Clinical trial results:
A randomized, double-blind, placebo-controlled, multi-center study to assess the safety and efficacy of different oral doses of BAY 94-8862 in subjects with type 2 diabetes mellitus and the clinical diagnosis of diabetic nephropathy

Summary

EudraCT number	2012-004179-38
Trial protocol	AT SE FI NL DE NO HU PT DK BG IT ES PL CZ
Global end of trial date	07 August 2014

Results information

Result version number	v1
This version publication date	12 July 2016
First version publication date	08 August 2015

Trial information

Trial identification

Sponsor protocol code	BAY94-8862/16243

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01874431
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer HealthCare AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.com
Scientific contact	Therapeutic Area Head, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.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	07 August 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective of the study was to investigate the change of urinary albumin-to-creatinine ratio (UACR) after treatment with different oral doses of BAY94-8862 given once daily over 90 days.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy:

Standard of care for renal and cardiovascular disease (CVD) protection (i.e. according to local guidelines: angiotensin-converting enzyme inhibitor [ACEI] or angiotensin receptor blocker [ARB] and optimal antihypertensive therapy; statins, anti-platelets, and beta-blockers; and glycemic control).

Evidence for comparator: -

Actual start date of recruitment	12 June 2013
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	Australia: 17
Country: Number of subjects enrolled	Austria: 27
Country: Number of subjects enrolled	Bulgaria: 84
Country: Number of subjects enrolled	Canada: 38
Country: Number of subjects enrolled	Czech Republic: 27
Country: Number of subjects enrolled	Denmark: 71
Country: Number of subjects enrolled	Finland: 52
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Hong Kong: 7
Country: Number of subjects enrolled	Hungary: 25
Country: Number of subjects enrolled	Israel: 64
Country: Number of subjects enrolled	Italy: 82
Country: Number of subjects enrolled	Netherlands: 22
Country: Number of subjects enrolled	Norway: 7

Country: Number of subjects enrolled	Poland: 23
Country: Number of subjects enrolled	Portugal: 9
Country: Number of subjects enrolled	South Africa: 51
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Spain: 67
Country: Number of subjects enrolled	Sweden: 45
Country: Number of subjects enrolled	Taiwan: 22
Country: Number of subjects enrolled	United States: 43
Worldwide total number of subjects	823
EEA total number of subjects	569

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)	388
From 65 to 84 years	431
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 148 study centers in 23 countries, from 12 June 2013 (first subject, first visit) to 07 August 2014 (last subject, last visit). The randomization was stratified by region (Europe, North America, Asia, others [Australia, Israel, and South Africa]), and type of albuminuria at screening (very high or high albuminuria).

Pre-assignment

Screening details:

Of 1501 subjects screened, 823 were randomized at 128 study centers and 678 were screening failures. The reasons were not fulfilled inclusion-/exclusion criteria's (635 subjects), withdrawal by subjects (37 subjects), adverse event (2 subjects), physician decision (2 subjects), logistical difficulties (1 subject) and lost to follow-up (1 subject).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Finerenone (BAY94-8862) (1.25 mg)

Arm description:

1.25 milligram (mg) BAY94-8862 tablet once daily in the morning for 90 days.

Arm type	Experimental
Investigational medicinal product name	Finerenone
Investigational medicinal product code	BAY94-8862
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Immediate-release (IR) light orange film-coated tablets, oval (modified oblong), containing 1.25 mg BAY94-8862, were administrated once daily in the morning for 90 days.

Arm title	Finerenone (BAY94-8862) (2.5 mg)

Arm description:

2.5 mg BAY94-8862 tablet once daily in the morning for 90 days.

Arm type	Experimental
Investigational medicinal product name	Finerenone
Investigational medicinal product code	BAY94-8862
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

IR light orange film-coated tablets, oval (modified oblong), containing 2.5 mg BAY94-8862, were administrated once daily in the morning for 90 days.

Arm title	Finerenone (BAY94-8862) (5 mg)

Arm description:

5 mg BAY94-8862 tablet once daily in the morning for 90 days.

Arm type	Experimental

Investigational medicinal product name	Finerenone
Investigational medicinal product code	BAY94-8862
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

IR light orange film-coated tablets, oval (modified oblong), containing 5 mg BAY94-8862, were administrated once daily in the morning for 90 days.

Arm title	Finerenone (BAY94-8862) (7.5 mg)

Arm description:

7.5 mg BAY94-8862 tablet once daily in the morning for 90 days.

Arm type	Experimental
Investigational medicinal product name	Finerenone
Investigational medicinal product code	BAY 94-8862
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

IR light orange film-coated tablets, oval (modified oblong), containing 7.5 mg BAY94-8862, were administrated once daily in the morning for 90 days.

Arm title	Finerenone (BAY94-8862) (10 mg)

Arm description:

10 mg BAY94-8862 tablet once daily in the morning for 90 days.

Arm type	Experimental
Investigational medicinal product name	Finerenone
Investigational medicinal product code	BAY94-8862
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

IR light orange film-coated tablets, oval (modified oblong), containing 10 mg BAY94-8862, were administrated once daily in the morning for 90 days.

Arm title	Finerenone (BAY94-8862) (15 mg)

Arm description:

15 mg BAY94-8862 tablet once daily in the morning for 90 days.

Arm type	Experimental
Investigational medicinal product name	Finerenone
Investigational medicinal product code	BAY94-8862
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

IR light orange film-coated tablets, oval (modified oblong), containing 15 mg BAY94-8862, were administrated once daily in the morning for 90 days.

Arm title	Finerenone (BAY94-8862) (20 mg)

Arm description:

20 mg BAY94-8862 tablet once daily in the morning for 90 days

Arm type	Experimental

Investigational medicinal product name	Finerenone
Investigational medicinal product code	BAY94-8862
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

IR light orange film-coated tablets, oval (modified oblong), containing 20 mg BAY94-8862, were administrated once daily in the morning for 90 days.

Arm title	Placebo

Arm description:

Placebo tablet once daily in the morning for 90 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets (matching BAY94-8862 tablets) were administrated once daily in the morning for 90 days.

Number of subjects in period 1	Finerenone (BAY94-8862) (1.25 mg)	Finerenone (BAY94-8862) (2.5 mg)	Finerenone (BAY94-8862) (5 mg)
Started	96	92	100
Subjects received treatment	96	92	100
Completed	90	87	90
Not completed	6	5	10
Physician decision	-	-	1
Consent withdrawn by subject	-	-	1
Logistical difficulties	-	-	-
Protocol violation	1	1	1
Adverse event	5	4	6
Non-compliance	-	-	-
Lost to follow-up	-	-	1
Sponsor decision	-	-	-

Number of subjects in period 1	Finerenone (BAY94-8862) (7.5 mg)	Finerenone (BAY94-8862) (10 mg)	Finerenone (BAY94-8862) (15 mg)
Started	98	98	125
Subjects received treatment	97	98	125
Completed	91	90	114
Not completed	7	8	11
Physician decision	-	-	-
Consent withdrawn by subject	2	1	1
Logistical difficulties	-	-	-

Protocol violation	-	3	2
Adverse event	5	2	8
Non-compliance	-	1	-
Lost to follow-up	-	-	-
Sponsor decision	-	1	-

Number of subjects in period 1	Finerenone (BAY94-8862) (20 mg)	Placebo
Started	120	94
Subjects received treatment	119	94
Completed	112	90
Not completed	8	4
Physician decision	-	-
Consent withdrawn by subject	3	-
Logistical difficulties	1	-
Protocol violation	1	1
Adverse event	2	3
Non-compliance	1	-
Lost to follow-up	-	-
Sponsor decision	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Finerenone (BAY94-8862) (1.25 mg)
Reporting group description:	
1.25 milligram (mg) BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (2.5 mg)
Reporting group description:	
2.5 mg BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (5 mg)
Reporting group description:	
5 mg BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (7.5 mg)
Reporting group description:	
7.5 mg BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (10 mg)
Reporting group description:	
10 mg BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (15 mg)
Reporting group description:	
15 mg BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (20 mg)
Reporting group description:	
20 mg BAY94-8862 tablet once daily in the morning for 90 days	
Reporting group title	Placebo
Reporting group description:	
Placebo tablet once daily in the morning for 90 days.	

Reporting group values	Finerenone (BAY94-8862) (1.25 mg)	Finerenone (BAY94-8862) (2.5 mg)	Finerenone (BAY94-8862) (5 mg)
Number of subjects	96	92	100
Age categorical Units: Subjects			
18 - 64 years	44	39	53
65 - 84 years	51	53	46
>=85 years	1	0	1
Gender categorical Units: Subjects			
Female	18	14	29
Male	78	78	71

Reporting group values	Finerenone (BAY94-8862) (7.5 mg)	Finerenone (BAY94-8862) (10 mg)	Finerenone (BAY94-8862) (15 mg)
Number of subjects	98	98	125
Age categorical Units: Subjects			
18 - 64 years	51	42	56
65 - 84 years	46	55	69
>=85 years	1	1	0

Gender categorical Units: Subjects			
Female	18	21	27
Male	80	77	98

Reporting group values	Finerenone (BAY94-8862) (20 mg)	Placebo	Total
Number of subjects	120	94	823
Age categorical Units: Subjects			
18 - 64 years	52	51	388
65 - 84 years	68	43	431
>=85 years	0	0	4
Gender categorical Units: Subjects			
Female	30	25	182
Male	90	69	641

End points

End points reporting groups

Reporting group title	Finerenone (BAY94-8862) (1.25 mg)
Reporting group description:	
1.25 milligram (mg) BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (2.5 mg)
Reporting group description:	
2.5 mg BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (5 mg)
Reporting group description:	
5 mg BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (7.5 mg)
Reporting group description:	
7.5 mg BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (10 mg)
Reporting group description:	
10 mg BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (15 mg)
Reporting group description:	
15 mg BAY94-8862 tablet once daily in the morning for 90 days.	
Reporting group title	Finerenone (BAY94-8862) (20 mg)
Reporting group description:	
20 mg BAY94-8862 tablet once daily in the morning for 90 days	
Reporting group title	Placebo
Reporting group description:	
Placebo tablet once daily in the morning for 90 days.	
Subject analysis set title	Safety Analysis Set (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
SAF (N=821) included all randomized subjects who took at least one dose of study drug and with data after beginning of treatment.	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
FAS (N=812) included all subjects of the SAF who had baseline and at least one post-baseline urinary albumin-to-creatinine ratio (UACR) value.	

Primary: Change of Urinary Albumin-to-Creatinine Ratio (UACR) at Visit 90

End point title	Change of Urinary Albumin-to-Creatinine Ratio (UACR) at Visit 90
End point description:	
UACR is defined as the ratio: milligram of albumin per gram of creatinine. The UACR was measured at baseline, Day 30, Day 60 and Day 90. UACR was determined from 3 first morning void samples taken on 3 consecutive days. The UACR data were log transformed prior to analysis. FAS-population was used to evaluate this endpoint.	
End point type	Primary
End point timeframe:	
From baseline to 90 days	

End point values	Finerenone (BAY94-8862) (1.25 mg)	Finerenone (BAY94-8862) (2.5 mg)	Finerenone (BAY94-8862) (5 mg)	Finerenone (BAY94-8862) (7.5 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	92	98	96
Units: Ratio				
least squares mean (confidence interval 90%)	0.869 (0.772 to 0.979)	0.89 (0.786 to 1.009)	0.824 (0.73 to 0.929)	0.739 (0.653 to 0.835)

End point values	Finerenone (BAY94-8862) (10 mg)	Finerenone (BAY94-8862) (15 mg)	Finerenone (BAY94-8862) (20 mg)	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	123	117	94
Units: Ratio				
least squares mean (confidence interval 90%)	0.708 (0.627 to 0.8)	0.63 (0.563 to 0.705)	0.585 (0.523 to 0.654)	0.938 (0.829 to 1.061)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

To demonstrate a dose-dependent effect of finerenone, an analysis of covariance (ANCOVA) with factors treatment group, type of albuminuria at screening and region, and log-transformed baseline value as covariate nested within type of albuminuria at screening was performed in the FAS using a last-observation carried-forward (LOCF) method for missing observations.

Comparison groups	Finerenone (BAY94-8862) (1.25 mg) v Placebo
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1973
Method	t-test, 1-sided
Parameter estimate	Least square mean ratio
Point estimate	0.926
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.799
upper limit	1.074

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

To demonstrate a dose-dependent effect of finerenone, an ANCOVA with factors treatment group, type

of albuminuria at screening and region, and log-transformed baseline value as covariate nested within type of albuminuria at screening was performed in the FAS using a LOCF method for missing observations.

Comparison groups	Finerenone (BAY94-8862) (2.5 mg) v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2808
Method	t-test, 1-sided
Parameter estimate	Least square mean ratio
Point estimate	0.949
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.818
upper limit	1.101

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

To demonstrate a dose-dependent effect of finerenone, an ANCOVA with factors treatment group, type of albuminuria at screening and region, and log-transformed baseline value as covariate nested within type of albuminuria at screening was performed in the FAS using a LOCF method for missing observations.

Comparison groups	Finerenone (BAY94-8862) (5 mg) v Placebo
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0723
Method	t-test, 1-sided
Parameter estimate	Least square mean ratio
Point estimate	0.878
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.758
upper limit	1.017

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

To demonstrate a dose-dependent effect of finerenone, an ANCOVA with factors treatment group, type of albuminuria at screening and region, and log-transformed baseline value as covariate nested within type of albuminuria at screening was performed in the FAS using a LOCF method for missing observations.

Comparison groups	Finerenone (BAY94-8862) (7.5 mg) v Placebo

Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0039
Method	t-test, 1-sided
Parameter estimate	Least square mean ratio
Point estimate	0.787
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.68
upper limit	0.912

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

To demonstrate a dose-dependent effect of finerenone, an ANCOVA with factors treatment group, type of albuminuria at screening and region, and log-transformed baseline value as covariate nested within type of albuminuria at screening was performed in the FAS using a LOCF method for missing observations.

Comparison groups	Finerenone (BAY94-8862) (10 mg) v Placebo
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0009
Method	t-test, 1-sided
Parameter estimate	Least square mean ratio
Point estimate	0.755
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.651
upper limit	0.875

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

To demonstrate a dose-dependent effect of finerenone, an ANCOVA with factors treatment group, type of albuminuria at screening and region, and log-transformed baseline value as covariate nested within type of albuminuria at screening was performed in the FAS using a LOCF method for missing observations.

Comparison groups	Finerenone (BAY94-8862) (15 mg) v Placebo
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	t-test, 1-sided
Parameter estimate	Least square mean ratio
Point estimate	0.671

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.584
upper limit	0.772

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

To demonstrate a dose-dependent effect of finerenone, an ANCOVA with factors treatment group, type of albuminuria at screening and region, and log-transformed baseline value as covariate nested within type of albuminuria at screening was performed in the FAS using a LOCF method for missing observations.

Comparison groups	Finerenone (BAY94-8862) (20 mg) v Placebo
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	t-test, 1-sided
Parameter estimate	Least square mean ratio
Point estimate	0.624
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.542
upper limit	0.718

Secondary: Change From Baseline to Day 90 in Serum Potassium

End point title	Change From Baseline to Day 90 in Serum Potassium

End point description:

Safety data was reported in the SAF with evaluable subjects for this endpoint.

End point type	Secondary

End point timeframe:

From baseline to Day 90

End point values	Finerenone (BAY94-8862) (1.25 mg)	Finerenone (BAY94-8862) (2.5 mg)	Finerenone (BAY94-8862) (5 mg)	Finerenone (BAY94-8862) (7.5 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	90	87	85	88
Units: millimole per liter				
least squares mean (confidence interval 90%)	0.109 (0.03 to 0.187)	0.123 (0.043 to 0.203)	0.202 (0.122 to 0.282)	0.127 (0.047 to 0.207)

End point values	Finerenone (BAY94-8862) (10 mg)	Finerenone (BAY94-8862) (15 mg)	Finerenone (BAY94-8862) (20 mg)	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	109	112	90
Units: millimole per liter				
least squares mean (confidence interval 90%)	0.167 (0.087 to 0.248)	0.238 (0.165 to 0.31)	0.188 (0.116 to 0.259)	0.002 (-0.077 to 0.081)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Finerenone (BAY94-8862) (1.25 mg) v Placebo
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0428
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	0.107
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.003
upper limit	0.21

Statistical analysis title	Statistical analysis 2
Comparison groups	Finerenone (BAY94-8862) (2.5 mg) v Placebo
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0223
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	0.121
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.017
upper limit	0.225

Statistical analysis title	Statistical analysis 3
Comparison groups	Finerenone (BAY94-8862) (5 mg) v Placebo

Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.096
upper limit	0.305

Statistical analysis title	Statistical analysis 4
Comparison groups	Finerenone (BAY94-8862) (7.5 mg) v Placebo
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0181
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	0.125
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.021
upper limit	0.229

Statistical analysis title	Statistical analysis 5
Comparison groups	Finerenone (BAY94-8862) (10 mg) v Placebo
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0019
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	0.166
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.061
upper limit	0.27

Statistical analysis title	Statistical analysis 6

Comparison groups	Finerenone (BAY94-8862) (15 mg) v Placebo
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	0.236
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.137
upper limit	0.334

Statistical analysis title	Statistical analysis 7
Comparison groups	Finerenone (BAY94-8862) (20 mg) v Placebo
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	0.186
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.088
upper limit	0.284

Secondary: Change From Baseline to Day 90 in Renal Function

End point title	Change From Baseline to Day 90 in Renal Function

End point description:

An estimated glomerular filtration rate (eGFR) indicates the renal function. An eGFR was calculated based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. Safety data was reported in the SAF with evaluable subjects for this endpoint.

End point type	Secondary

End point timeframe:

From baseline to Day 90

End point values	Finerenone (BAY94-8862) (1.25 mg)	Finerenone (BAY94-8862) (2.5 mg)	Finerenone (BAY94-8862) (5 mg)	Finerenone (BAY94-8862) (7.5 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	90	87	85	88
Units: mL/min/1.73m^2				
least squares mean (confidence interval 90%)	-2.364 (-4.311 to -0.418)	-3.189 (-5.164 to -1.213)	-2.497 (-4.475 to -0.518)	-3.378 (-5.341 to -1.415)

End point values	Finerenone (BAY94-8862) (10 mg)	Finerenone (BAY94-8862) (15 mg)	Finerenone (BAY94-8862) (20 mg)	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	113	112	90
Units: mL/min/1.73m^2				
least squares mean (confidence interval 90%)	-4.192 (-6.181 to -2.202)	-3.806 (-5.563 to -2.05)	-4.024 (-5.792 to -2.256)	-1.578 (-3.53 to 0.373)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Finerenone (BAY94-8862) (1.25 mg) v Placebo
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5454
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	-0.786
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.337
upper limit	1.765

Statistical analysis title	Statistical analysis 2
Comparison groups	Finerenone (BAY94-8862) (2.5 mg) v Placebo
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2186
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	-1.61

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.177
upper limit	0.957

Statistical analysis title	Statistical analysis 3
Comparison groups	Finerenone (BAY94-8862) (5 mg) v Placebo
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4859
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	-0.918
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.503
upper limit	1.667

Statistical analysis title	Statistical analysis 4
Comparison groups	Finerenone (BAY94-8862) (7.5 mg) v Placebo
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1677
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.358
upper limit	0.759

Statistical analysis title	Statistical analysis 5
Comparison groups	Finerenone (BAY94-8862) (10 mg) v Placebo

Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0462
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	-2.613
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.183
upper limit	-0.044

Statistical analysis title	Statistical analysis 6
Comparison groups	Finerenone (BAY94-8862) (15 mg) v Placebo
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0705
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	-2.228
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.643
upper limit	0.187

Statistical analysis title	Statistical analysis 7
Comparison groups	Finerenone (BAY94-8862) (20 mg) v Placebo
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.048
Method	t-test, 2-sided
Parameter estimate	Least squares mean difference
Point estimate	-2.446
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.869
upper limit	-0.022

Secondary: Change in Health-Related Quality of Life (HRQoL) (Kidney Disease QOL

[KDQOL]-36 Questionnaire)	
End point title	Change in Health-Related Quality of Life (HRQoL) (Kidney Disease QOL [KDQOL]-36 Questionnaire)

End point description:

The KDQOL-36 is a specific measure of HRQoL for chronic kidney disease (CKD) that includes effects and burden of kidney disease as well as physical and mental health scores. Index score ranges from 0 (serve problems in all items) to 100 (no problem in all items). FAS-population was used to evaluate this endpoint. "Effects of Kidney disease" subscore was analyzed.

End point type	Secondary

End point timeframe:

From baseline to Day 90

End point values	Finerenone (BAY94-8862) (1.25 mg)	Finerenone (BAY94-8862) (2.5 mg)	Finerenone (BAY94-8862) (5 mg)	Finerenone (BAY94-8862) (7.5 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[1]	84[2]	87[3]	89[4]
Units: scores on a scale				
least squares mean (confidence interval 95%)	-2.116 (-4.521 to 0.289)	0.104 (-2.369 to 2.577)	-1.229 (-3.643 to 1.185)	-1.185 (-3.597 to 1.226)

Notes:

[1] - FAS with evaluable subjects for this end point.

[2] - FAS with evaluable subjects for this end point.

[3] - FAS with evaluable subjects for this end point.

[4] - FAS with evaluable subjects for this end point.

End point values	Finerenone (BAY94-8862) (10 mg)	Finerenone (BAY94-8862) (15 mg)	Finerenone (BAY94-8862) (20 mg)	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88[5]	113[6]	109[7]	89[8]
Units: scores on a scale				
least squares mean (confidence interval 95%)	-2.596 (-5.049 to -0.142)	0.112 (-2.054 to 2.278)	0.058 (-2.146 to 2.263)	0.747 (-1.684 to 3.178)

Notes:

[5] - FAS with evaluable subjects for this end point.

[6] - FAS with evaluable subjects for this end point.

[7] - FAS with evaluable subjects for this end point.

[8] - FAS with evaluable subjects for this end point.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Finerenone (BAY94-8862) (1.25 mg) v Placebo
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0757
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-2.863

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.022
upper limit	0.297

Statistical analysis title	Statistical analysis 2
Comparison groups	Finerenone (BAY94-8862) (2.5 mg) v Placebo
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6941
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-0.643
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.851
upper limit	2.565

Statistical analysis title	Statistical analysis 3
Comparison groups	Finerenone (BAY94-8862) (5 mg) v Placebo
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2228
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-1.976
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.155
upper limit	1.203

Statistical analysis title	Statistical analysis 4
Comparison groups	Finerenone (BAY94-8862) (7.5 mg) v Placebo

Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2313
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-1.932
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.098
upper limit	1.234

Statistical analysis title	Statistical analysis 5
Comparison groups	Finerenone (BAY94-8862) (10 mg) v Placebo
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0386
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-3.342
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.509
upper limit	-0.176

Statistical analysis title	Statistical analysis 6
Comparison groups	Finerenone (BAY94-8862) (15 mg) v Placebo
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.677
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-0.634
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.624
upper limit	2.355

Statistical analysis title	Statistical analysis 7

Comparison groups	Finerenone (BAY94-8862) (20 mg) v Placebo
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6536
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-0.688
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.699
upper limit	2.322

Secondary: Change in Health-Related Quality of Life (EuroQol Group 5-Dimension, 3-Level [EQ-5D-3L] Questionnaire)

End point title	Change in Health-Related Quality of Life (EuroQol Group 5-Dimension, 3-Level [EQ-5D-3L] Questionnaire)

End point description:

EQ-5D-3L questionnaires consist of the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The EQ-5D-3L descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 3 levels: no problems, some problems, extreme problems. FAS-population was used to evaluate this endpoint. EQ VAS was analzyed for this endpoint and it ranges from 0 (worst possible health state) to 100 (best possible health state).

End point type	Secondary

End point timeframe:

From baseline to Day 90

End point values	Finerenone (BAY94-8862) (1.25 mg)	Finerenone (BAY94-8862) (2.5 mg)	Finerenone (BAY94-8862) (5 mg)	Finerenone (BAY94-8862) (7.5 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[9]	83[10]	86[11]	89[12]
Units: scores on a scale				
least squares mean (confidence interval 95%)	1.381 (-1.22 to 3.982)	3.888 (1.208 to 6.568)	3.124 (0.494 to 5.754)	2.851 (0.241 to 5.461)

Notes:

[9] - FAS with evaluable subjects for this endpoint.

[10] - FAS with evaluable subjects for this endpoint.

[11] - FAS with evaluable subjects for this endpoint.

[12] - FAS with evaluable subjects for this endpoint.

End point values	Finerenone (BAY94-8862) (10 mg)	Finerenone (BAY94-8862) (15 mg)	Finerenone (BAY94-8862) (20 mg)	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[13]	112[14]	109[15]	88[16]
Units: scores on a scale				
least squares mean (confidence interval 95%)	2.698 (0.026 to 5.37)	2.743 (0.394 to 5.092)	1.914 (-0.465 to 4.292)	4.425 (1.794 to 7.057)

Notes:
[13] - FAS with evaluable subjects for this endpoint.
[14] - FAS with evaluable subjects for this endpoint.
[15] - FAS with evaluable subjects for this endpoint.
[16] - FAS with evaluable subjects for this endpoint.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Finerenone (BAY94-8862) (1.25 mg) v Placebo
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0816
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-3.044
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.471
upper limit	0.383

Statistical analysis title	Statistical analysis 2
Comparison groups	Finerenone (BAY94-8862) (2.5 mg) v Placebo
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7625
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-0.537
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.027
upper limit	2.953

Statistical analysis title	Statistical analysis 3
Comparison groups	Finerenone (BAY94-8862) (5 mg) v Placebo

Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4603
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-1.301
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.759
upper limit	2.157

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo v Finerenone (BAY94-8862) (7.5 mg)
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3678
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-1.574
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.004
upper limit	1.855

Statistical analysis title	Statistical analysis 5
Comparison groups	Finerenone (BAY94-8862) (10 mg) v Placebo
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3279
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-1.727
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.191
upper limit	1.736

Statistical analysis title	Statistical analysis 6

Comparison groups	Finerenone (BAY94-8862) (15 mg) v Placebo
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3102
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-1.682
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.935
upper limit	1.57

Statistical analysis title	Statistical analysis 7
Comparison groups	Finerenone (BAY94-8862) (20 mg) v Placebo
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1317
Method	t-test, 2-sided
Parameter estimate	Least square mean difference
Point estimate	-2.511
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.778
upper limit	0.755

Adverse events

Adverse events information	
Timeframe for reporting adverse events: TEAEs collection starts with the first intake of study drug until 3 days after last study drug.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Finerenone (BAY 94-8862) (1.25 mg)
Reporting group description: 1.25 milligram (mg) BAY 94-8862 tablet once daily in the morning for 90 days	
Reporting group title	Finerenone (BAY 94-8862)(2.5 mg)
Reporting group description: 2.5 mg BAY 94-8862 tablet once daily in the morning for 90 days	
Reporting group title	Finerenone (BAY 94-8862)(5 mg)
Reporting group description: 5 mg BAY 94-8862 tablet once daily in the morning for 90 days	
Reporting group title	Finerenone (BAY 94-8862)(7.5 mg)
Reporting group description: 7.5 mg BAY 94-8862 tablet once daily in the morning for 90 days	
Reporting group title	Finerenone (BAY 94-8862)(10 mg)
Reporting group description: 10 mg BAY 94-8862 tablet once daily in the morning for 90 days	
Reporting group title	Finerenone (BAY 94-8862)(15 mg)
Reporting group description: 15 mg BAY 94-8862 tablet once daily in the morning for 90 days	
Reporting group title	Finerenone (BAY 94-8862)(20 mg)
Reporting group description: 20 mg BAY 94-8862 tablet once daily in the morning for 90 days	
Reporting group title	Placebo
Reporting group description: Placebo tablet once daily in the morning for 90 days	

Serious adverse events	Finerenone (BAY 94-8862) (1.25 mg)	Finerenone (BAY 94-8862)(2.5 mg)	Finerenone (BAY 94-8862)(5 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 96 (5.21%)	3 / 92 (3.26%)	7 / 100 (7.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			

subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 96 (1.04%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery stenosis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Coronary artery bypass			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toe amputation			
subjects affected / exposed	1 / 96 (1.04%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Local swelling			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 96 (0.00%)	1 / 92 (1.09%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Blood potassium increased			
subjects affected / exposed	0 / 96 (0.00%)	1 / 92 (1.09%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic enzymes increased			
subjects affected / exposed	0 / 96 (0.00%)	1 / 92 (1.09%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Subdural haemorrhage			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			

subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular disorder			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 96 (1.04%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Subcutaneous abscess			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 96 (0.00%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	2 / 96 (2.08%)	0 / 92 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 96 (1.04%)	0 / 92 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Finerenone (BAY 94-8862)(7.5 mg)	Finerenone (BAY 94-8862)(10 mg)	Finerenone (BAY 94-8862)(15 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 97 (8.25%)	2 / 98 (2.04%)	6 / 125 (4.80%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Bladder cancer			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 97 (1.03%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery stenosis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Coronary artery bypass			
subjects affected / exposed	1 / 97 (1.03%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toe amputation			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Local swelling			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			

subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood potassium increased			
subjects affected / exposed	1 / 97 (1.03%)	0 / 98 (0.00%)	2 / 125 (1.60%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic enzymes increased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Subdural haemorrhage			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 97 (0.00%)	1 / 98 (1.02%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 97 (1.03%)	1 / 98 (1.02%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 97 (1.03%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular disorder			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 97 (1.03%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal impairment			

subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Subcutaneous abscess			
subjects affected / exposed	1 / 97 (1.03%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 97 (1.03%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 97 (0.00%)	1 / 98 (1.02%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	1 / 97 (1.03%)	0 / 98 (0.00%)	2 / 125 (1.60%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Finerenone (BAY 94-8862)(20 mg)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 119 (3.36%)	3 / 94 (3.19%)	

number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Coronary artery bypass			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toe amputation			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Local swelling			
subjects affected / exposed	0 / 119 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Non-cardiac chest pain			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood potassium increased			
subjects affected / exposed	1 / 119 (0.84%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic enzymes increased			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Subdural haemorrhage			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 119 (0.84%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			

subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 119 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular disorder			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 119 (0.00%)	1 / 94 (1.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Subcutaneous abscess			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	2 / 119 (1.68%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Finerenone (BAY 94-8862) (1.25 mg)	Finerenone (BAY 94-8862)(2.5 mg)	Finerenone (BAY 94-8862)(5 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 96 (14.58%)	7 / 92 (7.61%)	13 / 100 (13.00%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 96 (6.25%)	1 / 92 (1.09%)	3 / 100 (3.00%)
occurrences (all)	6	1	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 96 (5.21%)	2 / 92 (2.17%)	4 / 100 (4.00%)
occurrences (all)	5	2	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 96 (7.29%)	4 / 92 (4.35%)	8 / 100 (8.00%)
occurrences (all)	7	4	8

Non-serious adverse events	Finerenone (BAY 94-8862)(7.5 mg)	Finerenone (BAY 94-8862)(10 mg)	Finerenone (BAY 94-8862)(15 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 97 (11.34%)	10 / 98 (10.20%)	11 / 125 (8.80%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 97 (1.03%)	3 / 98 (3.06%)	5 / 125 (4.00%)
occurrences (all)	1	3	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 97 (2.06%)	2 / 98 (2.04%)	3 / 125 (2.40%)
occurrences (all)	2	2	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 97 (9.28%)	5 / 98 (5.10%)	4 / 125 (3.20%)
occurrences (all)	9	5	4

Non-serious adverse events	Finerenone (BAY 94-8862)(20 mg)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 119 (10.08%)	8 / 94 (8.51%)	
Nervous system disorders			
Dizziness			

subjects affected / exposed occurrences (all)	1 / 119 (0.84%) 1	2 / 94 (2.13%) 2	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 5 / 119 (4.20%) 5	 2 / 94 (2.13%) 2	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 8 / 119 (6.72%) 9	 5 / 94 (5.32%) 6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2013	Amendment 1 was implemented globally. In this amendment changes to ensure consistency within the document and the central and local laboratory as well as clarifications of the study procedure have been implemented.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported