



Clinical trial results: Empagliflozin and its effect on heart failure in type 2 diabetes Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2016-000214-30 |
| Trial protocol | DE |
| Global end of trial date | 19 November 2020 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 25 January 2023 |
| First version publication date | 25 January 2023 |
| Summary attachment (see zip file) | Adverse_events Effort-2 (Adverse_events Effort_2.pdf) |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | P000805 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|--------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | DRKS: DRKS00009894 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Medical Center - University of Freiburg |
| Sponsor organisation address | Hugstetter Straße 55, Freiburg, Germany, 79106 |
| Public contact | Coordinating Investigator, Medical Center - University of Freiburg, jochen.seufert@uniklinik-freiburg.de |
| Scientific contact | Coordinating Investigator, Medical Center - University of Freiburg, jochen.seufert@uniklinik-freiburg.de |

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 | 04 April 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 November 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 November 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the EFFORT study is to investigate effects of empagliflozin on quality of life in diabetic patients with HFrEF or HFpEF.

Protection of trial subjects:

Before enrolment in the clinical trial, the patient was informed that participation in the clinical trial is voluntary and that he/she may withdraw from the clinical trial at any time without having to give reasons and without penalty or loss of benefits to which the patient is otherwise entitled.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 20 February 2017 |
| 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 | Germany: 63 |
| Worldwide total number of subjects | 63 |
| EEA total number of subjects | 63 |

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) | 26 |
| From 65 to 84 years | 37 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 63 |
| Number of subjects completed | 63 |

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 | Subject, Investigator |

Arms

| | |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Empagliflozin |

Arm description: -

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Empagliflozin |
| Investigational medicinal product code | |
| Other name | Jardiance |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Dose: 25 mg/day. The tablets were to be taken in the morning, with or without food, swallowed whole with water.

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

Arm description: -

| | |
|--|--------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo was supplied as optically identical tablets to the IMP containing lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, colloidal anhydrous silica, magnesium stearate, hypromellose 2910, titanium dioxide, talc, macrogol 400, iron oxide, yellow.

| Number of subjects in period 1 | Empagliflozin | Placebo |
|---------------------------------------|---------------|---------|
| Started | 32 | 31 |
| Completed | 32 | 31 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Empagliflozin |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Reporting group values | Empagliflozin | Placebo | Total |
|---------------------------------------|---------------|---------|-------|
| Number of subjects | 32 | 31 | 63 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 13 | 13 | 26 |
| From 65-84 years | 19 | 18 | 37 |
| Gender categorical Units: Subjects | | | |
| Female | 10 | 4 | 14 |
| Male | 22 | 27 | 49 |

Subject analysis sets

| | |
|----------------------------|---------------|
| Subject analysis set title | EFFORT-1 |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The primary objective of the EFFORT-1 study is to investigate effects of empagliflozin on quality of life in diabetic patients with heart failure (HF) with reduced ejection fraction (HFrEF). EFFORT-1 was planned as a confirmative study with respect to the primary endpoint, and had to be changed to an exploratory study due to slow recruitment. The primary objective is to evaluate quality of life under treatment with empagliflozin as compared to placebo in diabetic patients with HFrEF.

| | |
|----------------------------|---------------|
| Subject analysis set title | EFFORT-2 |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The primary objective of the EFFORT-2 study is to investigate effects of empagliflozin on quality of life in diabetic patients with heart failure (HF) with preserved ejection fraction (HFpEF). EFFORT-2 is an exploratory hypotheses generating study. The primary objective is to evaluate quality of life under treatment with empagliflozin as compared to placebo in diabetic patients with HFpEF.

| Reporting group values | EFFORT-1 | EFFORT-2 | |
|---------------------------------------|----------|----------|--|
| Number of subjects | 24 | 39 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 13 | 13 | |
| From 65-84 years | 11 | 26 | |
| Gender categorical Units: Subjects | | | |
| Female | 2 | 12 | |
| Male | 22 | 27 | |

End points

End points reporting groups

| | |
|--|---------------|
| Reporting group title | Empagliflozin |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Subject analysis set title | EFFORT-1 |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The primary objective of the EFFORT-1 study is to investigate effects of empagliflozin on quality of life in diabetic patients with heart failure (HF) with reduced ejection fraction (HFrEF). EFFORT-1 was planned as a confirmative study with respect to the primary endpoint, and had to be changed to an exploratory study due to slow recruitment. The primary objective is to evaluate quality of life under treatment with empagliflozin as compared to placebo in diabetic patients with HFrEF. | |
| Subject analysis set title | EFFORT-2 |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The primary objective of the EFFORT-2 study is to investigate effects of empagliflozin on quality of life in diabetic patients with heart failure (HF) with preserved ejection fraction (HFpEF). EFFORT-2 is an exploratory hypotheses generating study. The primary objective is to evaluate quality of life under treatment with empagliflozin as compared to placebo in diabetic patients with HFpEF. | |

Primary: EFFORT-1: Minnesota Living with Heart Failure Questionnaire (MLHFQ) total score

| | |
|--|---|
| End point title | EFFORT-1: Minnesota Living with Heart Failure Questionnaire (MLHFQ) total score |
| End point description: | |
| Difference of Minnesota Living with Heart Failure Questionnaire (MLHFQ) total score to baseline at 6 months after randomization. A lower MLHFQ score indicates less effect of heart failure on a patient's quality of life. A total score accounts for all 21 items. | |
| End point type | Primary |
| End point timeframe: | |
| 6 months | |

| End point values | Empagliflozin | Placebo | | |
|--|-----------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 12 | | |
| Units: MLHFQ total score | | | | |
| least squares mean (confidence interval 95%) | 2.01 (-6.31 to 10.34) | -2.96 (-11.66 to 5.75) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Mixed linear model for repeated measures (MMRM) |
| Statistical analysis description: | |
| MMRM with change from baseline of MLHFQ total score at month 1, month 3, month 6, month 9, month 12 as dependent variable and treatment, time point and interaction between treatment and time point and baseline MLHFQ as independent variables. Month 6 adjusted mean difference between treatments | |

was estimated with 95%-confidence interval.

| | |
|---|--------------------------------|
| Comparison groups | Placebo v Empagliflozin |
| Number of subjects included in analysis | 24 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4 |
| Method | Regression, Linear |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 4.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.09 |
| upper limit | 17.03 |

Primary: EFFORT-2: Minnesota Living with Heart Failure Questionnaire (MLHFQ) total score

| | |
|--|---|
| End point title | EFFORT-2: Minnesota Living with Heart Failure Questionnaire (MLHFQ) total score |
| End point description: Difference of Minnesota Living with Heart Failure Questionnaire (MLHFQ) total score to baseline at 6 months after randomization. A lower MLHFQ score indicates less effect of heart failure on a patient's quality of life. A total score accounts for all 21 items. | |
| End point type | Primary |
| End point timeframe: 6 months | |

| End point values | Empagliflozin | Placebo | | |
|--|------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 19 | | |
| Units: MLHFQ total score | | | | |
| least squares mean (confidence interval 95%) | -5.27 (-11.73 to 1.19) | 3.95 (-2.44 to 10.34) | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Mixed linear model for repeated measures (MMRM) |
| Statistical analysis description: MMRM with change from baseline of MLHFQ total score at month 1, month 3, month 6, month 9, month 12 as dependent variable and treatment, time point and interaction between treatment and time point and baseline MLHFQ as independent variables. Month 6 adjusted mean difference between treatments was estimated with 95%-confidence interval. | |
| Comparison groups | Empagliflozin v Placebo |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.048 |
| Method | Regression, Linear |
| Parameter estimate | Median difference (final values) |
| Point estimate | -9.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.35 |
| upper limit | -0.09 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Complete study

Adverse event reporting additional description:

Reported adverse events occurred in the EFFORT-1 substudy. Adverse events for EFFORT-2 are attached as PDF.

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 24 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Empagliflozin |
|-----------------------|---------------|

Reporting group description:

Empagliflozin

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

Reporting group description:

Placebo

| Serious adverse events | Empagliflozin | Placebo | |
|--|-----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 12 (33.33%) | 1 / 12 (8.33%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Cardiac disorders | | | |
| Coronary artery disease | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 12 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| 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 | | | |
| General physical health deterioration | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (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: 0 %

| | | | |
|---|-----------------|-----------------|--|
| Non-serious adverse events | Empagliflozin | Placebo | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 12 (66.67%) | 9 / 12 (75.00%) | |

| | | | |
|---|--|---|--|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Basal cell carcinoma subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| Surgical and medical procedures Finger amputation subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| General disorders and administration site conditions Chest discomfort subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 2 / 12 (16.67%) 2 0 / 12 (0.00%) 0 | 0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 | |
| Respiratory, thoracic and mediastinal disorders Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 | 0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 | |
| Investigations Blood creatinine increased subjects affected / exposed occurrences (all) Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 | 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 | |

| | | | |
|--|----------------------|---------------------|--|
| Serum ferritin decreased subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 2 | 0 / 12 (0.00%) 0 | |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 12 (0.00%) 0 | |
| Limb injury subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| Cardiac disorders | | | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 12 (0.00%) 0 | |
| Cardiac failure congestive subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| Coronary artery disease subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 12 (0.00%) 0 | |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 2 / 12 (16.67%) 2 | 0 / 12 (0.00%) 0 | |
| Blood and lymphatic system disorders | | | |
| Iron deficiency anaemia subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 12 (0.00%) 0 | |
| Eye disorders | | | |
| Ocular hyperaemia subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 12 (0.00%) 0 | |
| Panophthalmitis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| Gastrointestinal disorders | | | |

| | | | |
|--|----------------|----------------|--|
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 12 (8.33%) | |
| occurrences (all) | 1 | 1 | |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 2 | |
| Onychoclasia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Rash | | | |

| | | | |
|---|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 12 (0.00%) 0 | |
| Renal and urinary disorders Nocturia subjects affected / exposed occurrences (all) | 2 / 12 (16.67%) 2 | 1 / 12 (8.33%) 1 | |
| Renal pain subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| Musculoskeletal and connective tissue disorders Groin pain subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 12 (0.00%) 0 | |
| Tendon pain subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| Erysipelas subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| Influenza subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 1 / 12 (8.33%) 1 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 5 / 12 (41.67%) 5 | |
| Pneumonia subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 12 (0.00%) 0 | |
| Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 12 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 29 September 2017 | <ul style="list-style-type: none">• Visit 2 during the run-in phase has been omitted, as the visit was primarily implemented for controlling of patients' compliance which will be assessed anyway at randomization visit.• Inclusion criterion 1: new: ≤ 85 years old; old: < 85 years old.• Inclusion criterion 3: new: $\text{HbA1c} \geq 6.5\%$; old: $\text{HbA1c} > 7.0\%$.• Exclusion criterion 8 has been specified allowing investigators to assess individually a necessary lapse of time preceding registration for patients with implantable cardioverter-defibrillator (ICD) and pacemaker.• Exclusion criterion 16: new: active tumor disease; old: malignancies within the past 5 years (except carcinoma in situ of the cervix and non melanomatous skin cancer).• Definition of MRI compatibility has been included to optimize scheduling the cardiac MRI procedure.• Plasma volume assessment will only be performed in a subgroup of patients due to organizational issues. Patients will be assigned to this examination consecutively beginning from a certain time point in order not to compromise randomisation balance.• In addition to DNA extraction, the biobanking samples will be used for RNA extraction also.• Introduction of time range for randomisation visit. This visit may be postponed for a week due to e.g. bank holidays, patient's medical condition or other patient's related issues. The time range for visit 3 and visit 4 was also extended, up to 7 days.• CTP section related to adverse events of special interest was completed. |
| 17 April 2019 | <p>Until April 2019, 54 patients have been randomized within the recruitment period of approximately 29 months since enrolment of the first patient (22 patients in EFFORT-1, 32 patients in EFFORT-2). It was decided to terminate inclusion of patients into the study by the end of 2019, last patient last visit date in January 2021.</p> <p>From a statistical point of view, EFFORT-1, originally planned as a confirmatory study, with a calculated necessary sample size of 200 patients, will now have, with an expected sample size of less than 50 patients, only very low power to detect a difference between treatment arms. So, EFFORT-1, in the same way as planned from the beginning for EFFORT-2, is now regarded as an exploratory hypotheses generating study.</p> |

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 most important limitation is the small number of study participants. As such, the variability of all results is high leading to large confidence intervals of effect estimates.

Notes: