Clinical Trial Summary

A phase 2 study evaluating S95005 plus bevacizumab and capecitabine plus bevacizumab in patients with previously untreated colorectal cancer who are non-eligible for intensive therapy (TASCO1 study).

Full scientific title: An open-label, randomised, non-comparative phase 2 study evaluating S95005 (TAS-102) plus bevacizumab and capecitabine plus bevacizumab in patients with previously untreated Colorectal cancer who are non-eligible for intensive therapy (TASCO1 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 participants.
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 participants. For medical science to progress, many studies involving participants 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 2

24 September 2021

Final Version

In this summary:

Clinical Trial Summary (end of study)

A phase 2 study evaluating S95005 plus bevacizumab and capecitabine plus bevacizumab in patients with previously untreated colorectal cancer who are non-eligible for intensive therapy (TASCO1 study)

1 Why was this study done?

The study drug is called S95005 (trifluridine + tipiracil). It is approved to treat patients with colorectal cancer that has spread to other parts of the body when standard treatments are no longer effective. Colorectal cancer that has spread to other parts of the body is called metastatic colorectal cancer.

In this study, the medicine S95005 is combined with another marketed drug called bevacizumab.

This study is called a Phase 2 study. The main objective of the TASCO1 study was to explore the effect of the combination of S95005 with bevacizumab. Another combination (capecitabine with bevacizumab) served as reference.

Capecitabine with bevacizumab is a treatment recommended in participants with metastatic colorectal cancer.

- S95005 is a drug that blocks the growth of cancer cells.
- Bevacizumab is a drug that blocks the blood vessels that provide blood to the tumor. It slows the growth of the tumor.
- Capecitabine is a drug that also blocks the growth of cancer cells.

2 When and where did this study take place?

When did the study take place?

- This study started in April 2016.
- It ended in in September 2020.

This summary includes all information collected during the study.

- A first summary was done in November 2018 while the study was still ongoing. It is available on the Servier' Clinical Trial Data website (clinicaltrials.servier.com).

Where did the study take place?

The study took place in the following countries:

Country	Number of participants included
Australia	1
Belgium	5
Brazil	4
Denmark	7
France	7
Germany	6
Italy	9
Netherlands	28
Poland	21
Russia	22
Spain	20
United Kingdom	23

3 Who participated in the study?

Which participants were included in the study?

To take part, participants had to meet specific criteria including:

- 18 years of age or older.
- Diagnosed with metastatic colorectal cancer.
- The cancer had not been previously treated.
- Too frail to tolerate other therapies.
- Not eligible for surgery.

How many participants took part in the study?

154 participants took part in the study: 66 women and 88 men. Among them, one participant was not included and never took the treatment.

How old were the participants?

The average age of the participants was 71 years. The youngest participant was 33 years old and the oldest participant was 91 years old.

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4 Which treatments did the participants receive?

The participants received either:

- Study drug (S95005):
  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 participants continued the treatment as long as the cancer did not progress and/or until they had too severe side effects. Participants could also decide to stop the treatment at any time.

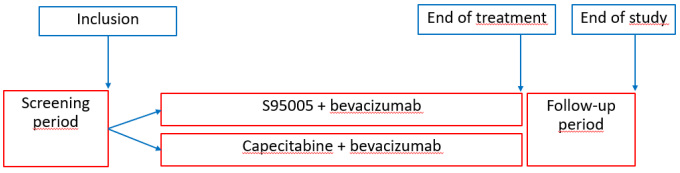
5 How was the study carried out?

The study is called a "randomised" study. It means that participants were put by chance into one of the 2 groups of treatment.
Among the 154 participants in the study:

- 77 participants took S95005 with bevacizumab
- 76 participants took capecitabine with bevacizumab
- 1 participant 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 knew which treatment was taken.

The study design is presented in the image below.



The duration of treatment was about 46 weeks for S95005 with bevacizumab. It was 36 weeks for capecitabine with bevacizumab.

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 treatment in the study.
In this summary, we describe unwanted medical events thought to be caused by S95005 or capecitabine or bevacizumab in the 2 treatment groups.
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 77 participants)	Capecitabine with bevacizumab (out of 76 participants)
Participants who had side effect(s)	75 (97%)	68 (90%)
Participants who had serious* side effect(s)	51 (66%)	45 (59%)
Participants who stopped the treatment because of side effect(s)	33 (43%)	32 (42%)

**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 (reported by at least 20% of the participants in one group).

	S95005 with bevacizumab (out of 77 participants)	Capecitabine with bevacizumab (out of 76 participants)
Lack of white blood cells called neutrophils	42 (54%)	4 (5%)
Diarrhoea	33 (43%)	28 (37%)
Feeling sick	31 (40%)	11 (15%)
Feeling tired	25 (33%)	19 (25%)
Decreased appetite	23 (30%)	13 (17%)
Decrease in the number of red blood cells	21 (27%)	4 (5%)
Decrease in the number of white blood cells called neutrophils	18 (23%)	2 (3%)
Vomiting	17 (22%)	7 (9%)
Hair loss	16 (21%)	0
Decrease in the number of white blood cells	15 (20%)	1 (1%)
Inflamed and sore mouth	14 (18%)	16 (21%)
Hand-foot syndrome*	3 (4%)	39 (51%)

= 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.

At the end of this study, 96 out of 153 participants (63%) had serious side effects.
The serious side effects reported by more than 2 participants in one group are described in the table below.

	S95005 with bevacizumab (out of 77 participants)	Capecitabine with bevacizumab (out of 76 participants)
Lack of white blood cells called neutrophils	4 (5%)	0
Fever with lack of white blood cells called neutrophils	3 (4%)	1 (1%)
Water loss	2 (3%)	3 (4%)
Diarrhoea	2 (3%)	6 (8%)
Blood clot in the lungs	0	3 (4%)
Blood clotting within veins	0	3 (4%)

= participants

In the study, 2 participants (3%) in each group died because of an unwanted event thought to be caused by the treatment.

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7 What were the study results?

The study was completed as planned.

To test the effectiveness, the researchers measured the time from starting the treatment until the cancer got worse or the patient died. This is called "progression-free survival". It was already calculated in 2018 when 100 patients had those events.

The average time from starting the treatment until the cancer got worse or the patient died was 9.2 months in the S95005 group and 7.8 months in the capecitabine group.

At the end of the study in 2020, the researchers also measured the time from starting the treatment until the patient died. It is called the "overall survival". The average time for overall survival was 22 months in the S95005 group and 18 months in the capecitabine group.

8 How has this study helped research?

Findings from this study were used in another study. This Phase 3 study is on-going in patients with metastatic colorectal cancer who can't receive an intensive therapy. It aims to confirm that the combination of S95005 with bevacizumab works better than the combination of capecitabine with bevacizumab.

9 Are there plans for further studies?

As mentioned above, there is an ongoing Phase 3 study for patients with metastatic colorectal cancer who can't receive an intensive therapy. There is also another Phase 3 study for patients with metastatic colorectal cancer when 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 Number: CL2-95005-002
- EudraCT Number: 2015-004544-18
- Clinicaltrials.gov: NCT02743221

Who did the study?

The companies that organised and funded the research, called the "sponsor" are:

- Institut de Recherches Internationales Servier based in Suresnes, France.
- Les Laboratoires Servier, Suresnes, France
- Laboratorios Servier, S.L., Madrid, Spain.

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 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/

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 Participants Committee of La Ligue Nationale contre le Cancer.