



Clinical trial results:

A Randomized, Open-Label, Five Period, Crossover Study to Evaluate the Single Dose Pharmacokinetics and Food Effect of two Pediatric AFQ056 Formulations in Healthy Adults

Summary

EudraCT number	2011-000365-12
Trial protocol	GB
Global end of trial date	05 July 2011

Results information

Result version number	v1 (current)
This version publication date	08 September 2018
First version publication date	08 September 2018

Trial information

Trial identification

Sponsor protocol code	CAFQ056A2166
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH 4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001003-PIP01-10
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	05 July 2011
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	05 July 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the pharmacokinetics (PKs) of two pediatric formulations relative to the capsule formulation of AFQ056 under fasting conditions at a single dose of 50 milligrams (mg).

- To assess the effect of a high fat meal on the relative bioavailability of the two pediatric formulations of AFQ056 at a single dose of 50 mg.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator:

For the objective of evaluating the PKs including the relative bioavailability of the two Powder for Oral Suspension (POS) formulations, the Final Market Image (FMI) formulation (hard gelatin capsule at a dose of 50 mg AFQ056) served as the reference.

Actual start date of recruitment	06 May 2011
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	United Kingdom: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at a single center in United Kingdom.

Pre-assignment

Screening details:

The study comprised of a screening period of up to 20 days, and five baseline visits (one before each treatment period). Subjects were randomized to one of the five treatment (T) sequences in an allocation ratio of 1:1:1:1:1. It was a single-dose, five period, five treatment, five sequence cross-over study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence 1: T1-T2-T3-T4-T5

Arm description:

Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 milliliter (mL) suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.

Arm type	Experimental
Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	POS-1
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

POS-1 at a dose of 50 mg AFQ056 was administered to subjects as 5 mL suspension with a 5 mL syringe, directly into the subject's mouth. An additional 235 mL of water was administered immediately after administration of the suspension.

Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	POS-2
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

POS-2 at a dose of 50 mg AFQ056 was administered to subjects as 5 mL suspension with a 5 mL syringe, directly into the subject's mouth. An additional 235 mL of water was administered immediately after administration of the suspension.

Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	FMI
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Two 25 mg hard gelatin capsules were administered orally with 240 mL of water in the morning.

Arm title	Sequence 2: T2-T3-T4-T5-T1
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Arm description:

Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.

Arm type	Experimental
Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	POS-1
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

POS-1 at a dose of 50 mg AFQ056 was administered to subjects as 5 mL suspension with a 5 mL syringe, directly into the subject's mouth.

Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	POS-2
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

POS-2 at a dose of 50 mg AFQ056 was administered to subjects as 5 mL suspension with a 5 mL syringe, directly into the subject's mouth. An additional 235 mL of water was administered immediately after administration of the suspension.

Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	FMI
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Two 25 mg hard gelatin capsules were administered orally with 240 mL of water in the morning.

Arm title	Sequence 3: T3-T4-T5-T1-T2
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Arm description:

Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.

Arm type	Experimental
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Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	POS-1
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

POS-1 at a dose of 50 mg AFQ056 was administered to subjects as 5 mL suspension with a 5 mL syringe, directly into the subject's mouth. An additional 235 mL of water was administered immediately after administration of the suspension.

Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	POS-2
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

POS-2 at a dose of 50 mg AFQ056 was administered to subjects as 5 mL suspension with a 5 mL syringe, directly into the subject's mouth. An additional 235 mL of water was administered immediately after administration of the suspension.

Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	FMI
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Two 25 mg hard gelatin capsules were administered orally with 240 mL of water in the morning.

Arm title	Sequence 4: T4-T5-T1-T2-T3
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Arm description:

Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.

Arm type	Experimental
Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	POS-2
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

POS-2 at a dose of 50 mg AFQ056 was administered to subjects as 5 mL suspension with a 5 mL syringe, directly into the subject's mouth. An additional 235 mL of water was administered immediately after administration of the suspension.

Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	POS-1
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

POS-1 at a dose of 50 mg AFQ056 was administered to subjects as 5 mL suspension with a 5 mL syringe, directly into the subject's mouth. An additional 235 mL of water was administered immediately after administration of the suspension.

Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	FMI
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Two 25 mg hard gelatin capsules were administered orally with 240 mL of water in the morning.

Arm title	Sequence 5: T5-T1-T2-T3-T4
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Arm description:

Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.

Arm type	Active comparator
Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	POS-1
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

POS-1 at a dose of 50 mg AFQ056 was administered to subjects as 5 mL suspension with a 5 mL syringe, directly into the subject's mouth. An additional 235 mL of water was administered immediately after administration of the suspension.

Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	POS-2
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

POS-2 at a dose of 50 mg AFQ056 was administered to subjects as 5 mL suspension with a 5 mL syringe, directly into the subject's mouth. An additional 235 mL of water was administered immediately after administration of the suspension.

Investigational medicinal product name	AFQ056
Investigational medicinal product code	
Other name	FMI
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Two 25 mg hard gelatin capsules were administered orally with 240 mL of water in the morning.

Number of subjects in period 1	Sequence 1: T1-T2-T3-T4-T5	Sequence 2: T2-T3-T4-T5-T1	Sequence 3: T3-T4-T5-T1-T2
Started	6	6	6
Completed	5	6	5
Not completed	1	0	1
Abnormal laboratory value(s)	-	-	-
Administrative problems	1	-	-
Adverse event	-	-	1

Number of subjects in period 1	Sequence 4: T4-T5-T1-T2-T3	Sequence 5: T5-T1-T2-T3-T4
Started	6	6
Completed	5	6
Not completed	1	0
Abnormal laboratory value(s)	1	-
Administrative problems	-	-
Adverse event	-	-

Baseline characteristics

Reporting groups

Reporting group title	Sequence 1: T1-T2-T3-T4-T5
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Reporting group description:

Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 milliliter (mL) suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.

Reporting group title	Sequence 2: T2-T3-T4-T5-T1
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Reporting group description:

Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.

Reporting group title	Sequence 3: T3-T4-T5-T1-T2
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Reporting group description:

Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.

Reporting group title	Sequence 4: T4-T5-T1-T2-T3
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Reporting group description:

Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.

Reporting group title	Sequence 5: T5-T1-T2-T3-T4
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Reporting group description:

Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.

Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.

Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.

Reporting group values	Sequence 1: T1-T2-T3-T4-T5	Sequence 2: T2-T3-T4-T5-T1	Sequence 3: T3-T4-T5-T1-T2
Number of subjects	6	6	6
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	30.8 ± 8.75	37.0 ± 11.61	30.0 ± 11.12
Gender categorical Units: Subjects			
Female	0	0	0
Male	6	6	6

Reporting group values	Sequence 4: T4-T5-T1-T2-T3	Sequence 5: T5-T1-T2-T3-T4	Total
Number of subjects	6	6	30
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	30.3 ± 7.74	35.2 ± 13.23	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	6	6	30

End points

End points reporting groups

Reporting group title	Sequence 1: T1-T2-T3-T4-T5
Reporting group description:	
Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 milliliter (mL) suspension under fasting condition, directly into the mouth on Day 1 of visit.	
Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.	
Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.	
Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.	
Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.	
Reporting group title	Sequence 2: T2-T3-T4-T5-T1
Reporting group description:	
Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.	
Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.	
Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.	
Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.	
Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.	
Reporting group title	Sequence 3: T3-T4-T5-T1-T2
Reporting group description:	
Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.	
Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.	
Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.	
Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.	
Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.	
Reporting group title	Sequence 4: T4-T5-T1-T2-T3
Reporting group description:	
Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.	
Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.	
Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.	
Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.	
Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.	
Reporting group title	Sequence 5: T5-T1-T2-T3-T4
Reporting group description:	
Treatment 1: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.	
Treatment 2: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.	
Treatment 3: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fasting condition, directly into the mouth on Day 1 of visit.	
Treatment 4: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension under fed condition, directly into the mouth on Day 1 of visit.	
Treatment 5: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition, on morning of Day 1 visit.	

Subject analysis set title	Treatment 1: 50mg AFQ056 POS-1, Fasted
Subject analysis set type	Full analysis
Subject analysis set description: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension with a 5 mL syringe under fasting condition, directly into the mouth.	
Subject analysis set title	Treatment 2: 50 mg AFQ056 POS-1, Fed
Subject analysis set type	Full analysis
Subject analysis set description: Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension with a 5 mL syringe under fed condition, directly into the mouth.	
Subject analysis set title	Treatment 3: 50 mg AFQ056 POS-2, Fasted
Subject analysis set type	Full analysis
Subject analysis set description: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension with a 5 mL syringe under fasting condition, directly into the mouth.	
Subject analysis set title	Treatment 4: 50 mg AFQ056 POS-2, Fed
Subject analysis set type	Full analysis
Subject analysis set description: Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension with a 5 mL syringe under fed condition, directly into the mouth.	
Subject analysis set title	Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted
Subject analysis set type	Full analysis
Subject analysis set description: Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition.	

Primary: Maximum Observed Plasma Concentration (C_{max}) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions

End point title	Maximum Observed Plasma Concentration (C _{max}) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions
End point description: The observed maximum plasma (or serum or blood) concentration following single dose AFQ056 administration was reported (mass / volume). It was determined by non-compartmental method(s) using WinNonlin Pro (Version 5.2). Analysis was performed in PK Analysis set which included subjects who had evaluable PK data for at least one period.	
End point type	Primary
End point timeframe: Pre-dose, 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 10, 14, 24, 36 and 48 hours in each treatment	

End point values	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 3: 50 mg AFQ056 POS-2, Fasted	Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	29	27	
Units: nanogram/mL (ng/mL)				
geometric mean (geometric coefficient of variation)	149.9 (± 58.94)	157.1 (± 47.54)	127.8 (± 61.46)	

Statistical analyses

Statistical analysis title	AFQ056 POS-1 vs Capsule Formulation
Statistical analysis description: The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% Confidence Interval (CI) for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.	
Comparison groups	Treatment 1: 50mg AFQ056 POS-1, Fasted v Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	1.179
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.04
upper limit	1.336

Statistical analysis title	AFQ056 POS-2 vs Capsule Formulation
Statistical analysis description: The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% CI for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.	
Comparison groups	Treatment 3: 50 mg AFQ056 POS-2, Fasted v Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	1.248
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.101
upper limit	1.414

Primary: Area Under The Plasma Concentration-Time Curve Infinity (AUCinf) of POS-1 and POS-2 Relative to the Capsule Formulation of AFQ056 Under Fasting Conditions

End point title	Area Under The Plasma Concentration-Time Curve Infinity (AUCinf) of POS-1 and POS-2 Relative to the Capsule Formulation of AFQ056 Under Fasting Conditions
End point description: The AUCinf represents area under the plasma (or serum or blood) concentration-time curve from time 0 to infinity (mass * time / volume). It was determined by non-compartmental method(s) using WinNonlin Pro (Version 5.2). Analysis was performed in PK Analysis set which included subjects who had evaluable PK data for at least one period.	
End point type	Primary

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 10, 14, 24, 36 and 48 hours in each treatment

End point values	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 3: 50 mg AFQ056 POS-2, Fasted	Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	27	28	23	
Units: hour (hr)*ng/mL				
geometric mean (geometric coefficient of variation)	832.4 (± 67.19)	794.8 (± 58.28)	849.8 (± 50.29)	

Statistical analyses

Statistical analysis title	AFQ056 POS-1 vs Capsule Formulation
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Statistical analysis description:

The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% CI for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.

Comparison groups	Treatment 1: 50mg AFQ056 POS-1, Fasted v Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	1.047
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.944
upper limit	1.16

Statistical analysis title	AFQ056 POS-2 vs Capsule Formulation
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Statistical analysis description:

The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% CI for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.

Comparison groups	Treatment 3: 50 mg AFQ056 POS-2, Fasted v Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted
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Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	1.005
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.907
upper limit	1.114

Primary: Area Under The Plasma Concentration-Time Curve Last (AUClast) of POS-1 and POS-2 Relative to the Capsule Formulation of AFQ056 Under Fasting Conditions

End point title	Area Under The Plasma Concentration-Time Curve Last (AUClast) of POS-1 and POS-2 Relative to the Capsule Formulation of AFQ056 Under Fasting Conditions
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End point description:

AUClast represents area under the plasma (or serum or blood) concentration-time curve from time 0 to the time of the last quantifiable concentration (mass * time / volume). It was determined by non-compartmental method(s) using WinNonlin Pro (Version 5.2). Analysis was performed in PK Analysis set which included subjects who had evaluable PK data for at least one period.

End point type	Primary
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End point timeframe:

Pre-dose, 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 10, 14, 24, 36 and 48 hours in each treatment

End point values	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 3: 50 mg AFQ056 POS-2, Fasted	Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	29	27	
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	764.7 (± 70.32)	736.4 (± 59.29)	686.7 (± 68.62)	

Statistical analyses

Statistical analysis title	AFQ056 POS-1 vs Capsule Formulation
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Statistical analysis description:

The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% CI for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.

Comparison groups	Treatment 1: 50mg AFQ056 POS-1, Fasted v Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted
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Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	1.102
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.996
upper limit	1.218

Statistical analysis title	AFQ056 POS-2 vs Capsule Formulation
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Statistical analysis description:

The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% CI for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.

Comparison groups	Treatment 3: 50 mg AFQ056 POS-2, Fasted v Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	1.072
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.97
upper limit	1.186

Primary: Effect of Food on the Relative Bioavailability of POS-1 and POS-2 of AFQ056 at a Single Dose as Determined Using Cmax

End point title	Effect of Food on the Relative Bioavailability of POS-1 and POS-2 of AFQ056 at a Single Dose as Determined Using Cmax
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End point description:

Bioavailability is the proportion of an administered dose of unchanged drug that reaches the systemic circulation when introduced into the body. Cmax represents observed maximum plasma (or serum or blood) concentration following single dose AFQ056 administration was reported (mass / volume). Analysis was performed in PK Analysis set which included subjects who had evaluable PK data for at least one period.

End point type	Primary
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End point timeframe:

Pre-dose, 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 10, 14, 24, 36 and 48 hours in each treatment

End point values	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 2: 50 mg AFQ056 POS-1, Fed	Treatment 3: 50 mg AFQ056 POS-2, Fasted	Treatment 4: 50 mg AFQ056 POS-2, Fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	28	29	28
Units: ng/mL				
geometric mean (geometric coefficient of variation)	149.9 (\pm 58.94)	115.2 (\pm 64.38)	157.1 (\pm 47.54)	105.9 (\pm 57.88)

Statistical analyses

Statistical analysis title	AFQ056 POS-1 Fed vs Fasted
Statistical analysis description:	
The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% CI for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.	
Comparison groups	Treatment 1: 50mg AFQ056 POS-1, Fasted v Treatment 2: 50 mg AFQ056 POS-1, Fed
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	0.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.681
upper limit	0.872

Statistical analysis title	AFQ056 POS-2 Fed vs Fasted
Statistical analysis description:	
The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% CI for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.	
Comparison groups	Treatment 3: 50 mg AFQ056 POS-2, Fasted v Treatment 4: 50 mg AFQ056 POS-2, Fed
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	0.665
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.586
upper limit	0.753

Primary: Effect of Food on the Relative Bioavailability of POS-1 and POS-2 of AFQ056 at a Single Dose as Determined Using AUCinf

End point title	Effect of Food on the Relative Bioavailability of POS-1 and POS-2 of AFQ056 at a Single Dose as Determined Using AUCinf
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End point description:

Bioavailability is the proportion of an administered dose of unchanged drug that reaches the systemic circulation when introduced into the body. The AUCinf represents area under the plasma (or serum or blood) concentration-time curve from time 0 to infinity (mass * time / volume).

Analysis was performed in PK Analysis set which included subjects who had evaluable PK data for at least one period.

End point type	Primary
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End point timeframe:

Pre-dose, 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 10, 14, 24, 36 and 48 hours in each treatment

End point values	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 2: 50 mg AFQ056 POS-1, Fed	Treatment 3: 50 mg AFQ056 POS-2, Fasted	Treatment 4: 50 mg AFQ056 POS-2, Fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	27	27	28	28
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	832.4 (± 67.19)	876.9 (± 59.38)	794.8 (± 58.28)	792 (± 65.88)

Statistical analyses

Statistical analysis title	AFQ056 POS-1 Fed vs Fasted
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Statistical analysis description:

The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% CI for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.

Comparison groups	Treatment 1: 50mg AFQ056 POS-1, Fasted v Treatment 2: 50 mg AFQ056 POS-1, Fed
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	1.053
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.955
upper limit	1.161

Statistical analysis title	AFQ056 POS-2 Fed vs Fasted
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Statistical analysis description:

The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% CI for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.

Comparison groups	Treatment 3: 50 mg AFQ056 POS-2, Fasted v Treatment 4: 50 mg AFQ056 POS-2, Fed
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	1.031
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.935
upper limit	1.136

Primary: Effect of Food on the Relative Bioavailability of POS-1 and POS-2 of AFQ056 at a Single Dose as Determined Using AUClast

End point title	Effect of Food on the Relative Bioavailability of POS-1 and POS-2 of AFQ056 at a Single Dose as Determined Using AUClast
End point description:	Bioavailability is the proportion of an administered dose of unchanged drug that reaches the systemic circulation when introduced into the body. AUClast represents area under the plasma (or serum or blood) concentration-time curve from time 0 to the time of the last quantifiable concentration (mass * time / volume). Analysis was performed in PK Analysis set which included subjects who had evaluable PK data for at least one period.
End point type	Primary
End point timeframe:	Pre-dose, 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 10, 14, 24, 36 and 48 hours in each treatment

End point values	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 2: 50 mg AFQ056 POS-1, Fed	Treatment 3: 50 mg AFQ056 POS-2, Fasted	Treatment 4: 50 mg AFQ056 POS-2, Fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	28	29	28
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	764.7 (± 70.32)	820.4 (± 59.78)	736.4 (± 59.29)	759.5 (± 67.62)

Statistical analyses

Statistical analysis title	AFQ056 POS-1 Fed vs Fasted
Statistical analysis description:	The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% CI for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.
Comparison groups	Treatment 1: 50mg AFQ056 POS-1, Fasted v Treatment 2: 50 mg AFQ056 POS-1, Fed

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	1.077
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.976
upper limit	1.19

Statistical analysis title	AFQ056 POS-2 Fed vs Fasted
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Statistical analysis description:

The ratio of geometric means (expressed as a percent) was obtained by exponentiating the mean differences of natural log-transformed data. The 90% CI for the ratio (expressed as a percent) was obtained by exponentiating the CI for the mean differences of natural log-transformed data.

Comparison groups	Treatment 3: 50 mg AFQ056 POS-2, Fasted v Treatment 4: 50 mg AFQ056 POS-2, Fed
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Ratio of geometric means
Point estimate	1.057
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.956
upper limit	1.168

Secondary: Palatability of POS-1 and POS-2 of AFQ056

End point title	Palatability of POS-1 and POS-2 of AFQ056
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End point description:

Palatability implies pleasure provided by foods or fluids, which often varies relative to the homeostatic satisfaction of nutritional, water, or energy needs. The Palatability Assessment was a questionnaire, developed internally at Novartis, to obtain feedback from subjects on the taste, smell and feeling of the powder for oral suspension. Subjects judged the smell, feeling (in mouth), and taste of both POS formulations as: good-very good, somewhat bad-somewhat good, bad, and missing. Analysis was performed on safety analysis set which included all subjects who received at least one dose of the study medication.

End point type	Secondary
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End point timeframe:

Day 1: 0 hour (immediately after dosing) in each treatment

End point values	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 2: 50 mg AFQ056 POS-1, Fed	Treatment 3: 50 mg AFQ056 POS-2, Fasted	Treatment 4: 50 mg AFQ056 POS-2, Fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	28	29	29
Units: subjects				
Smell: Good – Very good	5	3	7	7
Smell: Somewhat bad – Somewhat good	21	24	21	21
Smell: Very bad - Bad	0	0	0	0
Smell: Missing	2	1	1	1
Feeling: Good – Very good	6	5	8	10
Feeling: Somewhat bad – Somewhat good	21	22	21	19
Feeling: Very bad - Bad	0	1	0	0
Feeling: Missing	1	0	0	0
Taste: Good – Very good	5	5	8	9
Taste: Somewhat bad – Somewhat good	22	22	21	20
Taste: Very bad - Bad	0	1	0	0
Taste: Missing	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach the maximum concentration (Tmax) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions

End point title	Time to reach the maximum concentration (Tmax) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions
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End point description:

The Tmax represents time to reach the maximum concentration after drug administration. It was determined by non-compartmental method(s) using WinNonlin Pro (Version 5.2). Analysis was performed in PK Analysis set which included subjects who had evaluable PK data for at least one period.

End point type	Secondary
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End point timeframe:

Pre-dose, 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 10, 14, 24, 36 and 48 hours in each treatment

End point values	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 2: 50 mg AFQ056 POS-1, Fed	Treatment 3: 50 mg AFQ056 POS-2, Fasted	Treatment 4: 50 mg AFQ056 POS-2, Fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	28	29	28
Units: Hours				
median (full range (min-max))	1.50 (0.533 to 2.50)	4 (1 to 6.02)	1.50 (0.5 to 2.5)	4 (1 to 6)

End point values	Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: Hours				
median (full range (min-max))	1 (0.5 to 4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Lag time (Tlag) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions

End point title	Lag time (Tlag) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions
End point description: The Tlag represents lag time before the absorption and signifies the delay between the time of dosing and time of appearance of concentration in the sampling. It was determined by non-compartmental method(s) using WinNonlin Pro (Version 5.2). Analysis was performed in PK Analysis set which included subjects who had evaluable PK data for at least one period.	
End point type	Secondary
End point timeframe: Pre-dose, 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 10, 14, 24, 36 and 48 hours in each treatment	

End point values	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 2: 50 mg AFQ056 POS-1, Fed	Treatment 3: 50 mg AFQ056 POS-2, Fasted	Treatment 4: 50 mg AFQ056 POS-2, Fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	28	29	28
Units: Hours				
median (full range (min-max))	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.250)	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.250)

End point values	Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: Hours				
median (full range (min-max))	0.25 (0.00 to 0.283)			

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal elimination half-life (T_{1/2}) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions

End point title	Terminal elimination half-life (T _{1/2}) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions
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End point description:

The T_{1/2} represents terminal elimination half-life defined as time required for the concentration or amount of drug in the body to be reduced by one-half. It was determined by non-compartmental method(s) using WinNonlin Pro (Version 5.2). Analysis was performed in PK Analysis set which included subjects who had evaluable PK data for at least one period.

End point type	Secondary
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End point timeframe:

Pre-dose, 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 10, 14, 24, 36 and 48 hours in each treatment

End point values	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 2: 50 mg AFQ056 POS-1, Fed	Treatment 3: 50 mg AFQ056 POS-2, Fasted	Treatment 4: 50 mg AFQ056 POS-2, Fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	27	27	28	28
Units: Hours				
median (full range (min-max))	8.911 (3.01 to 14.96)	6.984 (2.35 to 18.08)	9.839 (2.15 to 20.13)	6.529 (1.91 to 21.05)

End point values	Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: Hours				
median (full range (min-max))	10.599 (2.77 to 15.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent systemic clearance from plasma (CL/F) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions

End point title	Apparent systemic clearance from plasma (CL/F) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions
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End point description:

The CL/F represents apparent systemic (or total body) clearance from plasma (or serum or blood) following extravascular administration (volume/time). It was determined by non-compartmental method(s) using WinNonlin Pro (Version 5.2). Analysis was performed in PK Analysis set which included subjects who had evaluable PK data for at least one period.

End point type	Secondary
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End point timeframe:

Pre-dose, 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 10, 14, 24, 36 and 48 hours in each treatment

End point values	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 2: 50 mg AFQ056 POS-1, Fed	Treatment 3: 50 mg AFQ056 POS-2, Fasted	Treatment 4: 50 mg AFQ056 POS-2, Fed
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	27	27	28	28
Units: L/hr				
geometric mean (geometric coefficient of variation)	60.06 (\pm 67.19)	57.02 (\pm 59.38)	62.91 (\pm 58.28)	63.13 (\pm 65.88)

End point values	Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: L/hr				
geometric mean (geometric coefficient of variation)	58.84 (\pm 50.29)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected from first treatment administration up to 7 days after last drug administration. Serious Adverse Events (SAEs), were collected from informed consent until 30 days after last dose of study drug.

Adverse event reporting additional description:

The analysis was performed in safety set population defined as all subjects who received study drug and have at least one postbaseline safety assessment were included in the safety data analysis.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.0
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Reporting groups

Reporting group title	Treatment 1: 50mg AFQ056 POS-1, Fasted
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Reporting group description:

Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension with a 5 mL syringe under fasting condition, directly into the mouth.

Reporting group title	Treatment 2: 50 mg AFQ056 POS-1, Fed
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Reporting group description:

Subjects were administered POS-1 at a dose of 50 mg AFQ056 as 5 mL suspension with a 5 mL syringe under fed condition, directly into the mouth.

Reporting group title	Treatment 3: 50 mg AFQ056 POS-2, Fasted
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Reporting group description:

Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension with a 5 mL syringe under fasting condition, directly into the mouth.

Reporting group title	Treatment 4: 50 mg AFQ056 POS-2, Fed
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Reporting group description:

Subjects were administered POS-2 at a dose of 50 mg AFQ056 as 5 mL suspension with a 5 mL syringe under fed condition, directly into the mouth.

Reporting group title	Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted
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Reporting group description:

Subjects were administered two 25 mg hard gelatin capsules orally under fasting condition.

Serious adverse events	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 2: 50 mg AFQ056 POS-1, Fed	Treatment 3: 50 mg AFQ056 POS-2, Fasted
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 29 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Treatment 4: 50 mg AFQ056 POS-2, Fed	Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	0 / 27 (0.00%)	

number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Treatment 1: 50mg AFQ056 POS-1, Fasted	Treatment 2: 50 mg AFQ056 POS-1, Fed	Treatment 3: 50 mg AFQ056 POS-2, Fasted
Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 28 (42.86%)	8 / 28 (28.57%)	8 / 29 (27.59%)
Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 28 (0.00%) 0	1 / 29 (3.45%) 1
Injury, poisoning and procedural complications Excoriation subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 28 (0.00%) 0	0 / 29 (0.00%) 0
Nervous system disorders Coordination abnormal subjects affected / exposed occurrences (all) Disturbance in attention subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Dizziness postural subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0 0 / 28 (0.00%) 0 9 / 28 (32.14%) 9 1 / 28 (3.57%) 1 3 / 28 (10.71%) 3	0 / 28 (0.00%) 0 0 / 28 (0.00%) 0 5 / 28 (17.86%) 5 0 / 28 (0.00%) 0 1 / 28 (3.57%) 1	1 / 29 (3.45%) 1 1 / 29 (3.45%) 1 6 / 29 (20.69%) 6 0 / 29 (0.00%) 0 0 / 29 (0.00%) 0
General disorders and administration site conditions			

Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 28 (0.00%) 0	0 / 29 (0.00%) 0
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 28 (0.00%) 0	0 / 29 (0.00%) 0
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Hypoaesthesia oral subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0 1 / 28 (3.57%) 1	1 / 28 (3.57%) 1 0 / 28 (0.00%) 0	0 / 29 (0.00%) 0 0 / 29 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal obstruction subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0 0 / 28 (0.00%) 0	1 / 28 (3.57%) 1 1 / 28 (3.57%) 1	0 / 29 (0.00%) 0 0 / 29 (0.00%) 0
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 28 (0.00%) 0	0 / 29 (0.00%) 0
Psychiatric disorders Euphoric mood subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 28 (0.00%) 0	0 / 29 (0.00%) 0
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	1 / 28 (3.57%) 1	1 / 29 (3.45%) 1

Non-serious adverse events	Treatment 4: 50 mg AFQ056 POS-2, Fed	Treatment 5: 50 mg AFQ056 Capsule Formulation, Fasted	
Total subjects affected by non-serious adverse events subjects affected / exposed	5 / 29 (17.24%)	10 / 27 (37.04%)	

Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 27 (0.00%) 0	
Injury, poisoning and procedural complications Excoriation subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	1 / 27 (3.70%) 1	
Nervous system disorders Coordination abnormal subjects affected / exposed occurrences (all) Disturbance in attention subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Dizziness postural subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0 2 / 29 (6.90%) 2 2 / 29 (6.90%) 2 0 / 29 (0.00%) 0 1 / 29 (3.45%) 1	0 / 27 (0.00%) 0 0 / 27 (0.00%) 0 9 / 27 (33.33%) 10 0 / 27 (0.00%) 0 2 / 27 (7.41%) 2	
General disorders and administration site conditions Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	1 / 27 (3.70%) 1	
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	1 / 27 (3.70%) 1	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 27 (0.00%) 0	

Hypoaesthesia oral subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 27 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal obstruction subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0 0 / 29 (0.00%) 0	0 / 27 (0.00%) 0 0 / 27 (0.00%) 0	
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	0 / 27 (0.00%) 0	
Psychiatric disorders Euphoric mood subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 27 (0.00%) 0	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 27 (0.00%) 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

None reported