Clinical trial results:
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

Summary

EudraCT number	2019-000919-85
Trial protocol	NL IT
Global end of trial date	02 May 2022

Results information

Result version number	v1 (current)
This version publication date	21 December 2023
First version publication date	21 December 2023

Trial information

Trial identification

Sponsor protocol code	DP13C201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04007406
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	DAMIAN Pharma AG
Sponsor organisation address	Haltli 6, Walchwil, Switzerland, 6318
Public contact	Teresa Gerlock, DAMIAN Pharma AG, 041 0616010978, teresa.gerlock@damianpharma.com
Scientific contact	Christoph Schumacher, DAMIAN Pharma AG, 041 0616010978, christoph.schumacher@damianpharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 January 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 May 2022
Global end of trial reached?	Yes
Global end of trial date	02 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To determine the efficacy of daily oral dexfadrostat phosphate (DP13) treatment (all dose arms combined) to decrease the plasma aldosterone-to-renin ratio (ARR) from baseline in patients with primary aldosteronism (PA) following 8 weeks of treatment
• To determine the efficacy of daily oral dexfadrostat phosphate (DP13) treatment (all dose arms combined) to reduce 24-hour ambulatory systolic blood pressure (aSBP) from baseline in patients with primary aldosteronism (PA) following 8 weeks of treatment

Protection of trial subjects:

The study was conducted in compliance with the study protocol, the recommendations on biomedical research on human subjects of the Declaration of Helsinki, International Conference of Harmonization (ICH)--Good Clinical Practice (GCP) Guidelines (ICH E6 (R2)), and all applicable laws and regulations.

Agreement to adhere to the protocol was established by Investigators signing and returning the protocol signature page.

Patient identities were kept confidential by assigning each patient a unique identifier consisting of a patient-specific numeric code, which was used throughout the study instead of the patient's name.

All study sites received the approval of the local Ethics Committee. Additionally, patients were treated to routine care by the site investigator/physician.

All patients were explained the nature and purpose of the study, the participation conditions and the risks and benefits to the patients before signing and dating the informed consent form.

Background therapy:

In order to prevent uncontrolled hypertension during the study, a fixed-dose regimen of doxazosin (1-8 mg QD), as first-line medication and, if necessary, verapamil slow release (40-120 mg BID) or diltiazem (slow release 90-360 mg daily) or amlodipine (2.5-10 mg QD) was implemented if clinically applicable 2 weeks prior to eligibility verification. Exceptionally, a calcium channel blocker could be used as first-line treatment if medically justified. Patients were not to take diagnosis-interfering medications as listed in the Endocrine Society Clinical Practice Guidelines (e.g., ACEi, ARB) for the duration of the study. Recently diagnosed patients on spironolactone were required to be washed out at least 8 weeks prior to study entry.

Evidence for comparator: -

Actual start date of recruitment	02 September 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Italy: 23

Country: Number of subjects enrolled	Switzerland: 10
Worldwide total number of subjects	35
EEA total number of subjects	25

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	35
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited as 'de novo' i.e., diagnosed with PA within 10 weeks of study entry or as 'recently diagnosed' i.e., diagnosed between 10 weeks and 1 year prior to study entry.

Pre-assignment

Screening details:

Patient screening ARR and blood pressure were reviewed and approved by the Eligibility Review Panel prior to enrolling in the study.
A suppression test also needed to be performed prior to study entry to confirm diagnosis of PA. Patients underwent a 2-week placebo run-in prior to randomization.

Pre-assignment period milestones

Number of subjects started	35
Number of subjects completed	35

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

IMP-containing jars were labeled/packed according to SOP based on the randomization list. The following controls were employed to maintain blinding:
1. Placebo capsules for the run-in period were identical in appearance to the DP13 capsules
2. The investigator and other members of staff involved in the study remained blinded to the treatment randomization code
3. Interim bioanalytical/hemodynamic data were provided to the central lab in a blinded manner

Emergency unblinding was possible

Arms

Are arms mutually exclusive?	No
Arm title	Baseline

Arm description:

Prior to active treatment but following 2-weeks single-blind placebo run-in

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Active treatment

Arm description:

Values after 8 weeks of dexfadrostat phosphate treatment

Arm type	Experimental
Investigational medicinal product name	dexfadrostat phosphate
Investigational medicinal product code	
Other name	DP13
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Once daily, before meals

Number of subjects in period 1	Baseline	Active treatment
Started	35	35
Completed	35	35

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	35	35	
Age categorical			
adults			
Units: Subjects			
Adults (18-64 years)	35	35	
Age continuous			
Units: years			
arithmetic mean	52		
standard deviation	± 9	-	
Gender categorical			
Units: Subjects			
Female	9	9	
Male	26	26	
Race			
Units: Subjects			
White	32	32	
Black or African American	2	2	
Asian	1	1	
Body mass index			
Vital signs at baseline all dose groups combined			
Units: kg/m2			
arithmetic mean	28		
standard deviation	± 3.5	-	
Office systolic blood pressure			
Units: mm Hg			
arithmetic mean	148		
standard deviation	± 12	-	
Potassium			
Units: mmol/L			
arithmetic mean	3.5		
standard deviation	± 0.4	-	
Office diastolic blood pressure			
Units: mm Hg			
arithmetic mean	92		
standard deviation	± 10	-	
24-hour ambulatory systolic blood pressure			
Units: mm Hg			
arithmetic mean	143		
standard deviation	± 14	-	
Aldosterone-to-renin ratio			
Units: ng*L/d?*mU			

arithmetic mean	17.6		
standard deviation	± 15	-	
24-hour ambulatory diastolic blood pressure			
Units: mm Hg			
arithmetic mean	88		
standard deviation	± 8	-	

Subject analysis sets

Subject analysis set title	Baseline
Subject analysis set type	Full analysis
Subject analysis set description: Baseline values after 2 weeks of placebo run-in	
Subject analysis set title	DP13 active treatment
Subject analysis set type	Full analysis
Subject analysis set description: Values following 8 weeks of once daily treatment with dexfadrostat phosphate	

Reporting group values	Baseline	DP13 active treatment	
Number of subjects	35	35	
Age categorical			
adults			
Units: Subjects			
Adults (18-64 years)	35	35	
Age continuous			
Units: years			
arithmetic mean	52	52	
standard deviation	± 9	± 9	
Gender categorical			
Units: Subjects			
Female	9	9	
Male	26	26	
Race			
Units: Subjects			
White	32	32	
Black or African American	2	2	
Asian	1	1	
Body mass index			
Vital signs at baseline all dose groups combined			
Units: kg/m2			
arithmetic mean	28	28	
standard deviation	± 3.5	± 3.5	
Office systolic blood pressure			
Units: mm Hg			
arithmetic mean	148	148	
standard deviation	± 12	± 12	
Potassium			
Units: mmol/L			
arithmetic mean	3.5	3.5	
standard deviation	± 0.4	± 0.4	

Office diastolic blood pressure Units: mm Hg			
arithmetic mean	92	92	
standard deviation	± 10	± 10	
24-hour ambulatory systolic blood pressure Units: mm Hg			
arithmetic mean	143	143	
standard deviation	± 14	± 14	
Aldosterone-to-renin ratio Units: ng*L/d?*mU			
arithmetic mean	17.6	17.6	
standard deviation	± 15	± 15	
24-hour ambulatory diastolic blood pressure Units: mm Hg			
arithmetic mean	88	88	
standard deviation	± 8	± 8	

End points

End points reporting groups

Reporting group title	Baseline
Reporting group description:	
Prior to active treatment but following 2-weeks single-blind placebo run-in	
Reporting group title	Active treatment
Reporting group description:	
Values after 8 weeks of dexfadrostat phosphate treatment	
Subject analysis set title	Baseline
Subject analysis set type	Full analysis
Subject analysis set description:	
Baseline values after 2 weeks of placebo run-in	
Subject analysis set title	DP13 active treatment
Subject analysis set type	Full analysis
Subject analysis set description:	
Values following 8 weeks of once daily treatment with dexfadrostat phosphate	

Primary: 24-hour ambulatory systolic blood pressure (SBP)

End point title	24-hour ambulatory systolic blood pressure (SBP)
End point description:	
End point type	Primary
End point timeframe:	
Change from baseline to end of active treatment (8 weeks) in ambulatory SBP	

End point values	Baseline	Active treatment	Baseline	DP13 active treatment
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	35	35
Units: mm Hg				
arithmetic mean (standard deviation)	143 (± 14)	132 (± 13)	143 (± 14)	132 (± 13)

Statistical analyses

Statistical analysis title	24-hour ambulatory SBP
Statistical analysis description:	
Change in mean 24-hour ambulatory systolic blood pressure (SBP) from baseline to the end of the 8-week DP13 treatment period for all dose arms combined	
Comparison groups	Baseline v DP13 active treatment

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Primary: Aldosterone-to-renin ratio (ARR)

End point title	Aldosterone-to-renin ratio (ARR)

End point description:

End point type	Primary

End point timeframe:

Change from baseline to end of active treatment (8 weeks), all dose groups combined

End point values	Baseline	Active treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: ng*L/dL*mU				
arithmetic mean (standard deviation)	17.6 (± 15)	2.2 (± 3.3)		

Statistical analyses

Statistical analysis title	Aldosterone-to-renin ratio (ARR)

Statistical analysis description:

Change in plasma ARR from baseline to the end of the 8-week DP13 treatment period for al dose arms combined

Comparison groups	Active treatment v Baseline
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANOVA
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: Potassium

End point title	Potassium

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to end of active treatment (8 weeks)

End point values	Baseline	Active treatment	Baseline	DP13 active treatment
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	35	35
Units: mmol/L				
arithmetic mean (standard deviation)	3.5 (± 0.4)	4.0 (± 0.3)	3.5 (± 0.4)	4.0 (± 0.3)

Statistical analyses

Statistical analysis title	Plasma potassium

Statistical analysis description:

Change in plasma potassium concentration from baseline to the end of the 8-week DP13 treatment period

Comparison groups	Baseline v DP13 active treatment
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Other pre-specified: 24-hour ambulatory diastolic blood pressure (aDBP)

End point title	24-hour ambulatory diastolic blood pressure (aDBP)

End point description:

End point type	Other pre-specified

End point timeframe:

Change from baseline to the end of the 8-week DP13 treatment period, all dose groups combined

End point values	Baseline	Active treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: mm Hg				
arithmetic mean (standard deviation)	88 (± 8)	82 (± 7)		

Statistical analyses

Statistical analysis title	4-hour ambulatory diastolic blood pressure (aDBP)
Statistical analysis description: Change in mean 24-hour ambulatory DBP from baseline to the end of DP13 treatment period (8 weeks)	
Comparison groups	Baseline v Active treatment
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANOVA
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were collected throughout the study including during the placebo run-in and withdrawal phases.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Safety analysis set
Reporting group description:	
All randomized patients who received at least one dose of active study drug	

Serious adverse events	Safety analysis set		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 35 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Safety analysis set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 35 (45.71%)		
Investigations			
Amylase increased			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Blood pressure diastolic increased			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Blood pressure increased			

subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	 1 / 35 (2.86%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 4 / 35 (11.43%) 4		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	 2 / 35 (5.71%) 2		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 1 / 35 (2.86%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Dental caries subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Duodenitis subjects affected / exposed occurrences (all) Gastritis	 1 / 35 (2.86%) 1 1 / 35 (2.86%) 1 1 / 35 (2.86%) 1 2 / 35 (5.71%) 2 1 / 35 (2.86%) 1		

subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Gastroesophageal reflux			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Breast tenderness			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Polymenorrhoea			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Renal and urinary disorders			
Cystitis			

subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Renal colic			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36914591