Summary of Clinical Trial Results

A study looking at cancer treatment choices guided by comprehensive genomic profiling in people with cancer of unknown primary (CUP)

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

About this summary

This is a 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 this document.

The study started in July 2018 and this summary includes the results that were collected and analysed until February 2023. At the time of writing this summary, this study is still happening – this summary presents the complete results for one part of the study. This summary will be updated when the study ends.

No single study can tell us everything about the risks and benefits of a particular treatment plan. 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 that included the same medicines.

- **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

1. General information about this study
2. Who is taking part in this study?
3. What is happening during the study?
4. What are the results of the study?
5. What are the side effects?
6. How does this study help research?
7. Are there plans for other studies?
8. Where can I find more information?

Glossary

- **Comprehensive genomic profiling:** a test that shows whether there are any alterations in the DNA of the tumour of a person with cancer.
- **Molecularly guided therapy:** a cancer treatment that targets DNA alterations in a person's tumour.
- **Platinum-based chemotherapy:** medicine that kills cancer cells using platinum.
- **Disease control:** when cancer does not progress (i.e. it does not get worse).
- **Cancer of unknown primary:** cancers where doctors are unable to find where in the body the cancer first started, before spreading to other parts of the body.

Thank you to the people who are taking part in this study

The people who are taking part in this study have helped researchers answer important questions about **cancer of unknown primary (CUP)** and the treatment plan being studied – molecularly guided therapy.

Key information about this study

- This study is being done to look at how well molecularly guided therapy and platinum-based chemotherapy work in certain people with CUP who achieved disease control after initial platinum-based chemotherapy treatment.
- In this study, 436 people with cancer from 34 countries are given either a therapy chosen based on alterations in the DNA of their tumour (molecularly guided therapy) or a continuation of platinum-based chemotherapy, decided using a computer programme that makes a random selection.
- So far, the study has shown that molecularly guided therapy increased the length of time it took for people's cancer to get worse or until they died compared with platinum-based chemotherapy.
    - In people given molecularly guided therapy, their cancer got worse or they died after 6.1 months on average.
    - In people given platinum-based chemotherapy, their cancer got worse or they died after 4.4 months on average.
- For every 100 patients during 1 year, there were around 23 serious side effects related to treatment in people who were given molecularly guided therapy and 27 serious side effects related to treatment in people who were given platinum-based chemotherapy.

1. General information about this study

Why is this study being done?

CUP describes a variety of cancers that have spread to other parts of the body, where doctors are unable to find where in the body the cancer first started, even after performing extensive tests at the time of diagnosis. CUP makes up only a small percentage of diagnoses of cancer, and a large proportion of people with CUP have a type called 'unfavourable' CUP. Unfavourable CUP is usually treated with a type of medicine called 'platinum-based chemotherapy'. Despite treatment with platinum-based chemotherapy, most people with unfavourable CUP die within a year. However, about a third of people with CUP have alterations in their tumour DNA that could allow treatment with molecularly guided therapies.

This study includes people with unfavourable CUP who achieved disease control after initial platinum-based chemotherapy treatment. The study looked at whether treatment choices guided by comprehensive genomic profiling (molecularly guided therapy) could lengthen the amount of time before the cancer got worse or until people died, compared with standard platinum-based chemotherapy. The study looked at how molecularly guided therapy affected people's quality of life and the safety (the side effects associated with a treatment) of molecularly guided therapy compared with platinum-based chemotherapy.

The study also includes people with unfavourable CUP whose cancer got worse after initial platinum-based chemotherapy treatment. The results from these people will be assessed separately and are not included in this summary.

What are the study treatments?

This study is looking at two treatment approaches:

- **Platinum-based chemotherapy** – the standard treatment plan.
- **Molecularly guided therapy** – the treatment plan being studied.

'**Platinum-based chemotherapy**' is currently the standard treatment for patients with unfavourable CUP.

- Platinum-based chemotherapy kills cancer cells using platinum.
- Platinum-based chemotherapy is used in the treatment of various types of cancers.

'**Molecularly guided therapy**' is the treatment plan being studied here – molecularly guided therapies work in a different way to platinum-based chemotherapy.

- Molecularly guided therapies are targeted therapies or cancer immunotherapies chosen based on the alterations in the tumour DNA of a person with cancer.
- Depending on the selected molecularly guided therapy, different signalling pathways involved in cancer development are blocked.
- This may mean that molecularly guided therapy can stop the growth and spread of cancer by targeting a specific alteration in the tumour DNA of a person with cancer and repairing the "normal" cell functions disturbed by the cancer.

