) in **Group B** had a treatment-related side effect.

Serious side effects

A side effect is considered ‘serious’ if it is life-threatening, needs hospital care, leads to death, or causes lasting problems.

During this study,

- 4 out of 15 people (27%) in **Group A** experienced a serious side effect.
- 7 out of 15 people (47%) in **Group B** experienced a serious side effect.

The serious side effects that the researchers thought were caused by the study medicines are shown below. Some people had more than one side effect – this means that they are included in more than one row in the table.

Treatment-related serious side effects reported in this study	People in Group A (15 people)	People in Group B (15 people)
Low levels of red blood cells or hemoglobin	0	6.7% (1 out of 15)
Multiple blood clots in the body	0	6.7% (1 out of 15)
Irregular heartbeat	0	6.7% (1 out of 15)
Fever	0	13.3% (2 out of 15)
Fatigue	6.7% (1 out of 15)	0
Allergic reaction or intolerance to medication	0	6.7% (1 out of 15)
Lowered levels of platelets (‘platelet count decreased’)	0	6.7% (1 out of 15)
Clot in a deep vein in the body	0	6.7% (1 out of 15)

Side effects that caused death

One person in **Group B** died because of a side effect of multiple blood clots in the body ('disseminated intravascular coagulation, DIC'), which the researchers thought was related to one of the study medicines. There were no fatal side effects in **Group A**.

Stopping the medicine because of side effects

During the study, some people decided to stop taking their medicine because of side effects.

- In **Group A**, no patient stopped taking their medicine because of a side effect.
- In **Group B**, 1 out of 15 people (6.7%) stopped taking their medicine because of side effects: multiple blood clots in the body ('disseminated intravascular coagulation, DIC') and clot in a deep vein in the body ('deep vein thrombosis, DVT').

8. What do these results mean for patients and researchers?

The information in this summary is from part of the larger MORPHEUS Pancreatic Cancer Study. These results are for a subgroup of patients who were given either atezolizumab together with BL-8040 or chemotherapy. These results have helped researchers learn more about how atezolizumab interacts with other medicines for the treatment of people with pancreatic cancer.

It is important to remember that **one study cannot tell us everything we need to know about how safe a medicine is and how well it works**. It takes a lot of people in many studies to truly understand everything we need to know. The results from this study may be different from results from other studies of the same medicines. **This means that you should not make medical decisions based on this one summary. Always speak with your study researchers before making any decisions about your treatment.**

9. Are there plans to add other people to this subgroup or to do other studies with these medicines?

Currently no other studies are looking at the use of atezolizumab together with BL-8040 in pancreatic cancer.

10. Where can I find more information?

You can find more information about this study on the following websites:

- <https://www.clinicaltrials.gov/ct2/show/NCT03193190>
- <https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-004126-42>
- <https://forpatients.roche.com/en/trials/cancer/pancreatic-cancer/a-study-of-multiple-immunotherapy-based-treatment-combinations-i2.html>

If you want to learn more about the results from this subgroup, see the following abstract/poster:

“Phase Ib/II Open-Label, Randomized Evaluation of 2L Atezolizumab (atezo) + BL-8040 vs Control in MORPHEUS-Pancreatic Ductal Adenocarcinoma (M-PDAC) and MORPHEUS-Gastric Cancer (M-GC).” The authors of the poster presented at Gastrointestinal Cancers Symposium (ASCO-GI) 2020 are Do-Youn Oh, Jaffer Ajani, Yung-Jue Bang, Hyun-Cheol Chung, Kyu-pyo Kim, Jill Lacy, Jeeyun Lee, Teresa Macarulla, Gulam A Manji, Eileen M O’Reilly, Kun-Huei Yeh, Simon Allen, Nedal Al-Sakaff, Hila Barak, Jilpa Patel, Jan Pintoffl, Colby S Shemesh, Wei Zhang, Xiaosong Zhang and Ian Chau. The link is here: https://ascopubs.org/doi/abs/10.1200/JCO.2020.38.4_suppl.712

Who can I contact if I have questions about this subgroup or the larger MORPHEUS Pancreatic Cancer Study?

If you have more questions, visit [ForPatients.roche.com](https://forpatients.roche.com) and fill out the contact form.

If you were part of this subgroup and have any questions about the results, talk to your study researchers or staff at the hospital or clinic where you were treated.

If you have questions about your own treatment, talk to the study researchers in charge of your treatment.

Who organised and paid for this subgroup and the larger MORPHEUS Pancreatic Cancer Study?

The MORPHEUS Pancreatic Cancer Study and this subgroup were organised and paid for by F. Hoffmann-La Roche Ltd whose headquarters are in Basel, Switzerland. The medicine BL-8040 was provided by BioLineRx Ltd.

Full title of the study and other identifying information

The full title of the study is: “A Study of Multiple Immunotherapy-Based Treatment Combinations in Participants with Metastatic Pancreatic Ductal Adenocarcinoma (Morpheus-Pancreatic Cancer)”

The study is also known as MORPHEUS-PDAC.

- The protocol number for this study is: WO39608.
- The ClinicalTrials.gov identifier for this study is: NCT03193190.
- The EudraCT number for this study is: 2016-004126-42.