



Clinical trial results:

A Phase 2/3 Randomized, Double-Blind, Placebo-Controlled, Dose-Finding Study of the Efficacy and Safety of Daily CF101 Administered Orally in Patients with Moderate-to-Severe Plaque Psoriasis

Summary

EudraCT number	2010-024196-83
Trial protocol	BG
Global end of trial date	03 February 2015

Results information

Result version number	v1 (current)
This version publication date	22 November 2020
First version publication date	22 November 2020

Trial information

Trial identification

Sponsor protocol code	CF101-202PS
-----------------------	-------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01235234
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Can-Fite BioPharma, Ltd
Sponsor organisation address	10 Bareket Street, Petach Tikva, Israel,
Public contact	Clinical Director, Can Fite BioPharma, Ltd, +972 528998672, sari@canfite.co.il
Scientific contact	Clinical Director, Can Fite BioPharma, Ltd, +972 528998672, sari@canfite.co.il

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?	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	28 April 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 February 2015
Global end of trial reached?	Yes
Global end of trial date	03 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Before Amendment 4:

The primary objectives of this study are to:

- Evaluate the efficacy of oral CF101 when administered at 2 mg twice daily (BID) for 16 weeks, compared with placebo, in patients with moderate-to-severe plaque psoriasis; and
- Evaluate the safety of oral CF101 in this patient population

After Amendment 4:

The primary objectives of this study were to:

- Evaluate the efficacy of oral CF101 when administered at 2 mg twice daily (BID) for 16 weeks, compared with placebo, in patients with moderate-to-severe plaque psoriasis; and
- Evaluate the safety of oral CF101 in this patient population

Protection of trial subjects:

This study was reviewed and approved by an Ethics Committee. The study was conducted in accordance with the protocol, standards of Good Clinical Practice, as defined by the International Conference on Harmonisation and all applicable national and local regulations. All associates assisting in the conduct of study were informed regarding their obligations.

A data monitoring committee, governed by a charter which stipulated operation procedures, met periodically to review interim data and results. It was chaired by Michael Goldfarb, PhD (Dermatologist at University of Michigan Department of Dermatology, MI, USA) and comprised Jay Herson, PhD (Biostatistician at Johns Hopkins University, ML, USA) and Michael Weintraub, MD (Clinical Research Physician [Pharmaceutical Consulting], Rochester, NY, USA).

Background therapy:

None

Evidence for comparator:

The results from nonclinical toxicology studies and clinical safety and efficacy studies performed to date support the safety of CF101 and provide evidence of efficacy of CF101 as potential therapy for mild-moderate plaque psoriasis. Efficacy data from Protocol CF101-201PS demonstrated that CF101 2 mg twice daily (BID) produced statistically significant improvements in Psoriasis Area and Severity Index (PASI), as compared to both baseline and to placebo, at the 12 week efficacy assessment. The same dose group showed statistically significant efficacy, as determined by the Physician Global Assessment (PGA) at 12 weeks. As originally written, the 2 mg BID dose group was studied in this trial, as well as a 1 mg BID dose group to further define the optimal dose of CF101.

Actual start date of recruitment	13 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 13
--------------------------------------	-------------------

Country: Number of subjects enrolled	Israel: 16
Country: Number of subjects enrolled	Romania: 110
Country: Number of subjects enrolled	Bulgaria: 154
Worldwide total number of subjects	293
EEA total number of subjects	264

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)	257
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

There were 325 subjects enrolled and randomised in 25 sites in 4 countries and included in the study

Pre-assignment

Screening details:

At a Screening Visit (within 28 days prior to the Baseline Visit), subjects who provided written informed consent and fulfilled the inclusion criteria (notably: diagnosis of moderate-to-severe chronic plaque-type psoriasis with BSA involvement $\geq 10\%$ and psoriasis for at least 6 months) underwent specified procedures.

Period 1

Period 1 title	BPCP
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Treatment assignment was blinded for the first 16-week dosing period, followed by an additional 16-week open-label treatment period (11 visits [1 via telephone], up to 36 weeks total).

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	CF101 2 mg
------------------	------------

Arm description:

Following Amendment 4, medication was taken orally BID for 16 weeks in a double-blinded fashion

Arm type	Active comparator
Investigational medicinal product name	Methyl 1-[N6-(3-iodobenzyl)-adenin-9-yl]- β -D-ribofuronamide
Investigational medicinal product code	CF101
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg tablet BID on an empty stomach 1 hour before or 2 hours after meals.

Arm title	Placebo
------------------	---------

Arm description:

Following Amendment 4, medication was taken orally BID for 16 weeks in a double-blinded fashion. Pooled set of subjects who received Placebo followed by CF101 1 mg (14 subjects), or Placebo followed by CF101 2 mg (134 subjects).

Arm type	Placebo
Investigational medicinal product name	Placebo, matching for methyl 1-[N6-(3-iodobenzyl)-adenin-9-yl]- β -D-ribofuronamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching CF1012 placebo tablet BID on an empty stomach 1 hour before or 2 hours after meals.

Number of subjects in period 1	CF101 2 mg	Placebo
Started	145	148
Completed	126	134
Not completed	19	14
Adverse event, serious fatal	1	-
Consent withdrawn by subject	3	4
Physician decision	4	1
Other	2	2
Lost to follow-up	4	2
Unacceptable concomitant medication or therapy	1	-
Unacceptable concomitant medication or therapy	-	1
Lack of efficacy	2	4
Protocol deviation	2	-

Period 2

Period 2 title	OLE
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Open label portion of the study.

Arms

Arm title	CF101 2 mg
-----------	------------

Arm description:

Following Amendment 4 subjects assigned to CF101 2 mg continued with CF101 2 mg, while subjects originally assigned to placebo were reassigned to CF101 2 mg BID. Therefore, dosing during Weeks 17 to 32 was open-label for both groups.

Arm type	Active comparator
Investigational medicinal product name	Methyl 1-[N6-(3-iodobenzyl)-adenin-9-yl]-β-D-ribofuronamide
Investigational medicinal product code	CF101
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 mg taken orally as 1 tablet BID on an empty stomach 1 hour before or 2 hours after meals.

Number of subjects in period 2^[1]	CF101 2 mg
Started	249
Completed	213
Not completed	36
Consent withdrawn by subject	13
Physician decision	3
Unacceptable toxicity developed	1
Other	6
Lost to follow-up	2
Unacceptable concomitant medication or therapy	1
Lack of efficacy	6
Protocol deviation	4

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Based on results of a planned interim analysis using data from the first 103 subjects enrolled in the trial (32 subjects in the CF101 1 mg BID dose group, 33 in the CF101 2 mg BID dose group, and 38 in the BID placebo group), the CF101 1 mg BID dose group was eliminated by Amendment 4 for futility, and the sample size of the remaining groups was increased.

Baseline characteristics

Reporting groups

Reporting group title	CF101 2 mg
Reporting group description: Following Amendment 4, medication was taken orally BID for 16 weeks in a double-blinded fashion	
Reporting group title	Placebo
Reporting group description: Following Amendment 4, medication was taken orally BID for 16 weeks in a double-blinded fashion. Pooled set of subjects who received Placebo followed by CF101 1 mg (14 subjects), or Placebo followed by CF101 2 mg (134 subjects).	

Reporting group values	CF101 2 mg	Placebo	Total
Number of subjects	145	148	293
Age categorical Units: Subjects			
Adults (18-80 years)	145	148	293
Gender categorical Units: Subjects			
Female	54	53	107
Male	91	95	186

End points

End points reporting groups

Reporting group title	CF101 2 mg
Reporting group description: Following Amendment 4, medication was taken orally BID for 16 weeks in a double-blinded fashion	
Reporting group title	Placebo
Reporting group description: Following Amendment 4, medication was taken orally BID for 16 weeks in a double-blinded fashion. Pooled set of subjects who received Placebo followed by CF101 1 mg (14 subjects), or Placebo followed by CF101 2 mg (134 subjects).	
Reporting group title	CF101 2 mg
Reporting group description: Following Amendment 4 subjects assigned to CF101 2 mg continued with CF101 2 mg, while subjects originally assigned to placebo were reassigned to CF101 2 mg BID. Therefore, dosing during Weeks 17 to 32 was open-label for both groups.	

Primary: Proportion of subjects achieving PASI 75 at Week 12

End point title	Proportion of subjects achieving PASI 75 at Week 12
End point description: The proportion of subjects achieving PASI 75 at Week 12.	
End point type	Primary
End point timeframe: Week 12	

End point values	CF101 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	144		
Units: Subjects	12	10		

Statistical analyses

Statistical analysis title	Subjects with PASI 75 at Wk 12
Statistical analysis description: Between-treatment comparisons of CF101 to placebo with respect to the proportion of subjects achieving PASI 75 at Week 12 were performed using the Cochran-Mantel Haenszel (CMH) test for the ITT population	
Comparison groups	CF101 2 mg v Placebo
Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	= 0.621
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.8

Confidence interval	
level	Other: 96.5 %
sides	2-sided
lower limit	0.31
upper limit	2.05

Notes:

[1] - To adjust for the interim analysis, the primary analysis of PASI 75 at Week 12 was performed at the 0.035 significance level.

Secondary: Proportion of subjects achieving PASI 75 at Week 16

End point title	Proportion of subjects achieving PASI 75 at Week 16
End point description: Proportion of subjects achieving PASI 75 at Week 16.	
End point type	Secondary
End point timeframe: Week 16	

End point values	CF101 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	144		
Units: Subjects	12	14		

Statistical analyses

Statistical analysis title	Subjects with PASI 75 at Wk 16
Statistical analysis description: Between-treatment comparisons of CF101 to placebo with respect to the proportion of subjects achieving PASI 75 at Week 12 were performed using the Cochran-Mantel Haenszel (CMH) test for the ITT population.	
Comparison groups	CF101 2 mg v Placebo
Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	other ^[2]
P-value	= 0.658
Method	Cochran-Mantel-Haenszel
Parameter estimate	Log odds ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	2.74

Notes:

[2] - Between-treatment comparisons of CF101 to placebo with respect to each of these variables were performed using the CMH test at the 0.05 level.

Secondary: Proportion of subjects with Physician Global Assessment (PGA) of 0 or 1 at Weeks 12

End point title	Proportion of subjects with Physician Global Assessment (PGA) of 0 or 1 at Weeks 12
End point description: Proportion of subjects with Physician Global Assessment (PGA) of 0 or 1 at Weeks 12.	
End point type	Secondary
End point timeframe: Week 12	

End point values	CF101 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	144		
Units: Subjects	9	5		

Statistical analyses

Statistical analysis title	Subjects with PGA 0 or 1 at Wk 12
Comparison groups	CF101 2 mg v Placebo
Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	other ^[3]
P-value	= 0.256
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	1.62

Notes:

[3] - Performed using the CMH test at the 0.05 level.

Secondary: Proportion of subjects with Physician Global Assessment (PGA) of 0 or 1 at Weeks 16

End point title	Proportion of subjects with Physician Global Assessment (PGA) of 0 or 1 at Weeks 16
End point description: Proportion of subjects with Physician Global Assessment (PGA) of 0 or 1 at Weeks 16.	
End point type	Secondary
End point timeframe: Week 16	

End point values	CF101 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	144		
Units: Subjects	4	8		

Statistical analyses

Statistical analysis title	Subjects with PGA 0 or 1 at Wk 16
Comparison groups	CF101 2 mg v Placebo
Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	other ^[4]
P-value	= 0.229
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	7.2

Notes:

[4] - Performed using the CMH test at the 0.05 level.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events reporting occurred from Baseline (Week 0) until Week 32

Adverse event reporting additional description:

AEs were coded using MedDRA. All TEAEs were summarized by treatment group. Counts and percent was presented by treatment group for each observed SOC and preferred term as defined in MedDRA.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	0
--------------------	---

Reporting groups

Reporting group title	CF101 2 mg BPCP
-----------------------	-----------------

Reporting group description:

Analysed as the Safety Population during the blinded placebo-controlled period.

Reporting group title	Placebo Pooled
-----------------------	----------------

Reporting group description:

Analysed as the Safety Population during the blinded placebo-controlled period.

Reporting group title	CF101 2mg OLE
-----------------------	---------------

Reporting group description:

Analysed as the Safety Population during the open-label extension period.

Reporting group title	CF101 1mg BPCP
-----------------------	----------------

Reporting group description:

Analysed as the Safety Population during the blinded placebo-controlled period.

Reporting group title	CF101 1.0 mg OLE
-----------------------	------------------

Reporting group description:

Analysed as the Safety Population during the open-label extension period.

Serious adverse events	CF101 2 mg BPCP	Placebo Pooled	CF101 2mg OLE
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 145 (4.83%)	1 / 148 (0.68%)	6 / 249 (2.41%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Thermal burn			

subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure chronic			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Sleep apnoea syndrome			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			

subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Glomerulonephritis chronic			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc disorder			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plica syndrome			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Subacute endocarditis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			

subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	CF101 1mg BPCP	CF101 1.0 mg OLE	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure chronic			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Sleep apnoea syndrome			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Psoriasis			

subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Glomerulonephritis chronic			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plica syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Subacute endocarditis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Peritonitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CF101 2 mg BPCP	Placebo Pooled	CF101 2mg OLE
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 145 (25.52%)	29 / 148 (19.59%)	46 / 249 (18.47%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid neoplasm			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	0 / 249 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Venous insufficiency			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	0	0	0
Angina pectoris			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	1	0	0
Arteriosclerosis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	0 / 249 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	1	0	1

Pyrexia subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	1 / 148 (0.68%) 1	1 / 249 (0.40%) 1
Immune system disorders Rhinitis allergic subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Food allergy subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Pulmonary arterial hypertension subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	1 / 148 (0.68%) 1	0 / 249 (0.00%) 0
Bronchitis chronic subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Lung disorder subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Influenza subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Investigations Red blood cells urine subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Bacterial test			

subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	0	0	0
Nitrite urine			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	1
Blood urea increased			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	1 / 249 (0.40%)
occurrences (all)	0	1	1
Helicobacter test positive			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	1 / 249 (0.40%)
occurrences (all)	0	2	1
Serum serotonin increased			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	1
Urine analysis abnormal			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	1
Blood phosphorus decreased			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram repolarisation abnormality			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			

Comminuted fracture subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Injury subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	1 / 148 (0.68%) 1	0 / 249 (0.00%) 0
Joint injury subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Thermal burn subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Cardiac disorders Tachyarrhythmia subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Supraventricular extrasystoles subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	1 / 148 (0.68%) 1	0 / 249 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Headache subjects affected / exposed occurrences (all)	4 / 145 (2.76%) 4	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Paraesthesia subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	2 / 249 (0.80%) 2
VIIth nerve paralysis subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Neuralgia			

subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	1 / 249 (0.40%)
occurrences (all)	0	1	1
Neutrophilia			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	0 / 249 (0.00%)
occurrences (all)	0	1	0
Anaemia			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	2 / 249 (0.80%)
occurrences (all)	1	0	2
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 145 (2.07%)	1 / 148 (0.68%)	1 / 249 (0.40%)
occurrences (all)	3	1	1
Abdominal pain upper			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	2 / 145 (1.38%)	1 / 148 (0.68%)	0 / 249 (0.00%)
occurrences (all)	2	1	0
Dysphagia			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	1
Enterocolitis			

subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	1 / 249 (0.40%)
occurrences (all)	0	1	1
Dry mouth			
subjects affected / exposed	2 / 145 (1.38%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	2	0	0
Oral candidiasis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	1
Gastroduodenitis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	2 / 145 (1.38%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	0 / 249 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	1
Lipodystrophy acquired			
subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	1	0	0
Angioedema			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	0 / 249 (0.00%)
occurrences (all)	0	1	0

Rash subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	1 / 148 (0.68%) 1	0 / 249 (0.00%) 0
Renal and urinary disorders			
Cystitis noninfective subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Proteinuria subjects affected / exposed occurrences (all)	2 / 145 (1.38%) 3	1 / 148 (0.68%) 1	3 / 249 (1.20%) 3
Nephrolithiasis subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	1 / 148 (0.68%) 3	0 / 249 (0.00%) 0
Glycosuria subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Hydronephrosis subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Haematuria subjects affected / exposed occurrences (all)	2 / 145 (1.38%) 3	2 / 148 (1.35%) 2	0 / 249 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	2 / 145 (1.38%) 2	0 / 148 (0.00%) 0	2 / 249 (0.80%) 2
Back pain subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	1 / 148 (0.68%) 1	0 / 249 (0.00%) 0
Musculoskeletal pain subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Pain in extremity subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Osteochondrosis			

subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	1 / 148 (0.68%) 1	0 / 249 (0.00%) 0
Infections and infestations			
Influenza			
subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	2 / 148 (1.35%) 2	1 / 249 (0.40%) 1
Pharyngitis			
subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	2 / 249 (0.80%) 2
Urinary tract infection			
subjects affected / exposed occurrences (all)	2 / 145 (1.38%) 3	4 / 148 (2.70%) 4	5 / 249 (2.01%) 6
Nasopharyngitis			
subjects affected / exposed occurrences (all)	2 / 145 (1.38%) 2	2 / 148 (1.35%) 2	5 / 249 (2.01%) 6
Cellulitis			
subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Tooth abscess			
subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Bronchitis			
subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Cystitis			
subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Oral candidiasis			
subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Pharyngotonsillitis			
subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Tooth infection			
subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	1 / 148 (0.68%) 1	1 / 249 (0.40%) 1

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	1 / 148 (0.68%) 1	2 / 249 (0.80%) 2
Erysipelas subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Viral infection subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Herpes zoster subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	1 / 148 (0.68%) 1	0 / 249 (0.00%) 0
Oral herpes subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	1 / 148 (0.68%) 1	0 / 249 (0.00%) 0
Pyelonephritis chronic subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Rhinitis subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	1 / 148 (0.68%) 1	0 / 249 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	1 / 148 (0.68%) 1	0 / 249 (0.00%) 0
Metabolism and nutrition disorders			
Diabetic nephropathy subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	0 / 249 (0.00%) 0
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Decreased appetite subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 148 (0.00%) 0	1 / 249 (0.40%) 1
Gout			

subjects affected / exposed	0 / 145 (0.00%)	0 / 148 (0.00%)	1 / 249 (0.40%)
occurrences (all)	0	0	2
Diabetes mellitus			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	0 / 249 (0.00%)
occurrences (all)	0	1	0
Hyperphosphataemia			
subjects affected / exposed	1 / 145 (0.69%)	0 / 148 (0.00%)	0 / 249 (0.00%)
occurrences (all)	1	0	0
Obesity			
subjects affected / exposed	0 / 145 (0.00%)	1 / 148 (0.68%)	0 / 249 (0.00%)
occurrences (all)	0	1	0
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 145 (0.69%)	2 / 148 (1.35%)	0 / 249 (0.00%)
occurrences (all)	1	2	0

Non-serious adverse events	CF101 1mg BPCP	CF101 1.0 mg OLE	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 32 (37.50%)	8 / 40 (20.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid neoplasm			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Venous insufficiency			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Angina pectoris			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Arteriosclerosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Haemorrhoids			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			

Chest pain subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Immune system disorders Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Food allergy subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Pulmonary arterial hypertension subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 40 (0.00%) 0	
Bronchitis chronic subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Lung disorder subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Influenza subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	1 / 40 (2.50%) 1	
Investigations Red blood cells urine			

subjects affected / exposed	1 / 32 (3.13%)	1 / 40 (2.50%)
occurrences (all)	1	1
Bacterial test		
subjects affected / exposed	0 / 32 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	1
Nitrite urine		
subjects affected / exposed	0 / 32 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	1
Liver function test abnormal		
subjects affected / exposed	0 / 32 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	1
Aspartate aminotransferase increased		
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0
Blood urea increased		
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0
Helicobacter test positive		
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0
Hepatic enzyme increased		
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0
Serum serotonin increased		
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0
Urine analysis abnormal		
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0
Blood phosphorus decreased		
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0
Electrocardiogram repolarisation abnormality		

subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Injury, poisoning and procedural complications			
Comminuted fracture			
subjects affected / exposed	0 / 32 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Injury			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Joint injury			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Thermal burn			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Tachyarrhythmia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Supraventricular extrasystoles			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
VIIth nerve paralysis			

subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Neuralgia subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Blood and lymphatic system disorders Leukocytosis subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 40 (0.00%) 0	
Neutrophilia subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 40 (0.00%) 0	
Anaemia subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Eye disorders Lacrimation increased subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 40 (0.00%) 0	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 40 (2.50%) 1	
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Abdominal pain subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Dysphagia			

subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Enterocolitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Dry mouth			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Gastroduodenitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Lipodystrophy acquired			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	

Angioedema subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Renal and urinary disorders Cystitis noninfective subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 40 (0.00%) 0	
Proteinuria subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 40 (2.50%) 1	
Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 40 (2.50%) 1	
Glycosuria subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 40 (0.00%) 0	
Hydronephrosis subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Haematuria subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 40 (0.00%) 0	
Back pain subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 40 (0.00%) 0	
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Pain in extremity			

subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Osteochondrosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
subjects affected / exposed	1 / 32 (3.13%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Cellulitis			
subjects affected / exposed	1 / 32 (3.13%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Tooth abscess			
subjects affected / exposed	1 / 32 (3.13%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Cystitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Pharyngotonsillitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	

Tooth infection subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Erysipelas subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Viral infection subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Herpes zoster subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Oral herpes subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Pyelonephritis chronic subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Rhinitis subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Sinusitis subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 40 (0.00%) 0	
Metabolism and nutrition disorders Diabetic nephropathy subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 40 (2.50%) 1	
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 40 (2.50%) 1	
Decreased appetite			

subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Gout			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Diabetes mellitus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Hyperphosphataemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Obesity			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 April 2010	Based on results of a planned interim analysis using data from the first 103 subjects enrolled in the trial (32 subjects in the CF101 1 mg BID dose group, 33 in the CF101 2 mg BID dose group, and 38 in the BID placebo group), the CF101 1 mg dose group was eliminated for futility, and the sample size of the remaining groups was increased. The safety profile and therapeutic index were favorable in this population and warranted continuing the 2 mg CF101 dose group, along with the placebo control. Therefore, only 2 treatment groups remained in the study. Objectives • Eliminated 1 mg dose • Eliminated 'optimal dose' objective • Eliminated PK objective • Changed order of efficacy assessments. PASI is now the primary efficacy endpoint (PGA was the former primary endpoint) so this is listed first. Design, Duration of Treatment • Changed from 3-arm to 2-arm study by eliminating 1 mg dose • Randomization changed from 2:2:1:1 to 1:1 to reflect removal of the CF101 1 mg followed by CF101 1 mg group and the Placebo followed by CF101 1 mg group • Changed the blinded period from 12 to 16 weeks • After cross-over at 16 weeks, changed from blinded to open-label because now all subjects will be on CF101 2 mg • Changed continued dosing period from 24 to 32 weeks • Added 2 visits (Visits 10 and 11), as needed for additional 8 weeks of study • Made Visit 3, Week 2, a telephone call only, eliminating all assessments except AEs and concomitant medications • Eliminated PK testing • Eliminated interim analysis Number of Subjects • Number of enrolled will be approximately 94 subjects in each group (CF101 2 mg and placebo), for a total of 188. • This will result in an overall total of 291 subjects when added to the 103 subjects included in the interim analysis.
25 August 2010	The rationale for this amendment was to incorporate modifications recommended by FDA. • Inclusion criterion: lower age range changed from 14 to 18 years of age. • Exclusion criterion: liver transaminase levels now greater than upper limit of normal, from 2 times upper limit of normal. • Discontinuation from dosing if a Grade 3 or 4 TEAE occurs in vital signs, systemic, or laboratory abnormalities in the Guidance for Industry: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research, September 2007), or other unacceptable toxicity develops.
02 December 2010	This amendment revised the statistical sections to incorporate • Recommendations from FDA • An interim analysis for dose selection and sample size re-estimation

29 August 2011	The original protocol inadvertently omitted an exclusion for topical Vitamin D analogs, which are utilized to treat psoriasis and whose uncontrolled use could confound the study results. This amendment added topical Vitamin D analogs to the list of medications excluded at screening and concomitantly throughout the trial.
24 December 2012	At Selected Sites An ex vivo analysis of peripheral blood mononuclear cell (PBMC) from patients with active psoriasis was performed. In PBMC from psoriasis patients, A3AR protein was highly over-expressed in comparison to the PBMC of healthy subjects. An increase of A3AR expression of approximately 16-fold was found in the psoriasis patients over normal control samples, which represents the highest level of A3AR over-expression documented to date in any population with immune-mediated inflammatory disease. Furthermore, analysis of mRNA in a biopsy of psoriatic skin revealed up-regulation of A3AR mRNA expression relative to normal skin, suggesting that CF101, a highly selective A3AR agonist, may demonstrate a very favorable therapeutic index in this disease. Finally, A3AR agonism by CF101 has been shown to de-regulate the PI3K-NF-kappaB signaling pathway, a pathway which is up-regulated in psoriatic epidermis and suppressed in response to clinically effective therapy. The objective of this amendment was to assess PBMC A3AR expression levels at Baseline and during treatment with CF101.
31 July 2013	At Selected Sites In the interests of gaining as much information as possible about A3AR behavior and relationship to response, this amendment removed the limit on the number of subjects who may be tested through PBMC sampling. The objective of this amendment is to clarify planned number of patients for PBMC A3AR expression levels assessment introduced to Protocol CF101-202PS with Amendment 5.
18 August 2014	Recent analyses from other trials of CF101, as well as of interim data from the current trial, indicated that the therapeutic response to CF101 may be strongly influenced by subject weight and/or BMI. The relationship between this clinical finding and systemic exposure to CF101 is unknown. By obtaining PK data in the treated population, this amendment will enable population PK analysis in this patient population and much more detailed analyses of the relationships between body weight/BMI, exposure, and efficacy of CF101, allowing dosing regimens to be optimized in future clinical use. Therefore, this Amendment added a secondary objective: Evaluate the PK of CF101 in this population.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None

Notes: