Clinical trial results:
Efficacy and safety of chlorthalidone 25 mg in hypertensive patients.

Summary

EudraCT number	2016-001809-16
Trial protocol	GR
Global end of trial date	20 March 2018

Results information

Result version number	v1 (current)
This version publication date	19 November 2021
First version publication date	19 November 2021

Trial information

Trial identification

Sponsor protocol code	Unidone-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Uni-Pharma Kleon Tsetis Pharmaceutical Laboratories SA
Sponsor organisation address	14th Km National Road 1, Kifissia, Greece, 14564
Public contact	Regulatory Affairs department, Uni-Pharma Kleon Tsetis Pharmaceutical Laboratories S.A., 30 2108072512374, soumelas@uni-pharma.gr
Scientific contact	Regulatory Affairs department, Uni-Pharma Kleon Tsetis Pharmaceutical Laboratories S.A., 30 2108072512374, soumelas@uni-pharma.gr

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	01 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 March 2018
Global end of trial reached?	Yes
Global end of trial date	20 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to address the BP lowering effect of chlorthalidone 25 mg in essential hypertensive patients. In parallel, safety following chlorthalidone administration will be evaluated in the patients that will be enrolled in the study. In specific:
Primary efficacy end-points
1.Changes in Office BP at 4 and 12 weeks.
2.Patients with controlled hypertension at 12 weeks.
Primary safety end-points
1.Changes in renal function by means of serum creatinine, estimated glomerular filtration rate (eGFR) and albuminuria at 4 and 12 weeks.
2.Changes in serum sodium, potassium and calcium levels at 4 and 12 weeks.
3.Changes in glycemic, lipid profile as well as uric acid levels at 4 and 12 weeks.
4.Hypotension episodes during follow-up.
5.Hospitalization for cardiovascular or any other systemic disease during follow-up.

Protection of trial subjects:

No specific measures applied

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2016
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	Greece: 44
Worldwide total number of subjects	44
EEA total number of subjects	44

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)	18
From 65 to 84 years	26
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was admitted to the study on 04.04.2017 and the last on 20.03.2018. A total of n = 44 hypertensive patients were recruited, who completed the study in 1 center: Hypertension Unit, First Cardiology Clinic University of Athens, Hippokration Hospital, Athens, Greece

Pre-assignment

Screening details:

44 patients (18 <Age≤75 years old) with untreated or treated uncontrolled essential hypertension characterized by office systolic BP ≥140 mmHg and/or office diastolic BP≥90 mmHg. Potential fertile women enrolled underwent a pregnancy test that excluded any possibility of present pregnancy and confirmed to use a safe contraceptive method.

Period 1

Period 1 title	Second visit
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Examination at 12 weeks of therapy

Arm description:

Patients will be examined in this final study visit and office systolic/diastolic BP will be evaluated along with metabolic profile determination. The percentage of patients with hypertension control (office BP<140/90 mmHg) will be estimated. During the week before the visit a drug intake diary will be kept by the patient.

Arm type	Experimental
Investigational medicinal product name	Unidone 25mg tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Same as First visit

Number of subjects in period 1	Examination at 12 weeks of therapy
Started	44
Completed	44

Period 2

Period 2 title	Baseline period
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Chlorthalidone 25mg

Arm description:

After subjects have given their informed consent to participate to the study, they will be examined at baseline and those with office systolic BP ≥140 mmHg and/or office diastolic BP≥90 mmHg using an automatic BP Monitor (Omron Healthcare, Inc., Bannockburn, Illinois, USA) will enter into the study in absence of any exclusion criteria.
If office systolic BP ≥140 mmHg and/or office diastolic BP≥90 mmHg is confirmed by ambulatory daytime systolic BP≥135 mmHg and/or daytime diastolic BP≥85 mmHg, using an ambulatory BP system (Spacelabs Healthcare, Inc., Issaquah, Washington, USA), therapy with chlorthalidone 25 mg once daily will be initiated. Moreover, before initiation of chlorthalidone therapy blood samples will be drawn for estimation of renal function and metabolic profile.

Arm type	Experimental
Investigational medicinal product name	Unidone 25mg tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Chlorthalidone 25 mg tablets once daily

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 is the baseline. This was assigned by mistake.

Number of subjects in period 2	Chlorthalidone 25mg
Started	44
Completed	44

Period 3

Period 3 title	First visit
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Examination at 4 weeks of therapy

Arm description:

Patients will be examined and office systolic/diastolic BP will be evaluated. In 1 out 4 consecutive patients ambulatory BP will be also evaluated on all time points of the study along with metabolic profile determination. If office systolic BP ≥140 mmHg and/or office diastolic BP≥90 mmHg step up of therapy with chlorthalidone 50 mg is in the discretion of the investigators. During the week before the visit a drug intake diary will be kept by the patient.

