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Clinical Trial Summary

A comparison of a single-pill combination of perindopril/ indapamide/ amlodipine/bisoprolol with perindopril, indapamide and amlodipine in patients with essential hypertension whose blood pressure remains high on perindopril, indapamide and amlodipine treatment

Full scientific title: Evaluation of the clinical efficacy and safety of perindopril 10 mg/indapamide 2.5 mg/ amlodipine 5 or 10 mg/bisoprolol 5 mg in single-pill combination after 8 weeks of treatment versus the free combination of perindopril 10 mg, indapamide 2.5 mg and amlodipine 5 or 10 mg in patients with uncontrolled essential hypertension. An international, multicentre, randomised, double-blind, 16-week 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. 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:
Cardiology

Disease:
Essential hypertension

Study phase:
Phase 3

Final version:
16/07/2024

In this summary:

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1 Why was this study done?

The aim of this study was to see if the addition of a 4th drug (bisoprolol) to a combination of 3 drugs used to treat high blood pressure (perindopril, indapamide and amlodipine) provides better control of high blood pressure than the combination of the 3 drugs.

These 4 drugs are not new drugs. They are well-known drugs, approved individually for marketing for more than 30 years and currently used in many countries. These drugs are prescribed by doctors for the treatment of high blood pressure. As their mode of action is different, these drugs can be combined to have a greater effect. They lower the blood pressure by:

- Slowing down the heart rate and reducing the force of contractions (bisoprolol).
- Widening the blood vessels. This makes it easier for the heart to pump the blood through them (perindopril).
- Relaxing the blood vessels (amlodipine).
- Promoting the elimination of salt through the urine (indapamide).

High blood pressure is a common health condition that may cause or increase the risk of health problems. Doctors make the diagnosis by measuring blood pressure. When blood pressure is measured, 2 values are recorded. The higher value is called systolic blood pressure (SBP). The lower value is called diastolic blood pressure (DBP). Blood pressure is written as SBP/DBP. For example, 120/80 mmHg (millimetres of mercury).

Patients may need several drugs to lower their high blood pressure. When this happens, patients may forget to take one of them or may dislike taking several pills, which means there is a chance that blood pressure remains uncontrolled. For these reasons, the researchers are focusing on developing "single-pill" option that combine the 4 drugs into a single-pill.

In this study, the test drug (called S05179) was the combination of the 4 drugs (perindopril, indapamide, amlodipine and bisoprolol) in a single-pill. It is developed for the treatment of difficult to control high blood pressure.

The main goal of this study was to test if S05179 works better than the free triple combination (perindopril, indapamide, and amlodipine) in lowering high SBP after 8 weeks of treatment, in participants suffering from uncontrolled high blood pressure.

In this study, the SBP was measured in a sitting position at the research doctor's office.

2 When and where did this study take place?

When did the study take place?

- This study started in February 2022.
- It ended in December 2023.

Where did the study take place?

The study took place in the following countries:

Country	Number of participants
Armenia	56
Russian Federation	30
Argentina	27
Poland	14
Latvia	10
Brazil	8
Czech Republic	8
Italy	8
Kazakhstan	7
Bulgaria	5
Hungary	5
Lithuania	4
Slovakia	1

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3 Who participated in the study?

Which participants were included in the study?

To take part, participants had to:

- Be men or women.
- Be at least 18 years old.
- Be diagnosed with uncontrolled high blood pressure despite treatment with 3 drugs used to treat high blood pressure. Uncontrolled means that the SBP was greater than or equal to 140 mmHg.

How many participants took part in the study?

A total of 469 participants were selected in the study and received 3 drugs (perindopril, indapamide, and amlodipine) for 8 weeks. Among these 469 participants, only those who were suffering from uncontrolled high blood pressure after having taken these 3 drugs were included in the study. A total of 183 participants were included (86 women and 97 men).

How old were the participants?

The average age of the participants was 57 years. The youngest participant was 22 years old and the oldest was 78 years old.

4 Which treatments did the participants receive?

All participants received perindopril 10 mg (milligrams), indapamide 2.5 mg, and amlodipine 5 mg or 10 mg as 3 tablets every morning for 8 weeks before being assigned to a treatment group.

After assignment to the treatment group, the participants received one of the following 2 treatments orally for 8 weeks every morning:

- **S05179 group**:
  - One single capsule of S05179 which is a combination of perindopril 10 mg, indapamide 2.5 mg, amlodipine 5 mg or 10 mg and bisoprolol 5 mg
  - One tablet of placebo
  - One capsule of placebo
- **Free triple combination group**:
  - One capsule of perindopril 10 mg
  - One tablet of indapamide 2.5 mg
  - One capsule of amlodipine 5 mg or 10 mg

A placebo looks like the study drug but does not contain any real medicine. In this study, the placebo capsules or tablets were used in the S05179 group. The placebo is only given so that participants took the same number of tablets or capsules, no matter to which treatment group they were assigned (S05179 group or free triple combination group). The participants in both groups therefore received a treatment that was strictly identical in appearance so that neither the participants nor the research doctors knew which treatment was taken.

5 How was the study carried out?

The study is called a “randomised” study. This means that the participants were put by chance into one of the 2 groups of treatment.

Participants had equal chances to be assigned to the S05179 group or the free triple combination group.

Among the 183 participants included in the study:

- 89 participants took S05179.
- 94 participants took free triple combination.

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One participant of S05179 group mistakenly received the free triple combination. This participant was counted in the S05179 group for the analysis of the changes in the SBP. However, for the analysis of the safety data, this participant was considered in the free triple combination group.

The study is called a "double-blind" study. This means that neither the participants nor the research doctors knew which treatment was taken. This was to avoid any influence on the results.

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 S05179 or the free triple combination. 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.

	S05179 group (out of 88 participants)	Free triple combination group (out of 95 participants)
Participants who had side effect(s)	1 (1%)	1 (1%)
Participants who had serious* side effect(s)	0 (0%)	0 (0%)
Participants who stopped the treatment because of side effect(s)	0 (0%)	0 (0%)

**See definition of serious side effects below*

What were the types of side effects?

The table below shows the side effects reported in the study.

	S05179 group (out of 88 participants)	Free triple combination group (out of 95 participants)
Slow heartbeat	1 (1%)	0 (0%)
Sensation of abnormal heartbeat	0 (0%)	1 (1%)

= participants

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.

In this study, no participants had serious side effects (serious unwanted medical events thought to be caused by the treatments in the study).

In the study, no participants died.

7 What were the study results?

In July 2023, the sponsor of the study (the company that organised and funded the study) decided to stop including new participants in the study before reaching the desired number of participants (the total desired was 968, that is 484 participants in each group). This decision was made because it was difficult to find enough participants for the study due to the strict selection criteria to identify patients with true resistant high blood pressure (that is patients with uncontrolled high blood pressure despite treatment with 3 drugs to lower the blood pressure).

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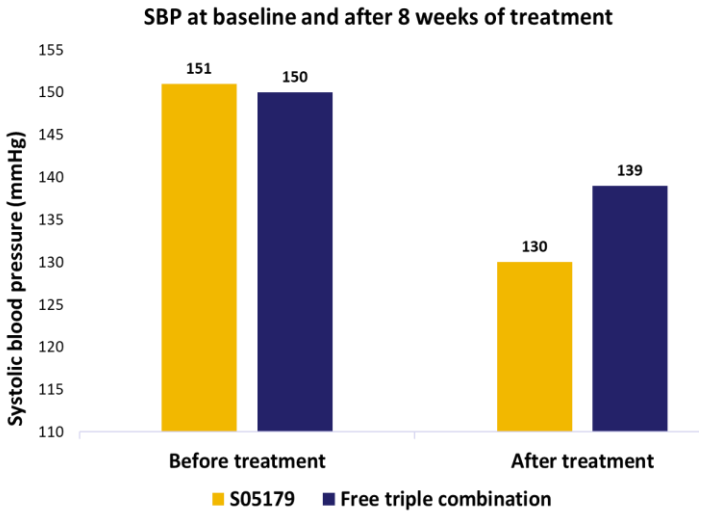
This document presents only the results for the main goal of the study. Other results are available in other documents listed in section 10.



The study found that after 8 weeks of treatment, participants who took S05179 showed a higher decrease in SBP than participants who took the free triple combination.

8 How has this study helped research?

This study helped researchers to gather more information on S05179 treatment in participants suffering from uncontrolled high blood pressure.

Research doctors found that single pill containing 4 drugs (perindopril, indapamide, amlodipine, bisoprolol) was better in controlling the high blood pressure than 3 drugs (perindopril, indapamide, amlodipine). Research doctors also found that S05179 was safe and well-tolerated.

The results of this study could be used to obtain approval for the use of S05179 in patients suffering from high blood pressure.

9 Are there plans for further studies?

No other studies with S05179 are planned so far.

10 Further information

What are the identification numbers of the study?

- Protocol code: CL3-05179-002
- EudraCT number: 2020-004891-16

Who did the study?

The company that organised and funded the research, called the "sponsor", is the Institut de Recherches Internationales Servier based in Gif-sur-Yvette, 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

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/