Clinical trial results:
Triiodothyronine for repair of left ventricular dysfunction and Remodeling in STEMI Patients

Summary

EudraCT number	2016-000631-40
Trial protocol	GR
Global end of trial date	12 November 2020

Results information

Result version number	v1 (current)
This version publication date	07 May 2022
First version publication date	07 May 2022
Summary attachment (see zip file)	Synopsis (Synopsis ThyRepair.pdf)

Trial information

Trial identification

Sponsor protocol code	T3inj-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 2108072512, soumelas@uni-pharma.gr
Scientific contact	Regulatory Affairs department, Uni-Pharma Kleon Tsetis Pharmaceutical Laboratories S.A., 0030 2108072512, 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	17 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 November 2020
Global end of trial reached?	Yes
Global end of trial date	12 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective will be the assessment of myocardial function by CMR after administration of liothyronine in patients with anterior or anterolateral STEMI.

Protection of trial subjects:

No specific measures applied

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 November 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Greece: 52
Worldwide total number of subjects	52
EEA total number of subjects	52

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)	52
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was admitted to the study on 13.11.2016 and the last on 12.11.2020. 155 patients were admitted to the centers and a total of n = 52 patients were finally enrolled, in 2 centers: 1. Cardiology Department, ELPIS General Hospital of Athens, Greece 2. Cardiology Department of Tzaneio General Hospital of Athens, Greece.

Pre-assignment

Screening details:

Patients (18 <Age≤75 years old) with anterior or anterolateral ST-Elevation Myocardial Infarctionwho presented within 12 hours after the onset of chest pain and were subjected to successful primary PCI.

Period 1

Period 1 title	Start of treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

In order to maintain blindness identical packs with identically appearing contents were used for both placebo and drug administration. The investigator site personnel involved in the monitoring or conducting of the trial was
blinded to the trial drug codes. Trial drug codes were not available to the above personnel except in the case of an emergency. All serum samples for thyroid hormone measurements were collected and analyzed at the end of the trial in order not to break the blindness.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Composition identical to the experimental drug apart from the active substance.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose administered was 0.8mcg.kg-1 intravenously bolus starting at reperfusion followed by an infusion of 0.113mcg. kg-1.h-1 intravenously for 48 hours. The selection of the dose and duration of treatment was based on preclinical and clinical evidence, adjusted for patient body weight.

Arm title	T3 inj sol

Arm description:

T3®Solution for injection 10µg/ml, having Liothyronine sodium as active substance, at the strength of 10µg/ml.

Arm type	Experimental
Investigational medicinal product name	T3®Solution for injection 10µg/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose administered was 0.8mcg.kg-1 intravenously bolus starting at reperfusion followed by an

infusion of 0.113mcg. kg-1.h-1 intravenously for 48 hours. The selection of the dose and duration of treatment was based on preclinical and clinical evidence, adjusted for patient body weight.

Number of subjects in period 1	Placebo	T3 inj sol
Started	24	28
Completed	24	28

Period 2

Period 2 title	Discharge
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

In order to maintain blindness identical packs with identically appearing contents were used for both placebo and drug administration. The investigator site personnel involved in the monitoring or conducting of the trial was
blinded to the trial drug codes. Trial drug codes were not available to the above personnel except in the case of an emergency. All serum samples for thyroid hormone measurements were collected and analyzed at the end of the trial in order not to break the blindness.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Composition identical to the experimental drug apart from the active substance.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose administered was 0.8mcg.kg-1 intravenously bolus starting at reperfusion followed by an infusion of 0.113mcg. kg-1.h-1 intravenously for 48 hours. The selection of the dose and duration of treatment was based on preclinical and clinical evidence, adjusted for patient body weight.

Arm title	T3 inj sol

Arm description:

T3®Solution for injection 10µg/ml, having Liothyronine sodium as active substance, at the strength of

10µg/ml.

Arm type	Experimental
Investigational medicinal product name	T3®Solution for injection 10µg/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose administered was 0.8mcg.kg-1 intravenously bolus starting at reperfusion followed by an infusion of 0.113mcg. kg-1.h-1 intravenously for 48 hours. The selection of the dose and duration of treatment was based on preclinical and clinical evidence, adjusted for patient body weight.

Number of subjects in period 2	Placebo	T3 inj sol
Started	24	28
Completed	22	24
Not completed	2	4
Adverse event, serious fatal	-	1
Protocol deviation	2	3

Period 3

Period 3 title	3 months visit
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

In order to maintain blindness identical packs with identically appearing contents were used for both placebo and drug administration. The investigator site personnel involved in the monitoring or conducting of the trial was
blinded to the trial drug codes. Trial drug codes were not available to the above personnel except in the case of an emergency. All serum samples for thyroid hormone measurements were collected and analyzed at the end of the trial in order not to break the blindness.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Composition identical to the experimental drug apart from the active substance.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose administered was 0.8mcg.kg-1 intravenously bolus starting at reperfusion followed by an infusion of 0.113mcg. kg-1.h-1 intravenously for 48 hours. The selection of the dose and duration of treatment was based on preclinical and clinical evidence, adjusted for patient body weight.

Arm title	T3 inj sol

Arm description:

T3®Solution for injection 10µg/ml, having Liothyronine sodium as active substance, at the strength of 10µg/ml.

Arm type	Experimental
Investigational medicinal product name	T3®Solution for injection 10µg/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose administered was 0.8mcg.kg-1 intravenously bolus starting at reperfusion followed by an infusion of 0.113mcg. kg-1.h-1 intravenously for 48 hours. The selection of the dose and duration of treatment was based on preclinical and clinical evidence, adjusted for patient body weight.

Number of subjects in period 3	Placebo	T3 inj sol
Started	22	24
Completed	21	22
Not completed	1	2
Adverse event, serious fatal	1	1
Lost to follow-up	-	1

Period 4

Period 4 title	6 months visit
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

In order to maintain blindness identical packs with identically appearing contents were used for both placebo and drug administration. The investigator site personnel involved in the monitoring or conducting of the trial was
blinded to the trial drug codes. Trial drug codes were not available to the above personnel except in the case of an emergency. All serum samples for thyroid hormone measurements were collected and analyzed at the end of the trial in order not to break the blindness.

Arms

Are arms mutually exclusive?	Yes

Arm title	Placebo

Arm description:

Composition identical to the experimental drug apart from the active substance.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose administered was 0.8mcg.kg-1 intravenously bolus starting at reperfusion followed by an infusion of 0.113mcg. kg-1.h-1 intravenously for 48 hours. The selection of the dose and duration of treatment was based on preclinical and clinical evidence, adjusted for patient body weight.

Arm title	T3 inj sol

Arm description:

T3®Solution for injection 10µg/ml, having Liothyronine sodium as active substance, at the strength of 10µg/ml.

Arm type	Experimental
Investigational medicinal product name	T3®Solution for injection 10µg/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose administered was 0.8mcg.kg-1 intravenously bolus starting at reperfusion followed by an infusion of 0.113mcg. kg-1.h-1 intravenously for 48 hours. The selection of the dose and duration of treatment was based on preclinical and clinical evidence, adjusted for patient body weight.

Number of subjects in period 4	Placebo	T3 inj sol
Started	21	22
Completed	21	21
Not completed	0	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	Start of treatment

Reporting group description: -

Reporting group values	Start of treatment	Total	
Number of subjects	52	52	
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)	52	52	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	56.1		
standard deviation	± 9.2	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	48	48	

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Composition identical to the experimental drug apart from the active substance.

Reporting group title	T3 inj sol

Reporting group description:

T3®Solution for injection 10µg/ml, having Liothyronine sodium as active substance, at the strength of 10µg/ml.

Reporting group title	Placebo

Reporting group description:

Composition identical to the experimental drug apart from the active substance.

Reporting group title	T3 inj sol

Reporting group description:

T3®Solution for injection 10µg/ml, having Liothyronine sodium as active substance, at the strength of 10µg/ml.

Reporting group title	Placebo

Reporting group description:

Composition identical to the experimental drug apart from the active substance.

Reporting group title	T3 inj sol

Reporting group description:

T3®Solution for injection 10µg/ml, having Liothyronine sodium as active substance, at the strength of 10µg/ml.

Reporting group title	Placebo

Reporting group description:

Composition identical to the experimental drug apart from the active substance.

Reporting group title	T3 inj sol

Reporting group description:

T3®Solution for injection 10µg/ml, having Liothyronine sodium as active substance, at the strength of 10µg/ml.

Primary: LVMI at 6 months

End point title	LVMI at 6 months[1]

End point description:

Left Ventricular Mass Index

End point type	Primary

End point timeframe:

6 months after acute myocardial infarction

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	Placebo	T3 inj sol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[2]	21		
Units: gram(s)/square metre				
arithmetic mean (standard deviation)	58.8 (± 13.9)	52.4 (± 7.5)		

Notes:

[2] - 1 patient not subjected to CMR due to claustrophobia, 4 excluded due to minimal infarct size

Statistical analyses

No statistical analyses for this end point

Primary: LVEDVI at 6 months

End point title	LVEDVI at 6 months[3]

End point description:

Left Ventricular End-Diastolic Volume Index

End point type	Primary

End point timeframe:

6 months after acute myocardial infarction

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	Placebo	T3 inj sol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[4]	21		
Units: millilitre(s)/square m				
arithmetic mean (standard deviation)	110 (± 32)	94.7 (± 17)		

Notes:

[4] - 1 patient not subjected to CMR due to claustrophobia, 4 excluded due to minimal infarct size

Statistical analyses

No statistical analyses for this end point

Primary: LVESVI

End point title	LVESVI[5]

End point description:

Left Ventricular End-Systolic Volume Index

End point type	Primary

End point timeframe:

6 months after acute myocardial infarction

Notes:

[5] - 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	Placebo	T3 inj sol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[6]	21		
Units: millilitre(s)/square m				
arithmetic mean (standard deviation)	59 (± 31.6)	44.9 (± 15.3)		

Notes:

[6] - 1 patient not subjected to CMR due to claustrophobia, 4 excluded due to minimal infarct size

Statistical analyses

No statistical analyses for this end point

Primary: LVEF, %

End point title	LVEF, %[7]

End point description:

percent of Left Ventricular Ejection Fraction

End point type	Primary

End point timeframe:

6 months after acute myocardial infarction

Notes:

[7] - 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	Placebo	T3 inj sol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[8]	21		
Units: percent				
arithmetic mean (standard deviation)	48.6 (± 11)	53.6 (± 9.5)		

Notes:

[8] - 1 patient not subjected to CMR due to claustrophobia, 4 excluded due to minimal infarct size

Statistical analyses

No statistical analyses for this end point

Primary: Infarct Size

End point title	Infarct Size[9]

End point description:

End point type	Primary

End point timeframe:

6 months after acute myocardial infarction

Notes:

[9] - 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	Placebo	T3 inj sol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[10]	21		
Units: millilitre(s)				
arithmetic mean (standard deviation)	25.9 (± 11.7)	18.7 (± 9.5)		

Notes:

[10] - 1 patient not subjected to CMR due to claustrophobia, 4 excluded due to minimal infarct size

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
6 months after acute myocardial infarction	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Composition identical to the experimental drug apart from the active substance.	
Reporting group title	T3 inj sol
Reporting group description:	
T3®Solution for injection 10µg/ml, having Liothyronine sodium as active substance, at the strength of 10µg/ml.	

Serious adverse events	Placebo	T3 inj sol	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 22 (31.82%)	16 / 26 (61.54%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Left ventricular failure	Additional description: LV thrombus formation		
subjects affected / exposed	6 / 22 (27.27%)	4 / 26 (15.38%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 22 (4.55%)	5 / 26 (19.23%)	
occurrences causally related to treatment / all	0 / 1	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis	Additional description: Pericarditis related to acute myocardial infarction		
subjects affected / exposed	1 / 22 (4.55%)	3 / 26 (11.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Pyrexia	Additional description: Transient episodes of increased temperature >37.8°C		

subjects affected / exposed	2 / 22 (9.09%)	8 / 26 (30.77%)	
occurrences causally related to treatment / all	0 / 2	8 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	T3 inj sol	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 22 (22.73%)	9 / 26 (34.62%)	
Vascular disorders			
Haemorrhage	Additional description: Minor episodes of nose bleeding		
subjects affected / exposed	3 / 22 (13.64%)	3 / 26 (11.54%)	
occurrences (all)	3	3	
Nervous system disorders			
Nervousness	Additional description: Nervousness during first 72h		
subjects affected / exposed	2 / 22 (9.09%)	6 / 26 (23.08%)	
occurrences (all)	2	6	

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