Arm type	Experimental
Investigational medicinal product name	Unidone 25mg tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Chlorthalidone 25 mg tablets once daily. If office systolic BP ≥140 mmHg and/or office diastolic BP≥90 mmHg step up of therapy with chlorthalidone 50 mg is in the discretion of the investigators.

Number of subjects in period 3	Examination at 4 weeks of therapy
Started	44
Completed	44

Baseline characteristics

Reporting groups	
Reporting group title	Baseline period

Reporting group description: -

Reporting group values	Baseline period	Total	
Number of subjects	44	44	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	18	18	
From 65-84 years	26	26	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	62		
standard deviation	± 9	-	
Gender categorical Units: Subjects			
Female	20	20	
Male	24	24	

End points

End points reporting groups

Reporting group title	Examination at 12 weeks of therapy

Reporting group description:

Patients will be examined in this final study visit and office systolic/diastolic BP will be evaluated along with metabolic profile determination. The percentage of patients with hypertension control (office BP<140/90 mmHg) will be estimated. During the week before the visit a drug intake diary will be kept by the patient.

Reporting group title	Chlorthalidone 25mg

Reporting group description:

After subjects have given their informed consent to participate to the study, they will be examined at baseline and those with office systolic BP ≥140 mmHg and/or office diastolic BP≥90 mmHg using an automatic BP Monitor (Omron Healthcare, Inc., Bannockburn, Illinois, USA) will enter into the study in absence of any exclusion criteria.
If office systolic BP ≥140 mmHg and/or office diastolic BP≥90 mmHg is confirmed by ambulatory daytime systolic BP≥135 mmHg and/or daytime diastolic BP≥85 mmHg, using an ambulatory BP system (Spacelabs Healthcare, Inc., Issaquah, Washington, USA), therapy with chlorthalidone 25 mg once daily will be initiated. Moreover, before initiation of chlorthalidone therapy blood samples will be drawn for estimation of renal function and metabolic profile.

Reporting group title	Examination at 4 weeks of therapy

Reporting group description:

Patients will be examined and office systolic/diastolic BP will be evaluated. In 1 out 4 consecutive patients ambulatory BP will be also evaluated on all time points of the study along with metabolic profile determination. If office systolic BP ≥140 mmHg and/or office diastolic BP≥90 mmHg step up of therapy with chlorthalidone 50 mg is in the discretion of the investigators. During the week before the visit a drug intake diary will be kept by the patient.

Primary: Changes in Office BP

End point title	Changes in Office BP[1]

End point description:

Changes in Office BP at 4 weeks

End point type	Primary

End point timeframe:

4 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: N/A

End point values	Examination at 4 weeks of therapy			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: mmHg				
arithmetic mean (standard deviation)	138 (± 15)			

Statistical analyses

No statistical analyses for this end point

Primary: Changes in Office BP

End point title	Changes in Office BP[2]

End point description:

Changes in Office BP at 12 weeks

End point type	Primary

End point timeframe:

12 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: N/A

End point values	Examination at 12 weeks of therapy			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: mmHg				
arithmetic mean (standard deviation)	134 (± 13)			

Statistical analyses

No statistical analyses for this end point

Primary: Patients with controlled hypertension

End point title	Patients with controlled hypertension[3]

End point description:

Patients with controlled hypertension at 12 weeks

End point type	Primary

End point timeframe:

12 weeks

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: N/A

End point values	Examination at 12 weeks of therapy			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: percent				
number (not applicable)	81.8			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 12 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0
Reporting groups	
Reporting group title	End of trial
Reporting group description: AEs reported after 12 weeks of treatment	

Serious adverse events	End of trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	End of trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Cardiac disorders			
Hypotension	Additional description: There was 1 episode of hypotension without syncope during follow-up which was attributed to dehydration of the patient.		
subjects affected / exposed[1]	1 / 1 (100.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea	Additional description: In 1 patient, diarrhoea occurred during the first 4 weeks of treatment which was treated symptomatically.		
subjects affected / exposed[2]	1 / 1 (100.00%)		
occurrences (all)	1		
Renal and urinary disorders			
Glomerular filtration rate increased	Additional description: In 1 patient there was an increase in glomerular filtration rate above 30% of baseline. By halving the dose of chlorthalidone and hydration, renal function was improved by the rate to baseline levels and treatment was continued		

subjects affected / exposed[3] occurrences (all)	1 / 1 (100.00%) 1		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The reporting group is referring to the end of the trial and to the total AEs reported.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The reporting group is referring to the end of the trial and to the total AEs reported.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The reporting group is referring to the end of the trial and to the total AEs reported.

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

None reported