Clinical trial results:
Relative bioavailability study to investigate the pharmacokinetics, safety and tolerability of single oral doses of finerenone 1.25 mg and 5 X 0.25 mg oro-dispersible tablet (pediatric formulation) in comparison to 10 mg tablet (adult formulation) in the fasting condition and to investigate the effect of a high fat, high calorie meal on 1.25 mg oro-dispersible tablet in healthy male subjects in a randomized, open-label, four-fold crossover design

Summary

EudraCT number	2016-002895-29
Trial protocol	DE
Global end of trial date	17 March 2017

Results information

Result version number	v1 (current)
This version publication date	25 October 2017
First version publication date	25 October 2017

Trial information

Trial identification

Sponsor protocol code	BAY94-8862/18290

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02956109
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, D-51368 Leverkusen, Germany,
Public contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001623-PIP01-14
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 March 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to:
• investigate the relative bioavailability of a single oral dose of 1.25 milligram (mg) finerenone (BAY94-8862) oro-dispersible tablet (ODT) and 5 X 0.25 mg ODTs (pediatric formulation) in comparison to 10 mg finerenone (adult formulation) tablet in the fasting condition,
• investigate the effect of a high fat, high calorie meal on the pharmacokinetics after a single oral dose of 1.25 mg finerenone ODT,
• investigate whether the finerenone ODTs are palatable and swallowable by using a questionnaire regarding overall impression, appearance, smell, taste, texture, and swallowability.

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: -

Evidence for comparator: -

Actual start date of recruitment	16 November 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	16
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at one study center in Germany, between 16 November 2016 (first subject first visit) and 22 December 2016 (last subject last visit).

Pre-assignment

Screening details:

Overall, 33 subjects were screened, of these 17 subjects were not included in the study; 13 were screen failures, 1 subject was lost to follow-up and 3 subjects were qualified but not needed. A total of 16 subjects were randomized and treated in a cross-over fashion, during the respective intervention periods (1st, 2nd, 3rd and 4th).

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment A-C-B-D

Arm description:

Subjects who followed treatment sequence A-C-B-D were reported.
Subjects received a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the first intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the second intervention period; followed by a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the third intervention period; and then a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

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

Dosage and administration details:

Treatment A: Subjects received a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state.
Treatment C: Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state.
Treatment B: Subjects received a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state.
Treatment D: Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state).

Arm title	Treatment B-A-D-C

Arm description:

Subjects who followed treatment sequence B-A-D-C were reported.
Subjects received a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the first intervention period; followed by a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the second intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the third intervention period; and then a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

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

Dosage and administration details:

Treatment B: Subjects received a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state.
Treatment A: Subjects received a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state.
Treatment D: Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state).
Treatment C: Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state.

Arm title	Treatment C-D-A-B

Arm description:

Subjects who followed treatment sequence C-D-A-B were reported.
Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the first intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the second intervention period; followed by a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the third intervention period; and then a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

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

Dosage and administration details:

Treatment C: Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state.
Treatment D: Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state).
Treatment A: Subjects received a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state.
Treatment B: Subjects received a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state.

Arm title	Treatment D-B-C-A

Arm description:

Subjects who followed treatment sequence D-B-C-A were reported.
Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the first intervention period; followed by a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the second intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the third intervention period; and then a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

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

Dosage and administration details:

Treatment D: Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state).
Treatment B: Subjects received a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state.
Treatment C: Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state.
Treatment A: Subjects received a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state.

Number of subjects in period 1	Treatment A-C-B-D	Treatment B-A-D-C	Treatment C-D-A-B
Started	4	4	4
Completed	3	4	4
Not completed	1	0	0
Adverse event	1	-	-

Number of subjects in period 1	Treatment D-B-C-A
Started	4
Completed	4
Not completed	0
Adverse event	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment A-C-B-D

Reporting group description:

Subjects who followed treatment sequence A-C-B-D were reported.
Subjects received a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the first intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the second intervention period; followed by a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the third intervention period; and then a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

Reporting group title	Treatment B-A-D-C

Reporting group description:

Subjects who followed treatment sequence B-A-D-C were reported.
Subjects received a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the first intervention period; followed by a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the second intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the third intervention period; and then a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

Reporting group title	Treatment C-D-A-B

Reporting group description:

Subjects who followed treatment sequence C-D-A-B were reported.
Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the first intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the second intervention period; followed by a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the third intervention period; and then a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

Reporting group title	Treatment D-B-C-A

Reporting group description:

Subjects who followed treatment sequence D-B-C-A were reported.
Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the first intervention period; followed by a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the second intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the third intervention period; and then a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

