Clinical trial results:
A multicenter, open-label, single-arm, two-step study to evaluate the safety and single-dose pharmacokinetics of famciclovir and multiple-dose safety after administration of famciclovir oral pediatric formulation to children 1 to 12 years of age with varicella zoster infection

Summary

EudraCT number	2015-004442-25
Trial protocol	Outside EU/EEA
Global end of trial date	30 July 2007

Results information

Result version number	v1 (current)
This version publication date	19 December 2016
First version publication date	19 December 2016

Trial information

Trial identification

Sponsor protocol code	CFAM810B2304

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00098046
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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes
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	30 July 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 July 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was:
Part A:
To evaluate the safety and tolerability, and pharmacokinetics (PK) of a single dose of famciclovir oral pediatric formulation in children from 1 to 12 years of age with varicella zoster virus (VZV) infection, in order to define the dose in this age group which gives a similar exposure to famciclovir 500 mg dose in adults
Part B:
To explore the safety and tolerability of multiple doses of famciclovir administered three times-daily over 7 days in children from 1 to 12 years of age who had VZV infection

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 July 2005
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	Costa Rica: 32
Country: Number of subjects enrolled	Panama: 34
Country: Number of subjects enrolled	Guatemala: 13
Worldwide total number of subjects	79
EEA total number of subjects	0

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	24

months)	
Children (2-11 years)	55
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at: Part A: 2 centers (1 in Panama, 1 in Costa Rica); Part B: 4 centers (2 in Panama, 1 in Costa Rica, 1 in Guatemala).

Pre-assignment

Screening details:

A total of 79 subjects (Part A: 26, Part B: 53) were enrolled in the study.

Period 1

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

Blinding implementation details:

The study was open label study, hence no blinding was performed

Arms

Are arms mutually exclusive?	Yes
Arm title	Famciclovir: Single dose (Part A)

Arm description:

Subjects were orally administered with a single body weight stratified dose of famciclovir of 12.5 milligram (mg)/kilogram (kg) body weight with a dose escalation up to a maximum dose of 500 mg. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Arm type	Experimental
Investigational medicinal product name	Famciclovir
Investigational medicinal product code	FAM810
Other name	Famvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects were orally administered with a single-dose closest to 12.5 mg/kg body weight with a maximum dose of 500 mg.

Arm title	Famciclovir: Multiple doses (Part B)

Arm description:

Subjects were orally administered with famciclovir sprinkle capsules thrice daily (t.i.d.) with a dose separation of 8 hours for a period of 7 days. Subjects were administered with a body weight stratified daily dose in 8-step from 150 mg t.i.d. up to a maximum of 500 mg t.i.d. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Arm type	Experimental
Investigational medicinal product name	Famciclovir
Investigational medicinal product code	FAM810
Other name	Famvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects were orally administered with a body weight stratified dose ranged from 150 mg to 500 mg t.i.d. of famciclovir sprinkle capsules with a dose separation of 8 hours for a period of 7 days.

Number of subjects in period 1	Famciclovir: Single dose (Part A)	Famciclovir: Multiple doses (Part B)
Started	26	53
Completed	26	48
Not completed	0	5
Abnormal lab values	-	2
Adverse event(s)	-	2
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	Famciclovir: Single dose (Part A)

Reporting group description:

Subjects were orally administered with a single body weight stratified dose of famciclovir of 12.5 milligram (mg)/kilogram (kg) body weight with a dose escalation up to a maximum dose of 500 mg. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Reporting group title	Famciclovir: Multiple doses (Part B)

Reporting group description:

Subjects were orally administered with famciclovir sprinkle capsules thrice daily (t.i.d.) with a dose separation of 8 hours for a period of 7 days. Subjects were administered with a body weight stratified daily dose in 8-step from 150 mg t.i.d. up to a maximum of 500 mg t.i.d. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Reporting group values	Famciclovir: Single dose (Part A)	Famciclovir: Multiple doses (Part B)	Total
Number of subjects	26	53	79
Age categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)	6	18	24
Children (2-11 years)	20	35	55
Age continuous			
Units: years			
arithmetic mean	4.8	4.2	
standard deviation	± 3.2	± 3.3	-
Gender categorical			
Units: Subjects			
Female	11	26	37
Male	15	27	42

Subject analysis sets

Subject analysis set title	Subjects aged: 1 to <2 years (Part A)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 1 to <2 years were orally administered with a single body weight stratified dose of famciclovir of 12.5 mg/kg weight with a maximum dose of 500 mg.

Subject analysis set title	Subjects aged: 2 to <6 years (Part A)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 2 to <6 years were orally administered with a single body weight stratified dose of famciclovir of 12.5 mg/kg weight with a maximum dose of 500 mg.

Subject analysis set title	Subjects aged: 6 to <=12 years (Part A)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 6 to <12 years were orally administered with a single body weight stratified dose of famciclovir of 12.5 mg/kg weight with a maximum dose of 500 mg.

Subject analysis set title	Subjects aged: 1 to <2 years (Part B)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 1 to <2 years were orally administered with famciclovir sprinkle capsule thrice daily with a dose separation of 8 hours for a period of 7
days. Subjects were administered with a body weight stratified daily dose in 8-step from 150 mg t.i.d. up to a maximum of 500 mg t.i.d. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Subject analysis set title	Subjects aged: 2 to <6 years (Part B)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 1 to <2 years were orally administered with famciclovir sprinkle capsule thrice daily with a dose separation of 8 hours for a period of 7
days. Subjects were administered with a body weight stratified daily dose in 8-step from 150 mg t.i.d.up to a maximum of 500 mg t.i.d. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Subject analysis set title	Subjects aged: 6 to <=12 years (Part B)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 1 to <2 years were orally administered with famciclovir sprinkle capsule thrice daily with a dose separation of 8 hours for a period of 7
days. Subjects were administered with a body weight stratified daily dose in 8-step from 150 mg t.i.d.up to a maximum of 500 mg t.i.d. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Reporting group values	Subjects aged: 1 to <2 years (Part A)	Subjects aged: 2 to <6 years (Part A)	Subjects aged: 6 to <=12 years (Part A)
Number of subjects	6	11	9
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Age continuous Units: years			
arithmetic mean	1	3.9	8.3
standard deviation	± 0	± 1	± 2
Gender categorical Units: Subjects			
Female	4	4	3
Male	2	7	6

Reporting group values	Subjects aged: 1 to <2 years (Part B)	Subjects aged: 2 to <6 years (Part B)	Subjects aged: 6 to <=12 years (Part B)
Number of subjects	18	19	16
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Age continuous Units: years			
arithmetic mean	1	3.5	8.6
standard deviation	± 0	± 1.1	± 1.4
Gender categorical Units: Subjects			
Female	10	5	11
Male	8	14	5

End points

End points reporting groups

Reporting group title	Famciclovir: Single dose (Part A)

Reporting group description:

Subjects were orally administered with a single body weight stratified dose of famciclovir of 12.5 milligram (mg)/kilogram (kg) body weight with a dose escalation up to a maximum dose of 500 mg. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Reporting group title	Famciclovir: Multiple doses (Part B)

Reporting group description:

Subjects were orally administered with famciclovir sprinkle capsules thrice daily (t.i.d.) with a dose separation of 8 hours for a period of 7 days. Subjects were administered with a body weight stratified daily dose in 8-step from 150 mg t.i.d. up to a maximum of 500 mg t.i.d. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Subject analysis set title	Subjects aged: 1 to <2 years (Part A)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 1 to <2 years were orally administered with a single body weight stratified dose of famciclovir of 12.5 mg/kg weight with a maximum dose of 500 mg.

Subject analysis set title	Subjects aged: 2 to <6 years (Part A)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 2 to <6 years were orally administered with a single body weight stratified dose of famciclovir of 12.5 mg/kg weight with a maximum dose of 500 mg.

Subject analysis set title	Subjects aged: 6 to <=12 years (Part A)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 6 to <12 years were orally administered with a single body weight stratified dose of famciclovir of 12.5 mg/kg weight with a maximum dose of 500 mg.

Subject analysis set title	Subjects aged: 1 to <2 years (Part B)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 1 to <2 years were orally administered with famciclovir sprinkle capsule thrice daily with a dose separation of 8 hours for a period of 7
days. Subjects were administered with a body weight stratified daily dose in 8-step from 150 mg t.i.d. up to a maximum of 500 mg t.i.d. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Subject analysis set title	Subjects aged: 2 to <6 years (Part B)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 1 to <2 years were orally administered with famciclovir sprinkle capsule thrice daily with a dose separation of 8 hours for a period of 7
days. Subjects were administered with a body weight stratified daily dose in 8-step from 150 mg t.i.d.up to a maximum of 500 mg t.i.d. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Subject analysis set title	Subjects aged: 6 to <=12 years (Part B)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects aged between 1 to <2 years were orally administered with famciclovir sprinkle capsule thrice daily with a dose separation of 8 hours for a period of 7
days. Subjects were administered with a body weight stratified daily dose in 8-step from 150 mg t.i.d.up to a maximum of 500 mg t.i.d. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Primary: Time to maximum plasma concentration (Tmax) of famciclovir during Part A

End point title	Time to maximum plasma concentration (Tmax) of famciclovir during Part A[1]

End point description:

Tmax was defined as the time to reach maximum plasma concentration. Penciclovir (metabolite of famciclovir) plasma concentrations were determined by using a validated liquid chromatography/tandem mass spectrometry (LC/MS/MS) method. The limit of quantification was 0.15 microgram (µg)/millilitre (mL) for both compounds. The analysis was performed in pharmacokinetic analysis set (PAS) population, defined as all subjects who received at least one scheduled dose of famciclovir and provided all primary PK parameters in at least one treatment period.

End point type	Primary

End point timeframe:

At pre-dose, 1, 2, 3, 4, and 5 hours post treatment administration

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: ONLY SUMMARY STATS ARE AVAILABLE

End point values	Subjects aged: 1 to <2 years (Part A)	Subjects aged: 2 to <6 years (Part A)	Subjects aged: 6 to <=12 years (Part A)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	11	9	
Units: Hours				
median (full range (min-max))	1.08 (1 to 1.42)	1.07 (0.93 to 3.03)	1 (1 to 1.17)	

Statistical analyses

No statistical analyses for this end point

Primary: Maximum plasma concentration (Cmax) of famciclovir during Part A

End point title	Maximum plasma concentration (Cmax) of famciclovir during Part A[2]

End point description:

Cmax was defined as the maximum plasma concentration. Penciclovir (metabolite of famciclovir)plasma concentrations were determined by using a validated LC/MS/MS method. The limit of quantification was 0.15 µg/mL for both compounds. The analysis was performed in PAS population.

End point type	Primary

End point timeframe:

At pre-dose, 1, 2, 3, 4, and 5 hours post treatment administration

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: ONLY SUMMARY STATS ARE AVAILABLE

End point values	Subjects aged: 1 to <2 years (Part A)	Subjects aged: 2 to <6 years (Part A)	Subjects aged: 6 to <=12 years (Part A)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	11	9	
Units: microgram(µg)/milliliter(mL)				
geometric mean (geometric coefficient	3.09 (± 31.6)	3.09 (± 24.6)	3.86 (± 22.7)	

of variation)

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration time curve from time zero to the time point of the last measurable concentration (AUC 0-tlast) of famciclovir during Part A

End point title	Area under the plasma concentration time curve from time zero to the time point of the last measurable concentration (AUC 0-tlast) of famciclovir during Part A[3]

End point description:

AUC 0-tlast was defined as the area under the plasma concentration time curve from time zero to the time point of the last measurable concentration. Penciclovir (metabolite of famciclovir)plasma concentrations were determined by using a validated LC/MS/MS method. The limit of quantification was 0.15 µg/mL for both compounds. The analysis was performed in PAS population.

End point type	Primary

End point timeframe:

At pre-dose, 1, 2, 3, 4, and 5 hours post treatment administration

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: ONLY SUMMARY STATS ARE AVAILABLE

End point values	Subjects aged: 1 to <2 years (Part A)	Subjects aged: 2 to <6 years (Part A)	Subjects aged: 6 to <=12 years (Part A)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	11	9	
Units: (microgram(µg)/milliliter(mL))*hour(h))				
geometric mean (geometric coefficient of variation)	6.76 (± 35.2)	6.85 (± 25.2)	8.76 (± 17)	

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration time curve from time zero to infinity (AUC 0-infinity) of famciclovir during Part A

End point title	Area under the plasma concentration time curve from time zero to infinity (AUC 0-infinity) of famciclovir during Part A[4]

End point description:

AUC 0-infinity was defined as the area under the plasma concentration time curve from time zero to infinity. Penciclovir (metabolite of famciclovir) plasma concentrations were determined by using a validated LC/MS/MS method. The limit of quantification was 0.15 µg/mL for both compounds. The analysis was performed in PAS population.

End point type	Primary

End point timeframe:

At pre-dose, 1, 2, 3, 4, and 5 hours post treatment administration

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: ONLY SUMMARY STATS ARE AVAILABLE

End point values	Subjects aged: 1 to <2 years (Part A)	Subjects aged: 2 to <6 years (Part A)	Subjects aged: 6 to <=12 years (Part A)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	11	9	
Units: µg/mL*h				
geometric mean (geometric coefficient of variation)	7.46 (± 38)	7.56 (± 29.8)	10.24 (± 17.5)	

Statistical analyses

No statistical analyses for this end point

Primary: Terminal elimination half-life (T½) of famciclovir during Part A

End point title	Terminal elimination half-life (T½) of famciclovir during Part

End point description:

T½ was defined as the terminal elimination half-life. Penciclovir (metabolite of famciclovir)plasma concentrations were determined by using a validated LC/MS/MS method. The limit of quantification was 0.15 µg/mL for both compounds. The analysis was performed in PAS population.

End point type	Primary

End point timeframe:

At pre-dose, 1, 2, 3, 4, and 5 hours post treatment administration

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: ONLY SUMMARY STATS ARE AVAILABLE

End point values	Subjects aged: 1 to <2 years (Part A)	Subjects aged: 2 to <6 years (Part A)	Subjects aged: 6 to <=12 years (Part A)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	11	9	
Units: Hours				
median (full range (min-max))	1.26 (1.08 to 1.53)	1.17 (0.83 to 1.38)	1.68 (1.16 to 1.99)	

Statistical analyses

No statistical analyses for this end point

Primary: Apparent oral clearance (CL/F) of famciclovir during Part A

End point title	Apparent oral clearance (CL/F) of famciclovir during Part A[6]

End point description:

CL/F was defined as the apparent oral clearance. Penciclovir (metabolite of famciclovir)plasma concentrations were determined by using a validated LC/MS/MS method. The limit of quantification was 0.15 µg/mL for both compounds. The analysis was performed in PAS population.

End point type	Primary

End point timeframe:

At pre-dose, 1, 2, 3, 4, and 5 hours post treatment administration

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: ONLY SUMMARY STATS ARE AVAILABLE

End point values	Subjects aged: 1 to <2 years (Part A)	Subjects aged: 2 to <6 years (Part A)	Subjects aged: 6 to <=12 years (Part A)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	11	9	
Units: Lites(L)/Hour(h)				
geometric mean (geometric coefficient of variation)	13.1 (± 30.8)	23.3 (± 18.6)	26.1 (± 23.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with Adverse Events (AEs), Serious Adverse Events(SAEs), AE leading to discontinuation and who died

End point title	Number of subjects with Adverse Events (AEs), Serious Adverse Events(SAEs), AE leading to discontinuation and who died[7]

End point description:

AEs are defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during study, having been absent at baseline, or, if present at baseline, appears to worsen. Serious adverse events are any untoward medical occurrences that result in death, are life threatening, require (or prolong) hospitalization, cause persistent or significant disability/incapacity, result in congenital anomalies or birth defects, or are other conditions which in judgment of investigators represent significant hazards. The analysis was performed on safety set population defined as all subjects who received at least one of the study treatment.

End point type	Primary

End point timeframe:

From Day 1 up to Day 15

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: NO STATS COMPARING SAFETY

End point values	Subjects aged: 1 to <2 years (Part A)	Subjects aged: 2 to <6 years (Part A)	Subjects aged: 6 to <=12 years (Part A)	Subjects aged: 1 to <2 years (Part B)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	11	9	18
Units: Subjects				
AEs	0	0	0	7
SAEs	0	0	0	0

Deaths	0	0	0	0
AEs leading to discontinuation	0	0	0	0
AE requiring concomitant medication	0	0	0	3

End point values	Subjects aged: 2 to <6 years (Part B)	Subjects aged: 6 to <=12 years (Part B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	16		
Units: Subjects				
AEs	10	7		
SAEs	0	0		
Deaths	0	0		
AEs leading to discontinuation	0	2		
AE requiring concomitant medication	7	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with clinically significant laboratory abnormalities

End point title	Number of subjects with clinically significant laboratory abnormalities[8]

End point description:

Subjects with laboratory values outside the defined normal range were graded as clinically significant laboratory abnormalities. Laboratory values were assessed according to the National Cancer Institute-Common terminology criteria for Adverse Events (NCI-CTCAE). Hematology and clinical chemistry were performed. The analysis was performed on the safety set.

End point type	Primary

End point timeframe:

From Day 1 up to Day 15

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: NO STATS COMPARING SAFETY

End point values	Subjects aged: 1 to <2 years (Part A)	Subjects aged: 2 to <6 years (Part A)	Subjects aged: 6 to <=12 years (Part A)	Subjects aged: 1 to <2 years (Part B)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	11	9	18
Units: Subjects				
Hematology	0	0	0	0
Clinical chemistry	0	0	0	0

End point values	Subjects aged: 2 to <6 years	Subjects aged: 6 to <=12		

	(Part B)	years (Part B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	16		
Units: Subjects				
Hematology	0	0		
Clinical chemistry	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of acceptability of pediatric formulation during Part A

End point title	Assessment of acceptability of pediatric formulation during Part A

End point description:

Assessment of acceptability was done using a modified, 5-point facial hedonic scale, subjects or caregivers were asked to complete an assessment of study medication. Subjects marked the scale with their response of choice. The scale represented a balance of choices from 'I did not like it' to 'I like it very much' with a mid-point of neither like nor dislike, with qualitative evaluation. The analysis was performed on the safety set.

End point type	Secondary

End point timeframe:

At Day 1

End point values	Subjects aged: 1 to <2 years (Part A)	Subjects aged: 2 to <6 years (Part A)	Subjects aged: 6 to <=12 years (Part A)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	11	9	
Units: Subjects				
Bitter	0	4	7	
Sweet	1	6	3	
Other	5	1	0	
Very badly / Unacceptable	0	0	0	
Badly but accepted	1	1	1	
Neither good nor bad	1	1	1	
Well accepted	2	8	5	
Very well accepted	2	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of acceptability of pediatric formulation during Part B

End point title	Assessment of acceptability of pediatric formulation during Part B

End point description:

Assessment of acceptability was done using a modified, 5-point facial hedonic scale, subjects orcaregivers were asked to complete an assessment of study medication. Subjects marked the scale with their response of choice. The scale represented a balance of choices from 'I did not like it' to 'I like it
very much' with a mid-point of neither like nor dislike, with qualitative evaluation. The analysis was performed on the safety set. Here, 'clinic' and 'home' signifies post-first dose in clinic and home respectively and day 8 have been reported for post-last dose at home.

End point type	Secondary

End point timeframe:

From Day 1 to Day 8

End point values	Subjects aged: 1 to <2 years (Part B)	Subjects aged: 2 to <6 years (Part B)	Subjects aged: 6 to <=12 years (Part B)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	18	19	16	
Units: Subjects				
Bitter	4	6	7	
Sweet	6	10	6	
Other	8	3	3	
Very badly/unacceptable:Day 1(clinic)	4	0	0	
Badly but accepted: Day 1(clinic)	7	3	2	
Neither good nor bad: Day 1(clinic)	6	2	1	
Well accepted: Day 1(clinic)	1	10	7	
Very well accepted: Day 1(clinic)	0	4	6	
Very badly/unacceptable:Day 1(home)	2	0	0	
Badly but accepted: Day 1(home)	9	6	3	
Neither good nor bad: Day 1(home)	4	4	3	
Well accepted: Day 1(home)	1	6	4	
Very well accepted: Day 1(home)	0	3	5	
Very badly/unacceptable: EoS/early discontinuation	1	0	0	
Badly but accepted: EoS/early discontinuation	5	5	3	
Neither good nor bad: EoS/early discontinuation	5	4	1	
Well accepted: EoS/early discontinuation	5	2	3	
Very well accepted: EoS/early discontinuation	0	8	9	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events are monitored from date of First Subject First Visit (FSFV) until Last Subject Last Visit (LSLV). All other adverse events are monitored from First Subject First Treatment until LSLV

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	Famciclovir: Multiple doses (Part B)

Reporting group description:

Subjects were orally administered with famciclovir sprinkle capsules t.i.d. with a dose separation of 8 hours for a period of 7 days. Subjects were administered with a body weight stratified daily dose in 8-step from 150 mg t.i.d. up to a maximum of 500 mg t.i.d. Subjects who had weight >= 40 kg received a famciclovir dose of 500 mg.

Serious adverse events	Famciclovir: Multiple doses (Part B)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 53 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Famciclovir: Multiple doses (Part B)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 53 (32.08%)		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Gastrointestinal disorders			

Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	2 / 53 (3.77%) 2 6 / 53 (11.32%) 7 2 / 53 (3.77%) 2 5 / 53 (9.43%) 5		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	2 / 53 (3.77%) 2		
Infections and infestations Cellulitis subjects affected / exposed occurrences (all)	2 / 53 (3.77%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 July 2006	Dosing scheme for Part B was adjusted according to interim results from Part A of both studies (i.e. CFAM810B2303 and CFAM810B2304) and discussions with FDA. It also added a criterion to exclude subjects who weighed <9 kg and deleted the requirement that subjects without laboratory confirmation of their infection must discontinue drug.
17 November 2006	Requirement for PK and multiple-dose safety assessments in a cohort of subjects, 12 to 18 years of age and the upper age limit of the pediatric subjects to be studied from 12 to 18 years old was amended. The amendment created a new cohort for these adolescent subjects .
18 June 2007	Cancelled the requirement for inclusion of adolescent subjects in the study by deleting the new cohort (which had been designated as cohort 4 to include subjects 12 to 18 years of age), amending the upper age limit of the pediatric subjects to be studied from 18 back to 12 years, and deleting the requirement for single-dose PK for 3 to 4 subjects in cohort 4. The amendment also readjusted the number of subjects per cohort in Part B to compensate for the removal of cohort 4.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported