Clinical trials
LAY SUMMARY

SHORT STUDY TITLE

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)

Therapeutic area:
Oncology

Indication:
Colorectal cancer

Study phase:
Phase 2

Date:
15 November 2018
Final version

IN THIS LAY SUMMARY:

CLINICAL TRIALS LAY SUMMARY

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Welcome

This document summaries how the TASCO1 study was performed as well as its results. Researchers need many studies to decide which medicines work best and are safest for the patient. It takes a lot of people in many studies all around the world to advance medical science. This summary only shows the results from the TASCO1 study. Other studies may find different results.

1 WHAT WAS THE OBJECTIVE OF THE STUDY?

The study drug is called S95005 (trifluridine + tipiracil). It was approved to treat patients with colorectal cancer that has spread to other parts of the body when standard treatments are no longer effective.
In this study, the medicine 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 plus bevacizumab is a treatment recommended in patients with colorectal cancer that has spread to other parts of the body.

- S95005 is a drug that blocks cancer cells proliferation.
- Bevacizumab is a drug that blocks the blood vessels which 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 was it performed?

- This study started in April 2016.
- Inclusions in the study are now complete
- The study is still ongoing.

This summary includes information collected up to January 2018.

Where did the study take place?

The study included 153 patients in the following countries:

Country	Number of patients
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?

What patients were included in the study?

Patients in the study had to meet the following criteria:

- 18 years and older.
- Diagnosed with a colorectal cancer.
- The cancer had spread to other parts of the body and had not been previously treated.
- Too frail to tolerate other therapies.
- Not eligible to surgery.

How many men and women were in the study?

WOMEN	MEN
66 patients (43 %)	87 patients (57 %)

How old the patients were?

33 to 65 years	66 to 75 years	76 to 91 years
39 patients (25%)	48 patients (31 %)	66 patients (43%)

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4 WHAT TREATMENTS DID PATIENTS RECEIVE?

The study is called a "randomized" study. It means that patients were put by chance into 2 groups:

- Study drug (S95005) group.
  Patients took the study drug orally twice daily, for 10 days during 28 days cycles. They received bevacizumab every 2 weeks.
- Capecitabine group.
  Patients took capecitabine orally twice daily, for 14 days over 21 days cycles. They received bevacizumab every 3 weeks.

In both groups, each patient received bevacizumab in solution for injection into veins.

Patients continued the treatment until their cancer got worse or until they had too severe side effects.

This is called an "open-label" study. It means that patients and doctors knew who was given which treatment.

5 WHAT WERE THE SIDE EFFECTS?

What about side effects?

Like all medicines, these drugs can cause side effects although not everybody gets them.
Side effects are unwanted events thought to be related to the study drug (S95005) or capecitabine or bevacizumab.

All the 153 included patients were treated.
The table below shows the number of patients who experienced side effects. More side effects were seen with the study drug (S95005) and bevacizumab than with capecitabine and bevacizumab.

	Related to study drug or bevacizumab	Related to capecitabine or bevacizumab
Patients who had side effect(s)	75 patients (97%)	68 patients (90%)
Patients who had serious* side effect(s)	25 patients (33%)	17 patients (22%)
Patients who had withdrew because of side effect(s)	14 patients (18%)	11 patients (15%)

**See definition below*

How many patients experienced serious side effects?

A side effect is defined as serious when:

- The patient needs to be hospitalized.
- The patient's life is in danger.
- It causes permanent damage or death.
- Or it may put at risk the patient and requires a medical intervention to prevent the situations listed above.

In this study, 42 patients (28%) experienced serious side effects.
The serious side effects reported by more than 2 patients are described in the table below.

	Related to study drug or bevacizumab	Related to capecitabine or bevacizumab
Diarrhoea	2 patients (3%)	5 patients (7%)
Fever with lack of white blood cells called neutrophils	3 patients (4%)	1 patient (1%)
Lack of white blood cells called neutrophils	4 patients (5%)	0
Water loss	2 patients (3%)	3 patients (4%)
Blood clot in the lungs	0	3 patients (4%)

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Serious side effects led to withdrawal of 13 patients. Among them, 9 patients (12%) in the study drug group and 4 patients (5%) in the capecitabine group.

In the study, 13 patients died during the treatment period: 4 (5%) in the study drug group and 9 (12%) in the capecitabine group.
After the treatment was stopped and up to January 2018, 18 patients (23%) died in the study drug group and 24 patients (32%) in the capecitabine group.

In most cases, patients died because of the progression of the colorectal cancer. For 2 patients in each group, the death was due to an unwanted event thought to be related to the study drug (S95005) or capecitabine or bevacizumab.

What were the other side effects?

The table below shows the other side effects reported in the study. Only the most common effects (reported by at least 20% of patients) are presented.

	Related to study drug or bevacizumab	Related to capecitabine or bevacizumab
Feeling sick	31 patients (40%)	10 patients (13%)
Diarrhoea	30 patients (39%)	24 patients (32%)
Feeling tired	24 patients (31%)	20 patients (26%)
Decreased appetite	23 patients (30%)	13 patients (17%)
Vomiting	17 patients (22%)	6 patients (8%)
Hair loss	15 patients (20%)	-
Inflamed and sore mouth	13 patients (17%)	16 patients (21%)
Hand-foot syndrome*	3 patients (4%)	38 patients (50%)

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

The table below shows the other side effects found on blood tests. Only the most common (reported by at least 20% of patients) are presented.

	Related to study drug or bevacizumab	Related to capecitabine or bevacizumab
Lack of white blood cells called neutrophils	40 patients (52%)	3 patients (4%)
Decrease in the number of white blood cells called neutrophils	17 patients (22%)	1 patient (1%)
Decrease in the number of red blood cells	16 patients (21%)	4 patients (5%)
Decrease in the number of white blood cells	15 patients (20%)	1 patient (1%)

6 WHAT WERE THE STUDY RESULTS?

Results described in this summary include information collected up to January 2018.
To test the effectiveness, the researchers measure the time from starting the treatment until the cancer got worse or the patient died. It is called "progression-free survival" or "PFS". This calculation was done when 100 patients had those events.

The study is still on-going. Further calculations will be done when the study is complete.

What are the results of the clinical study?

The average time from starting the treatment until the cancer got worse or the patient died was 9.2 months in the test drug group and 7.8 months in the capecitabine group.
The difference between groups could be due to chance.

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What does it mean?

It means that the number of patients alive or for whom the cancer did not get worse was higher with the test drug + bevacizumab than with capecitabine + bevacizumab.
This result has to be confirmed in a further study to be sure that it was not obtained by chance.

7 HOW HAS THIS STUDY HELPED PATIENTS AND RESEARCHERS?

Findings from this study will be used in other studies to obtain an approval for using this treatment for patients with colorectal cancer that has spread to other parts of the body and who can't receive an intensive therapy.

8 ARE THERE PLANS FOR FURTHER STUDIES?

Further clinical studies with S95005 are planned.

9 FURTHER INFORMATION

What is the full title name of the clinical study ?

The full title of the TASCO1 study is "An open-label, randomised, non-comparative phase 2 study evaluating S95005 (TAS-102) plus bevacizumab and capecitabine plus bevacizumab in patients with previously untreated metastatic COlorectal cancer who are non-eligible for intensive therapy"

What are the trade names of the treatment?

For S95005: Lonsurf®

What is the identification number of the clinical study?

- Protocol Number: CL2-95005-002.
- EudraCT Number: 2015-004544-18.
- Clinicaltrials.gov: NCT02743221

What is the name of the Sponsor?

The companies organizing and funding the research, called sponsors, 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 Servier website (www.servier.com).

Where can you learn more about this study?

- The scientific summary is also available on Servier Clinical Trial Data website. (www.clinicaltrials.servier.com)
- In this document, we translated medical terms into lay terms. You can find the corresponding medical terms in the Servier glossary on Servier Clinical Trial Data website.