# 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 |

**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) | EMEA-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 |
|---|---|

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 |
|---|---|

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. 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 |

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 |
|---|---|

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 |
|---|---|

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.

| **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<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years | | | |
| arithmetic mean | 30.8 | 37.0 | 30.0 |
| standard deviation | ± 8.75 | ± 11.61 | ± 11.12 |
| Gender categorical<br>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<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years | | | |
| arithmetic mean | 30.3 | 35.2 | |
| standard deviation | ± 7.74 | ± 13.23 | - |
| Gender categorical<br>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 (Cmax) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions

| | |
|---|---|
| End point title | Maximum Observed Plasma Concentration (Cmax) 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 |
|---|---|

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 |
|---|---|

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 | 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 |

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 |

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 |
|---|---|

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 | 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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 (± 58.94) | 115.2 (± 64.38) | 157.1 (± 47.54) | 105.9 (± 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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 (T1/2) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions

| End point title | Terminal elimination half-life (T1/2) of POS-1 and POS-2 to the Capsule Formulation of AFQ056 Under Fasting Conditions |
|---|---|

End point description:

The T1/2 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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 (± 67.19) | 57.02 (± 59.38) | 62.91 (± 58.28) | 63.13 (± 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 (± 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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 13.0 |

### Reporting groups

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

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 |

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 |

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 |

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 |

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 | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| Excoriation | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Coordination abnormal | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Dizziness | | | |
| subjects affected / exposed | 9 / 28 (32.14%) | 5 / 28 (17.86%) | 6 / 29 (20.69%) |
| occurrences (all) | 9 | 5 | 6 |
| Dizziness postural | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 1 / 28 (3.57%) | 0 / 29 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypoaesthesia oral | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasal obstruction | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Eczema | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Euphoric mood | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 1 / 28 (3.57%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 1 | 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 | 0 / 29 (0.00%) | 0 / 27 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Excoriation | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 27 (3.70%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| Coordination abnormal | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 27 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Disturbance in attention | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 27 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 9 / 27 (33.33%) | |
| occurrences (all) | 2 | 10 | |
| Dizziness postural | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 27 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 2 / 27 (7.41%) | |
| occurrences (all) | 1 | 2 | |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 27 (3.70%) | |
| occurrences (all) | 0 | 1 | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 27 (3.70%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 27 (0.00%) | |
| occurrences (all) | 0 | 0 | |

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