Clinical trial results:
Relative bioavailability study to investigate the pharmacokinetics, safety and tolerability of a single oral dose of finerenone 20 mg as suspension (pediatric formulation), intact tablet and crushed tablet (adult formulation) in the fasting condition, and to investigate the effect of a high fat, high calorie meal on the suspension in healthy male subjects in a randomized, open-label, four-fold crossover design

Summary

EudraCT number	2016-002813-24
Trial protocol	DE
Global end of trial date	01 March 2017

Results information

Result version number	v1 (current)
This version publication date	25 January 2018
First version publication date	25 January 2018

Trial information

Trial identification

Sponsor protocol code	BAY94-8862/16538

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02957396
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, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, 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	01 March 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 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
1. investigate the relative bioavailability of a single oral dose of 20 milligram (mg) finerenone suspension and 20 mg crushed and re-suspended tablet in comparison to 20 mg finerenone tablet in the fasting condition;
2. investigate the effect of a high fat, high calorie meal on the pharmacokinetics (PK) of a single oral dose of 20 mg finerenone suspension;
3. investigate whether 20 mg finerenone suspension and 20 mg crushed and re-suspended tablet 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	17 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 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)	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 17 November 2016 (first subject first visit) and 13 January 2017 (last subject last visit).

Pre-assignment

Screening details:

Overall, 36 subjects were enrolled, of them 20 subjects were not included into the study. A total of 16 subjects were randomized and received all the treatments in a four-fold cross-over fashion (A-D-C-B, B-C-D-A, C-A-B-D, or D-B-A-C) and completed the study.

Period 1

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

Arms

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

Arm description:

Subjects who followed treatment sequence A-D-C-B in fasted and fed state were reported.
Subjects received a single oral dose of 20 mg finerenone (BAY94-8862) intact film-coated tablet in fasted state (Treatment A) in the first intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 milliliter [mL]) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the second intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the third intervention period; followed by a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

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

Dosage and administration details:

Treatment A: Subjects received a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state.
Treatment D: Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state.
Treatment C: Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state.
Treatment B: Subjects received a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state.

Arm title	Treatment B-C-D-A

Arm description:

Subjects who followed treatment sequence B-C-D-A in fasted and fed state were reported.
Subjects received a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the first intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the second intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the third intervention period; followed by a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state (Treatment A) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

Arm type	Experimental

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

Dosage and administration details:

Treatment B: Subjects received a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state.
Treatment C: Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state.
Treatment D: Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state.
Treatment A: Subjects received a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state.

Arm title	Treatment C-A-B-D

Arm description:

Subjects who followed treatment sequence C-A-B-D in fasted and fed state were reported.
Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the first intervention period; followed by a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state (Treatment A) in the second intervention period; followed by a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the third intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

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

Dosage and administration details:

Treatment C: Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state.
Treatment A: Subjects received a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state.
Treatment B: Subjects received a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state.
Treatment D: Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state.

Arm title	Treatment D-B-A-C

Arm description:

Subjects who followed treatment sequence D-B-A-C in fed and fasted state were reported.
Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the first intervention period; followed by a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the second intervention period; followed by a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state (Treatment A) in the third intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

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

Dosage and administration details:

Treatment D: Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state.

Treatment B: Subjects received a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state.
Treatment A: Subjects received a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state.
Treatment C: Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state.

Number of subjects in period 1	Treatment A-D-C-B	Treatment B-C-D-A	Treatment C-A-B-D
Started	4	4	4
Completed	4	4	4

Number of subjects in period 1	Treatment D-B-A-C
Started	4
Completed	4

Baseline characteristics

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

Reporting group description:

Subjects who followed treatment sequence A-D-C-B in fasted and fed state were reported.
Subjects received a single oral dose of 20 mg finerenone (BAY94-8862) intact film-coated tablet in fasted state (Treatment A) in the first intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 milliliter [mL]) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the second intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the third intervention period; followed by a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

Reporting group title	Treatment B-C-D-A

Reporting group description:

Subjects who followed treatment sequence B-C-D-A in fasted and fed state were reported.
Subjects received a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the first intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the second intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the third intervention period; followed by a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state (Treatment A) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

Reporting group title	Treatment C-A-B-D

Reporting group description:

Subjects who followed treatment sequence C-A-B-D in fasted and fed state were reported.
Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the first intervention period; followed by a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state (Treatment A) in the second intervention period; followed by a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the third intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

Reporting group title	Treatment D-B-A-C

Reporting group description:

Subjects who followed treatment sequence D-B-A-C in fed and fasted state were reported.
Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the first intervention period; followed by a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the second intervention period; followed by a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state (Treatment A) in the third intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

Reporting group values	Treatment A-D-C-B	Treatment B-C-D-A	Treatment C-A-B-D
Number of subjects	4	4	4
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	35.3	35.3	36.8
standard deviation	± 7.3	± 7.0	± 5.0

Gender Categorical Units: Subjects			
Male	4	4	4

Reporting group values	Treatment D-B-A-C	Total	
Number of subjects	4	16	
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	36.8		
standard deviation	± 10.9	-	
Gender Categorical Units: Subjects			
Male	4	16	

End points

End points reporting groups

Reporting group title	Treatment A-D-C-B

Reporting group description:

Subjects who followed treatment sequence A-D-C-B in fasted and fed state were reported.
Subjects received a single oral dose of 20 mg finerenone (BAY94-8862) intact film-coated tablet in fasted state (Treatment A) in the first intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 milliliter [mL]) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the second intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the third intervention period; followed by a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

Reporting group title	Treatment B-C-D-A

Reporting group description:

Subjects who followed treatment sequence B-C-D-A in fasted and fed state were reported.
Subjects received a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the first intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the second intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the third intervention period; followed by a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state (Treatment A) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

Reporting group title	Treatment C-A-B-D

Reporting group description:

Subjects who followed treatment sequence C-A-B-D in fasted and fed state were reported.
Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the first intervention period; followed by a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state (Treatment A) in the second intervention period; followed by a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the third intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

Reporting group title	Treatment D-B-A-C

Reporting group description:

Subjects who followed treatment sequence D-B-A-C in fed and fasted state were reported.
Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state (Treatment D) in the first intervention period; followed by a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state (Treatment B) in the second intervention period; followed by a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state (Treatment A) in the third intervention period; followed by a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state (Treatment C) in the fourth intervention period. A wash-out period of at least 72 hours was maintained between finerenone administrations.

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

Subject analysis set description:

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

Subject analysis set title	Pharmacokinetic analysis set (PKS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PKS (N=16) included all subjects with a valid PK profile for at least two of the treatments relevant for comparison (Treatment A and B or Treatment A and C or Treatment C and D).

Subject analysis set title	Finerenone 20 mg Intact Tablet Fasted (Treatment A)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects (N=16) received a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state

during any intervention period.

Subject analysis set title	Finerenone 20 mg Crushed Tablet Fasted (Treatment B)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects (N=16) received a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state during any intervention period.

Subject analysis set title	Finerenone 20 mg Suspension Fasted (Treatment C)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects (N=16) received a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state during any intervention period.

Subject analysis set title	Finerenone 20 mg Suspension Fed (Treatment D)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects (N=16) received a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state during any intervention period.

Primary: Maximum Observed Concentration (Cmax) After Single Dose Administration of Finerenone in Plasma

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

End point description:

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

End point type	Primary

End point timeframe:

Pre-dose to 24 hours post-dose

End point values	Finerenone 20 mg Intact Tablet Fasted (Treatment A)	Finerenone 20 mg Crushed Tablet Fasted (Treatment B)	Finerenone 20 mg Suspension Fasted (Treatment C)	Finerenone 20 mg Suspension Fed (Treatment D)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	16	16	16
Units: microgram per liter (mcg/L)				
geometric mean (geometric coefficient of variation)	154 (± 29.9)	138 (± 35.9)	190 (± 32.3)	110 (± 27.3)

Statistical analyses

Statistical analysis title	Statistical analysis: Treatment (C)/Treatment (A)

Statistical analysis description:

Cmax of finerenone were analyzed using analysis of variance (ANOVA) including sequence, subject (sequence), period, and treatment effects. Based on these analysis point estimates (least squares (LS)-means) and exploratory 90 percent (%) confidence intervals (CIs) for the ratios "20 mg suspension fasted (C)/20 mg intact tablet fasted (A)" of Cmax were calculated. Database auto-calculate number of subjects analysed, but the actual number of subjects analysed was 16.

Comparison groups	Finerenone 20 mg Intact Tablet Fasted (Treatment A) v Finerenone 20 mg Suspension Fasted (Treatment C)

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Estimated ratio in percent [%]
Point estimate	122.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	104.48
upper limit	144.56

Statistical analysis title	Statistical analysis: Treatment (D)/Treatment (C)

Statistical analysis description:

Cmax of finerenone were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. Based on these analysis point estimates (LS-means) and exploratory 90% CIs for the ratios "20 mg suspension fed (D)/20 mg suspension fasted (C)" of Cmax were calculated. Database auto-calculate number of subjects analysed, but the actual number of subjects analysed was 16.

Comparison groups	Finerenone 20 mg Suspension Fasted (Treatment C) v Finerenone 20 mg Suspension Fed (Treatment D)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Estimated ratio in %
Point estimate	58.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	49.32
upper limit	68.25

Statistical analysis title	Statistical analysis: Treatment (B)/Treatment (A)

Statistical analysis description:

Cmax of finerenone were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. Based on these analysis point estimates (LS-means) and exploratory 90% CIs for the ratios "20 mg crushed/re-suspended tablet fasted (B)/20 mg intact tablet fasted (A)" of Cmax were calculated. Database auto-calculate number of subjects analysed, but the actual number of subjects analysed was 16.

Comparison groups	Finerenone 20 mg Intact Tablet Fasted (Treatment A) v Finerenone 20 mg Crushed Tablet Fasted (Treatment B)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Estimated ratio in %
Point estimate	89.04

Confidence interval	
level	90 %
sides	2-sided
lower limit	75.69
upper limit	104.74

Primary: Area Under Concentration Versus Time Curve From Zero to Infinity (AUC) After Single Dose Administration of Finerenone in Plasma

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

End point description:

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

End point type	Primary

End point timeframe:

Pre-dose to 24 hours post-dose

End point values	Finerenone 20 mg Intact Tablet Fasted (Treatment A)	Finerenone 20 mg Crushed Tablet Fasted (Treatment B)	Finerenone 20 mg Suspension Fasted (Treatment C)	Finerenone 20 mg Suspension Fed (Treatment D)
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]	16[4]
Units: microgram * hour per liter (mcg*h/L)				
geometric mean (geometric coefficient of variation)	432 (± 33.0)	352 (± 37.7)	451 (± 28.7)	453 (± 26.4)

Notes:

[1] - PKS

[2] - PKS

[3] - PKS

[4] - PKS

Statistical analyses

Statistical analysis title	Statistical analysis: Treatment (C)/Treatment (A)

Statistical analysis description:

AUC of finerenone were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. Based on these analysis point estimates (LS-means) and exploratory 90% CIs for the ratios "20 mg suspension fasted (C)/20 mg intact tablet fasted (A)" of AUC were calculated. Database auto calculate number of subjects analyzed, but the actual number of subjects analyzed was 16.

Comparison groups	Finerenone 20 mg Intact Tablet Fasted (Treatment A) v Finerenone 20 mg Suspension Fasted (Treatment C)

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Estimated ratio in %
Point estimate	104.55
Confidence interval	
level	90 %
sides	2-sided
lower limit	95.85
upper limit	114.04

Statistical analysis title	Statistical analysis: Treatment (B)/Treatment (A)

Statistical analysis description:

AUC of finerenone were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. Based on these analysis point estimates (LS-means) and exploratory 90% CIs for the ratios "20 mg crushed/re-suspended tablet fasted (B)/20 mg intact tablet fasted (A)" of AUC were calculated. Database auto calculate number of subjects analyzed, but the actual number of subjects analyzed was 16.

Comparison groups	Finerenone 20 mg Intact Tablet Fasted (Treatment A) v Finerenone 20 mg Crushed Tablet Fasted (Treatment B)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Estimated ratio in %
Point estimate	81.61
Confidence interval	
level	90 %
sides	2-sided
lower limit	74.82
upper limit	89.02

Statistical analysis title	Statistical analysis: Treatment (D)/Treatment (C)

Statistical analysis description:

AUC of finerenone were analyzed using ANOVA including sequence, subject (sequence), period, and treatment effects. Based on these analysis point estimates (LS-means) and exploratory 90% CIs for the ratios "20 mg suspension fed (D)/20 mg suspension fasted (C)" of AUC were calculated. Database auto calculate number of subjects analyzed, but the actual number of subjects analyzed was 16.

Comparison groups	Finerenone 20 mg Suspension Fasted (Treatment C) v Finerenone 20 mg Suspension Fed (Treatment D)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Estimated ratio in %
Point estimate	100.37

Confidence interval	
level	90 %
sides	2-sided
lower limit	92.02
upper limit	109.48

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 subject who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) was an AE resulting in any of 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/birth defect and another serious or important medical event as judged by the investigator. AE/SAEs that started or worsened after study drug treatment were recorded as TEAE/TESAEs.

End point type	Secondary

End point timeframe:

From start of study drug administration up to 1 week after last drug administration (Day 16)

End point values	Finerenone 20 mg Intact Tablet Fasted (Treatment A)	Finerenone 20 mg Crushed Tablet Fasted (Treatment B)	Finerenone 20 mg Suspension Fasted (Treatment C)	Finerenone 20 mg Suspension Fed (Treatment D)
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]	16[8]
Units: subjects				
TEAE	2	2	3	4
TESAE	0	0	0	0

Notes:

[5] - SAF

[6] - SAF

[7] - SAF

[8] - SAF

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Appearance of the Formulation Assessed by Questionnaire

End point title	Appearance of the Formulation Assessed by Questionnaire

End point description:

Subjects completed a questionnaire regarding appearance immediately after study drug administration. Subjects were asked the question as 'I like the appearance of the medium', where subjects were selected their response from one of the five items: '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".

End point type	Other pre-specified

End point timeframe:

Immediately after study drug administration

End point values	Finerenone 20 mg Crushed Tablet Fasted (Treatment B)	Finerenone 20 mg Suspension Fasted (Treatment C)	Finerenone 20 mg Suspension Fed (Treatment D)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[9]	16[10]	16[11]	
Units: subjects				
Disliked	0	3	3	
Neutral	6	7	8	
Liked	10	6	5	

Notes:

[9] - SAF

[10] - SAF

[11] - SAF

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Taste of the Formulation Assessed by Questionnaire

End point title	Taste of the Formulation Assessed by Questionnaire

End point description:

Subjects completed a questionnaire regarding taste immediately after study drug administration. Subjects were asked the question as 'I like the taste after swallowing', where subjects were selected their response from one of the five items: '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".

End point type	Other pre-specified

End point timeframe:

Immediately after study drug administration

End point values	Finerenone 20 mg Crushed Tablet Fasted (Treatment B)	Finerenone 20 mg Suspension Fasted (Treatment C)	Finerenone 20 mg Suspension Fed (Treatment D)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[12]	16[13]	16[14]	
Units: subjects				
Disliked	1	4	3	
Neutral	2	8	5	
Liked	13	4	8	

Notes:

[12] - SAF

[13] - SAF

[14] - SAF

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Smell of the Formulation Assessed by Questionnaire

End point title	Smell of the Formulation Assessed by Questionnaire

End point description:

Subjects completed a questionnaire regarding smell immediately after study drug administration. Subjects were asked the question as 'I like the smell of the medium', where subjects were selected their response from one of the five items: '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".

End point type	Other pre-specified

End point timeframe:

Immediately after study drug administration

End point values	Finerenone 20 mg Crushed Tablet Fasted (Treatment B)	Finerenone 20 mg Suspension Fasted (Treatment C)	Finerenone 20 mg Suspension Fed (Treatment D)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[15]	16[16]	16[17]	
Units: subjects				
Disliked	0	2	2	
Neutral	4	12	11	
Liked	12	1	3	

Notes:

[15] - SAF

[16] - SAF

[17] - SAF

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Overall Impression of the Formulation Assessed by Questionnaire

End point title	Overall Impression of the Formulation Assessed by Questionnaire

End point description:

Subjects completed a questionnaire regarding overall impression immediately after study drug administration. Subjects were asked the question as 'I like the medium overall', where subjects were selected their response from one of the five items: '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".

End point type	Other pre-specified

End point timeframe:

Immediately after study drug administration

End point values	Finerenone 20 mg Crushed Tablet Fasted (Treatment B)	Finerenone 20 mg Suspension Fasted (Treatment C)	Finerenone 20 mg Suspension Fed (Treatment D)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[18]	16[19]	16[20]	
Units: subjects				
Disliked	0	2	1	
Neutral	3	5	5	
Liked	13	9	10	

Notes:

[18] - SAF

[19] - SAF

[20] - SAF

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Texture of the Formulation Assessed by Questionnaire

End point title	Texture of the Formulation Assessed by Questionnaire

End point description:

Subjects completed a questionnaire regarding texture immediately after study drug administration. Subjects were asked the question as 'texture like sand, sticky, dry, creamy and strange (unlike any of the above mentioned) or other feeling', where subjects were selected their response from one of the five items: '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".

End point type	Other pre-specified

End point timeframe:

Immediately after study drug administration

End point values	Finerenone 20 mg Crushed Tablet Fasted (Treatment B)	Finerenone 20 mg Suspension Fasted (Treatment C)	Finerenone 20 mg Suspension Fed (Treatment D)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[21]	16[22]	16[23]	
Units: subjects				
Sand: Disliked	16	15	16	
Sand: Neutral	0	0	0	
Sand: Liked	0	1	0	
Sticky: Disliked	13	11	11	
Sticky: Neutral	1	1	0	
Sticky: Liked	2	4	5	

Dry: Disliked	16	15	16	
Dry: Neutral	0	1	0	
Dry: Liked	0	0	0	
Creamy: Disliked	6	2	2	
Creamy: Neutral	4	4	4	
Creamy: Liked	6	10	10	
Strange: Disliked	14	15	14	
Strange: Neutral	1	0	1	
Strange: Liked	1	1	1	

Notes:

[21] - SAF

[22] - SAF

[23] - SAF

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Whether Oro-dispersible Tablets are Palatable and Swallowable Assessed by Questionnaire

End point title	Whether Oro-dispersible Tablets are Palatable and Swallowable Assessed by Questionnaire

End point description:

Subjects completed a questionnaire regarding palatable and swallowable immediately after study drug administration. Subjects were asked the question as 'It was easy for me to swallow', where subjects were selected their response from one of the two items: 'somewhat disagree', and 'completely agree'. In the below table, the response for category 'somewhat disagree' was summarized under "disliked" and response from category 'completely agree' was summarized under "liked".

End point type	Other pre-specified

End point timeframe:

Immediately after study drug administration

End point values	Finerenone 20 mg Crushed Tablet Fasted (Treatment B)	Finerenone 20 mg Suspension Fasted (Treatment C)	Finerenone 20 mg Suspension Fed (Treatment D)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[24]	16[25]	16[26]	
Units: subjects				
Disliked	0	0	0	
Neutral	0	0	0	
Liked	16	16	16	

Notes:

[24] - SAF

[25] - SAF

[26] - 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 drug administration up to 1 week after the last drug administration (Day 16)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Finerenone, 20mg Intact Tablet Fasted

Reporting group description:

Subjects received a single oral dose of 20 mg finerenone intact film-coated tablet in fasted state during any intervention period.

Reporting group title	Finerenone, 20mg Crushed Tablet Fasted

Reporting group description:

Subjects received a single oral dose of 20 mg finerenone crushed and re-suspended film-coated tablet in fasted state during any intervention period.

Reporting group title	Finerenone, 20mg Suspension Fasted

Reporting group description:

Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) in fasted state during any intervention period.

Reporting group title	Finerenone, 20mg Suspension Fed

Reporting group description:

Subjects received a single oral dose of 20 mg finerenone suspension (10 mL) after a standardized high-fat, high-calorie American breakfast in fed state during any intervention period.

Serious adverse events	Finerenone, 20mg Intact Tablet Fasted	Finerenone, 20mg Crushed Tablet Fasted	Finerenone, 20mg Suspension 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, 20mg Suspension Fed		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (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, 20mg Intact Tablet Fasted	Finerenone, 20mg Crushed Tablet Fasted	Finerenone, 20mg Suspension Fasted
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 16 (12.50%)	2 / 16 (12.50%)	3 / 16 (18.75%)
Investigations			
Amylase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Lipase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			

subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Rhinitis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0

Non-serious adverse events	Finerenone, 20mg Suspension Fed		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 16 (25.00%)		
Investigations			
Amylase increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Lipase increased			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
White blood cell count increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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: