Summary of Clinical Trial Results

MY PATHWAY Solid Tumor Study: data from people who were treated with trastuzumab and pertuzumab together, erlotinib, vemurafenib alone, vemurafenib and cobimetinib together, vismodegib, alectinib, or atezolizumab

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

About this summary

This is a summary of the results from small groups of people (called 'subgroups') who were part of a large clinical trial (called a 'study' in this document) called My Pathway. This summary was written for:

- members of the public and
- people who took part in the study.

This summary is based on information known at the time of writing.

The study started in April 2014 and finished in May 2023. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.

Contents of the summary

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about solid tumors with rare mutations and the medicines studied – **trastuzumab with pertuzumab**, **atezolizumab**, **vemurafenib alone**, **vemurafenib with cobimetinib**, **vismodegib**, **alectinib**, and **erlotinib**.

The subgroups were: (1) the **trastuzumab with pertuzumab** group, (2) the **atezolizumab** group, (3) the **vemurafenib alone** group, (4) the **vemurafenib with cobimetinib** group, (5) the **vismodegib** group, (6) the **alectinib** group, and (7) the **erlotinib** group.

As the company that organized and funded this study (the '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 important role you have played in medical research. If

you have questions about the results outlined in this document, please speak with the doctor, research nurse, or another team member at your study site.

1. General information about this study

Why was this study done?

There are a lot of mutations that can cause cancer. In some cases, there are medications that can treat cancers that have specific kinds of mutations. These medications are called targeted therapies.

This study looked at a few targeted therapies in a couple of kinds of solid tumors. Each of the eight medications in this study target specific mutations that happen in some people's tumors. Overall, the eight medications included in this study were given to seven groups of people, depending on what kind of mutation each group of people had:

(1) **trastuzumab with pertuzumab**

(2) **atezolizumab**

(3) **vemurafenib alone**

(4) **vemurafenib with cobimetinib**

(5) **vismodegib**

(6) **alectinib**

(7) **erlotinib**

What did researchers want to find out?

- Researchers did this study to see how well looking for specific mutations could help to figure out the correct treatment to use (see section 4 "What were the results of the study?").
- They also wanted to find out how safe each of the medicines were – by checking how many people had side effects and seeing how serious they were, when taking each of the treatments during this study (see section 5 "What were the side effects?").

The main questions that researchers wanted to answer were:

1. If targeted therapies that are approved for specific types of solid tumors can be used to help people with different kinds of solid tumors that have the same mutations.

Other questions that researchers wanted to answer included:

2. Whether the medications used were safe – by checking how many people had side effects and seeing how serious they were.
3. Figuring out if the information about the mutations could help other patients in the future.

What kind of study was this?

This study was a 'Phase 2' study. Before this study, all eight treatments had been tested in a number of people with solid tumors. In this study, people with solid tumors were put into seven groups depending on what type of mutation their tumor had.

When and where did the study take place?

The study started in April 2014 and finished in May 2023. This summary was written after the study had ended.

The study took place at 54 study centers – across the U.S.

2. Who took part in this study?

In this study, 672 people with advanced solid tumors took part.

People who took part in the study were between 23 and 90 years of age. 326 of the 672 people (48.5%) were male and 346 of the 672 people (51.5%) were female.

People could take part in the study if:
- they had an advanced or metastatic solid tumor with specific types of mutations
- there was no medication currently approved for their type of tumor and no better treatment option available

People could not take part in the study if:
- they had a blood cancer instead of a solid tumor
- they were taking other anti-cancer medicines
- they had a brain metastasis

3. What happened during the study?

During the study, people were put into groups based on what kind of mutations their tumor had.

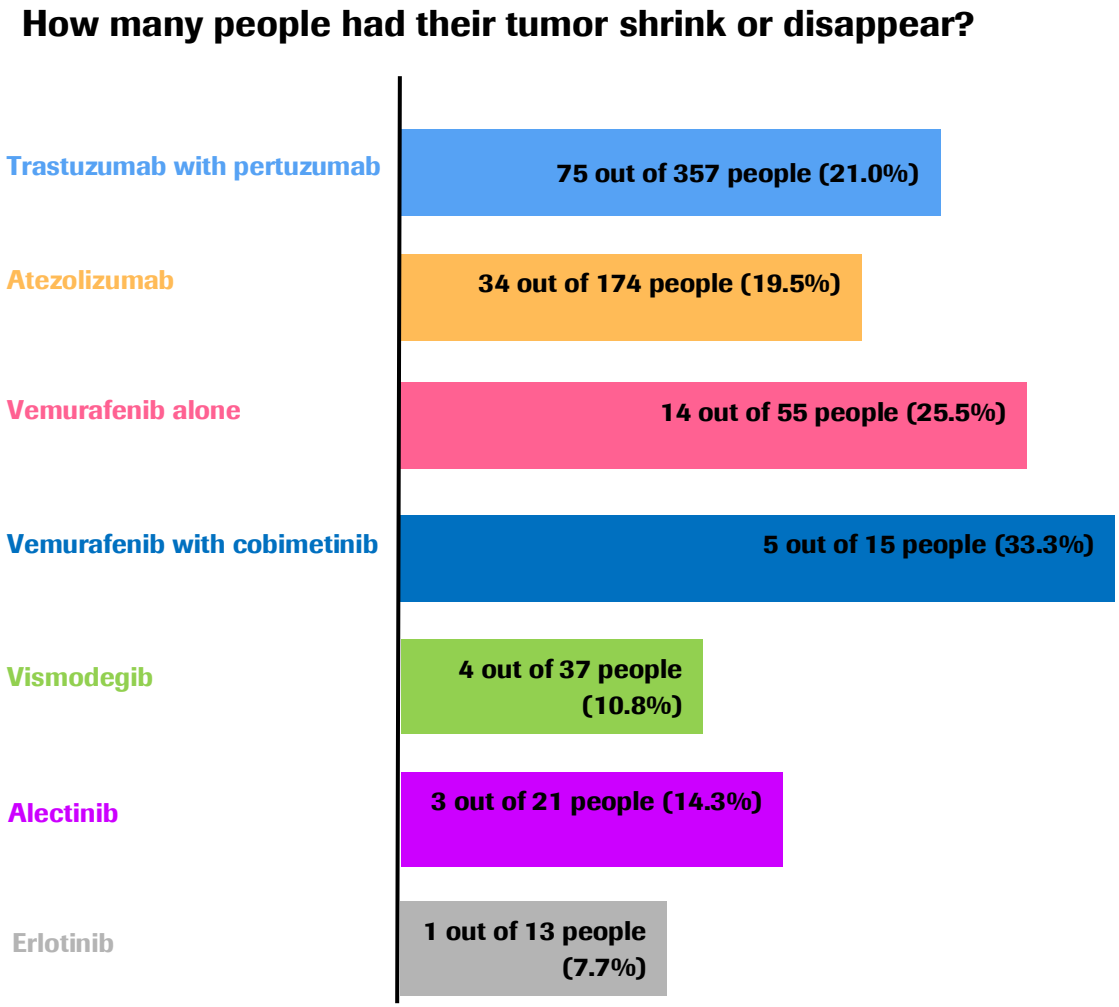
The treatment groups were:
- **trastuzumab with pertuzumab**
- **atezolizumab**
- **vemurafenib alone**
- **vemurafenib with cobimetinib**
- **vismodegib**
- **alectinib**
- **erlotinib**

People in the study took the treatments for 16 weeks for **erlotinib**, **vemurafenib alone**, **vemurafenib with cobimetinib**, **vismodegib**, and **alectinib** and 12 weeks for **trastuzumab with pertuzumab** and **atezolizumab**. If the medication was working for the patient, they were allowed to continue taking it until their cancer got worse or they had side effects. During the study, the people who took part were asked to go back to their study center for scheduled visits – to check their overall health. Look below to see more information about what happened in the study.

4. What were the results of the study?

Question 1: Can targeted therapies that are approved for specific types of solid tumors be used to help people with different kinds of solid tumors that have the same mutations?

Researchers looked at how many patients had smaller or no tumors after treatment.



The results of this study show that this type of study can be used to help researchers find treatment options for people with rare types of solid tumors that don't currently have treatment options.

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happen during the study.

- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine prescribing information sheet.
- Serious and common side effects are listed in the following sections.

Serious side effects

A side effect is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems.

In the **trastuzumab with pertuzumab** group, serious side effects happened in **26.6%** of people. The most common serious side effects were intestinal blockages, infections, anemia (or low red blood cells), and infusion-related reactions.

In the **atezolizumab** group, serious side effects happened in **35.6%** of people. The most common serious side effects were pneumonia, infections, and kidney injury.

In the **vemurafenib only** group, serious side effects happened in **38.2%** of people. The most common serious side effects were stomach problems, infections, inflammation of the pancreas, and shortness of breath.

In the **vemurafenib with cobimetinib** group, serious side effects happened in **73.3%** of people. The most common serious side effects were intestinal blockages.

In the **vismodegib** group, serious side effects happened in **35.1%** of people. The most common serious side effects were intestinal blockages, infections, and problems with blood clotting.

In the **alectinib** group, serious side effects happened in **33.3%** of people. The most common serious side effects were increases in liver values, which may mean lower liver activity.

In the **erlotinib** group, serious side effects happened in **23.1%** of people. The most common serious side effects were intestinal blockages, pneumonia, confusion, and falling.

There were some people in the study who died due to side effects that may have been related to one of the study medicines. These were:

- **2 out of 357** people (0.6%) in the **trastuzumab with pertuzumab** group.
- **0 out of 175** people in the **atezolizumab** group.
- **0 out of 55** people in the **vemurafenib only** group.
- **0 out of 15** people in the **vemurafenib with cobimetinib** group.
- **0 out of 37** people in the **vismodegib** group.
- **0 out of 21** people in the **alectinib** group.
- **0 out of 13** people in the **erlotinib** group.

Common side effects

Not all side effects are considered 'serious'. Side effects may be mild to very serious and can be different from person to person.

In the **trastuzumab with pertuzumab** group, side effects happened in **93.6%** of people. The most common side effects were diarrhea, fatigue (or feeling tired), nausea, anemia (or low red blood cells), and infusion-related reactions.

In the **atezolizumab** group, side effects happened in **93.1%** of people. The most common side effects were fatigue (or feeling tired), nausea, diarrhea, cough, and anemia (or low red blood cells).

In the **vemurafenib only** group, side effects happened in **98.2%** of people. The most common side effects were fatigue (or feeling tired), nausea, arthralgia (or joint stiffness), vomiting, maculo-papular rash (or a rash with raised bumps), and diarrhea.

In the **vemurafenib with cobimetinib** group, side effects happened in **100%** of people. The most common side effects were nausea, diarrhea, and fatigue (or feeling tired).

In the **vismodegib** group, side effects happened in **94.6%** of people. The most common side effects were fatigue (or feeling tired), diarrhea, nausea, dysgeusia (or a metal taste in the mouth), and muscle spasms.

In the **alectinib** group, side effects happened in **100%** of people. The most common side effects were constipation, fatigue (or feeling tired), edema peripheral (or swelling in the legs), nausea, back pain, and dyspnea (or shortness of breath).

In the **erlotinib** group, side effects happened in **92.3%** of people. The most common side effects were diarrhea, decreased appetite, fatigue (or feeling tired), nausea, and pyrexia (or fever).

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

6. How has this study helped research?

The information presented here is from a single study of 672 people with advanced solid tumors. These results helped researchers learn more about advanced solid tumors and **trastuzumab with pertuzumab**, **atezolizumab**, **vemurafenib alone**, **vemurafenib with cobimetinib**, **vismodegib**, **alectinib**, and **erlotinib**.

The results of this study show that this type of study can be used in the future to help researchers find treatment options for people with rare types of solid tumors.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

7. Are there plans for other studies?

Studies with these medications are still happening, and further studies will be planned based on the results of current studies.

8. Where can I find more information?

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

- https://clinicaltrials.gov/ct2/show/results/NCT02091141
- https://forpatients.roche.com/en/trials/cancer/my-pathway--a-study-evaluating-herceptin-perjeta--tarceva--zelbo.html

If you would like to find out more about the results of this study, there are five relevant scientific papers:

- "Pertuzumab plus trastuzumab for HER2-amplified metastatic colorectal cancer (MyPathway): an updated report from a multicentre, open-label, phase 2a, multiple basket study". The authors of the scientific paper are: F Meric-Bernstam, H Hurwitz, KPS Raghav, and others. The paper is published in the journal 'Lancet Oncology', volume number 20, on pages 518-350.
- "Targeted therapy for advanced salivary gland carcinoma based on molecular profiling: results from MyPathway, a phase IIa multiple basket study". The authors of the scientific paper are: R Kurzrock, DW Bowles, H Kang, and others. The paper is published in the journal 'Annals of Oncology', volume number 31, on pages 412-421.
- "Pertuzumab and trastuzumab for HER2-positive, metastatic biliary tract cancer (MyPathway): a multicentre, open-label, phase 2a, multiple basket study". The authors of the scientific paper are: M Javie, MJ Borad, NS Azad, and others. The paper is published in the journal 'Lancet Oncology', volume number 22, on pages 1290-1300.
- "Atezolizumab Treatment of Tumors with High Tumor Mutational Burden from MyPathway, a Multicenter, Open-Label, Phase IIa Multiple Basket Study". The authors of the scientific paper are: CF Friedman, JD Hainsworth, R Kurzrock, and others. The paper is published in the journal 'Cancer Discovery', volume number 12, on pages 654-669.
- "MyPathway Human Epidermal Growth Factor Receptor 2 Basket Study: Pertuzumab + Trastuzumab Treatment of a Tissue-Agnostic Cohort of Patients With Human Epidermal Growth Factor Receptor 2-Altered Advanced Solid Tumors". The authors of the scientific paper are: CJ Sweeney, JD Hainsworth, R Bose, and others. The paper is published in the journal 'Journal of Clinical Oncology', volume number 42, on pages 258-265.

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/trials/cancer/my-pathway--a-study-evaluating-herceptin-perjeta--tarceva--zelbo.html
- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organised and paid for this study?

This study was organized and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: My Pathway: An Open-Label Phase IIA Study Evaluating Trastuzumab/Pertuzumab, Erlotinib, Vemurafenib/Cobimetinib, Vismodegib, Alectinib, and Atezolizumab in Patients who have Advanced Solid Tumors with Mutations or Gene Expression Abnormalities Predictive of Response to One of these Agents.

The study is known as 'My Pathway'.

- The ClinicalTrials.gov identifier for this study is: NCT02091141