Clinical Trial Summary

A study comparing S95005 plus bevacizumab to capecitabine plus bevacizumab in patients with untreated colorectal cancer who are non-eligible for intensive therapy.

Full scientific title: An open-label, randomised, phase III study comparing trifluridine/tipiracil (S95005) in combination with bevacizumab to capecitabine in combination with bevacizumab in first-line treatment of patients with metastatic colorectal cancer who are not candidate for intensive therapy (SOLSTICE 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

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Final Version

In this summary:

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1 Why was this study done?

The study was done to confirm the effectiveness of a drug called S95005 (study drug), when combined with another drug in patients with metastatic colorectal cancer. Metastatic means that the cancer has spread to other parts of the body.

S95005 is a combination of two drugs: trifluridine and tipiracil. It is used to treat patients with metastatic gastric or 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 a combination of capecitabine with bevacizumab. This treatment (capecitabine with bevacizumab) is recommended for patients with metastatic colorectal cancer who cannot receive strong chemotherapy, called intensive chemotherapy.

- 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.
- Capecitabine is a drug that also blocks the growth of cancer cells.

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

2 When and where did this study take place?

When did the study take place?

- This study started in March 2019.
- The study is still ongoing. Participant inclusions are now complete.

This summary only includes data collected up to 09 June 2021.

Where did the study take place?

The study took place in the following countries:

Country	Number of participants
Argentina	15
Australia	15
Austria	13
Brazil	42
Bulgaria	23
Czech Republic	12
Denmark	36
Estonia	14
France	33
Germany	3
Hungary	74
Ireland	2
Italy	57
Latvia	11
Lithuania	14
Netherlands	21
Poland	34
Portugal	6
Romania	23
Russian federation	126
Slovakia	4
Spain	83
Sweden	10
United Kingdom	53
Ukraine	132

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
- Not previously treated for colorectal cancer that has spread to other parts of the body
- Not eligible for intensive therapy
- Not eligible for surgery.

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How many participants took part in the study?

A total of 856 participants took part in the study: 390 women and 466 men.

How old were the participants?

The average age of the participants was 71 years. The youngest participant was 22 years old and the oldest was 93 years old.

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 (study drug):
  Participants took the study drug orally twice daily, for 10 days, over 28 day-cycles. They also received bevacizumab into a vein every 2 weeks.
- Capecitabine:
  Participants took capecitabine orally twice daily, for 14 days, over 21 day-cycles. They also received bevacizumab into a vein every 3 weeks.

These 28 or 21 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.

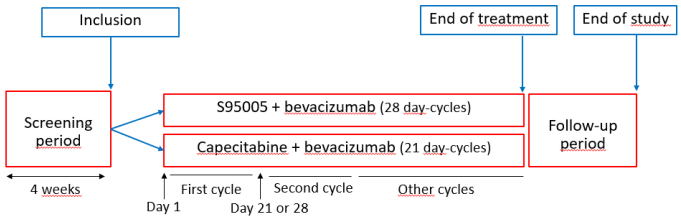
5 How was the study carried out?

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 856 participants in the study:

- 423 participants took S95005 with bevacizumab
- 427 participants took capecitabine with bevacizumab
- 6 participants stopped the study before receiving the treatment

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.

The duration of treatment in the study was about 8 months in both groups.

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 capecitabine and/or bevacizumab 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 423 participants)	Capecitabine with bevacizumab (out of 427 participants)
Participants who had side effect(s)	396 (94%)	375 (88%)
Participants who had serious* side effect(s)	83 (20%)	96 (23%)
Participants who stopped the treatment because of side effect(s)	49 (12%)	68 (16%)

**See definition of serious side effects below*

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What were the 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 the two groups).

	S95005 with bevacizumab (out of 423 participants)	Capecitabine with bevacizumab (out of 427 participants)
Lack of white blood cells called neutrophils	277 (66%)	36 (8%)
Decrease in the number of red blood cells	148 (35%)	42 (10%)
Feeling sick	135 (32%)	88 (21%)
Diarrhoea	131 (31%)	127 (30%)
Decrease in the number of white blood cells called neutrophils	90 (21%)	9 (2%)
Feeling tired	78 (18%)	89 (21%)
Hand-foot syndrome*	5 (1%)	223 (52%)

= participants

**redness, swelling, pain and sometimes blisters on the palms of the hands and/or the soles of the feet.*

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 the two groups are described in the following table.

	S95005 with bevacizumab (out of 423 participants)	Capecitabine with bevacizumab (out of 427 participants)
Decrease in the number of red blood cells	19 (5%)	5 (1%)
Lack of white blood cells called neutrophils	12 (3%)	1 (below 1%)
Fever with lack of white blood cells called neutrophils	9 (2%)	2 (below 1%)
Blood clot in the lungs	8 (2%)	19 (4%)
Diarrhoea	8 (2%)	10 (2%)
Blood clotting within veins	4 (below 1%)	11 (3%)
Water loss	4 (below 1%)	9 (2%)

= participants

In the study, 9 participants died because of an unwanted event thought to be caused by the treatment: 5 participants in the group S95005/ bevacizumab and 4 in the group capecitabine/ bevacizumab.

7 What were the study results?

The results included in this summary include information collected up to 09 June 2021

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

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The main goal of the study was to show that S95005 with bevacizumab worked better than capecitabine with bevacizumab. For this, the researchers measured the time from starting the treatment until the cancer got worse or the participant died. This is called “progression-free survival”.

The average progression-free survival was 9.4 months in the S95005/bevacizumab group and 9.3 months in the capecitabine/bevacizumab group. However, the difference between the two groups was too small. That means that in this study, S95005 with bevacizumab did not work better than capecitabine with bevacizumab for patients with colorectal cancer.

During this study, the safety of the treatments was similar to the safety already known. The progression-free survival was close in both groups. This is why the study is continuing as initially planned. When the study is complete, another calculation will be done for the time from starting the treatment until the patient died. This is called “overall survival”.

8 How has this study helped research?

This study helped researchers gather more information on the treatment of participants with 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 metastatic colorectal cancer not previously treated and not eligible for intensive therapies.

Another study is ongoing: it is being carried out in patients with metastatic colorectal cancer for whom standard treatments are no longer effective. This study aims to show that the combination of S95005 with bevacizumab works better than S95005 alone.

10 Further information

What are the identification numbers of the study?

- Protocol code: CL3-95005-006
- EudraCT number: 2017-004059-22
- US NCT number: NCT03869892
- Universal Trial Number: U1111-1206-3198

Who did the study?

The company that organised and funded the research, called the “sponsor”, is the Institut de Recherches Internationales Servier based in Suresnes, France.

How can you contact the sponsor?

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

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 medical terms were translated into lay terms on purpose. 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 at https://clinicaltrials.servier.com/

In accordance with the recommendations of the French National Cancer Plan III (Measure 5.4), this document was submitted for review and guidance to the Clinical Cancer Research Patients Committee of La Ligue Nationale contre le Cancer.