

**Clinical trial results:****A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of CF102 in the Second-Line Treatment of Advanced Hepatocellular Carcinoma in Subjects with Child-Pugh Class B Cirrhosis
Summary**

| | |
|--------------------------|----------------|
| EudraCT number | 2014-000489-23 |
| Trial protocol | BG |
| Global end of trial date | 17 March 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 04 July 2021 |
| First version publication date | 04 July 2021 |

Trial information**Trial identification**

| | |
|-----------------------|--------------|
| Sponsor protocol code | CF102-201HCC |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02128958 |
| 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 | 27 November 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 27 November 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 March 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of orally administered CF102 25 mg twice daily (BID) as compared to placebo, as determined by Overall Survival (OS), when used as second-line therapy in subjects with advanced hepatocellular carcinoma (HCC) and Child-Pugh Class B (CPB) cirrhosis.

Protection of trial subjects:

This study was reviewed and approved by the IRB/EC representing each participating institution prior to enrolling subjects. It was conducted in accordance with the ethical principles that have their origin in the current Declaration of Helsinki and was consistent with International Conference on Harmonization Good Clinical Practice (ICH GCP) and applicable regulatory requirements.

Background therapy:

None

Evidence for comparator:

Placebo as control

| | |
|---|------------------|
| Actual start date of recruitment | 07 December 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Romania: 41 |
| Country: Number of subjects enrolled | Bulgaria: 11 |
| Country: Number of subjects enrolled | Serbia: 15 |
| Country: Number of subjects enrolled | Israel: 4 |
| Country: Number of subjects enrolled | United States: 7 |
| Worldwide total number of subjects | 78 |
| EEA total number of subjects | 52 |

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) | 41 |
| From 65 to 84 years | 37 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 15 sites in 5 countries (3 sites in Bulgaria, 2 sites in Serbia, 1 site in Israel, 7 sites in Romania, 2 sites in the United States) . There were 78 subjects randomized to treatment between 07 Dec 2014 and 27 Nov 2017.

Pre-assignment

Screening details:

At a Screening Visit subjects who provided written informed consent had procedures performed including medical history, physical examination, eligibility criteria check, body weight, vital signs, laboratory tests, ECOG, concomitant medications, tumour imaging (double blind period only), and adverse events (open label period only).

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Subject |

Blinding implementation details:

The trial was double-blind, meaning the subject and Investigator/staff did not have access to or knowledge of the subject's treatment assignment.

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | CF102 25 mg |

Arm description:

Medication (CF102 25 mg) was taken orally BID for consecutive 28-day cycles.

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

Dosage and administration details:

25 mg capsule BID

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

Arm description:

Medication (placebo) was taken orally BID for consecutive 28 day cycles in a double-blinded fashion

| | |
|--|---|
| 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 | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Matching CF102 placebo capsule BID

| Number of subjects in period 1 | CF102 25 mg | Placebo |
|---------------------------------------|-------------|---------|
| Started | 50 | 28 |
| Completed | 29 | 18 |
| Not completed | 21 | 10 |
| Adverse event, serious fatal | 19 | 9 |
| Consent withdrawn by subject | 2 | 1 |

Baseline characteristics

Reporting groups

| | |
|---|-------------|
| Reporting group title | CF102 25 mg |
| Reporting group description: Medication (CF102 25 mg) was taken orally BID for consecutive 28-day cycles. | |
| Reporting group title | Placebo |
| Reporting group description: Medication (placebo) was taken orally BID for consecutive 28 day cycles in a double-blinded fashion | |

| Reporting group values | CF102 25 mg | Placebo | Total |
|--|-------------|---------|-------|
| Number of subjects | 50 | 28 | 78 |
| Age categorical | | | |
| Subjects with advanced hepatocellular carcinoma (HCC) and Child-Pugh Class B (CPB) cirrhosis | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 28 | 13 | 41 |
| From 65-84 years | 22 | 15 | 37 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 25 | 14 | 39 |
| Male | 25 | 14 | 39 |

Subject analysis sets

| | |
|---|-------------------------------|
| Subject analysis set title | Safety Analysis Population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The Safety Population consisted of all subjects who received at least one dose of study medication. Analyses of safety assessments were performed using the Safety Population. | |
| Subject analysis set title | Intention-To-Treat Population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: The Intent-To-Treat (ITT) Population was defined as all subjects in the Safety Population with any post-Baseline assessment recorded. Exclusion of subjects from the ITT Population was determined prior to unblinding. All efficacy analyses were performed using the ITT Population. | |
| Subject analysis set title | Per Protocol Population |
| Subject analysis set type | Per protocol |
| Subject analysis set description: The Per Protocol (PP) Population was defined as all subjects in the ITT Population with no major protocol deviations, including major violations of inclusion and exclusion criteria and violation of RECIST requirements regarding the number of target lesions at Screening. Exclusion of subjects from the PP Population was determined prior to unblinding. Tumor response was analyzed for the PP Population. | |

| Reporting group values | Safety Analysis Population | Intention-To-Treat Population | Per Protocol Population |
|--|----------------------------|-------------------------------|-------------------------|
| Number of subjects | 78 | 78 | 78 |
| Age categorical | | | |
| Subjects with advanced hepatocellular carcinoma (HCC) and Child-Pugh Class B (CPB) cirrhosis | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 41 | 41 | 41 |
| From 65-84 years | 37 | 37 | 37 |

| | | | |
|--------------------|----|---|---|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 39 | 0 | 0 |
| Male | 39 | 0 | 0 |

End points

End points reporting groups

| | |
|---|-------------------------------|
| Reporting group title | CF102 25 mg |
| Reporting group description: Medication (CF102 25 mg) was taken orally BID for consecutive 28-day cycles. | |
| Reporting group title | Placebo |
| Reporting group description: Medication (placebo) was taken orally BID for consecutive 28 day cycles in a double-blinded fashion | |
| Subject analysis set title | Safety Analysis Population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The Safety Population consisted of all subjects who received at least one dose of study medication. Analyses of safety assessments were performed using the Safety Population. | |
| Subject analysis set title | Intention-To-Treat Population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: The Intent-To-Treat (ITT) Population was defined as all subjects in the Safety Population with any post-Baseline assessment recorded. Exclusion of subjects from the ITT Population was determined prior to unblinding. All efficacy analyses were performed using the ITT Population. | |
| Subject analysis set title | Per Protocol Population |
| Subject analysis set type | Per protocol |
| Subject analysis set description: The Per Protocol (PP) Population was defined as all subjects in the ITT Population with no major protocol deviations, including major violations of inclusion and exclusion criteria and violation of RECIST requirements regarding the number of target lesions at Screening. Exclusion of subjects from the PP Population was determined prior to unblinding. Tumor response was analyzed for the PP Population. | |

Primary: Overall survival - Primary

| | |
|---|----------------------------|
| End point title | Overall survival - Primary |
| End point description: The time to event assessment for OS was the number of days from Day 1 of Cycle 1 to the day of death+1, where a death could have been due to any cause. | |
| End point type | Primary |
| End point timeframe: Baseline to time of death | |

| End point values | CF102 25 mg | Placebo | | |
|---------------------------------------|-------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 28 | | |
| Units: Months | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Overall survival | 4.1 (2.2 to 14.8) | 4.3 (2.0 to 8.9) | | |

| | |
|-----------------------------------|---|
| Attachments (see zip file) | Product Limit Survival Estimates, OS (ITT Pop)/CF102- |
|-----------------------------------|---|

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Time to Event - Overall Survival (months) |
|-----------------------------------|---|

Statistical analysis description:

Time to event variables were summarized using the number observed, number censored, median, and 25th and 75th percentiles from Kaplan-Meier curves. Data were summarized using descriptive statistics (number of subjects (n), mean, median, standard deviation, minimum, and maximum) for continuous variables. Categorical variables were summarized using frequencies and percentages.

| | |
|---|------------------------|
| Comparison groups | CF102 25 mg v Placebo |
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | = 0.508 ^[2] |
| Method | Logrank |

Notes:

[1] - Kaplan Meier log-rank test.

[2] - Calculated using logrank test

| | |
|-----------------------------------|--|
| Statistical analysis title | Time to Event - Disease Progression (months) |
|-----------------------------------|--|

Statistical analysis description:

Time to event variables were summarized using the number observed, number censored, median, and 25th and 75th percentiles from Kaplan-Meier curves. Data were summarized using descriptive statistics (number of subjects (n), mean, median, standard deviation, minimum, and maximum) for continuous variables. Categorical variables were summarized using frequencies and percentages.

| | |
|---|-----------------------|
| Comparison groups | CF102 25 mg v Placebo |
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[3] |
| P-value | = 0.371 |
| Method | Logrank |

Notes:

[3] - Kaplan Meier log-rank test.

Secondary: Disease Progression

| | |
|------------------------|---------------------|
| End point title | Disease Progression |
|------------------------|---------------------|

End point description:

Time to Progression (TTP) was the number of days from Day 1 of Cycle 1 to the day of PD+1.

Progression Free Survival was the number of days from Day 1 of Cycle 1 to the day of death or PD+1.

| | |
|-----------------------|-----------|
| End point type | Secondary |
|-----------------------|-----------|

End point timeframe:

Baseline to time to event

| End point values | CF102 25 mg | Placebo | | |
|---------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 28 | | |
| Units: Months | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| TTP | 5.1 (1.9 to 11.2) | 3.3 (1.9 to 33.2) | | |

| | |
|-----------------------------------|--|
| Attachments (see zip file) | KM Curve for TTP (ITT)/CF102-201HCC_2014_000489_23 |
|-----------------------------------|--|

Statistical analyses

| | |
|-----------------------------------|-----|
| Statistical analysis title | TPP |
|-----------------------------------|-----|

Statistical analysis description:

Time to Progression (TTP) was the number of days from Day 1 of Cycle 1 to the day of PD+1.

Progression Free Survival was the number of days from Day 1 of Cycle 1 to the day of death or PD+1

| | |
|---|-----------------------|
| Comparison groups | Placebo v CF102 25 mg |
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[4] |
| P-value | = 0.371 |
| Method | Logrank |

Notes:

[4] - Kaplan Meier - Logrank

Secondary: Progression-free Survival

| | |
|-----------------|---------------------------|
| End point title | Progression-free Survival |
|-----------------|---------------------------|

End point description:

Progression Free Survival was the number of days from Day 1 of Cycle 1 to the day of death or PD+1.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to time of event

| End point values | CF102 25 mg | Placebo | | |
|---------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 28 | | |
| Units: Months | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| PFS | 2.5 (1.8 to 6.1) | 1.9 (1.8 to 3.8) | | |

| | |
|-----------------------------------|--|
| Attachments (see zip file) | KM Curve for PFS (ITT)/CF102-201HCC_2014_000489_23 |
|-----------------------------------|--|

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Time to Event - Progression-free Survival (months) |
| Statistical analysis description: Progression Free Survival was the number of days from Day 1 of Cycle 1 to the day of death or PD+1. | |
| Comparison groups | CF102 25 mg v Placebo |
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[5] |
| P-value | = 0.521 |
| Method | Logrank |

Notes:

[5] - Kaplan Meier - Logrank test

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events that occurred during the study (Weeks 0 to 28 days)

Adverse event reporting additional description:

AEs coded by MedDRA v 21.0. No and % of subjects with AEs were tabulated by SOC and PT. Assessments included AE type, incidence, severity, seriousness, and treatment relationship. Dose interruptions/reductions, SAEs, AEs resulting in discontinuation, and deaths were collected. Severity grade were according to NCI-CTCAE criteria, v4.0.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | CF102 |
|-----------------------|-------|

Reporting group description:

Analysed as the Safety Population during the treatment period (Baseline to Day 28).

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Analysed as the Safety Population during the treatment period (Baseline to Day 28).

| Serious adverse events | CF102 | Placebo | |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 37 / 50 (74.00%) | 20 / 28 (71.43%) | |
| number of deaths (all causes) | 46 | 26 | |
| number of deaths resulting from adverse events | 23 | 10 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Hepatocellular carcinoma | | | |
| subjects affected / exposed | 5 / 50 (10.00%) | 2 / 28 (7.14%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 5 | 0 / 2 | |
| Metastases to lung | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |

| | | | |
|--|------------------|-----------------|--|
| Vascular disorders | | | |
| Vena cava thrombosis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Superior vena cava occlusion | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Death | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Disease progression | | | |
| subjects affected / exposed | 14 / 50 (28.00%) | 5 / 28 (17.86%) | |
| occurrences causally related to treatment / all | 0 / 14 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 14 | 0 / 5 | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Bilirubin conjugated increased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiac disorders | | | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Nervous system disorders | | | |
| Coma | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Subileus | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal adhesions | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Ascites | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Peritoneal haematoma | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Oesophageal varices haemorrhage | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic failure | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 50 (0.00%) | 2 / 28 (7.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | CF102 | Placebo | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 46 / 50 (92.00%) | 26 / 28 (92.86%) | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pallor | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 1 | 1 | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 1 | 1 | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 2 | 2 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 10 / 50 (20.00%) | 5 / 28 (17.86%) | |
| occurrences (all) | 13 | 6 | |
| Chills | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Fatigue | | | |
| subjects affected / exposed | 9 / 50 (18.00%) | 3 / 28 (10.71%) | |
| occurrences (all) | 11 | 4 | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 4 | 2 | |
| Chest pain | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 50 (4.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 2 | 2 | |
| Asthenia | | | |
| subjects affected / exposed | 6 / 50 (12.00%) | 6 / 28 (21.43%) | |
| occurrences (all) | 6 | 9 | |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 1 | 2 | |
| Facial pain | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Swelling | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 5 / 50 (10.00%) | 3 / 28 (10.71%) | |
| occurrences (all) | 5 | 3 | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 3 | 2 | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Epistaxis | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 2 | 1 | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Alveolitis | | | |

| | | | |
|--|---------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 1 | 0 / 28 (0.00%) 0 | |
| Rhinitis allergic subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 1 | 0 / 28 (0.00%) 0 | |
| Productive cough subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 1 | 1 / 28 (3.57%) 1 | |
| Psychiatric disorders | | | |
| Confusional state subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 0 | 1 / 28 (3.57%) 0 | |
| Insomnia subjects affected / exposed occurrences (all) | 2 / 50 (4.00%) 5 | 1 / 28 (3.57%) 1 | |
| Investigations | | | |
| Blood uric acid increased subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 1 | 0 / 28 (0.00%) 0 | |
| Aspartate aminotransferase decreased subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 1 | 0 / 28 (0.00%) 0 | |
| Blood thyroid stimulating hormone increased subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 1 | 3 / 28 (10.71%) 4 | |
| Weight decreased subjects affected / exposed occurrences (all) | 4 / 50 (8.00%) 7 | 4 / 28 (14.29%) 5 | |
| International normalised ratio abnormal subjects affected / exposed occurrences (all) | 0 / 50 (0.00%) 0 | 1 / 28 (3.57%) 1 | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 4 | 0 / 28 (0.00%) 0 | |
| Blood bilirubin increased | | | |

| | | | |
|--|----------------|-----------------|--|
| subjects affected / exposed | 0 / 50 (0.00%) | 3 / 28 (10.71%) | |
| occurrences (all) | 0 | 3 | |
| Weight increased | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | 3 / 28 (10.71%) | |
| occurrences (all) | 5 | 4 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 4 | 2 | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 2 | 2 | |
| Blood creatine increased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 0 | 4 | |
| Bilirubin conjugated increased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 0 | 2 | |
| Tri-iodothyronine free decreased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 0 | 2 | |
| Neutrophil count increased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Liver function test increased | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---------------------|---------------------|--|
| Traumatic haematoma subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 1 | 0 / 28 (0.00%) 0 | |
| Cardiac disorders | | | |
| Sinus bradycardia subjects affected / exposed occurrences (all) | 0 / 50 (0.00%) 0 | 1 / 28 (3.57%) 2 | |
| Atrioventricular block first degree subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 1 | 1 / 28 (3.57%) 5 | |
| Bundle branch block left subjects affected / exposed occurrences (all) | 0 / 50 (0.00%) 0 | 1 / 28 (3.57%) 1 | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 50 (0.00%) 0 | 1 / 28 (3.57%) 1 | |
| Sinus tachycardia subjects affected / exposed occurrences (all) | 2 / 50 (4.00%) 3 | 1 / 28 (3.57%) 1 | |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 3 / 50 (6.00%) 3 | 1 / 28 (3.57%) 1 | |
| Speech disorder subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 1 | 0 / 28 (0.00%) 0 | |
| Movement disorder subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 2 | 0 / 28 (0.00%) 0 | |
| Sciatica subjects affected / exposed occurrences (all) | 0 / 50 (0.00%) 0 | 1 / 28 (3.57%) 1 | |
| Dizziness subjects affected / exposed occurrences (all) | 3 / 50 (6.00%) 5 | 2 / 28 (7.14%) 2 | |
| Neuralgia | | | |

| | | | |
|--------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 7 / 50 (14.00%) | 6 / 28 (21.43%) | |
| occurrences (all) | 8 | 11 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Leukopenia | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ear and labyrinth disorders | | | |
| Tinnitus | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 9 / 50 (18.00%) | 6 / 28 (21.43%) | |
| occurrences (all) | 9 | 7 | |
| Abdominal pain | | | |

| | | |
|------------------------------|-----------------|-----------------|
| subjects affected / exposed | 7 / 50 (14.00%) | 3 / 28 (10.71%) |
| occurrences (all) | 7 | 5 |
| Vomiting | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 4 / 28 (14.29%) |
| occurrences (all) | 3 | 5 |
| Constipation | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 2 / 28 (7.14%) |
| occurrences (all) | 0 | 2 |
| Oropharyngeal pain | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 |
| Ascites | | |
| subjects affected / exposed | 8 / 50 (16.00%) | 3 / 28 (10.71%) |
| occurrences (all) | 19 | 3 |
| Gastrointestinal haemorrhage | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dysphagia | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 |
| Diarrhoea | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 2 / 28 (7.14%) |
| occurrences (all) | 2 | 2 |
| Haematemesis | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 |
| Abdominal distension | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 2 | 0 |
| Dyspepsia | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 1 / 28 (3.57%) |
| occurrences (all) | 0 | 0 |
| Gingival bleeding | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 |
| Abdominal pain upper | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 2 / 50 (4.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 3 | 2 | |
| Flatulence | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hepatobiliary disorders | | | |
| Jaundice | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hepatomegaly | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pruritus | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Eczema | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Swelling face | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|------------------------------------|----------------|-----------------|--|
| Back pain | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 3 | 1 | |
| Bone pain | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 1 | 1 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 3 / 28 (10.71%) | |
| occurrences (all) | 2 | 3 | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infections and infestations | | | |
| Infective glossitis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Onychomycosis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 4 | 1 | |
| Hypoalbuminaemia | | | |

| | | | |
|-----------------------------|----------------|-----------------|--|
| subjects affected / exposed | 4 / 50 (8.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 5 | 2 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 3 / 28 (10.71%) | |
| occurrences (all) | 2 | 3 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 4 | 2 | |
| Hypoproteinaemia | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 28 (3.57%) | |
| occurrences (all) | 0 | 1 | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 28 (0.00%) | |
| occurrences (all) | 1 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 16 June 2014 | <p>The original protocol CF102-201HCC was approved on 07 January 2014. Subsequently, the protocol was amended a first time on 16 June 2014:</p> <ul style="list-style-type: none">• Addressed comments and requests for information from FDA in correspondence dated 15 May 2014.• Clearly described rules for dose interruption due to toxicity and criteria for dose modification.• Revised eligibility to require prior treatment with sorafenib.• Required collection of data documenting the reasons for sorafenib intolerance and the duration of prior sorafenib treatment.• Added collection of sparse pharmacokinetic samples to allow for exploratory analyses of exposure-response relationships for CF102.• Added collection of additional ECGs at the anticipated maximal CF102 concentrations at steady state. |
| 03 October 2014 | <p>The original protocol CF102-201HCC was approved on 07 January 2014. Subsequently, the protocol was amended a second time on 03 October 2014:</p> <ul style="list-style-type: none">• The Sponsor had recently completed the in-life portion of 90-day toxicology studies in monkeys and rats. In a 90-day monkey study (30, 100, 300 mg/kg/day), preliminary data indicated that there was a dose-related increase in incidence and severity of microscopic thyroid follicular atrophy/degeneration with or without a concurrent neutrophil infiltrate. Thyroid follicular change was noted as minimal in severity in 1 of 6 animals at the low dose, minimal-to-mild severity in 2 of 6 animals at the mid dose, and mild-to-moderate severity in 4 of 6 animals at the high dose. Recovery was not evaluated in this study. The highest non-severely toxic dose in this study was 30 mg/kg. This information was added to the protocol. |
| 21 October 2015 | <p>The original protocol CF102-201HCC was approved on 07 January 2014. Subsequently, the protocol was amended a third time on 21 October 2015:</p> <ul style="list-style-type: none">• Changed the assay methodology for A3AR expression determination.• Revised information which was previously clarified, corrected or changed as per the following:<ul style="list-style-type: none">o Global Note to File GLO_P_Am. 01_16Jun2014 dated 11 August 2014o Global Note to File GLO_P_PBMC_08Oct2014 dated 01 April 2015o Global Note to File GLO_P_WBC_08Oct2014 dated 02 June 2015 <p>The protocol was modified to reflect the new procedure and correct already existing information.</p> |

| | |
|-------------------|---|
| 21 September 2018 | <p>The original protocol CF102-201HCC was approved on 07 January 2014. Subsequently, the protocol was amended a fourth time on 21 September 2018:</p> <ul style="list-style-type: none"> • Eliminated the requirement for 75 deaths prior to the end of the post-accrual period • Terminated the double-blind period of the study prior to the occurrence of 75 deaths • Deleted the MITT population • Added the PP population • Efficacy analyses were to be performed on the ITT population • Tumor response was to be analyzed using the PP population • Subjects who remained on blinded drug were offered the opportunity to continue dosing with open-label CF102 25 mg BID indefinitely, following the protocol-specified schedule of events. |
| 06 November 2018 | <p>The original protocol CF102-201HCC was approved on 07 January 2014. Subsequently, the protocol was amended a fifth time on 06 November 2018:</p> <ul style="list-style-type: none"> • Added Table 1-2: Schedule of Events for Open Label (OL) Treatment. • Amendment 5 implemented the transition to open-label (OL) dosing for patients who were surviving and remaining on drug at the time of analysis; and established the assessments and schedule of visits for the OL dosing aspect of the trial. This included defining the OL eligibility criteria; detailing the visit and assessment schedule; and specifying that the only patients still on treatment in this trial at the time of this amendment were in Romania. • Required a separate signed ICF prior to subject's continuation on OL treatment. • Provided for self-administration of CF102 or placebo BID in continuous 28-day cycles beginning on Day 1 of Cycle 1. • Provided for collection of information regarding the occurrence of adverse events during the OL period, up 28 days following the last dose of study drug (OL Follow-Up Visit). Any data for AEs related to study drug that were ongoing at the OL Follow-Up Visit would be collected until the AE resolved or stabilized. • Provided for PE, laboratory testing, ECG, liver chemistry, INR, and measuring of viral load during the OL period and OL Follow-Up. |

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.

The primary endpoint was not met but the subgroup analysis showed a positive efficacy signal (OS) in subjects with CPB7.

Notes: