SERVIER TAIHO ONCOLOGY

Clinical Trial Summary

A study of trifluridine/tipiracil and bevacizumab in patients with resistant colorectal cancer that has spread (metastatic)

Full scientific title: An open-label, randomised, phase III study comparing trifluridine/tipiracil in combination with bevacizumab to trifluridine/tipiracil monotherapy in patients with refractory metastatic colorectal cancer (SUNLIGHT study).

We thank all the participants who took part in the study. Clinical study participants are very important for making progress in science, for the benefit of patients.
This document is a summary of the study. It is written for a general audience.

Researchers need many studies to decide which medicines work the best and are the safest for patients. For medical science to progress, many studies involving patients are running all around the world. This summary only shows the results from this one study. Other studies, evaluating the same drug, may find different results. You should not change your current treatment based on the results of this single study. If you have any questions about this study, please talk to your doctor.

Therapeutic area:
Oncology

Disease:
Colorectal cancer

Study phase:
Phase 3

25 April 2023

Final Version

In this summary:

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1 Why was this study done?

The study was done to confirm the effectiveness of the study drug called trifluridine/tipiracil or S95005, when combined with another drug in patients with metastatic colorectal cancer. Colorectal cancer means cancer of the colon or rectum. Metastatic means that the cancer has spread to other parts of the body.

S95005 is a combination of two drugs, trifluridine and tipiracil, together in the same pill. It is used to treat patients with metastatic colorectal cancer when standard treatments are no longer effective.

In this study, S95005 was combined with another marketed drug called bevacizumab. It was compared to S95005 given alone.

- S95005 is a drug that blocks the growth of cancer cells.
- Bevacizumab is a drug that blocks the blood vessels that supply the tumour. It slows the growth of the tumour.

The main goal of the study was to test if S95005 in combination with bevacizumab worked better than S95005 alone in patients with metastatic colorectal cancer.

2 When and where did this study take place?

When did the study take place?

- This study started in November 2020.
- The study is still ongoing. Participant inclusions are now complete.

This summary only includes data collected up to 19 July 2022.

Where did the study take place?

The study took place in the following countries:

Country	Number of participants
Spain	115
Russian federation	77
Brazil	63
Hungary	47
Italy	39
Poland	34
France	28
Ukraine	21
Denmark	20
United States of America	16
Austria	15
Germany	10
Belgium	7

3 Who participated in the study?

Which participants were included in the study?

To be eligible to the study, participants had to be:

- 18 years of age or older
- Diagnosed with metastatic colorectal cancer
- Resistant to previous treatments for metastatic colorectal cancer and
- Not eligible for surgery

How many participants took part in the study?

A total of 492 participants took part in the study: 236 women and 256 men.

How old were the participants?

The average age of the participants was 62 years. The youngest participant was 20 years old and the oldest was 90 years old.

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4 Which treatments did the participants receive?

The participants took the drugs during time periods called "cycles". They received one of the following treatments:

- S95005 and bevacizumab:
  Participants took S95005 orally over 28-day cycles, for 5 days twice daily each of the first 2 weeks then no intake for the 2 remaining weeks. They were also given bevacizumab into a vein every 2 weeks.
- S95005 alone:
  Participants took S95005 orally over 28 day-cycles, for 5 days twice daily each of the first 2 weeks then no intake for the 2 remaining weeks.

These 28-day cycles were repeated for as long as the cancer did not progress and if the participant did not have too severe side effects. Participants could also decide to stop the treatment at any time.

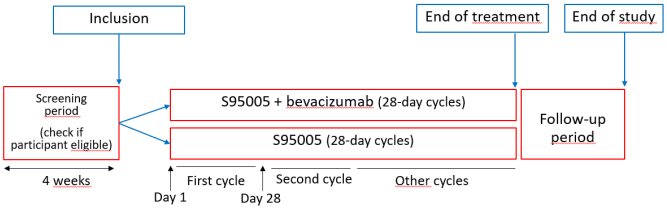
5 How was the study carried out?

The study is called a "randomised" study. This means that the participants were put into one of the two treatment groups by chance.
Of the 492 participants in the study:

- 246 participants took S95005 with bevacizumab
- 246 participants took S95005 alone

The study is called an "open-label" study. This means that both the participants and the research doctors were aware of the treatment being taken.

The study design is presented in the image below.



The participants visited the doctors regularly. During the visits, the doctors collected information about the participants' health.

6 What were the side effects?

Side effects are unwanted medical events that the doctors think may be caused by the treatments in the study.
In this summary, we describe unwanted medical events thought to be caused by S95005 and/or bevacizumab in one group and S95005 in the other group.
The results may be presented differently in other documents related to the study.

The table below shows the number of participants who had side effects.

	S95005 with bevacizumab (out of 246 participants)	S95005 (out of 246 participants)
Participants who had side effect(s)	223 (91%)	200 (81%)
Participants who had serious* side effect(s)	13 (5%)	20 (8%)
Participants who stopped the treatment because of side effect(s)	31 (13%)	31 (13%)

**See definition of serious side effects below*

What were the types of side effects?

The table below shows the most common side effects reported in the study (by at least 20% of the participants in one group or both groups).

	S95005 with bevacizumab (out of 246 participants)	S95005 (out of 246 participants)
Low level of neutrophils, a type of white blood cells	148 (60%)	119 (48%)
Feeling sick	82 (33%)	51 (21%)
Decrease in the number of red blood cells	58 (24%)	62 (25%)

= participants

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What were the serious side effects?

A side effect is considered serious when:

- the participant needs to be hospitalised,
- it causes lasting damage or death,
- the participant's life is in danger or,
- it is medically important in the doctor's opinion.

The serious side effects reported by more than 1% of participants in one group or both groups are described in the following table.

	S95005 with bevacizumab (out of 246 participants)	S95005 (out of 246 participants)
Decrease in the number of red blood cells	1 (below 1%)	6 (2%)
Low level of neutrophils with fever	1 (below 1%)	6 (2%)

In the study, none of the participants died because of an unwanted event thought to be caused by the treatment.

7 What were the study results?

The results included in this summary include information collected up to July 2022.

This document presents only the results for the main aim of the study. Other results are available in other documents listed in section 10.

The main aim of the study was to show that S95005 with bevacizumab worked better than S95005 alone. For this, the researchers measured the time from starting the treatment until the participant died. This is called "overall survival".

The average overall survival was around 11 months in the S95005/bevacizumab group and 7 months in the S95005 group. The difference between the two groups was large enough to conclude that S95005 with bevacizumab worked better than S95005 alone for patients with metastatic colorectal cancer.

The study is continuing until the end of 2023 as defined in the study protocol.

8 How has this study helped research?

Findings from this study will be used to obtain approval for use of the combination of S95005 with bevacizumab for patients with metastatic colorectal cancer.

9 Are there plans for further studies?

To date, no other studies with the combination of S95005 with bevacizumab are planned in participants with resistant metastatic colorectal cancer.

10 Further information

What are the identification numbers of the study?

- Protocol code: CL3-95005-007
- EudraCT number: 2020-001976-14
- US NCT number: NCT04737187

Who did the study?

The companies that organised and funded the research, called the "sponsors", are the Institut de Recherches Internationales Servier based in Suresnes, France and Taiho Oncology Inc. based in Princeton, New Jersey, USA

How can you contact the sponsor?

Contact us on the Servier or Taiho website
https://servier.com/en/
https://taihooncology.com/

Where can you learn more about this study?

You can find more information about this study on these websites:

- https://clinicaltrials.servier.com/find-clinical-trials
- www.clinicaltrialsregister.eu/ctr-search
- www.clinicaltrials.gov

In this document we translated medical terms into lay terms. You can find the corresponding medical terms in the Servier glossary at https://clinicaltrials.servier.com/glossary/

You can find general information about clinical trials on https://clinicaltrials.servier.com/