What do researchers want to find out?

- Researchers are doing this study to look at molecularly guided therapy and platinum-based chemotherapy – to see how well molecularly guided therapy works (see section 4, "What are the results of the study?").
- They also want to find out how safe the treatment plan is – by checking how many people have side effects and seeing how serious they are, when taking each of the treatment approaches being used during this study (see section 5, "What are the side effects?").

The main question that researchers want to answer is:

1. In people who have achieved disease control after initial platinum-based chemotherapy, do therapy decisions guided by comprehensive genomic profiling increase the length of time it takes for their cancer to get worse or until they die compared with platinum-based chemotherapy?

Other questions that researchers want to answer include:

2. In people who have achieved disease control after initial platinum-based chemotherapy, do therapy decisions guided by comprehensive genomic profiling make them live longer compared with platinum-based chemotherapy?

3. In people who have achieved disease control after initial platinum-based chemotherapy, do therapy decisions guided by comprehensive genomic profiling improve their quality of life compared with platinum-based chemotherapy?

4. How many people whose therapy decisions are guided by comprehensive genomic profiling experience side effects caused by the molecularly guided therapy compared with platinum-based chemotherapy – and how serious are the side effects?

What kind of study is this?

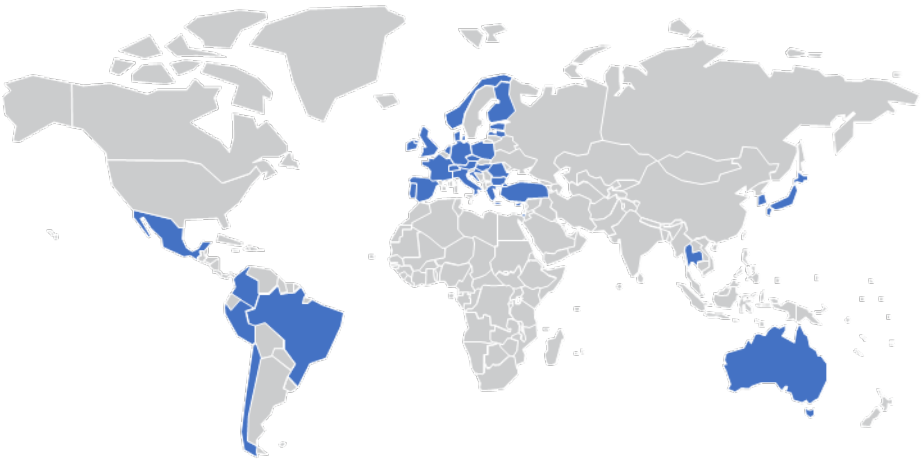
This study is a 'Phase 2' study. This means that the medicines that are being given to people who took molecularly guided therapy have been tested in a number of people with or without CUP before this study. In this study, people with CUP are taking either molecularly guided therapy or platinum-based chemotherapy – this is to find out if the use of comprehensive genomic profiling to guide the choice of molecularly guided therapy lengthens the amount of time it takes for people's cancer to get worse or until they die compared with platinum-based chemotherapy.

The study is 'randomised'. This means that it is decided by chance whether the person is given molecularly guided therapy or platinum-based chemotherapy. Randomly choosing whether people take molecularly guided therapy or platinum-based chemotherapy makes it more likely that the types of people in both groups (for example, age, race) will be a similar mix.

When and where is the study taking place?

The study started in July 2018 and this summary includes the results up until February 2023. At the time of writing this summary, further safety information is being collected.

The study is taking place at 159 study centres – across 34 countries in Europe, South America and Asia-Pacific. The following map shows the countries where this study is taking place.



- Australia
- Austria
- Brazil
- Bulgaria
- Chile
- Colombia
- Croatia
- Cyprus
- Czech Republic
- Denmark
- Estonia
- Finland
- France
- Germany
- Greece
- Hungary
- Ireland
- Israel
- Italy
- Japan
- Latvia
- Mexico
- Netherlands
- Norway
- Peru
- Poland
- Portugal
- Romania
- South Korea
- Spain
- Switzerland
- Thailand
- Turkey
- United Kingdom

2. Who is taking part in this study?

In this study, 436 people with unfavourable CUP, who have achieved disease control after initial platinum-based chemotherapy treatment, are taking part.

People taking part in the study are between 24 and 84 years of age; 222 of the 436 people (50.9%) are male and 214 of the 436 people (49.1%) are female.

People could take part in the study if they:

- Were at least 18 years old.
- Had unfavourable CUP – a panel of experts decided which specific cases to include in the study.
- Had a tumour that could be accurately measured in size.
- Could provide cancer tissue and/or a blood sample for comprehensive genomic profiling.

People could not take part in the study if they:

- Had already been given medicine for CUP that works throughout the whole of the body.
- Were not able to take platinum-based chemotherapy.

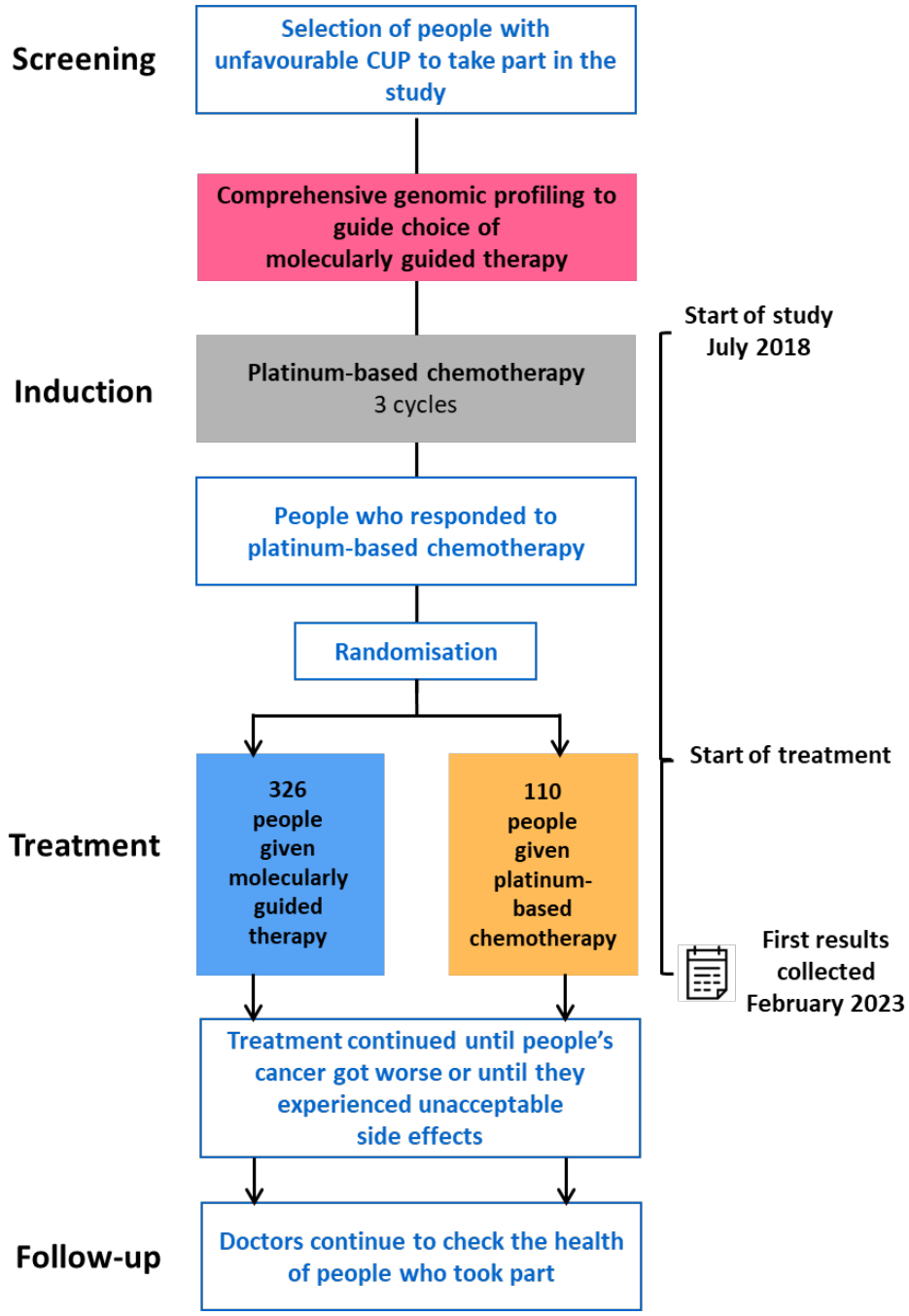
3. What is happening during the study?

During the study, all people were given three cycles of platinum-based chemotherapy. People who achieved disease control after this initial platinum-based chemotherapy treatment were then selected by chance to get one of two treatment approaches. The type of treatment approach was selected at random – by a computer.

The treatment groups are:

- **Molecularly guided therapy** (the treatment plan being studied).
- **Platinum-based chemotherapy** (the standard treatment plan).

Some people are still being treated with the study treatments. When the study finishes, the people who took part will be asked to go back to their study centre for more visits – to check their overall health. Look below to see more information about what has happened in the study so far – and what the next steps are.



This study is still happening, so the symbol on the timeline (📋) shows when the information shown in this summary was collected – after approximately 4.5 years (February 2023).

4. What are the results of the study?

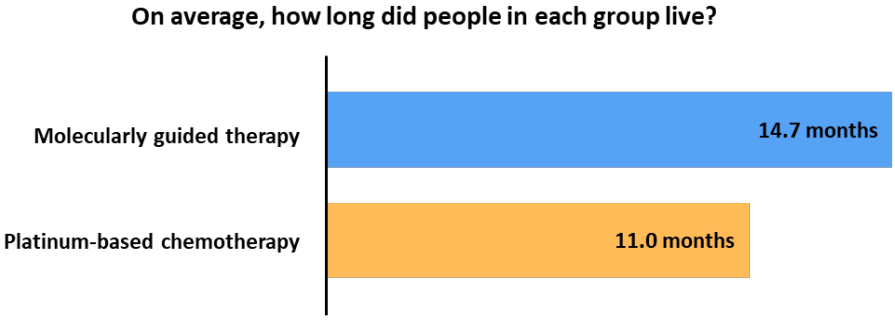
This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8).

Question 1: In people who have achieved disease control after initial platinum-based chemotherapy, do therapy decisions guided by comprehensive genomic profiling increase the length of time it takes for their cancer to get worse or until they die compared with platinum-based chemotherapy?

In people whose therapy was chosen based on comprehensive genomic profiling (molecularly guided therapy), their cancer got worse or they died after 6.1 months on average. Some people's cancer got worse or they died more quickly than this, and some people's cancer got worse or they died slower than this. This compares with 4.4 months for people who were given platinum-based chemotherapy. This is a real difference that was not caused by chance.

Question 2: In people who have achieved disease control after initial platinum-based chemotherapy, do therapy decisions guided by comprehensive genomic profiling make them live longer compared with platinum-based chemotherapy?

People whose therapy was chosen based on comprehensive genomic profiling (molecularly guided therapy) lived for 14.7 months on average. This compares with 11.0 months for people who were given platinum-based chemotherapy. However, as the researchers do not have enough information yet, we do not know whether this is a real difference or whether it is caused by chance.



Question 3: In people who have achieved disease control after initial platinum-based chemotherapy, do therapy decisions guided by comprehensive genomic profiling improve their quality of life compared with platinum-based chemotherapy?

The 'EQ-5D-5L VAS score' measures people's overall health-related quality of life, while the 'FACT-G total score' measures people's physical, social, emotional and functional wellbeing. For both of these measures, there was no evidence that molecularly guided therapy increased the time to worsening of quality of life compared with platinum-based chemotherapy.

5. What are the side effects?

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

- They are described in this summary because the study doctor believes the side effects are related to the treatments in the study.
- Not all of the people in this study have 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 leaflets.

Side effects

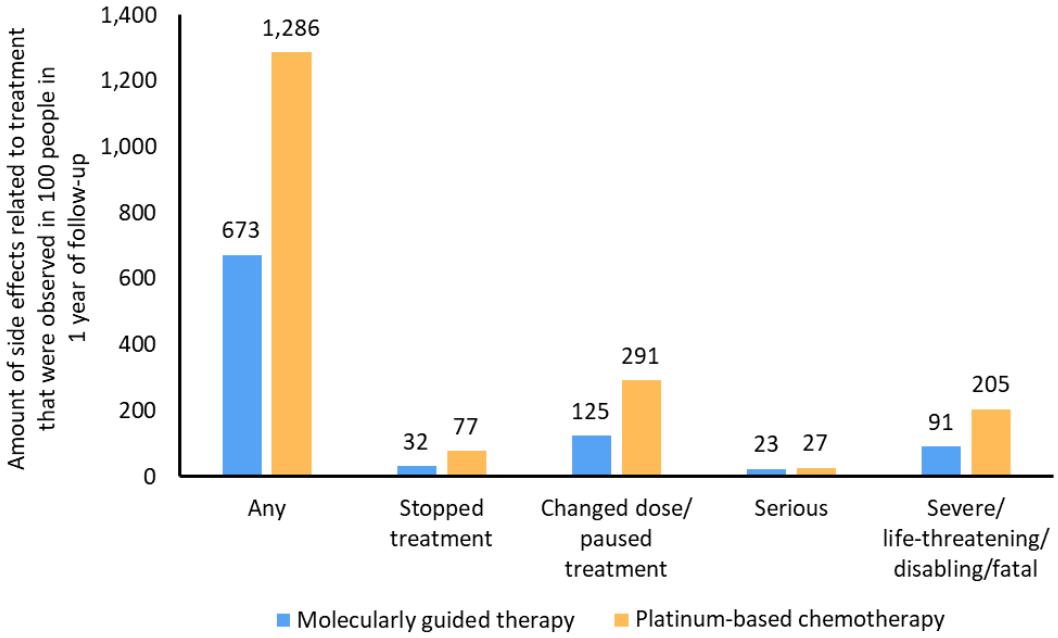
A side effect is considered 'serious' if it is life-threatening, needs hospital care or causes lasting problems. For every 100 patients during 1 year, there were around 23 serious side effects in people who were given molecularly guided therapy and 27 in people who were given platinum-based chemotherapy.

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

- Although side effects depend on the specific therapy used in the molecularly guided therapy group, there were a total of 32 patients with side effects for every 100 patients during 1 year, which led to them stopping treatment.
- In the platinum-based chemotherapy group, there were a total of 77 patients with side effects for every 100 patients during 1 year, which led to them stopping treatment.

Although side effects depend on the specific therapy used in the molecularly guided therapy group, there were around 673 side effects for every 100 patients during 1 year that were not considered serious. In the platinum-based chemotherapy group, there were 1,286 side effects that were not considered serious.

A summary of side effects related to treatment is shown in the following graph.



No people in the study died due to side effects that may have been related to one of the study medicines.

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 does this study help research?

The information presented here is from a single study of 436 people with unfavourable CUP who achieved disease control after initial platinum-based chemotherapy treatment. These results help researchers learn more about unfavourable CUP and treatment approaches with molecularly guided therapy.

Indeed, this study demonstrates the value of including comprehensive genomic profiling at the start of people's cancer journey to inform treatment decisions in people with CUP. Overall, molecularly guided therapy increased the length of time it took for people's cancer to progress compared with platinum-based chemotherapy. These initial results showed no evidence that molecularly guided therapy made people live longer. Quality of life was comparable between people treated with molecularly guided therapy and platinum-based chemotherapy. The number of people who had side effects related to treatment was generally similar or lower for molecularly guided therapy than for platinum-based chemotherapy. Researchers will continue to collect results from this study to see whether molecularly guided therapy makes people with unfavourable CUP live longer compared with platinum-based chemotherapy.

No single study can tell us everything about the risks and benefits of a treatment plan. 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 that included the same medicines.

- **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?

At the time of writing this summary, no more studies looking at treatment decisions guided by comprehensive genomic profiling (molecularly guided therapy) are planned at the current time.

8. Where can I find more information?

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

- https://clinicaltrials.gov/study/NCT03498521
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2017-003040-20/results
- https://forpatients.roche.com/en/trials/cancer/a-phase-ii-randomized-study-comparing-the-efficacy-and-safety-of.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Molecularly guided therapy versus chemotherapy after disease control in unfavourable cancer of unknown primary (CUPISCO): an open-label, randomised, phase 2 study”. The authors of the scientific paper are: Alwin Krämer, Tilmann Bochtler, Chantal Pauli, Kai-Keen Shiu, Natalie Cook and others. The paper is published in the journal ‘The Lancet’, volume number 404, on pages 527–539.

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, click on the ‘Contact Us’ button and fill out the contact form – https://forpatients.roche.com/en/trials/cancer/a-phase-ii-randomized-study-comparing-the-efficacy-and-safety-of.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, which has its headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: “A Phase II, Randomized, Active-Controlled, Multi-Center Study Comparing the Efficacy and Safety of Targeted Therapy or Cancer Immunotherapy Guided by Genomic Profiling Versus Platinum-Based Chemotherapy in Patients With Cancer of Unknown Primary Site Who Have Received Three Cycles of Platinum Doublet Chemotherapy”.

The study is known as ‘CUPISCO’.

- The protocol number for this study is: MX39795.
- The ClinicalTrials.gov identifier for this study is: NCT03498521.
- The EudraCT number for this study is: 2017-003040-20.