Summary of Clinical Trial Results

MYTACTIC: A Study Looking at Targeted Cancer Medications in Patients with Advanced Solid Tumors with Mutations

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 MYTACTIC. 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 January 2021 and finished in December 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.

The subgroups were:

(1) **entrectinib in people with ROS1 mutations**

(2) **inavisolib in people with PI3K mutations**

(3) **alectinib in people with ALK mutations**

(4) **ipatasertib in people with PTEN or AKT mutations**

(5) **atezolizumab plus chemotherapy in people with DNA repair mutations**

(6) **trastuzumab emtansine plus atezolizumab in people with HER2 mutations without DNA repair mutations**

(7) **PH FDC SC in people with HER2 mutations**

(8) **PH FDC SC plus chemotherapy in people with HER2 mutations**

(9) **trastuzumab emtansine plus tucatinib in people with HER2 mutations**

(10) **trastuzumab emtansine plus atezolizumab in people with HER2 and DNA repair mutations**

(11) **ipatasertib plus atezolizumab in people with PI3K mutations**

(12) **ipatasertib plus atezolizumab in people with PTEN or AKT mutations**

(13) **ipatasertib plus paclitaxel in people with PI3K and PTEN or AKT mutations**

(14) **atezolizumab plus tiragolumab in people with DNA repair mutations**

(15) **pralsetinib in people with RET mutations**

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 or combinations of targeted therapies in a couple of kinds of solid tumors. Each of the medications in this study target specific mutations that happen in some people's tumors. Overall, the medications included in this study were given to 15 groups of people, depending on what kind of mutation each group of people had.

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 or combinations of therapies are effective in people with advanced or metastatic solid tumors.

Other questions that researchers wanted to answer included:

2. How long the treatment prevented a person's cancer from getting worse.

What kind of study was this?

This study was a 'Phase 2' study. Before this study, all ten treatments had been tested in many other people with solid tumors. In this study, people with solid tumors were put into 15 groups depending on what type of mutation their tumor had.

When and where did the study take place?

The study started in January 2021 and finished in December 2023. This summary was written after the study had ended.

The study took place at 38 study centers – across the U.S.

2. Who took part in this study?

In this study, 252 people with advanced solid tumors took part.

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:

(1) **entrectinib in people with ROS1 mutations**

(2) **inavisolib in people with PI3K mutations**

(3) **alectinib in people with ALK mutations**

(4) **ipatasertib in people with PTEN or AKT mutations**

(5) **atezolizumab plus chemotherapy in people with DNA repair mutations**

(6) **trastuzumab emtansine plus atezolizumab in people with HER2 mutations without DNA repair mutations**

(7) **PH FDC SC in people with HER2 mutations**

(8) **PH FDC SC plus chemotherapy in people with HER2 mutations**

(9) **trastuzumab emtansine plus tucatinib in people with HER2 mutations**

(10) **trastuzumab emtansine plus atezolizumab in people with HER2 and DNA repair mutations**

(11) **ipatasertib plus atezolizumab in people with PI3K mutations**

(12) **ipatasertib plus atezolizumab in people with PTEN or AKT mutations**

(13) **ipatasertib plus paclitaxel in people with PI3K and PTEN or AKT mutations**

(14) **atezolizumab plus tiragolumab in people with DNA repair mutations**

(15) **pralsetinib in people with RET mutations**

No patients were enrolled in Group 1: **entrectinib in people with ROS1 mutations**. All other groups had patients enrolled who were treated. If the medication was working for the patient, they were allowed to continue taking it until the end of the study. 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.

How many people had their tumor shrink or disappear?

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 **entrectinib (ROS1 mutations)** group, there were no serious side effects because no patients were enrolled in this group.

In the **inavisolib (PI3K mutations)** group, serious side effects happened in **5** out of **26** people **(19.2%)**. The most common serious side effects were dehydration, device malfunction, low blood potassium, and infections.

In the **alectinib (ALK mutations)** group, serious side effects happened in **2** out of **5** people **(40.0%)**. The most common serious side effects were acute liver failure and pneumonia.

In the **ipatasertib (PTEN or AKT mutations)** group, serious side effects happened in **6** out of **26** people **(23.1%)**. The most common serious side effects were back pain, dehydration, diarrhea, bone fracture, heart attack, and infections.

In the **atezolizumab plus chemotherapy (DNA repair mutations)** group, serious side effects happened in **11** out of **25** people **(44.0%)**. The most common serious side effect was cardiac arrest.

In the **trastuzumab emtansine plus atezolizumab (HER2 mutations without DNA repair mutations)** group, serious side effects happened in **9** out of **25** people **(36.0%)**. The most common serious side effects were stomach and intestine problems, infections, kidney problems, low blood platelets, and fast heartbeat.

In the **PH FDC SC (HER2 mutations)** group, serious side effects happened in **2** out of **13** people **(15.4%)**. The most common serious side effects were inflammation of the intestines, bone fractures, and falling.

In the **PH FDC SC plus chemotherapy (HER2 mutations)** group, serious side effects happened in **2** out of **8** people **(25.0%)**. The most common serious side effects were swollen stomach, dehydration, diarrhea, inflammation of the intestines, and low blood potassium.

In the **trastuzumab emtansine plus tucatinib (HER2 mutations)** group, serious side effects happened in **6** out of **23** people **(26.1%)**. The most common serious side effect was anemia (or low red blood cells).

In the **trastuzumab emtansine plus atezolizumab (HER2 and DNA repair mutations)** group, serious side effects happened in **7** out of **19** people **(36.8%)** of people. The most common serious side effects were stroke, exhaustion, vomiting, too much blood calcium, and infections.

In the **ipatasertib plus atezolizumab (PI3K mutations)** group, serious side effects happened in **10** out of **28** people **(35.7%)**. The most common serious side effect was diarrhea.

In the **ipatasertib plus atezolizumab (PTEN or AKT mutations)** group, serious side effects happened in **8** out of **25** people **(32.0%)**. The most common serious side effects were kidney injury and lung inflammation.

In the **ipatasertib plus paclitaxel (PI3K and PTEN or AKT mutations)** group, serious side effects happened in **2** out of **3** people **(66.7%)**. The most common serious side effects were infections and hemorrhages.

In the **atezolizumab plus tiragolumab (DNA repair mutations)** group, serious side effects happened in **6** out of **23** people **(26.1%)**. The most common serious side effects were heart attacks.

In the **pralsetinib (RET mutations)** group, serious side effects happened in **2** out of **3** people **(66.7%)**. The most common serious side effects were anemia (or low red blood cells), brain swelling, infections, diarrhea, and a seizure.

There were some people in the study who died, but none of the causes of death were due to the study medicines. Also, none of the side effects that occurred in this study were different from the side effects that are already known to happen with these medications.

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://www.clinicaltrials.gov/study/NCT04632992
- https://forpatients.roche.com/en/trials/cancer/solid-tumors/a-study-evaluating-targeted-therapies-in-participants-w-28698.html

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

- "MyTACTIC: Activity of targeted therapy in patients (pts) with advanced solid tumors harboring specific biomarkers [abstract]". The authors of the scientific paper are: LS Schwartzberg, DR Spigel, A VanderWalde, and others. The paper is published in the journal 'Journal of Clinical Oncology', volume number 42, Supplement 16 on page 3100.
- "MyTACTIC: Afficacy and safety of atezolizumab (atezo) + chemotherapy (chemo) in patients (pts) with advanced unresectable/metastatic solid tumors with high tumor mutational burden (TMB-H) or high microsatellite instability (MSI-H)/deficient mismatch repair (dMMR) [abstract]". The authors of the scientific paper are: DR Spigel, MA Hussein, R Zuniga, and others. The paper is published in the journal 'Journal of Clinical Oncology, volume number 41, Supplement 16 on page 2612.
- "Activity and safety of ipatasertib (ipat) for AKT activating mutation and/ or PTEN loss/loss of function solid tumors from MyTACTIC [abstract]". The authors of the

scientific paper are: A VanderWalde, DR Spiget, WC Darbonne, and others. The paper is published in the journal 'European Journal of Cancer', volume number 174, Supplement 1 on page S71.

- "Improving ethnic and racial diversity within clinical trial populations through community recruitment and inclusion initiatives: Experience from MyTACTIC [abstract]". The authors of the scientific paper are: RM Zuniga, DR Spigel, LS Schwartzberg, and others. The paper is published in the journal 'Journal of Clinical Oncology', volume number 42, Supplement 16 on page e13679.

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/solid-tumors/a-study-evaluating-targeted-therapies-in-participants-w-28698.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: Final CSR Study ML42439, MYTACTIC: An Open-Label Phase II Study Evaluating Targeted Therapies in Patients Who Have Advanced Solid Tumors With Genomic Alterations Or Protein Expression Patterns Predictive Of Response.

The study is known as 'MY TACTIC'.

- The ClinicalTrials.gov identifier for this study is: NCT04632992