Clinical trial results:
A randomized, double-blinded, single-center, placebo controlled, cross-over study to assess the effect of QVA149 (indacaterol maleate/glycopyrronium bromide) on cardiac function in patients with chronic obstructive pulmonary disease (COPD).

Due to EudraCT system limitations, which EMA is aware of, results of crossover studies are not accurately represented in this record. Please go to https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Summary

EudraCT number	2014-004680-21
Trial protocol	DE
Global end of trial date	15 May 2017
Results information	
Result version number	v1 (current)
This version publication date	12 July 2018
First version publication date	12 July 2018

Trial information

Trial identification	
Sponsor protocol code	CQVA149ADE05
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02442206
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 May 2017
Global end of trial reached?	Yes
Global end of trial date	15 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to determine the effect of once-daily QVA149 (110/50) compared with placebo on left ventricular end-diastolic volume (LV EDV), as measured by magnetic resonance imaging (MRI) after 2 weeks of treatment in hyperinflated COPD patients.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 May 2015
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	Germany: 62
Worldwide total number of subjects	62
EEA total number of subjects	62

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)	29
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This was a randomized, double-blind, placebo controlled, single-center, 2-period cross-over study to compare the effects of a 2 week therapy each with QVA149 versus placebo. The study duration was about 13 weeks

Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind[1]
Roles blinded	Subject, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment sequence 1

Arm description:

QVA149 from day 1 to day 15 followed by Placebo from day 29 to day 43

Arm type	Experimental
Investigational medicinal product name	QVA149 (110/50 µg) followed by placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Inhalation use

Dosage and administration details:

QVA149 (110/50 µg) o.d. from Day 1 to Day 15, followed by placebo o.d. from Day 29 to Day 43.

Arm title	Treatment sequence 2

Arm description:

Placebo from day 1 to day 15 followed by QVA149 from day 29 to day 43

Arm type	Experimental
Investigational medicinal product name	Placebo followed by QVA149 (110/50 µg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo o.d. from Day 1 to Day 15, followed by QVA149 (110/50 µg) o.d. from Day 29 to Day 43.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: All data verified

Number of subjects in period 1	Treatment sequence 1	Treatment sequence 2
Started	30	32
Completed	29	29
Not completed	1	3
withdrew consent	-	1
Adverse event, non-fatal	1	1
COPD exacerbation	-	1

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment sequence 1

Arm description:

QVA149 from day 1 to day 15 followed by Placebo from day 29 to day 43

Arm type	Experimental
Investigational medicinal product name	QVA149 (110/50 µg) followed by placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Inhalation use

Dosage and administration details:

QVA149 (110/50 µg) o.d. from Day 1 to Day 15, followed by placebo o.d. from Day 29 to Day 43.

Arm title	Treatment sequence 2

Arm description:

Placebo from day 1 to day 15 followed by QVA149 from day 29 to day 43

Arm type	Experimental
Investigational medicinal product name	Placebo followed by QVA149 (110/50 µg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo o.d. from Day 1 to Day 15, followed by QVA149 (110/50 µg) o.d. from Day 29 to Day 43.

Notes:

[2] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: All data verified

Number of subjects in period 2	Treatment sequence 1	Treatment sequence 2
Started	29	29
Completed	28	29
Not completed	1	0
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment sequence 1
Reporting group description:	
QVA149 from day 1 to day 15 followed by Placebo from day 29 to day 43	
Reporting group title	Treatment sequence 2
Reporting group description:	
Placebo from day 1 to day 15 followed by QVA149 from day 29 to day 43	

Reporting group values	Treatment sequence 1	Treatment sequence 2	Total
Number of subjects	30	32	62
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	15	14	29
From 65-84 years	15	18	33
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	64.1	63.8	
standard deviation	± 8.00	± 7.80	-
Sex: Female, Male Units: Subjects			
Female	8	9	17
Male	22	23	45
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	30	32	62
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Treatment sequence 1
Reporting group description: QVA149 from day 1 to day 15 followed by Placebo from day 29 to day 43	
Reporting group title	Treatment sequence 2
Reporting group description: Placebo from day 1 to day 15 followed by QVA149 from day 29 to day 43	
Reporting group title	Treatment sequence 1
Reporting group description: QVA149 from day 1 to day 15 followed by Placebo from day 29 to day 43	
Reporting group title	Treatment sequence 2
Reporting group description: Placebo from day 1 to day 15 followed by QVA149 from day 29 to day 43	
Subject analysis set title	QVA149
Subject analysis set type	Per protocol
Subject analysis set description: QVA149 from day 1 to day 15 followed by Placebo from day 29 to day 43	
Subject analysis set title	Placebo
Subject analysis set type	Per protocol
Subject analysis set description: Placebo from day 1 to day 15 followed by QVA149 from day 29 to day 43	
Subject analysis set title	QVA149
Subject analysis set type	Per protocol
Subject analysis set description: QVA149 from day 1 to day 15 followed by Placebo from day 29 to day 43	
Subject analysis set title	Placebo
Subject analysis set type	Per protocol
Subject analysis set description: Placebo from day 1 to day 15 followed by QVA149 from day 29 to day 43	

