Clinical trial results:
Renin-Angiotensin System Quantification in patients treated with Aliskiren or Candesartan (RASQAL)

Summary

EudraCT number	2012-000250-55
Trial protocol	AT
Global end of trial date	25 January 2016

Results information

Result version number	v1 (current)
This version publication date	26 January 2020
First version publication date	26 January 2020

Trial information

Trial identification

Sponsor protocol code	RASQAL

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01827202
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Spitalgasse 23, Vienna, Austria,
Public contact	Study investigator, Medical University of Vienna, marlies.antlanger@kepleruniklinikum.at
Scientific contact	Study investigator, Medical University of Vienna, marlies.antlanger@kepleruniklinikum.at

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	25 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 January 2016
Global end of trial reached?	Yes
Global end of trial date	25 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the quantity of differences in the renin-angiotensin peptide profiles in patients receiving direct renin inhibition or angiotensin receptor blockade.

Protection of trial subjects:

Clinical and laboratory control one week after initiation of study medication. Biweekly clinical and laboratory controls thereafter. Patients were given the opportunity to contact study staff at all times by phone.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 December 2012
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	Austria: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	20
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients were recruited from the outpatient Nephrology clinic of the Medical University of Vienna. Patients were recruited from December 13th, 2012 to November 12th, 2015.

Pre-assignment

Screening details:

Inclusion criteria:
- Chronic kidney disease stages III-IV (defined by MDRD formula)
- Urinary albumin to creatinine ratio (UACR) >300mg/g, UACR >200mg/g if already receiving RAS blockade
- Hypertension
--> 2-week run-in phase after inclusion: standardization of blood pressure medication, no RAS-blocking agent

Period 1

Period 1 title	Baseline visit
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Candesartan

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Atacand
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

8 mg once daily for 4 weeks, thereafter 16 mg once daily for 4 weeks

Arm title	Aliskiren

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Rasilez
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg once daily for 4 weeks, thereafter 300 mg once daily for 4 weeks.

Number of subjects in period 1	Candesartan	Aliskiren
Started	12	12
Baseline visit	12	12
Completed	12	12

Period 2	
Period 2 title	Study end visit
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Candesartan

Arm description: -

Arm type	Comparator
Investigational medicinal product name	Atacand
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

8 mg once daily for 4 weeks, thereafter 16 mg once daily for 4 weeks

Arm title	Aliskiren

Arm description: -

Arm type	Intervention
Investigational medicinal product name	Rasilez
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg once daily for 4 weeks, thereafter 300 mg once daily for 4 weeks.

Number of subjects in period 2	Candesartan	Aliskiren
Started	12	12
Completed	12	12

Baseline characteristics

Reporting groups	
Reporting group title	Candesartan
Reporting group description: -	
Reporting group title	Aliskiren
Reporting group description: -	

Reporting group values	Candesartan	Aliskiren	Total
Number of subjects	12	12	24
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	54	51	
standard deviation	± 15	± 14	-
Gender categorical Units: Subjects			
Female	2	4	6
Male	10	8	18
Angiotensin I Units: pg/ml			
median	75.8	68.8	
inter-quartile range (Q1-Q3)	45.5 to 130.4	19.6 to 136.4	-
Angiotensin II Units: pg/ml			
median	109.6	65	
inter-quartile range (Q1-Q3)	32.4 to 164.6	34.4 to 132	-
Angiotensin 1-7 Units: pg/ml			
median	1.2	1.2	
inter-quartile range (Q1-Q3)	1.1 to 1.6	1.1 to 1.3	-

End points

End points reporting groups

Reporting group title	Candesartan
Reporting group description: -	
Reporting group title	Aliskiren
Reporting group description: -	
Reporting group title	Candesartan
Reporting group description: -	
Reporting group title	Aliskiren
Reporting group description: -	

Primary: Angiotensin I

End point title	Angiotensin I
End point description:	
End point type	Primary
End point timeframe:	
8 weeks	

End point values	Candesartan	Aliskiren	Candesartan	Aliskiren
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12[1]	12[2]	12[3]	12[4]
Units: pg/ml				
median (inter-quartile range (Q1-Q3))	332.8 (187.3 to 563)	6.8 (2.1 to 13.3)	75.8 (45.5 to 130.4)	68.8 (19.6 to 136.4)

Notes:

[1] - End of study

[2] - End of study

[3] - Baseline

[4] - Baseline

Statistical analyses

Statistical analysis title	Angiotensin I pre/post
Statistical analysis description:	
Comparison of Angiotensin I change with Candesartan versus Aliskiren treatment	
Comparison groups	Candesartan v Aliskiren v Candesartan v Aliskiren
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[5] - Wilcoxon signed-rank test was applied to compare Angiotensin change within the Candesartan and within the Aliskiren group.

Primary: Angiotensin II

End point title	Angiotensin II

End point description:

End point type	Primary

End point timeframe:

8 weeks

End point values	Candesartan	Aliskiren	Candesartan	Aliskiren
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12[6]	12[7]
Units: pg/ml				
median (inter-quartile range (Q1-Q3))	442.9 (292.2 to 635)	14.4 (1.7 to 28.2)	109.6 (32.4 to 164.6)	65 (34.4 to 132)

Notes:

[6] - Baseline

[7] - Baseline

Statistical analyses

Statistical analysis title	Angiotensin II pre/post

Statistical analysis description:

Comparison of Angiotensin II levels before and after treatment with Candesartan or Aliskiren

Comparison groups	Candesartan v Aliskiren v Candesartan v Aliskiren
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[8] - Wilcoxon signed-rank test was applied to compare Angiotensin II levels before and after Candesartan or Aliskiren treatment.

Primary: Angiotensin 1-7

End point title	Angiotensin 1-7

End point description:

End point type	Primary

End point timeframe:

8 weeks

End point values	Candesartan	Aliskiren	Candesartan	Aliskiren
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12[9]	12[10]
Units: pg/ml				
median (inter-quartile range (Q1-Q3))	1.3 (1.3 to 10.1)	1.2 (1.1 to 1.3)	1.2 (1.1 to 1.6)	1.2 (1.1 to 1.3)

Notes:

[9] - Baseline

[10] - Baseline

Statistical analyses

Statistical analysis title	Angiotensin 1-7 pre/post

Statistical analysis description:

Comparison of change in Angiotensin 1-7 with Candesartan versus Aliskiren use.

Comparison groups	Candesartan v Aliskiren v Candesartan v Aliskiren
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[11] - Wilcoxon signed-rank test was applied compare Angiotensin 1-7 levels before and after treatment with Candesartan and Aliskiren.

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Patients were assessed for (S)AEs at every study visit, i.e. after the run-in phase (= at baseline visit), 1 week after study medication initiation, 4 weeks after initiation, 6 weeks after initiation and at the study end visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15

Reporting groups

Reporting group title	Candesartan
Reporting group description: -	
Reporting group title	Aliskiren
Reporting group description: -	

Serious adverse events	Candesartan	Aliskiren	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Candesartan	Aliskiren	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	

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: Study duration was relatively short (8 weeks) and the study was carried out in a stable cohort of patients with a chronic disease with study medications with long-standing regulatory approval. No events/laboratory changes requiring reporting were detected/documented.

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