Clinical Trial Results

The summary results presented are from one study in patients with primary aldosteronism. Researchers must look at more than one study from patients all around the world to determine if a medicine is safe and effective to be prescribed to patients. Results from this study may not be the same as results from other studies in patients with primary aldosteronism or in patients with other diseases.

Research sponsor: DAMIAN Pharma AG
Sponsor headquarters: Walchwil, Switzerland; +41 61 601 09 78
Medicine evaluated: dexfadrostat phosphate (DP13)
Protocol number: DP13C201
Dates of study: 19 December 2019 to 2 May 2022
Study title: DP13 – A Phase II Study in Patients with Primary Aldosteronism to Evaluate the Efficacy, Safety and Tolerability of the Aldosterone Synthase Inhibitor, DP13, over an 8-week Treatment Period
EudraCT number: 2019-000919-85
NCT number: NCT04007406

THANK YOU

Thank you for participating in the clinical study which evaluated how dexfadrostat phosphate affects primary aldosteronism. Your kind participation helped researchers learn more about dexfadrostat phosphate.

This summary will describe the study results and was prepared to provide you with information about what researchers learned from the trial. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is primary aldosteronism?

Primary aldosteronism is a disease caused by the uncontrolled over production of aldosterone. Aldosterone is a hormone produced by the adrenals, glands that sit on top of the kidney. Aldosterone regulates salt, potassium, and water balance in the body to control blood pressure and how the blood vessels of the body expand and contract to pump blood through the body. If left untreated, it can lead to long-term damage of blood vessels, heart, kidney, and the brain. Primary aldosteronism is sometimes abbreviated as PA.

What is dexfadrostat phosphate?

Dexfadrostat phosphate has not been approved for use outside of a research study. Dexfadrostat phosphate is a new experimental medication that works directly at the source of aldosterone overproduction by decreasing the activity of the enzyme responsible for making aldosterone. In a separate clinical study of healthy volunteers, dexfadrostat phosphate was shown to lower the amount of aldosterone in the blood and urine.

What was the purpose of the study?

To bring the body back into balance, the underlying aldosterone production must be controlled. Therefore, the aim of the study was to evaluate if dexfadrostat phosphate was able to decrease the amount of aldosterone in the blood and urine and decrease blood pressure in patients with PA. This study was a phase 2 study. This means that the new medication was tested in a small number of patients with the disease. The study was 'double blind' which means that neither patients nor doctors knew who was given which dose of the experimental medication. This was done to make sure that the trial results were not influenced in any way. The study was also 'randomized' which means that patients were given a specific dose 'by chance' which makes the comparison between groups fairer. The study also included 2 periods where patients took a 'placebo' pill. A placebo is an identical looking capsule but with no medicine.

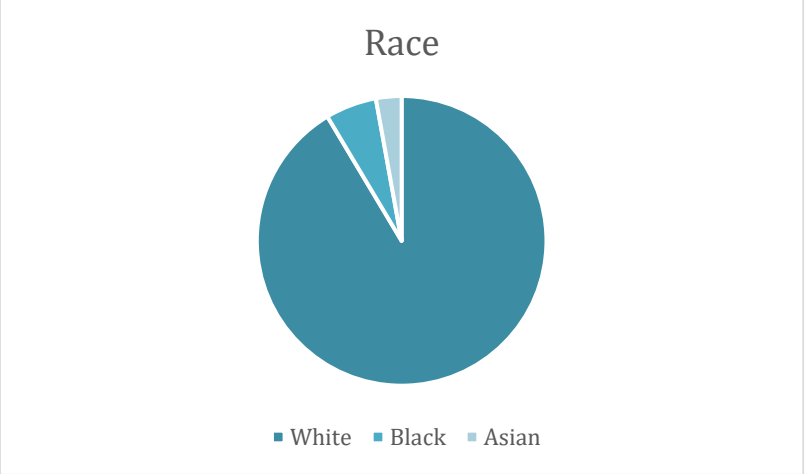
How long was the study?

The total time in the study was 84 days. All patients in the study took 1 capsule of placebo per day in the morning by mouth for 14 days (2 weeks) before receiving dexfadrostat phosphate. Patients took 1 capsule of dexfadrostat phosphate each day for 56 days (8 weeks) by mouth before breakfast. After 56 days, all patients then switched back to placebo capsules, taken once each day, for another 14 days (2 weeks).

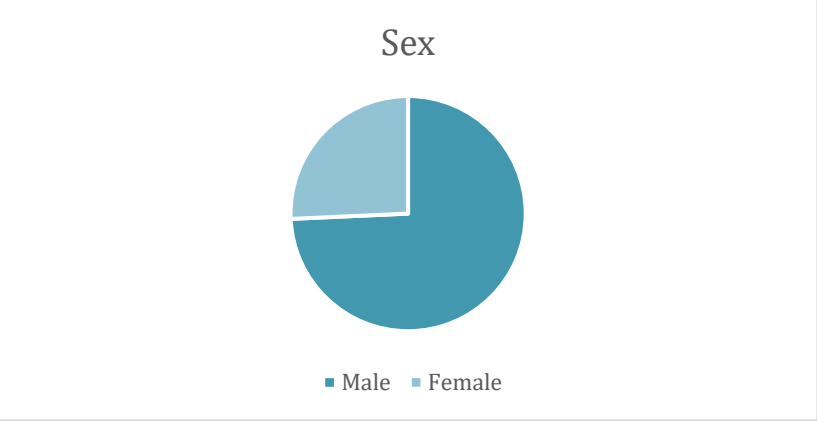
Who participated in the study?

All patients in the study were required to have a diagnosis of PA. There were 35 patients in the study from three countries: 23 patients from Italy; 10 patients from Switzerland; 2 patients from The Netherlands. Other patient characteristics are listed below.

Number of patients in the study: 35
All patients were between 18 and 65 years of age



White	91.4%
Black	5.7%
Asian	2.9%

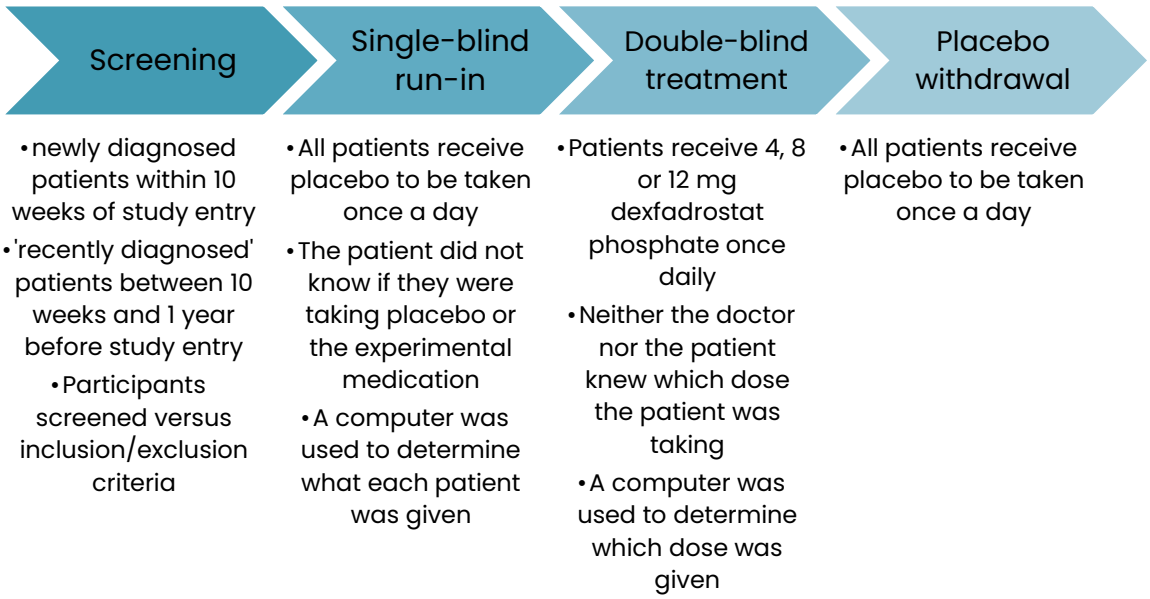


Male	74%
Female	26%

How was the study done?

The study consisted of 4 periods:

- Screening to assess study eligibility and washout of not allowed medications
- Single-blind run-in (2 weeks) to assess baseline parameters
- Randomized double-blind treatment (8 weeks) to test treatment effects and tolerability
- Placebo withdrawal period (2 weeks) to assess parameters after removal of medication



What was evaluated in the study?

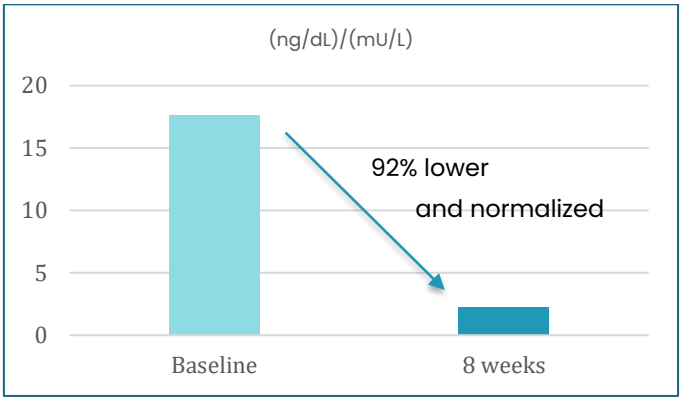
In this study, the researchers wanted to know how the experimental medication worked in patients with primary aldosteronism. Patients with this disease have unusually high levels of aldosterone, a hormone that maintains water and salt balance in the body, that cause very high blood pressure, and also long-term negative effects on body organs such as the heart, the kidneys and the brain. The study tested whether dexfadrostat phosphate could reduce the blood level of aldosterone causing a reduction of systolic blood pressure and whether it caused any medical problems in the patients. The study tested three doses of the experimental medication, (individually and all together) and showed the difference between what was measured before the experimental medication and after it was taken for 8 weeks.

Primary objectives	**Definition**
• To determine whether daily oral dexfadrostat phosphate (all doses combined) reduced blood **aldosterone-to-renin ratio (ARR)** after 8 weeks of treatment in patients with PA. • To determine whether daily oral dexfadrostat phosphate (all doses combined) reduced **24-hour ambulatory systolic blood pressure** (aSBP) after 8 weeks of treatment in patients with PA.	• The aldosterone-to-renin ratio compares the amount of aldosterone to the amount of renin (a hormone produced by cells in the kidney that, like aldosterone, helps to control blood pressure) in the blood. A high ARR indicates PA. A reduction in ARR generally indicates normal levels of aldosterone. • 24-hour ambulatory blood pressure monitoring measures blood pressures at regular intervals over 24 hours. This type of blood pressure measurement allows the patient to perform regular daily activities and sleep normally. It is generally a more accurate measurement since it reduces 'white coat syndrome', which is the general increase in blood pressure due to anxiety when a person visits a doctor's office. Systolic blood pressure is the pressure exerted on arteries as blood is pumped through the body by the heart.
Main secondary objectives	**Definition**
• To determine the **safety and tolerability** of DP13 in patients with PA. • To determine whether daily oral dexfadrostat phosphate (all dose arms combined) reduced **office systolic blood pressure** (oSBP) after 8 weeks of treatment in patients with PA.	• Safety and tolerability monitoring measures the medical problems seen while taking an experimental medication which may or may not be due to the medication. • Office blood pressure monitoring averages 3 blood pressure measurements, 10 minutes apart. Office blood pressure is generally less reliable than ambulatory blood pressure due to 'white coat syndrome'. Systolic blood pressure is the pressure exerted on arteries as blood is pumped through the body by the heart.
Main exploratory objectives	**Definition**
• To determine whether daily oral dexfadrostat phosphate reduces 24-hour **urinary aldosterone excretion** after 8 weeks of treatment in patients with PA. • To determine whether daily oral dexfadrostat phosphate raised **blood potassium** values after 8 weeks of treatment in patients with PA.	• Urine is collected over 24 hours and the amount of aldosterone is measured. • Blood is collected and the amount of potassium is measured. Low potassium levels affect cardiac function.

What were the results of the study?

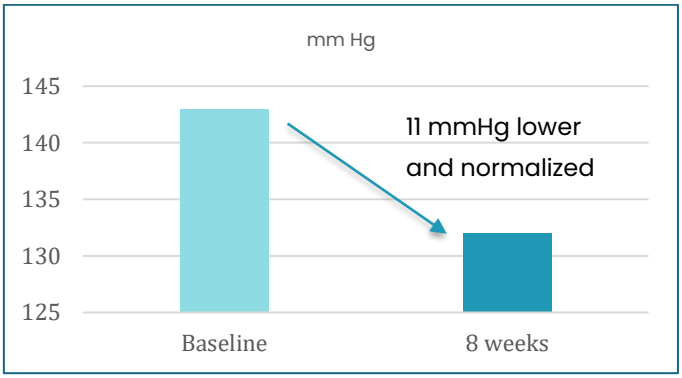
Is there a reduction in blood aldosterone-to-renin ratio after 8 weeks of treatment with dexfadrostat phosphate?

Aldosterone-to-renin ratio (ng/dL)/(mU/L)	
Baseline	Day 56
17.6 ± 15.2	2.2 ± 3.3



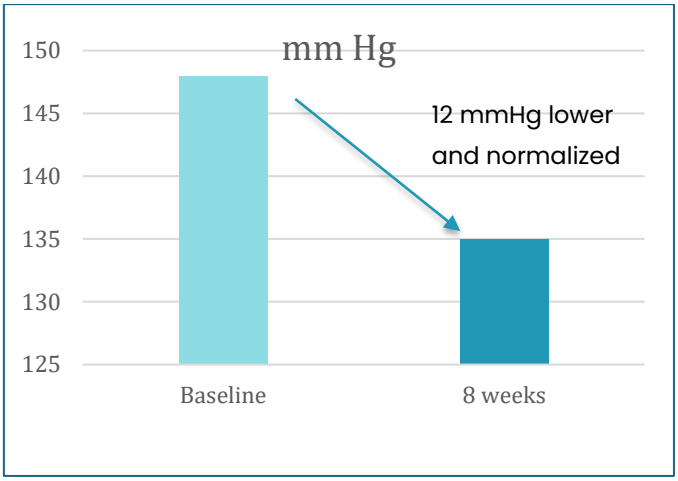
Is there a reduction in 24-hour ambulatory blood pressure after 8 weeks of treatment with dexfadrostat phosphate?

Ambulatory systolic blood pressure (mmHg)	
Baseline	Day 56
143 ± 14	132 ± 13



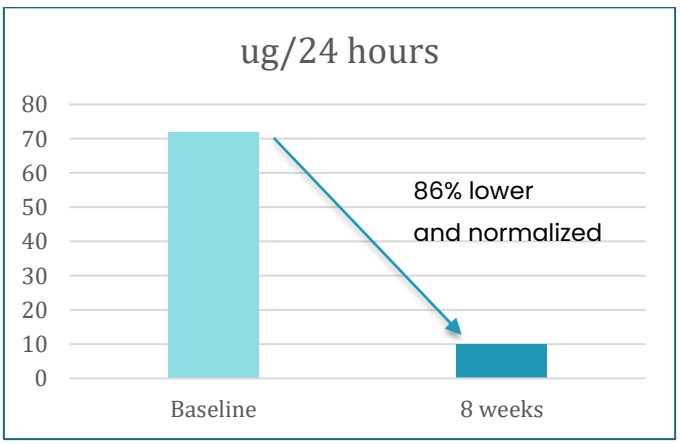
Is there a reduction in office blood pressure after 8 weeks of treatment with dexfadrostat phosphate?

Office systolic blood pressure (mmHg)	
Baseline (mean ± SD)	Day 56 (mean ± SD)
148 ± 12	136 ± 12



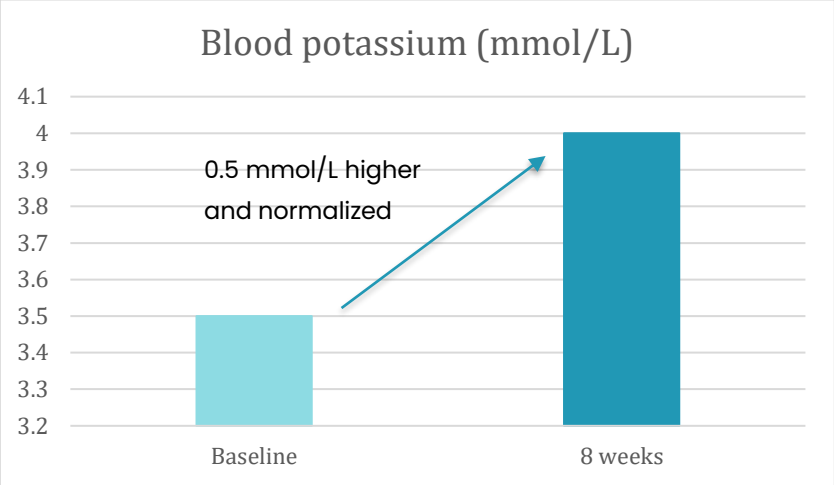
Is there a reduction in urinary aldosterone excretion after 8 weeks of treatment with dexfadrostat phosphate?

Urinary aldosterone (µg/24 hours)	
Baseline (mean ± SD)	Day 56 (mean ± SD)
72 ± 43	10 ± 10



Is there an increase in blood potassium levels after 8 weeks of treatment with dexfadrostat phosphate?

Blood potassium (mmol/L)	
Baseline (mean ± SD)	Day 56 (mean ± SD)
3.5 ± 0.4	4.0 ± 0.3



What side effects did the participants have during the study?

Unwanted medical effects that occur during the study are called 'adverse events'. Adverse events are collected by the researcher to understand how the patient is doing. Adverse events are categorized as mild, moderate, or severe. Researchers also collect information on how long the adverse event occurred or if it didn't stop at all during the study. Researchers also collect information on 'serious adverse events'. This type of event causes the patient to go to the hospital, causes lasting problems or is considered life-threatening. Adverse events can be related to the experimental medication, or they can be considered by the researcher to be unrelated to the experimental medication.

This study showed the dexfadrostat phosphate is generally safe and well tolerated. Not all patients in the trial had side effects. Side effects collected during this study were the same as what is seen in the normal patient population. No patients had serious medical problems during this study, and no one died. Most of the side effects were considered by the researcher to be mild in severity and all recovered during the study. The most common side effect reported by the

patients during the study was headache, followed by diarrhea and feeling tired.

The following table shows the most common side effects reported by at least 5% of the study participants.

Most common adverse events at any time during the study*	
Adverse event reported in at least 5% of any group	Number out of 35 participants
Diarrhea	2 (5.7%)
Fatigue	2 (5.7%)
Headache	4 (11.4%)

*Participants could have experienced more than one adverse event during the study.

What was learned from the study?

This is the first study to test this experimental medication in patients with PA. All patients who took the experimental medication had less aldosterone in their blood and their blood pressure went down. Few people had any medical problems while they were taking the experimental medication and if they did, the problems were mild and went away quickly.

Additional studies will be done in patients with primary aldosteronism to better understand the effects of the experimental medication in patients. The results of this study will be added to the results of other studies of the experimental medication before it is approved to be used by doctors to treat patients with primary aldosteronism.

Where can I learn more about the study?

- If you have questions about the results of your study, please speak with the doctor or staff at your study site.
- For more details on primary aldosteronism, please see the mechanism of disease video at www.damianpharma.com/treatment under 'The Disease'.
- For more information on dexfadrostat phosphate, please see the mechanism of disease video at www.damianpharma.com/treatment under 'DP13' and the medical publication of the study.
- This trial was registered on the following websites where you can find more information:
  - ClinicalTrials.gov—https://clinicaltrials.gov. Use the study identifier NCT04007406
  - European Union Clinical Trials Register—https://www.clinicaltrialsregister.eu. Use the study identifier 2019-000919-85
- Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.