Clinical trial SUMMARY

Short study title

Study evaluating one chewable tablet of MPFF 1000 mg in people with venous disease.

Full scientific title:

Clinical non-inferiority study between Micronized Purified Flavonoid Fraction (MPFF) 1000 mg, one chewable tablet per day and MPFF 500 mg, 2 tablets daily after eight weeks of treatment in patients suffering from symptomatic Chronic Venous Disease (CVD).

In this summary:

Therapeutic area:
Cardiovascular

Indication:
Chronic venous disease

Study phase:
Phase 3

16 October 2020
Final version

CLINICAL TRIAL SUMMARY

Study evaluating one chewable tablet of MPFF 1000 mg in people with venous disease.

We would like to thank all the patients who participated in the study. As clinical study participants, they help researchers discover new medicines for the benefit of all 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. It involves a lot of people in many studies all around the world for medical science to progress. 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 on this study, please speak to your doctor.

1 Why was this study done?

Venous disease is due to insufficient blood circulation in the veins of the legs. The name of the study drug is Micronized Purified Flavonoid Fraction (MPFF). It is used to improve the symptoms of venous disease like leg discomfort (leg pain, leg heaviness, tiredness and feeling of swelling).

This study is called a Phase 3. It compared the same medicine (MPFF) in 2 different forms:
- The chewable tablet of 1000 mg is a new form.
- The tablet of 500 mg is already on the market.

One chewable tablet contains the same dose of MPFF as 2 tablets.
For the patient, one chewable tablet may be easier to take than 2 tablets.

The aim of this study was to show that one chewable tablet of 1000 mg works as well or almost as well as 2 tablets of 500 mg.

2 When and where did this study take place?

When was it performed?

- This study started in July 2018.
- It ended in October 2019.

Where did the study take place?

The study took place in the following countries:

Country	Number of patients included
Argentina	125
Austria	4
Brazil	78
Hungary	43
Romania	87
Russia	173
Vietnam	32
Thailand	55
Turkey	14

3 Who participated in the study?

Which patients were included in the study?

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

- Be aged from 20 to 75 years old (inclusive).
- Have venous disease.
- Have leg discomfort.
  The feeling of discomfort was to be greater than or equal to 4 cm on the following scale.

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How many patients participated in the study?

Overall 611 patients joined the study, including 502 women and 109 men. Of those included, 27 patients did not complete the study, mainly for non-medical reasons.

How old were the patients?

The average age of the patients was 48 years. The youngest patient was 21 years old and the oldest one was 76 years old (75 years old and few months, rounded to 76).

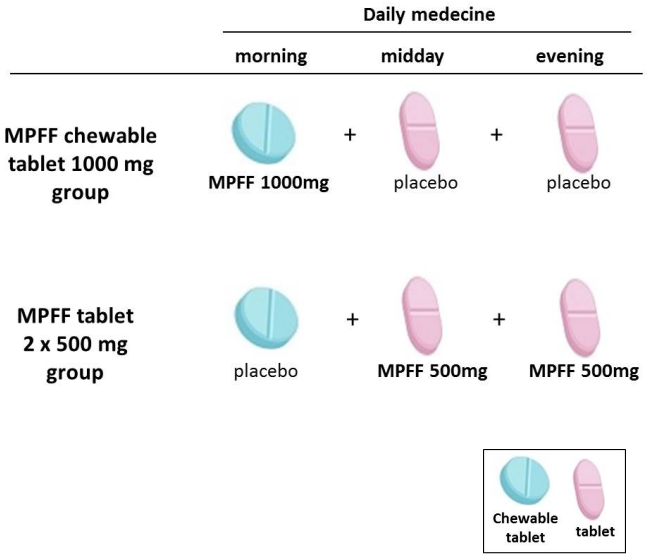
4 Which treatments did patients receive?

The study drug was the Micronized Purified Flavonoid Fraction (MPFF).
In this study, 1 chewable tablet of MPFF 1000 mg was compared to 2 tablets of MPFF 500 mg. Every day, patients received either:

- 1 MPFF chewable tablet and placebo.
- or 2 MPFF tablets and placebo.

The placebo looked like MPFF but did not have any real medicine in it.

Patients took the oral treatment with meals as shown below:



5 How was the study done?

This study is called a "randomized" study. It means that patients were put into one of the 2 groups by chance.

- 307 patients took 1 MPFF chewable tablet 1000 mg
- 301 patients took 2 MPFF tablets 500 mg.

In addition, 3 patients stopped the study before receiving the treatment.

The study is called a "double-blind" study. This means that neither patients nor doctors knew who was given which treatment. Therefore, there is no influence of patients and doctors on the study results.

The treatment lasted 8 weeks. At the beginning of the study and each week, the patients rated their leg discomfort, at home, on the scale described in the Section 3.

6 What were the side effects?

What about side effects?

Like all medicines, the study drug can cause side effects, although not everybody gets them.
Side effects are unwanted events thought to be related to the treatments in the study.

The table below shows the number of patients who experienced side effects. Be aware that the results may be presented differently elsewhere.

	1 chewable tablet of MPFF 1000 mg	2 tablets of MPFF 500 mg
Patients who had side effect(s)	8 patients (2.6%)	6 patients (2.0%)
Patients who had serious* side effect(s)	0 patient	0 patient
Patients who withdrew the study because of side effect(s)	2 patients (0.7%)	0 patient

See definition below on the next page

How many patients had serious side effects?

A side effect is 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 the patient at risk and requires a medical intervention to prevent the situations listed above.

In this study, no patient had serious side effects.

What were the other side effects?

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

	1 chewable tablet of MPFF 1000 mg	2 tablets of MPFF 500 mg
Feeling sick	5 patients (1.6%)	1 patient (0.3%)
Headache	2 patients (0.7%)	1 patient (0.3%)
Diarrhoea	1 patient (0.3%)	1 patient (0.3%)
Darkening of the skin	1 patient (0.3%)	1 patient (0.3%)
Bowel pain	1 patient (0.3%)	0 patient
Dizziness	1 patient (0.3%)	0 patient
Rash	1 patient (0.3%)	0 patient
Unusual weakness	1 patient (0.3%)	0 patient
Indigestion	0 patient	1 patient (0.3%)
Soft stools	0 patient	1 patient (0.3%)

7 What were the study results?

The study was completed as planned.

This lay summary presents only the results for the main goal of the study. Other results can be found in the scientific study summary on www.clinicaltrials.servier.com

- At the beginning of the study, all patients had similar leg discomfort. Patients rated their discomfort as 7.3, on average, on the scale (from 0 = no discomfort to 10 = extreme discomfort).
- After 8 weeks of treatment, patients rated their leg discomfort as 3.6, on average, on the scale. With either one chewable tablet of 1000 mg or 2 tablets of 500 mg per day, leg discomfort decreased in a similar way.

This study found that after 8 weeks of treatment, one chewable tablet of MPFF 1000 mg works as well or almost as well as 2 tablets of 500 mg per day on leg discomfort.

8 How has this study helped patients and researchers?

Results from this study will be used to obtain an authorisation for the use of MPFF chewable tablet 1000 mg. This authorisation will be requested from the Health Authorities.

9 Are there plans for further studies?

No other studies with the MPFF chewable tablet 1000 mg are foreseen to date.

10 Further information

What is the identification number of the clinical study?

- Protocol Number: CL3-05682-109
- EudraCT Number: 2017-003633-28

Who did the study?

The company organizing and funding 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 (www.servier.com).

Where can you learn more about this study?

- The scientific study summary is also available on the 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 the Servier Clinical Trial Data website.