

Summary of Clinical Trial Results

An early phase clinical research study evaluating the safety, efficacy, and pharmacokinetics* of ipatasertib in combination with atezolizumab and docetaxel in metastatic castration-resistant prostate cancer

Please see on page 5, at the end of the summary, the full study title and the other study protocol details

About this summary

This is a lay person summary of the results of a clinical trial (called a 'study' in this document) – 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 (January 2024) .

The study started in July 2020 and stopped early – in December 2021 – due to side effects of the study drugs.

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. **Therefore, should you currently receive a similar treatment as those described in this summary, you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

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Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about prostate cancer and about treatment with ipatasertib in combination with atezolizumab and docetaxel.

Layperson summary date: <February-2024>

* A pharmacokinetic study in people measures how a study treatment is absorbed, processed and eliminated by the human body

1. General information about this study

Why was this study done?

Men with prostate cancer that has spread to other parts of the body are often treated with drugs that lower the amount of male hormones in the body, and more precisely testosterone. Male hormones may help the tumours grow, so taking drugs that reduce the amount of male hormones in the body can stop the tumours from getting bigger or even make them shrink. However, despite the reduction of testosterone, some tumours start growing again. Doctors may then use combinations of drugs that act in different ways to help prevent tumours from growing for a longer period of time. In this study, researchers wanted to see if the addition of a combination of a new drug (ipatasertib) with immunotherapy (atezolizumab) and chemotherapy (docetaxel) would stop cancer from growing for longer after the failure of hormone reducing drugs. They also wanted to see whether the combination of drugs would be well enough tolerated by people.

What were the study medicines?

The medicines called 'atezolizumab' and 'ipatasertib' were the focus of this study

You say this 'ah-tez-oh-liz-uh-mab'

You say this as 'eye – pat – uh – sir – tib'

What did researchers want to find out?

In men who have prostate cancer that has spread, researchers wanted to see how well tolerated the combination of medicines (ipatasertib plus atezolizumab /docetaxel) is when taking the study medicines together, and see if their disease gets better.

The study consisted of two parts:

Part A: Safety run-in cohort of approximately 12 people

Part B: Expansion cohort of approximately 38 people

What kind of study was this?

This study was a 'Phase 1b' study. This means that it is the first time the combination of ipatasertib plus atezolizumab has been tested in people with prostate cancer.

Phase 1b studies are done in a small number of people to see if a drug or a combination of drugs are well tolerated. Once established, the drug or combination of

drugs can be tested in a larger number of people to see if it works better than the usual treatment and is well enough tolerated to be allowed by the health authorities as a treatment that can be prescribed by your doctor.

The study was 'open label'. This means that both the people taking part in the study and the study doctors knew the treatments which were given.

When and where did the study take place?

The study started in July 2020 but stopped earlier than planned because the study drugs did not work as well as expected. This summary presents the results of the study up until it was stopped in December 2021.

The study took place at 9 hospitals in France, Italy, Spain and Switzerland.

2. Who took part in this study?

In this study, 6 men with prostate cancer that had spread to other parts of the body took part. Men could take part in the study if:

- Age >18 years
- Disease worsened but no curative treatment options
- Pretreated with last generation hormone therapy for the disease

3. What happened during the study?

The study stopped earlier than planned (after only 6 people were enrolled) because side effects observed from the drugs were too many and difficult to manage by the study doctors despite the precautionary measures taken to prevent/limit these side effects.

4. What were the results of the study?

The study showed that the combination of ipatasertib, atezolizumab and docetaxel, was not well tolerated enough to continue to be administered to people.

5. What were the side effects?

Overall, the side effects were similar to those observed previously with ipatasertib, atezolizumab, or docetaxel.

The majority of people were elderly with multiple co-morbidities and in an advanced stage of their disease. Despite multiple risk-minimization strategies in place, such as prevention measures, controlled enrolment, etc, the combination of ipatasertib plus atezolizumab and docetaxel was shown to be challenging to manage in terms of toxicity, which made further enrollment of further participants at this dose level inappropriate.

Severe or medically significant adverse events (Grade 3 or higher AEs) were reported in 5 out of 6 people (83.3%) with decreased red blood cells (anemia), decreased white blood cells (neutropenia), feeling weak and having no energy (asthenia) and decreased appetite in 2 people [33.3%, each).

6. How has this study helped research?

The aim of this study was to evaluate if combining a new targeted therapy drug in combination with an immuno-and chemotherapy would be well tolerated for people to take, and would stop cancer from growing for longer after failure of a new generation of hormone-reducing drug.

The majority of people who took part in the study were elderly, with multiple co-morbidities and in an advanced stage disease. Despite multiple strategies to minimise side effects of this study treatments by e.g. prophylactic measures, the combination of ipatasertib plus atezolizumab and docetaxel was shown to be challenging due to side effect issues. Hence, it was necessary to stop the study earlier than planned.

7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at ipatasertib plus atezolizumab and chemotherapy are planned.

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/NCT04404140>
- <https://forpatients.roche.com/en/trials/cancer/prostate-cancer/a-study-evaluating-the-safety--efficacy-and-pharmacokin-79210.html>

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/prostate-cancer/a-study-evaluating-the-safety--efficacy-and-pharmacokin-79210.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 organised 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: “A Phase Ib, Open-Label, Multicenter Study Evaluating the Safety, Efficacy, and Pharmacokinetics of ipatasertib in Combination with Atezolizumab and Docetaxel in Metastatic Castration-Resistant Prostate Cancer”.

- The protocol number for this study is: CO41792.
- The ClinicalTrials.gov identifier for this study is: NCT04404140.
- The EudraCT number for this study is: 2019-004591-19.