Clinical Trial Summary

An early access study of trifluridine / tipiracil (S95005/TAS-102) in patients with a pretreated metastatic colorectal cancer.

Full scientific title: An open-label early access phase IIIb study of trifluridine / tipiracil (S95005/TAS-102) in patients with a pretreated metastatic colorectal cancer (PRECONNECT 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:

1. Why was this study done?
2. When and where did this study take place?
3. Who participated in the study?
4. Which treatments did the participants receive?
5. How was the study carried out?
6. What were the side effects?
7. What were the study results?
8. How has this study helped research?
9. Are there plans for further studies?
10. Further information

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1 Why was this study done?

The study drug is a combination of two drugs: trifluridine and tipiracil. It is called S95005 or TAS-102.

S95005 (trifluridine + tipiracil) is marketed in several countries around the world. It is used to treat patients with gastric or colorectal cancer that has spread to other parts of the body when standard treatments are no longer effective.

It is a drug that blocks the growth of cancer cells.

The present study is an early access study. The aim was for patients with colorectal cancer to gain access to S95005 before it was marketed in the patient's country.

This study is a Phase IIIb study. The purpose was to obtain more data on a drug.

The main objective of the study was to have more safety data on the study drug.

2 When and where did this study take place?

When did the study take place?

- This study started in November 2016.
- It ended in in November 2020.

Where did the study take place?

The study took place in the following countries:

Country	Number of participants
Australia	71
Belgium	45
Brazil	55
Bulgaria	12
Croatia	16
France	292
Ireland	7
Italy	161
Panama	17
Poland	54
Portugal	24
Romania	30
Slovakia	16
Slovenia	4
Turkey	100
Ukraine	12

3 Who participated in the study?

Which participants were included in the study?

Participants in the study had to meet specific criteria, including:

- Be at least 18 years old.
- Diagnosed with a colorectal cancer.
- Whose cancer had spread to other parts of the body.
- Previously treated for colorectal cancer.
- For who standard treatments can't be used anymore.

How many participants took part in the study?

Overall, 916 participants joined the study: 375 women and 541 men.

Among the 916 participants:

- 914 participants took the study drug. All of them stopped the treatment: 80% because of the progression of the cancer.
- 2 participants stopped the study before receiving the treatment: 1 participant made the decision to stop, and 1 participant stopped based on the doctor's decision.

How old were the participants?

The average age of the participants taking the study drug was 61 years. The youngest participant was 24 years old and the oldest participant was 89 years old.

Clinical Trial Summary

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4 Which treatments did the participants receive?

All participants received the study drug as tablets, at the dose of 35 milligrams per square meter (m^2) of body surface area. This means that the dose depended on the size of the participant's body.

Participants took the study drug during time periods called "cycles". A cycle lasted 28 days, as follows:

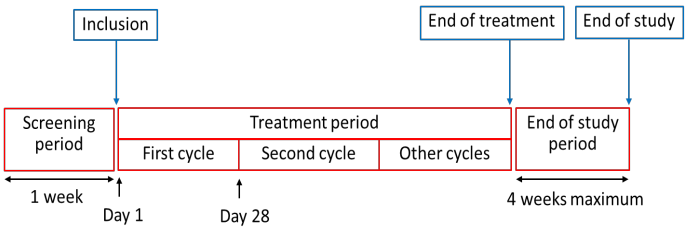
- Participants took the study drug orally twice a day,
  5 days per week, for 2 weeks.
- Then, there were 2 weeks without treatment.

This cycle was repeated 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?

In the study, all participants took the same 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 16 weeks in the study.

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.

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

	Number of participants (out of 914 participants)
Participants who had side effect(s)	721 (79%)
Participants who had serious* side effect(s)	97 (11%)
Participants who stopped the treatment because of side effect(s)	31 (3%)

**See definition of serious side effects below*

What were the side effects?

The table below shows the most common side effects reported in the study (reported by at least 5% of the participants).

	Number of participants (out of 914 participants)
Lack of white blood cells called neutrophils	427 (47%)
Feeling sick	237 (26%)
Decrease in the number of red blood cells	189 (21%)
Diarrhoea	184 (20%)
Unusual weakness	121 (13%)
Tiredness	119 (13%)
Vomiting	116 (13%)
Decreased appetite	83 (9%)
Lack of platelets, cells that help the blood to clot	59 (7%)
Decrease in the number of white blood cells called neutrophils	58 (6%)

= 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 table below shows the serious side effects that were reported by at least 1% of the participants.

	Number of participants (out of 914 participants)
Decrease in the number of red blood cells	25 (2.7%)
Lack of white blood cells called neutrophils	20 (2.2%)
Diarrhoea	10 (1.1%)
Fever with lack of white blood cells called neutrophils	9 (1%)
Vomiting	9 (1%)

= participants

In the study, 3 participants died because of an unwanted event thought to be caused by the study drug.

7 What were the study results?

The study was completed as planned.

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

The most frequent side effects observed in the study were blood events and gastrointestinal events (refer to section 6).

The safety data with S95005 in this study was quite similar to the already known data.

8 How has this study helped research?

This study allowed patients to gain access to the study drug before it was marketed in the patient's country.

This study helped researchers to know more about the safety of the study drug.

9 Are there plans for further studies?

Clinical studies with S95005 in combination with another anticancer drug are ongoing. Further studies are planned.

10 Further information

What are the identification numbers of the study?

- Protocol Number: CL3-95005-004
- EudraCT Number: 2016-002311-18
- ClinicalTrials.gov: NCT03306394

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
- https://www.clinicaltrialsregister.eu/ctr-search
- https://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 Patients Committee of La Ligue Nationale contre le Cancer.