Primary: Left ventricular end-diastolic volume (LVEDV)

End point title	Left ventricular end-diastolic volume (LVEDV)
End point description: Left ventricular enddiastolic volume (LVEDV) is a measurement of the volume of blood in the heart's left ventricular chamber at the end of the chamber's filling with blood and will be determined as measured by MRI.	
End point type	Primary
End point timeframe: week 2	

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	59		
Units: ML				
arithmetic mean (standard deviation)	11.873 (± 14.3215)	-0.954 (± 12.2463)		

Statistical analyses

Statistical analysis title	Left ventricular enddiastolic volume (LVEDV)
Comparison groups	Placebo v QVA149
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	10.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.209
upper limit	14.331

Secondary: Forced Expiratory Volume in one second (FEV1) at each time-point

End point title	Forced Expiratory Volume in one second (FEV1) at each time-point

End point description:

Forced Expiratory Volume in one second (FEV1) will be calculated as the volume of air forcibly exhaled in one second as measured by spirometry.

End point type	Secondary

End point timeframe:

week 2

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	59		
Units: Liter				
arithmetic mean (standard deviation)	0.42 (± 0.211)	-0.01 (± 0.168)		

Statistical analyses

Statistical analysis title	Forced Expiratory Volume in one second (FEV1)
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	0.49

Secondary: Forced Vital Capacity (FVC) at each time-point	
End point title	Forced Vital Capacity (FVC) at each time-point
End point description: Forced Vital Capacity (FVC) is the amount of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. FVC will be assessed via spirometry.	
End point type	Secondary
End point timeframe: week 2	

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	59		
Units: Liter				
arithmetic mean (standard deviation)	0.67 (± 0.434)	0.00 (± 0.293)		

Statistical analyses

Statistical analysis title	Forced Vital Capacity (FVC)
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	0.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.8

Secondary: Inspiratory Capacity (IC) at each time-point

End point title	Inspiratory Capacity (IC) at each time-point

End point description:

Inspiratory capacity (IC) was defined as the mean of the maximum IC over 3 values measured by bodyplethysmography according to internationally accepted standards.

End point type	Secondary

End point timeframe:

week 2

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	59		
Units: Liters				
arithmetic mean (standard deviation)	0.475 (± 0.3284)	0.014 (± 0.2388)		

Statistical analyses

Statistical analysis title	Inspiratory capacity (IC)
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	0.446
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.352
upper limit	0.541

Secondary: Total Lung Capacity (TLC) at each time-point

End point title	Total Lung Capacity (TLC) at each time-point

End point description:

Total Lung Capacity (TLC) will be calculated from the mean Functional Residual Capacity (FRC) plus the highest value of the Inspiratory Capacity, both measured by bodyplethymography according to internationally accepted standards.

End point type	Secondary

End point timeframe:

week 2

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	59		
Units: Liters				
arithmetic mean (standard deviation)	-0.181 (± 0.3408)	-0.001 (± 0.3618)		

Statistical analyses

Statistical analysis title	Total Lung Capacity (TLC)
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0017
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.177
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.285
upper limit	-0.07

Secondary: Residual Volume (RVol) at each time-point

End point title	Residual Volume (RVol) at each time-point

End point description:

Residual Volume (RVol) will be calculated from the value of Total Lung Capacity (TLC) minus the highest value of the Slow Vital Capacity, both measured by bodyplethymography according to internationally accepted standards.

End point type	Secondary

End point timeframe:

week 2

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	59		
Units: Liters				
arithmetic mean (standard deviation)	-0.757 (± 0.5833)	0.012 (± 0.5141)		

Statistical analyses

Statistical analysis title	Residual Volume (RVol)
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.751
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.925
upper limit	-0.577

Secondary: Specific Airway Resistance (sRaw) at each time-point

End point title	Specific Airway Resistance (sRaw) at each time-point

End point description:

Specific Airway Resistance (sRaw) will be documented as effective resistance (sReff) calculated as the median of five acceptable measurements. Values will be measured by bodyplethymography according to internationally accepted standards.

End point type	Secondary

End point timeframe:

week 2

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	56	55		
Units: kilopascal (kPa)				
arithmetic mean (standard deviation)	1.887 (± 1.0979)	0.037 (± 1.0383)		

Statistical analyses

Statistical analysis title	Specific Airway Resistance (sRaw)
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-1.639
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.945
upper limit	-1.332

Secondary: Functional Residual Capacity (FRC) at each time-point	
End point title	Functional Residual Capacity (FRC) at each time-point
End point description:	
Functional Residual Capacity (FRC) will be calculated as the mean of three reproducible values as measured by bodyplethymography according to internationally accepted standards.	
End point type	Secondary
End point timeframe:	
week 2	

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	59		
Units: Liters				
arithmetic mean (standard deviation)	-0.656 (± 0.4602)	-0.015 (± 0.4257)		

Statistical analyses

Statistical analysis title	Functional Residual Capacity (FRC)
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.625

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.761
upper limit	-0.489

Secondary: Right ventricular (RV) and left ventricular (LV) ejection fraction (EF) at each time-point

End point title	Right ventricular (RV) and left ventricular (LV) ejection fraction (EF) at each time-point

End point description:

Right and left ventricular ejection fraction is the fraction of blood (in percent) pumped out of the heart's left and right ventricular chamber, respectively, with each heart beat and will be determined as measured by MRI.

End point type	Secondary

End point timeframe:

week 2

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	59		
Units: Percentage				
arithmetic mean (standard deviation)				
LV-EF|	1.893 (± 5.8486)	1.313 (± 5.4261)		
RV-EF|	2.046 (± 5.8746)	0.361 (± 6.1936)		

Statistical analyses

Statistical analysis title	Right and left ventricular ejection fraction

Statistical analysis description:

LV EF

Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.142
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	1.209

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.419
upper limit	2.836

Statistical analysis title	Right and left ventricular ejection fraction
Statistical analysis description:	
RV EF	
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1732
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	1.131
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.512
upper limit	2.774

Secondary: Left and right ventricular end-systolic volumeat each time-point	
End point title	Left and right ventricular end-systolic volumeat each time-point
End point description:	
Right ventricular end-systolic volume (RV-ESV) and left ventricular end-systolic volume (LV-ESV) is a measurement of the volume of blood in the heart’s right and left ventricular chamber, respectively, at the end of the heart's contraction and will be determined as measured by MRI.	
End point type	Secondary
End point timeframe:	
week 2	

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	59		
Units: ML				
arithmetic mean (standard deviation)				
LV-ESV|	1.898 (± 8.4565)	-2.283 (± 8.1489)		
RV-ESV|	2.183 (± 8.7063)	0.133 (± 9.3370)		

Statistical analyses

Statistical analysis title	(RV-ESV) and (LV-ESV)
Statistical analysis description: LV ESV	
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0437
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	2.241
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.066
upper limit	4.417

Statistical analysis title	(RV-ESV) and (LV-ESV)
Statistical analysis description: RV ESV	
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1236
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	2.095
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.591
upper limit	4.782

Secondary: Right ventricular enddiastolic volume at each time-point

End point title	Right ventricular enddiastolic volume at each time-point

End point description:

Right ventricular end-diastolic volume is a measurement of the volume of blood in the heart’s right

ventricular chamber at the end of the chamber's filling with blood and will be determined as measured by MRI.

End point type	Secondary

End point timeframe:

week 2

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	59		
Units: ML				
arithmetic mean (standard deviation)	12.323 (± 13.9683)	1.758 (± 14.7904)		

Statistical analyses

Statistical analysis title	Right ventricular end-diastolic volume
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	9.357
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.649
upper limit	14.065

Secondary: Cardiac output at each time-point, left and right ventricular cardiac output (LVCO and RVCO)

End point title	Cardiac output at each time-point, left and right ventricular cardiac output (LVCO and RVCO)

End point description:

Cardiac output is calculated as the heart rate multiplied by the stroke volume (= difference between ventricular enddiastolic volume and endsystolic volume) that will be determined as measured by MRI.

End point type	Secondary

End point timeframe:

week 2

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	59		
Units: Liter/min				
arithmetic mean (standard deviation)				
LVCO|	0.504 (± 0.7919)	0.119 (± 0.8970)		
RVCO|	0.517 (± 0.8063)	0.144 (± 0.9523)		

Statistical analyses

Statistical analysis title	Cardiac output
Statistical analysis description: RVCO	
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0182
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	0.281
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.512

Statistical analysis title	Cardiac output
Statistical analysis description: LVCO	
Comparison groups	QVA149 v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0032
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	0.337
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.118
upper limit	0.555

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: For the study duration of about 13 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Frequency threshold for reporting non-serious adverse events: 5 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: All data verified

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 May 2015	Echocardiographic measures were included as additional exploratory objectives. To account for blood pressure changes as potential confounder of ventricular function, blood pressure measurements were to be performed 4 times during MRI and the mean was considered during data analysis. Changes to the exclusion criteria were made as follows: a. To allow patients with stents to be enrolled in the study as stent material does not interfere with MRI and the indication for stent implantation does not per se influence the outcome of the study unless significant ischemic cardiac changes were present. b. To exclude patients with uncontrolled hypertension from the study. c. To allow patients with a history of hypersensitivity to i.v. contrast medium to participate in the study. In case patients suffered from such a hypersensitivity, the last MRI protocol sequence that required i.v. contrast medium was not performed.
14 July 2015	19F MRI technique was included as an optional measurement to assess regional pulmonary ventilation during steady state breathing. Hence, an additional explorative objective of regional lung 19F gas wash-out time was included in the protocol as optional measurement in a subgroup of patients
20 April 2016	The possibility of re-screening patients who failed the screening (before Visit 4) due to increased blood pressure (mean sitting SBP >160 mmHg and/or mean sitting DBP > 90 mmHg) was implemented in the exclusion criteria. Therefore, these patients were permitted to be re-screened in case they achieved controlled disease status following initiation or intensification of antihypertensive therapy

Notes:

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.

Due to EudraCT system limitations, which EMA is aware of, results of crossover studies are not accurately represented in this record. Please go to https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: