Clinical Trial Summary

A clinical study evaluating the efficacy and safety of a combined treatment Perindopril/Indapamide/Amlodipine into a single-pill in patients with high blood pressure.

Full scientific title: Evaluation of the clinical efficacy and safety of perindopril 5 mg / indapamide 1.25 mg / amlodipine 5 mg fixed combination in single-pill after 2 months of treatment versus free combination, perindopril 4 mg / indapamide 1.25 mg + amlodipine 5 mg given separately at the same time, with conditional titration based on blood pressure control in patients with essential hypertension uncontrolled after 1 month with perindopril 4 mg / indapamide 1.25 mg bi-therapy.

A national, multicentre, randomised, double blind, 7 months 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 best and are 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:
Cardiovascular

Disease:
Uncontrolled essential hypertension

Study phase:
Phase 3

14/06/2023

Final version

In this summary:

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1 Why was this study done?

The study was done to test the combination of 3 drugs (perindopril, indapamide and amlodipine) that lower blood pressure in a single-pill (called a fixed combination) in patients with high blood pressure.

The study was designed for the registration of the combination in China.

High blood pressure is a common condition that may cause health problems, such as heart disease. Doctors make the diagnosis by measuring blood pressure.

When blood pressure is measured, two values are recorded. The higher value is called systolic blood pressure (SBP) and is produced when the heart contracts (this is your pulse). The lower value is called diastolic blood pressure (DBP) and is the "background" pressure of the blood. Blood pressure is written as SBP/DBP. For example, 120/80 mmHg (millimetres of mercury).

Some patients have their blood pressure well controlled with a single drug treatment. Others require two or more drugs to get the desired effect. When this happens, patients may forget to take one of them or dislike taking several pills, and so there is a chance that blood pressure remains uncontrolled. For these reasons, it can be desirable to combine several drugs into a single pill. This is the reason why researchers have developed the study drug.

The main objective of the study was to test whether the combination of perindopril, indapamide and amlodipine in a single pill (fixed combination) works as well or almost as well as the combination of perindopril and indapamide (in a single-pill) plus a tablet of amlodipine (called free combination), in lowering SBP after 2 months of treatment. "Free combination" can apply to any number of pills from 2 upwards.

2 When and where did this study take place?

When did the study take place?

- This study started in May 2019.
- It ended in February 2022.

Where did the study take place?

The study took place in China.

3 Who participated in the study?

Which participants were included in the study?

To take part, participants had to be:

- men or women of Asian origin.
- 18 years of age or older.
- diagnosed with uncontrolled high blood pressure despite a treatment. Uncontrolled means that:
  - The SBP was between 140 and 180 mmHg.
  - The DBP was between 90 and 110 mmHg.

How many participants took part in the study?

A total of 532 participants took part in the study: 209 women and 323 men.

How old were the participants?

The average age of the participants was 56 years. The youngest participant was 24 years old and the oldest was 73 years old.

4 Which treatments did the participants receive?

Participants received either:

- the fixed combination.
- or the free combination,

The fixed combinations consisted of:

- 1 tablet of 5 mg of perindopril, 1.25 mg of indapamide and 5 mg of amlodipine or
- 1 tablet of 10 mg of perindopril, 2.5 mg of indapamide and 5 mg of amlodipine or
- 1 tablet of 10 mg of perindopril, 2.5 mg of indapamide and 10 mg of amlodipine

The free combination consisted of:

- 1 or 2 tablets of 4 mg of perindopril and of 1.25 mg of indapamide and
- 1 or 2 tablets of 5 mg of amlodipine.

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The medication started at low dose, and then every 2 months, the dose was gradually increased, if the blood pressure was still high.
Each participant took 2 capsules orally in the morning either:

- 1 capsule containing the fixed combination and 1 placebo capsule or
- 1 capsule containing perindopril and indapamide and 1 capsule containing amlodipine.

The placebo looks like the treatment but does not contain any real medicine.

5 How was the study carried out?

The study was split into 2 periods:

A one-month period under treatment called **run-in period**. During this period, the doctors checked if the study was suitable for the participant.

The **treatment period.**
The study is called a "randomised" study. This means that the participants were put by chance into one of the 2 groups of treatment.
Among the 532 participants included in the study:

- 262 participants took the fixed combination.
- 269 participants took the free combination.
- 1 participant did not receive any study treatment

Participants took the treatment for 6 months.

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 and measured the blood pressure.
Participants whose blood pressure was still not controlled after 2 months or 4 months received a higher dose.

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 the fixed combination or the free 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.

	Fixed combination (out of 262 participants)	Free combination (out of 269 participants)
Participants who had side effect(s)	110 (42%)	108 (40.1%)
Participants who had serious* side effect(s)	0	3 (1.1%)
Participants who stopped the treatment because of side effect(s)	7 (2.7%)	10 (3.7%)

**See definition of serious side effects below*

= participants

What were the type of side effects?

The table below shows the most common side effects reported in the study (reported by at least 3 participants in either treatment group).

	Fixed combination (out of 262 participants)	Free combination (out of 269 participants)
High blood acid uric level that can cause pain in the joints, called gout	47 (17.9%)	45 (16.7%)
Low blood potassium level	34 (13.0%)	33 (12.3%)
Cough	13 (5.0%)	14 (5.2%)
High blood levels of triglycerides, a type of fat	10 (3.8%)	9 (3.3%)
Increase in blood sugar	10 (3.8%)	7 (2.6%)
High blood level of cholesterol	9 (3.4%)	5 (1.9%)
Increase in blood level of acid uric. It can cause pain in the joints, called gout	3 (1.1%)	6 (2.2%)

= 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.

In this study, 3 participants (4.0%) treated by free combination had serious side effects (serious unwanted medical events thought to be caused by the treatments in the study). No patient treated by fixed combination reported serious side effect.

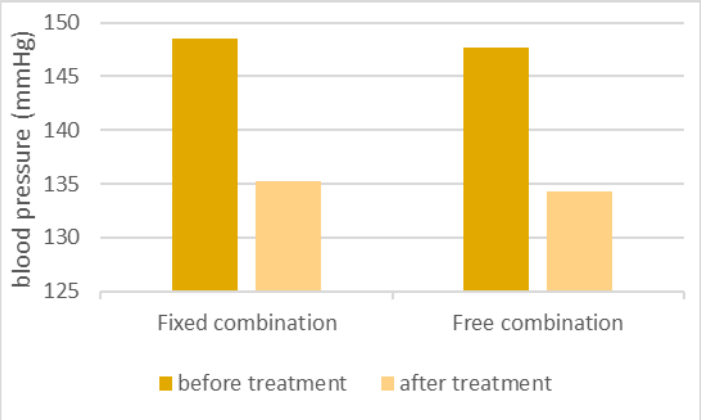
The serious side effects reported were stroke due to interruption of blood flow to parts of the brain, breakdown of the covering around nerve fibres, and a type of asthma with dry cough
In the study, no participants died because of an unwanted event thought to be caused by study treatments.

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.

Changes in SBP over the two first months



The study found that participants with the fixed combination (study drug) had similar decrease in blood pressure to participants with the free combination.

8 How has this study helped research?

This study helped researchers to gather more information on the treatment of participants with high blood pressure.
This summary shows only the main results from this one study. Other studies, evaluating the same drug, may find different results.

9 Are there plans for further studies?

No other studies with the study drug are planned so far.

10 Further information

What are the identification numbers of the study?

- Protocol code: CL3-06593-018
- US NCT number: *NCT05820880*

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.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/