Reporting group values	Treatment A-C-B-D	Treatment B-A-D-C	Treatment C-D-A-B
Number of subjects	4	4	4
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	27.8	36.8	31
standard deviation	± 4.3	± 7.7	± 4.1

Gender categorical Units: Subjects			
Male	4	4	4

Reporting group values	Treatment D-B-C-A	Total	
Number of subjects	4	16	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	28.5		
standard deviation	± 3.3	-	
Gender categorical Units: Subjects			
Male	4	16	

End points

End points reporting groups

Reporting group title	Treatment A-C-B-D

Reporting group description:

Subjects who followed treatment sequence A-C-B-D were reported.
Subjects received a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the first intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the second intervention period; followed by a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the third intervention period; and then a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

Reporting group title	Treatment B-A-D-C

Reporting group description:

Subjects who followed treatment sequence B-A-D-C were reported.
Subjects received a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the first intervention period; followed by a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the second intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the third intervention period; and then a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

Reporting group title	Treatment C-D-A-B

Reporting group description:

Subjects who followed treatment sequence C-D-A-B were reported.
Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the first intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the second intervention period; followed by a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the third intervention period; and then a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

Reporting group title	Treatment D-B-C-A

Reporting group description:

Subjects who followed treatment sequence D-B-C-A were reported.
Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) (Treatment D) in the first intervention period; followed by a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state (Treatment B) in the second intervention period; followed by a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state (Treatment C) in the third intervention period; and then a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state (Treatment A) in the fourth intervention period. A wash-out phase of at least 72 hours was maintained between the finerenone administrations.

Subject analysis set title	Safety Analysis Set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

SAF included all subjects who received at least one dose of the study medication (N= 16).

Subject analysis set title	Pharmacokinetics Analysis Set (PKS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PKS included all subjects with valid pharmacokinetic profiles for at least two of the treatments relevant for comparison (that is treatment A and B or treatment A and C or treatment C and D or treatment B and C) were included (N= 16).

Subject analysis set title	Finerenone, 10 mg tablet, fasted
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a single oral dose of 10 mg (1 X 10 mg) finerenone tablet in fasted state during any of

the intervention periods (N= 16).

Subject analysis set title	Finerenone, 5 X 0.25 mg ODTs, fasted
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a single oral dose of 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state during any of the intervention periods (N= 16).

Subject analysis set title	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state during any of the intervention periods (N= 16).

Subject analysis set title	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a single oral dose of 1.25 mg (1 X 1.25 mg) finerenone ODT after a standardized high-fat, high-calorie American breakfast (fed state) during any of the intervention periods (N= 15).

Primary: Area Under the Concentration Versus Time Curve From Zero to Infinity Divided by Dose (AUC/D) After Single Dose of Finerenone in Plasma

End point title	Area Under the Concentration Versus Time Curve From Zero to Infinity Divided by Dose (AUC/D) After Single Dose of Finerenone in Plasma

End point description:

Area under the concentration versus time curve from zero to infinity divided by dose in plasma after single dose of finerenone was calculated. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Primary

End point timeframe:

0 hour (pre-dose) to 24 hours post-dose of finerenone

End point values	Finerenone, 10 mg tablet, fasted	Finerenone, 5 X 0.25 mg ODTs, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16[1]	16[2]	16[3]	14[4]
Units: hour per liter * 10^-3 (h/L*10^-3)				
geometric mean (geometric coefficient of variation)	17.1 (± 29.9)	16 (± 28)	16.9 (± 30.8)	19.9 (± 31.5)

Notes:

[1] - PKS

[2] - PKS

[3] - PKS

[4] - PKS with evaluable subjects for this endpoint

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Logarithms of AUC/D were analyzed using analysis of variance (ANOVA) including sequence, subject (sequence), period, and treatment effects. Least square (LS)-Means and exploratory 90 percent (%) confidence intervals (CIs) for ratio C/A (1.25 mg [1 X 1.25 mg] ODT fasted/10 mg tablet fasted) were calculated by re-transformation of logarithmic data by intra-individual standard deviation of the ANOVA.

Database auto-calculates total number of subjects erroneously, analysed number of subjects were 16

Comparison groups	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted v Finerenone, 10 mg tablet, fasted
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	0.9888
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9221
upper limit	1.0604

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Logarithms of AUC/D were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. LS-Means and exploratory 90 % CIs for ratio B/A (1.25 mg [5 X 0.25 mg] ODT fasted/10 mg tablet fasted) were calculated by re-transformation of logarithmic data by intra-individual standard deviation of the ANOVA. Database auto-calculates total number of subjects erroneously, analysed number of subjects were 16.

Comparison groups	Finerenone, 5 X 0.25 mg ODTs, fasted v Finerenone, 10 mg tablet, fasted
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	0.9388
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8755
upper limit	1.0068

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Logarithms of AUC/D were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. LS-Means and exploratory 90 % CIs for ratio B/C (1.25 mg [5 X 0.25 mg] ODT fasted/1.25 mg [1 X 1.25 mg] ODT fasted) were calculated by re-transformation of logarithmic data by intra-individual standard deviation of the ANOVA. Database auto-calculates total number of subjects erroneously, analysed number of subjects were 16.

Comparison groups	Finerenone, 5 X 0.25 mg ODTs, fasted v Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	0.9495
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8854
upper limit	1.0182

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Logarithms of AUC/D were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. LS-Means and exploratory 90 % CIs for ratio D/C (1.25 mg [1 X 1.25 mg] ODT fed/1.25 mg [1 X 0.25 mg] ODT, fasted) were calculated by re-transformation of logarithmic data by intra-individual standard deviation of the ANOVA. Database auto-calculates total number of subjects erroneously, analysed number of subjects were 14.

Comparison groups	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed v Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	1.2075
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.1222
upper limit	1.2993

Primary: Maximum Observed Finerenone Concentration in Measured Matrix Divided by Dose (Cmax/D) After Single Dose Administration of Finerenone

End point title	Maximum Observed Finerenone Concentration in Measured Matrix Divided by Dose (Cmax/D) After Single Dose Administration of Finerenone

End point description:

Maximum observed finerenone concentration in measured matrix divided by dose after single dose administration of finerenone was calculated. Geometric mean and percentage geometric coefficient of variation (%CV)
were reported.

End point type	Primary

End point timeframe:

0 hour (pre-dose) to 24 hours post-dose of finerenone

End point values	Finerenone, 10 mg tablet, fasted	Finerenone, 5 X 0.25 mg ODTs, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16[5]	16[6]	16[7]	14[8]
Units: per liter * 10^-3 (/L*10^-3)				
geometric mean (geometric coefficient of variation)	7.27 (± 31.1)	7.14 (± 29.8)	7.12 (± 29.2)	5.04 (± 50.1)

Notes:

[5] - PKS

[6] - PKS

[7] - PKS

[8] - PKS with evaluable subjects for this endpoint

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Logarithms of Cmax/D were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. LS-Means and exploratory 90 % CIs for ratio C/A (1.25 mg [1 X 1.25 mg] ODT fasted/10 mg tablet fasted) were calculated by re-transformation of logarithmic data by intra-individual standard deviation of the ANOVA. Database auto-calculates total number of subjects erroneously, analysed number of subjects were 16.

Comparison groups	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted v Finerenone, 10 mg tablet, fasted
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	0.979
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8492
upper limit	1.1286

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Logarithms of Cmax/D were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. LS-Means and exploratory 90 % CIs for ratio B/A (1.25 mg [5 X 0.25 mg] ODT fasted/10 mg tablet fasted) were calculated by re-transformation of logarithmic data by intra-individual standard deviation of the ANOVA. Database auto-calculates total number of subjects erroneously, analysed number of subjects were 16.

Comparison groups	Finerenone, 5 X 0.25 mg ODTs, fasted v Finerenone, 10 mg tablet, fasted
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	0.9822

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.852
upper limit	1.1322

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Logarithms of Cmax/D were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. LS-Means and exploratory 90 % CIs for ratio B/C (1.25 mg [5 X 0.25 mg] ODT fasted/1.25 mg [1 X 1.25 mg] ODT fasted) were calculated by re-transformation of logarithmic data by intra-individual standard deviation of the ANOVA. Database auto-calculates total number of subjects erroneously, analysed number of subjects were 16.

Comparison groups	Finerenone, 5 X 0.25 mg ODTs, fasted v Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	1.0032
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.873
upper limit	1.1565

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Logarithms of Cmax/D were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. LS-Means and exploratory 90 % CIs for ratio D/C (1.25 mg [1 X 1.25 mg] ODT fed/1.25 mg [1 X 0.25 mg] ODT, fasted) were calculated by re-transformation of logarithmic data by intra-individual standard deviation of the ANOVA. Database auto-calculates total number of subjects erroneously, analysed number of subjects were 14.

Comparison groups	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed v Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	LS-Mean
Point estimate	0.7155
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.6164
upper limit	0.8306

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly and another serious or important medical event as judged by the investigator. TEAEs were defined as AEs that started or worsened up to 3 days after the last finerenone dose administration.

End point type	Secondary

End point timeframe:

From start of study treatment up to 3 days after the last finerenone dose administration

End point values	Finerenone, 10 mg tablet, fasted	Finerenone, 5 X 0.25 mg ODTs, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16[9]	16[10]	16[11]	15[12]
Units: subjects				
TEAE	1	1	2	0
TESAE	0	0	0	0

Notes:

[9] - SAF

[10] - SAF

[11] - SAF

[12] - SAF

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Area Under the Concentration Versus Time Curve From Zero to Infinity (AUC) After Single Dose of Finerenone in Plasma

End point title	Area Under the Concentration Versus Time Curve From Zero to Infinity (AUC) After Single Dose of Finerenone in Plasma

End point description:

Area under the concentration versus time curve from zero to infinity after single dose of finerenone in plasma was calculated. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Other pre-specified

End point timeframe:

0 hour (pre-dose) to 24 hours post-dose of finerenone

End point values	Finerenone, 10 mg tablet, fasted	Finerenone, 5 X 0.25 mg ODTs, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16[13]	16[14]	16[15]	14[16]
Units: microgram*hour per liter (mcg*h/L)				
geometric mean (geometric coefficient of variation)	171 (± 29.9)	20 (± 28)	21.1 (± 30.8)	24.8 (± 31.5)

Notes:

[13] - PKS

[14] - PKS

[15] - PKS

[16] - PKS with evaluable subjects for this endpoint

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Maximum Observed Drug Concentration (Cmax) After Single Dose Administration of Finerenone in Plasma

End point title	Maximum Observed Drug Concentration (Cmax) After Single Dose Administration of Finerenone in Plasma

End point description:

Maximum observed drug concentration in plasma after single dose of finerenone was calculated. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Other pre-specified

End point timeframe:

0 hour (pre-dose) to 24 hours post-dose of finerenone

End point values	Finerenone, 10 mg tablet, fasted	Finerenone, 5 X 0.25 mg ODTs, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16[17]	16[18]	16[19]	14[20]
Units: microgram per liter (mcg/L)				
geometric mean (geometric coefficient of variation)	72.7 (± 31.1)	8.92 (± 29.8)	8.9 (± 29.2)	6.3 (± 50.1)

Notes:

[17] - PKS

[18] - PKS

[19] - PKS

[20] - PKS with evaluable subjects for this endpoint

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Various Acceptance Regarding the Appearance of the Oro-dispersible Tablets Assessed by Questionnaire

End point title	Number of Subjects With Various Acceptance Regarding the Appearance of the Oro-dispersible Tablets Assessed by Questionnaire

End point description:

Subjects completed a questionnaire regarding the taste and palatability immediately after study drug administration. The questionnaire included statement judging the appearance, taste, smell, and overall impression. Subjects selected their response from one of the five options: 'completely disagree', 'somewhat disagree', 'neutral', 'somewhat agree' and 'completely agree'. In the below table, the response for categories 'completely disagree', 'somewhat disagree' were summarized under "disliked" and response from categories 'somewhat agree' and 'completely agree' were summarized under "liked". Number of subjects with various acceptance regarding appearance of oro-dispersible tablets were reported.

End point type	Other pre-specified

End point timeframe:

immediately after study drug administration

End point values	Finerenone, 5 X 0.25 mg ODTs, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[21]	16[22]	15[23]	
Units: subjects				
Disliked	0	1	0	
Neutral	2	4	4	
Liked	14	11	11	

Notes:

[21] - SAF

[22] - SAF

[23] - SAF

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Various Acceptance Regarding the Taste of the Oro-dispersible Tablets Assessed by Questionnaire

End point title	Number of Subjects With Various Acceptance Regarding the Taste of the Oro-dispersible Tablets Assessed by Questionnaire

End point description:

Subjects completed a questionnaire regarding the taste and palatability immediately after study drug administration. The questionnaire included statement judging the appearance, taste, smell, and overall impression. Subjects selected their response from one of the five options: 'completely disagree', 'somewhat disagree', 'neutral', 'somewhat agree' and 'completely agree'. In the below table, the response for categories 'completely disagree', 'somewhat disagree' were summarized under "disliked" and response from categories 'somewhat agree' and 'completely agree' were summarized under "liked". Number of subjects with various acceptance regarding taste of oro-dispersible tablets were reported.

End point type	Other pre-specified

End point timeframe:

immediately after study drug administration

End point values	Finerenone, 5 X 0.25 mg ODTs, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[24]	16[25]	15[26]	
Units: subjects				
Taste: Disliked	1	1	0	
Taste: Neutral	11	12	10	
Taste: Liked	4	3	5	
Aftertaste: Disliked	0	0	1	
Aftertaste: Neutral	15	14	12	
Aftertaste: Liked	1	2	2	
Swallowability: Disliked	2	0	0	
Swallowability: Neutral	0	0	1	
Swallowability: Liked	14	16	14	

Notes:

[24] - SAF

[25] - SAF

[26] - SAF

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Various Acceptance Regarding the Smell of the Oro-dispersible Tablets Assessed by Questionnaire

End point title	Number of Subjects With Various Acceptance Regarding the Smell of the Oro-dispersible Tablets Assessed by Questionnaire

End point description:

Subjects completed a questionnaire regarding the taste and palatability immediately after study drug administration. The questionnaire included statement judging the appearance, taste, smell, and overall impression. Subjects selected their response from one of the five options: ‘completely disagree’, ‘somewhat disagree’, ‘neutral’, ‘somewhat agree’ and ‘completely agree’. In the below table, the response for categories ‘completely disagree’, ‘somewhat disagree’ were summarized under "disliked" and response from categories ‘somewhat agree’ and ‘completely agree’ were summarized under "liked". Number of subjects with various acceptance regarding smell of oro-dispersible tablets were reported.

End point type	Other pre-specified

End point timeframe:

immediately after study drug administration

End point values	Finerenone, 5 X 0.25 mg ODTs, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[27]	16[28]	15[29]	
Units: subjects				
Disliked	1	0	0	

Neutral	12	15	14	
Liked	3	1	1	

Notes:

[27] - SAF

[28] - SAF

[29] - SAF

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Various Acceptance Regarding the Overall Impression of the Oro-dispersible Tablets Assessed by Questionnaire

End point title	Number of Subjects With Various Acceptance Regarding the Overall Impression of the Oro-dispersible Tablets Assessed by Questionnaire

End point description:

Subjects completed a questionnaire regarding the taste and palatability immediately after study drug administration. The questionnaire included statement judging the appearance, taste, smell, and overall impression. Subjects selected their response from one of the five options: 'completely disagree', 'somewhat disagree', 'neutral', 'somewhat agree' and 'completely agree'. In the below table, the response for categories 'completely disagree', 'somewhat disagree' were summarized under "disliked" and response from categories 'somewhat agree' and 'completely agree' were summarized under "liked". Number of subjects with various acceptance regarding overall impression of oro-dispersible tablets were reported.

End point type	Other pre-specified

End point timeframe:

immediately after study drug administration

End point values	Finerenone, 5 X 0.25 mg ODTs, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[30]	16[31]	15[32]	
Units: subjects				
Disliked	1	0	0	
Neutral	3	4	1	
Liked	12	12	14	

Notes:

[30] - SAF

[31] - SAF

[32] - SAF

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the start of study treatment up to 3 days after the last dose of study drug	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Finerenone, 10 mg tablet fasted
Reporting group description:	
Subjects received a single oral dose 10 mg (1 X 10 mg) finerenone tablet in fasted state during any of the intervention periods.	
Reporting group title	Finerenone, 5 X 0.25 mg ODTs, fasted
Reporting group description:	
Subjects received a single oral dose 1.25 mg (5 X 0.25 mg) finerenone ODTs in fasted state during any of the intervention periods.	
Reporting group title	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted
Reporting group description:	
Subjects received a single oral dose 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state during any of the intervention periods.	
Reporting group title	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed
Reporting group description:	
Subjects received a single oral dose 1.25 mg (1 X 1.25 mg) finerenone ODT in fasted state during any of the intervention periods.	

Serious adverse events	Finerenone, 10 mg tablet fasted	Finerenone, 5 X 0.25 mg ODTs, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Finerenone, 10 mg tablet fasted	Finerenone, 5 X 0.25 mg ODTs, fasted	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fasted
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	2 / 16 (12.50%)
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Non-serious adverse events	Finerenone, 1.25 mg (1 X 1.25 mg) ODT, fed		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	 0 / 15 (0.00%) 0		
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2016	This amendment included the following changes: • Administrative changes: change of deputy investigator and role of the signatory on the signature page • Correction of number of overnight stays from 3 to 2 nights in each period for consistency • Change of one serum chemistry parameter: leucine aminopeptidase could not be determined any longer due to lack of CE-marked test. Alternatively, the bone-specific alkaline phosphatase (ostase) was determined if an increase in alkaline phosphatase was observed.

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.

Occurrence of "±" in relation with geometric CV is auto-generated and cannot be deleted. Decimal places were automatically truncated if last decimal equals zero.

Notes: