



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 | 0 / 145 (0.00%) | 1 / 148 (0.68%) | 0 / 249 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Renal and urinary disorders | | | |
| Cystitis noninfective | | | |
| subjects affected / exposed | 0 / 145 (0.00%) | 0 / 148 (0.00%) | 0 / 249 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 2 / 145 (1.38%) | 1 / 148 (0.68%) | 3 / 249 (1.20%) |
| occurrences (all) | 3 | 1 | 3 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 145 (0.69%) | 1 / 148 (0.68%) | 0 / 249 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Glycosuria | | | |
| subjects affected / exposed | 0 / 145 (0.00%) | 0 / 148 (0.00%) | 0 / 249 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 145 (0.00%) | 0 / 148 (0.00%) | 1 / 249 (0.40%) |
| occurrences (all) | 0 | 0 | 1 |
| Haematuria | | | |
| subjects affected / exposed | 2 / 145 (1.38%) | 2 / 148 (1.35%) | 0 / 249 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 145 (1.38%) | 0 / 148 (0.00%) | 2 / 249 (0.80%) |
| occurrences (all) | 2 | 0 | 2 |
| Back pain | | | |
| subjects affected / exposed | 1 / 145 (0.69%) | 1 / 148 (0.68%) | 0 / 249 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 145 (0.69%) | 0 / 148 (0.00%) | 1 / 249 (0.40%) |
| occurrences (all) | 1 | 0 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 145 (0.00%) | 0 / 148 (0.00%) | 1 / 249 (0.40%) |
| occurrences (all) | 0 | 0 | 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 | <p>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.</p> <p>Objectives</p> <ul style="list-style-type: none">• 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. <p>Design, Duration of Treatment</p> <ul style="list-style-type: none">• 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 <p>Number of Subjects</p> <ul style="list-style-type: none">• 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 | <p>The rationale for this amendment was to incorporate modifications recommended by FDA.</p> <ul style="list-style-type: none">• 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 | <p>This amendment revised the statistical sections to incorporate</p> <ul style="list-style-type: none">• 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 | <p>At Selected Sites</p> <p>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.</p> <p>The objective of this amendment was to assess PBMC A3AR expression levels at Baseline and during treatment with CF101.</p> |
| 31 July 2013 | <p>At Selected Sites</p> <p>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.</p> <p>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.</p> |
| 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: