Clinical trial results:
Randomised, double-blind, placebo-controlled and parallel dose group trial to investigate efficacy and safety of multiple doses of oral BI 690517 over 14 weeks, alone and in combination with empagliflozin, in patients with diabetic and non-diabetic chronic kidney disease

Summary

EudraCT number	2021-001434-19
Trial protocol	BE FI IT NO SE CZ HU ES DK BG GR PT PL
Global end of trial date	10 July 2023

Results information

Result version number	v2 (current)
This version publication date	04 October 2024
First version publication date	21 July 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	1378.5

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05182840
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com

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	01 August 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 June 2023
Global end of trial reached?	Yes
Global end of trial date	10 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of the trial were to demonstrate the efficacy of BI 690517, alone and in combination with empagliflozin, and to characterise the BI 690517 dose-response relationship in patients with diabetic and non-diabetic chronic kidney disease (CKD) by assessing three doses and placebo.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all subjects as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 February 2022
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	Argentina: 128
Country: Number of subjects enrolled	Australia: 10
Country: Number of subjects enrolled	Belgium: 24
Country: Number of subjects enrolled	Brazil: 204
Country: Number of subjects enrolled	Bulgaria: 36
Country: Number of subjects enrolled	Canada: 20
Country: Number of subjects enrolled	China: 21
Country: Number of subjects enrolled	Czechia: 16
Country: Number of subjects enrolled	Finland: 30
Country: Number of subjects enrolled	Germany: 43
Country: Number of subjects enrolled	Greece: 15
Country: Number of subjects enrolled	Hong Kong: 6
Country: Number of subjects enrolled	Hungary: 41
Country: Number of subjects enrolled	India: 63
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Japan: 84
Country: Number of subjects enrolled	Korea, Republic of: 21
Country: Number of subjects enrolled	Malaysia: 31

Country: Number of subjects enrolled	Mexico: 70
Country: Number of subjects enrolled	Norway: 7
Country: Number of subjects enrolled	Philippines: 127
Country: Number of subjects enrolled	Poland: 75
Country: Number of subjects enrolled	Portugal: 22
Country: Number of subjects enrolled	South Africa: 58
Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Türkiye: 5
Country: Number of subjects enrolled	United States: 518
Worldwide total number of subjects	1714
EEA total number of subjects	346

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)	764
From 65 to 84 years	950
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In the run-in period patients got empagliflozin or placebo to empagliflozin. The run-in period was followed by a second randomization at which patients were 1:1:1:1 randomized to a treatment period to receive one of three doses of BI 690517 or placebo matching BI 690517 in combination with the background medication assigned in the run-in period.

Pre-assignment

Screening details:

Due to limitations of the EudraCT Results Form 2 patients who did not complete the Run-in period (RP) for the Placebo arm are entered under the milestone completed of the RP.
The 2 patients who did not complete the RP were mistakenly randomized to the treatment period (TP) but were not treated during the TP with BI 690517 or placebo to BI 690517.

Period 1

Period 1 title	Run-in period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

Patients, investigators and everyone involved in trial conduct or analysis or with any other interest in this double-blind trial remained blinded with regard to the randomised treatment assignments.

Arms

Are arms mutually exclusive?	Yes
Arm title	Run-in period: 10 mg Empa

Arm description:

Patients received during the run-in period 10 milligrams (mg) of empagliflozin (Empa) once daily orally for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Empagliflozin film-coated tablets 10mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received during the run-in period one film-coated tablet of 10 milligrams (mg) of empagliflozin (Empa) once daily orally for 8 weeks.

Arm title	Run-in period: Placebo to Empa 10 mg

Arm description:

Patients received during the run-in period placebo matching empagliflozin (Empa) 10 milligrams (mg) once daily orally for 8 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo to empagliflozin film-coated tablets 10mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received during the run-in period one film-coated tablet of 10 milligrams (mg) of placebo matching empagliflozin (Empa) once daily orally for 8 weeks.

Number of subjects in period 1	Run-in period: 10 mg Empa	Run-in period: Placebo to Empa 10 mg
Started	356	358
Treated with Empa or Placebo to Empa	356	357
Completed	332	332
Not completed	24	26
Adverse event, non-fatal	5	5
No reason available	2	2
Burden of study procedures	2	2
Other reason but not sponsor termination	14	16
Change of residence	1	-
Not treated	-	1

Period 2

Period 2 title	Screened for treatment period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

Patients, investigators and everyone involved in trial conduct or analysis or with any other interest in this double-blind trial remained blinded with regard to the randomised treatment assignments.

Arms

Are arms mutually exclusive?	Yes
Arm title	Run-in period: 10 mg Empa

Arm description:

Patients received during the run-in period 10 milligrams (mg) of empagliflozin (Empa) once daily orally for 8 weeks.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Run-in period: Placebo to Empa 10 mg

Arm description:

Patients received during the run-in period placebo matching empagliflozin (Empa) 10 milligrams (mg) once daily orally for 8 weeks.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Run-in period: 10 mg Empa	Run-in period: Placebo to Empa 10 mg
Started	332	332
Completed the RP and screened for TP	332	330
Entered to TP without completing the RP	0 [1]	2 [2]
Completed	298	288
Not completed	34	44
Did not meet Treatment Period eligibility criteria	34	44

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Only 2 patients in the arm were eligible for this milestone.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: None of the patients who in this arm were eligible for this milestone.

Period 3

Period 3 title	Treatment period
Is this the baseline period?	Yes[3]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

Patients, investigators and everyone involved in trial conduct or analysis or with any other interest in this double-blind trial remained blinded with regard to the randomised treatment assignments.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment period: 10 mg Empa + 3 mg BI 690517

Arm description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 3 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 3 mg BI 690517 and 10 mg empagliflozin for 14 weeks.

Arm type	Experimental
Investigational medicinal product name	Empagliflozin film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 10 mg of empagliflozin once daily (QD) orally for 14 weeks.

Investigational medicinal product name	BI 690517 film-coated tablets 3 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 3 milligrams (mg) of BI 690517 once daily (QD) for 14 weeks.

Arm title	Treatment period: 10 mg Empa + 10 mg BI 690517

Arm description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 10 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 10 mg BI 690517 and 10 mg empagliflozin for 14 weeks.

Arm type	Experimental
Investigational medicinal product name	Empagliflozin film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 10 mg of empagliflozin once daily (QD) orally for 14 weeks.

Investigational medicinal product name	BI 690517 film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 10 milligrams (mg) of BI 690517 orally for 14 weeks.

Arm title	Treatment period: 10 mg Empa + 20 mg BI 690517

Arm description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 20 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 20 mg BI 690517 and 10 mg empagliflozin for 14 weeks.

Arm type	Experimental
Investigational medicinal product name	Empagliflozin film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 10 mg of empagliflozin once daily (QD) orally for 14 weeks.

Investigational medicinal product name	BI 690517 film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received two film-coated tablets of 10 milligrams (mg) of BI 690517 (total BI 690517 dose=20 mg) orally for 14 weeks.

Arm title	Treatment period: 10 mg Empa + Placebo to BI 690517

Arm description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received placebo matching BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received placebo matching BI 690517 and 10 mg empagliflozin for 14 weeks.

Arm type	Placebo

Investigational medicinal product name	Placebo to BI 690517 film-coated tablets 3 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 3 mg of placebo to BI 690517 orally for 14 weeks.

Investigational medicinal product name	Empagliflozin film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 10 mg of empagliflozin once daily (QD) orally for 14 weeks.

Investigational medicinal product name	Placebo to BI 690517 film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received either one film-coated tablet of 10 mg of placebo to BI 690517 or 2 film-coated tablets of 10 mg of placebo to BI 690517 orally for 14 weeks.

Arm title	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517

Arm description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 3 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 3 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Arm type	Experimental
Investigational medicinal product name	Placebo to empagliflozin film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 10 milligrams (mg) of placebo to empagliflozin once daily (QD) orally for 14 weeks.

Investigational medicinal product name	BI 690517 film-coated tablets 3 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 3 milligrams (mg) of BI 690517 once daily (QD) orally for 14 weeks.

Arm title	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517

Arm description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 10 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 10 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Arm type	Experimental

Investigational medicinal product name	Placebo to empagliflozin film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 10 milligrams (mg) of placebo to empagliflozin once daily (QD) orally for 14 weeks.

Investigational medicinal product name	BI 690517 film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 10 milligrams (mg) of BI 690517 once daily (QD) orally for 14 weeks.

Arm title	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517

Arm description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 20 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 20 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Arm type	Experimental
Investigational medicinal product name	Placebo to empagliflozin film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received one film-coated tablet of 10 milligrams (mg) of placebo to empagliflozin once daily (QD) orally for 14 weeks.

Investigational medicinal product name	BI 690517 film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received two film-coated tablets of 10 milligrams (mg) of BI 690517 (total BI 690517 dose=20 mg) orally for 14 weeks.

Arm title	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517

Arm description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received placebo matching BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received placebo matching BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo to BI 690517 film-coated tablets 3 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:	
Patients received one film-coated tablet of 3 mg of placebo to BI 690517 orally for 14 weeks.	
Investigational medicinal product name	Placebo to BI 690517 film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Patients received either one film-coated tablet of 10 mg of placebo to BI 690517 or 2 film-coated tablets of 10 mg of placebo to BI 690517 orally for 14 weeks.	
Investigational medicinal product name	Empagliflozin film-coated tablets 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Patients received one film-coated tablet of 10 milligrams (mg) of placebo to empagliflozin once daily (QD) orally for 14 weeks.	

Notes:

[3] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Baseline characteristics are reported for the participants who started the Treatment Period. 586 subjects were randomized to treatment period.

Number of subjects in period 3[4]	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517
Started	76	74	74
Got BI 690517/Placebo to BI 690517	76	73	74
Completed	63	50	55
Not completed	13	24	19
Adverse event, non-fatal	4	16	12
Did not get BI/Placebo to BI	-	1	-
No reason available	-	1	-
Protocol deviation	-	-	-
Burden of study procedures	-	-	1
Change of residence	-	-	-
Other but not sponsor termination	8	6	6
Reason missing	1	-	-

Number of subjects in period 3[4]	Treatment period: 10 mg Empa + Placebo to BI 690517	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517
Started	74	71	72
Got BI 690517/Placebo to BI 690517	74	70	71
Completed	58	61	54
Not completed	16	10	18
Adverse event, non-fatal	6	4	8
Did not get BI/Placebo to BI	-	1	1
No reason available	2	-	1

Protocol deviation	-	-	-
Burden of study procedures	-	-	-
Change of residence	1	-	-
Other but not sponsor termination	7	5	8
Reason missing	-	-	-

Number of subjects in period 3[4]	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Started	72	73
Got BI 690517/Placebo to BI 690517	72	73
Completed	48	66
Not completed	24	7
Adverse event, non-fatal	16	5
Did not get BI/Placebo to BI	-	-
No reason available	-	-
Protocol deviation	1	-
Burden of study procedures	-	-
Change of residence	-	-
Other but not sponsor termination	7	2
Reason missing	-	-

Notes:

[4] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of 1714 participants that were screened only 714 were randomized to the Run-in period.

Baseline characteristics

Reporting groups

Reporting group title	Treatment period: 10 mg Empa + 3 mg BI 690517

Reporting group description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 3 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 3 mg BI 690517 and 10 mg empagliflozin for 14 weeks.

Reporting group title	Treatment period: 10 mg Empa + 10 mg BI 690517

Reporting group description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 10 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 10 mg BI 690517 and 10 mg empagliflozin for 14 weeks.

Reporting group title	Treatment period: 10 mg Empa + 20 mg BI 690517

Reporting group description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 20 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 20 mg BI 690517 and 10 mg empagliflozin for 14 weeks.

Reporting group title	Treatment period: 10 mg Empa + Placebo to BI 690517

Reporting group description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received placebo matching BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received placebo matching BI 690517 and 10 mg empagliflozin for 14 weeks.

Reporting group title	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517

Reporting group description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 3 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 3 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Reporting group title	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517

Reporting group description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 10 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 10 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Reporting group title	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517

Reporting group description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 20 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 20 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Reporting group title	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517

Reporting group description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received placebo matching BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received placebo matching BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Reporting group values	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517
Number of subjects	76	74	74
Age categorical			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	32	30	40
From 65-84 years	41	44	33
85 years and over	3	0	1
Age Continuous			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: years			
arithmetic mean	65.4	64.4	61.8
standard deviation	± 11.2	± 12.3	± 12.2
Sex: Female, Male			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Participants			
Male	49	44	54
Female	27	30	20
Ethnicity (NIH/OMB)			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Subjects			
Hispanic or Latino	25	21	12
Not Hispanic or Latino	51	53	62
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Subjects			
American Indian or Alaska Native	0	2	1
Asian	17	27	20
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	9	6	7
White	49	35	45
More than one race	1	4	1
Unknown or Not Reported	0	0	0

Urine Albumin Creatinine Ratio (UACR) at baseline			
UACR is a ratio between two measured substances i.e., albumine and creatinine and it is calculated as: (Urine albumin (milligram (mg)/deciliter (dL)))/(urine creatinine gram (g)/deciliter (dL))= UACR in mg/g. Albuminuria is present when UACR is greater than 30 mg/g and is a marker for chronic kidney disease (CKD). UACR measurements were collected on 2 consecutive days at 3 timepoints from Week -2 to Week 0 (i.e. Week 6-8 of Run-in period) for treatment period baseline. The randomised set (RS) was used to report the UACR at baseline.			
Units: milligram/gram			
arithmetic mean	780.3	740.8	695.4
standard deviation	± 828.8	± 915.0	± 748.0

Reporting group values	Treatment period: 10 mg Empa + Placebo to BI 690517	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517
Number of subjects	74	71	72
Age categorical			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	35	32	30
From 65-84 years	39	37	41
85 years and over	0	2	1
Age Continuous			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: years			
arithmetic mean	63.4	64.4	64.8
standard deviation	± 10.3	± 11.8	± 9.9
Sex: Female, Male			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Participants			
Male	43	51	49
Female	31	20	23
Ethnicity (NIH/OMB)			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Subjects			
Hispanic or Latino	20	22	21
Not Hispanic or Latino	54	49	51
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they			

were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Subjects			
American Indian or Alaska Native	2	2	2
Asian	19	23	15
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	10	3	9
White	42	42	45
More than one race	1	1	1
Unknown or Not Reported	0	0	0
Urine Albumin Creatinine Ratio (UACR) at baseline			
UACR is a ratio between two measured substances i.e., albumine and creatinine and it is calculated as: (Urine albumin (milligram (mg)/deciliter (dL)))/(urine creatinine gram (g)/deciliter (dL))= UACR in mg/g. Albuminuria is present when UACR is greater than 30 mg/g and is a marker for chronic kidney disease (CKD). UACR measurements were collected on 2 consecutive days at 3 timepoints from Week -2 to Week 0 (i.e. Week 6-8 of Run-in period) for treatment period baseline. The randomised set (RS) was used to report the UACR at baseline.			
Units: milligram/gram			
arithmetic mean	801.4	934.0	646.2
standard deviation	± 1132.3	± 1363.6	± 685.2

Reporting group values	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517	Total
Number of subjects	72	73	586
Age categorical			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	29	39	267
From 65-84 years	42	34	311
85 years and over	1	0	8
Age Continuous			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: years			
arithmetic mean	64.3	62.3	
standard deviation	± 10.7	± 11.4	-
Sex: Female, Male			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Participants			
Male	45	55	390

Female	27	18	196

Ethnicity (NIH/OMB)			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Subjects			
Hispanic or Latino	18	24	163
Not Hispanic or Latino	54	49	423
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Randomised Set (RS): included all entered and randomised patients based on the treatment groups they were randomised to at the randomisation prior to the treatment period (i.e. at second randomisation (R2)), regardless of being treated by BI 690517 or not.			
Units: Subjects			
American Indian or Alaska Native	3	1	13
Asian	19	16	156
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	9	10	63
White	40	44	342
More than one race	1	1	11
Unknown or Not Reported	0	0	0
Urine Albumin Creatinine Ratio (UACR) at baseline			
UACR is a ratio between two measured substances i.e., albumine and creatinine and it is calculated as: (Urine albumin (milligram (mg)/deciliter (dL)))/(urine creatinine gram (g)/deciliter (dL))= UACR in mg/g. Albuminuria is present when UACR is greater than 30 mg/g and is a marker for chronic kidney disease (CKD). UACR measurements were collected on 2 consecutive days at 3 timepoints from Week -2 to Week 0 (i.e. Week 6-8 of Run-in period) for treatment period baseline. The randomised set (RS) was used to report the UACR at baseline.			
Units: milligram/gram			
arithmetic mean	785.0	684.4	
standard deviation	± 885.7	± 715.1	-

End points

End points reporting groups

Reporting group title	Run-in period: 10 mg Empa
Reporting group description:	
Patients received during the run-in period 10 milligrams (mg) of empagliflozin (Empa) once daily orally for 8 weeks.	
Reporting group title	Run-in period: Placebo to Empa 10 mg
Reporting group description:	
Patients received during the run-in period placebo matching empagliflozin (Empa) 10 milligrams (mg) once daily orally for 8 weeks.	
Reporting group title	Run-in period: 10 mg Empa
Reporting group description:	
Patients received during the run-in period 10 milligrams (mg) of empagliflozin (Empa) once daily orally for 8 weeks.	
Reporting group title	Run-in period: Placebo to Empa 10 mg
Reporting group description:	
Patients received during the run-in period placebo matching empagliflozin (Empa) 10 milligrams (mg) once daily orally for 8 weeks.	
Reporting group title	Treatment period: 10 mg Empa + 3 mg BI 690517
Reporting group description:	
This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 3 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 3 mg BI 690517 and 10 mg empagliflozin for 14 weeks.	
Reporting group title	Treatment period: 10 mg Empa + 10 mg BI 690517
Reporting group description:	
This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 10 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 10 mg BI 690517 and 10 mg empagliflozin for 14 weeks.	
Reporting group title	Treatment period: 10 mg Empa + 20 mg BI 690517
Reporting group description:	
This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 20 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 20 mg BI 690517 and 10 mg empagliflozin for 14 weeks.	
Reporting group title	Treatment period: 10 mg Empa + Placebo to BI 690517
Reporting group description:	
This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received placebo matching BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received placebo matching BI 690517 and 10 mg empagliflozin for 14 weeks.	
Reporting group title	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517
Reporting group description:	
This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 3 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 3 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.	
Reporting group title	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517
Reporting group description:	
This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 10 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 10 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.	

Reporting group title	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517

Reporting group description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 20 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 20 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Reporting group title	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517

Reporting group description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received placebo matching BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received placebo matching BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Subject analysis set title	3 mg BI 690517
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes patients who received during the Treatment Period 3 milligram (mg) of BI 690517 + 10 mg Empagliflozin (i.e. arm "Treatment period: 10 mg empagliflozin + 3 mg BI 690517" in the Participant Flow) and patients who received during the Treatment period 3 mg BI 690517 + Placebo matching Empagliflozin 10 mg (i.e. arm "Treatment period: Placebo to empagliflozin 10 mg + 3 mg BI 690517" in the Participant Flow).

Subject analysis set title	10 mg BI 690517
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes patients who received during the Treatment Period 10 milligram (mg) of BI 690517 + 10 mg Empagliflozin (i.e. arm "Treatment period: 10 mg empagliflozin + 10 mg BI 690517" in the Participant Flow) and patients who received during the Treatment period 10 mg BI 690517 + Placebo matching Empagliflozin 10 mg (i.e. arm "Treatment period: Placebo to empagliflozin 10 mg + 10 mg BI 690517" in the Participant Flow).

Subject analysis set title	20 mg BI 690517
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes patients who received during the Treatment Period 20 milligram (mg) of BI 690517 + 10 mg Empagliflozin (i.e. arm "Treatment period: 10 mg empagliflozin + 20 mg BI 690517" in the Participant Flow) and patients who received during the Treatment period 20 mg BI 690517 + Placebo matching Empagliflozin 10 mg (i.e. arm "Treatment period: Placebo to empagliflozin 10 mg + 20 mg BI 690517" in the Participant Flow).

Subject analysis set title	Placebo to BI 690517
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes patients who received during the Treatment Period Placebo to BI 690517 + 10 mg Empagliflozin (i.e. arm "Treatment period: 10 mg empagliflozin + Placebo to BI 690517" in the Participant Flow) and patients who received during the Treatment period Placebo to BI 690517 + Placebo matching Empagliflozin 10 mg (i.e. arm "Treatment period: Placebo to empagliflozin 10 mg + Placebo to BI 690517" in the Participant Flow).

Subject analysis set title	3 mg BI 690517
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes patients who received during the Treatment Period 3 milligram (mg) of BI 690517 + 10 mg Empagliflozin (i.e. arm "Treatment period: 10 mg empagliflozin + 3 mg BI 690517" in the Participant Flow) and patients who received during the Treatment period 3 mg BI 690517 + Placebo matching Empagliflozin 10 mg (i.e. arm "Treatment period: Placebo to empagliflozin 10 mg + 3 mg BI 690517" in the Participant flow).

Subject analysis set title	BI 690517 3 mg
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes patients who received during the Treatment Period 3 milligram (mg) of BI 690517 + 10 mg Empagliflozin (i.e. arm "Treatment period: 10 mg empagliflozin + 3 mg BI 690517" in the

Participant Flow) and patients who received during the Treatment period 3 mg BI 690517 + Placebo matching Empagliflozin 10 mg (i.e. arm "Treatment period: Placebo to empagliflozin 10 mg + 3 mg BI 690517" in the Participant flow).

Subject analysis set title	3 mg BI 690517
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes patients who received during the Treatment Period 3 milligram (mg) of BI 690517 + 10 mg Empagliflozin (i.e. arm "Treatment period: 10 mg empagliflozin + 3 mg BI 690517" in the Participant Flow) and patients who received during the Treatment period 3 mg BI 690517 + Placebo matching Empagliflozin 10 mg (i.e. arm "Treatment period: Placebo to empagliflozin 10 mg + 3 mg BI 690517" in the Participant Flow).

Subject analysis set title	10 mg BI 690517
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes patients who received during the Treatment Period 10 milligram (mg) of BI 690517 + 10 mg Empagliflozin (i.e. arm "Treatment period: 10 mg empagliflozin + 10 mg BI 690517" in the Participant Flow) and patients who received during the Treatment period 10 mg BI 690517 + Placebo matching Empagliflozin 10 mg (i.e. arm "Treatment period: Placebo to empagliflozin 10 mg + 10 mg BI 690517" in the Participant Flow).

Subject analysis set title	20 mg BI 690517
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes patients who received during the Treatment Period 20 milligram (mg) of BI 690517 + 10 mg Empagliflozin (i.e. arm "Treatment period: 10 mg empagliflozin + 20 mg BI 690517" in the Participant Flow) and patients who received during the Treatment period 20 mg BI 690517 + Placebo matching Empagliflozin 10 mg (i.e. arm "Treatment period: Placebo to empagliflozin 10 mg + 20 mg BI 690517" in the Participant Flow).

Subject analysis set title	Placebo to BI 690517
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes patients who received during the Treatment Period Placebo to BI 690517 + 10 mg Empagliflozin (i.e. arm "Treatment period: 10 mg empagliflozin + Placebo to BI 690517" in the Participant Flow) and patients who received during the Treatment period Placebo to BI 690517 + Placebo matching Empagliflozin 10 mg (i.e. arm "Treatment period: Placebo to empagliflozin 10 mg + Placebo to BI 690517" in the Participant Flow).

Primary: Change from treatment period baseline in log transformed Urine Albumin Creatinine Ratio (UACR) measured in First Morning Void (FMV) urine after 14 weeks - all patients

End point title	Change from treatment period baseline in log transformed Urine Albumin Creatinine Ratio (UACR) measured in First Morning Void (FMV) urine after 14 weeks - all patients

End point description:

The adjusted mean change (95% confidence interval) in log transformed FMV UACR from baseline at 14 weeks is presented.
The adjusted means and 95 % confidence intervals were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which includes the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Full Analysis Set (FAS): This patient set included all randomised patients to one of 3 doses of BI 690517 (3mg QD, 10 mg QD or 20 mg QD) or placebo matching BI 690517 who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6, 7 or 8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment of BI 690517 or placebo matching BI 690517.

End point type	Primary

End point timeframe:

The MMRM model is a longitudinal analysis and it incorporated UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period.

End point values	3 mg BI 690517	10 mg BI 690517	20 mg BI 690517	Placebo to BI 690517
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	128	121	121	133
Units: log transformed FMV UACR				
least squares mean (confidence interval 95%)	-0.235 (-0.355 to -0.114)	-0.553 (-0.681 to -0.425)	-0.487 (-0.616 to -0.357)	-0.066 (-0.184 to 0.051)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference of adjusted means and 95 % confidence interval were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Comparison groups	3 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.0499
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.168
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.337
upper limit	0

Notes:

[1] - Least Squares Mean of "3 mg BI 690517" - Least Squares Mean of "Placebo to BI 690517".

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The difference of adjusted means and 95 % confidence interval were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Comparison groups	10 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 0.0001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.486

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	-0.313

Notes:

[2] - Least Squares Mean of "10 mg BI 690517" - Least Squares Mean of "Placebo to BI 690517".

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

A flat vs. non-flat dose-response relationship across the 3 doses of BI 690517 and placebo was tested using the Multiple Comparison Procedure - Modelling (MCP-Mod). MMRM estimates were used as input for the MCP-Mod. MMRM included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Comparison groups	3 mg BI 690517 v 10 mg BI 690517 v 20 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	503
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0 [4]
Method	MCPMod linear model fit

Notes:

[3] - Null hypothesis: The dose-response curve is flat across the 3 BI 690517 doses and the placebo.

Linear model fit assumption: No assumption is needed.
[4] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

A flat vs. non-flat dose-response relationship across the 3 doses of BI 690517 and placebo was tested using the Multiple Comparison Procedure - Modelling (MCP-Mod). MMRM estimates were used as input for the MCP-Mod. MMRM included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Comparison groups	3 mg BI 690517 v 10 mg BI 690517 v 20 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	503
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0 [6]
Method	MCPMod Emax model fit

Notes:

[5] - Null hypothesis: The dose-response curve is flat across the 3 BI 690517 doses and the placebo.

Emax model fit assumption: 80% of the maximum effect is achieved at 10 mg.
[6] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

A flat vs. non-flat dose-response relationship across the 3 doses of BI 690517 and placebo was tested using the Multiple Comparison Procedure - Modelling (MCP-Mod). MMRM estimates were used as input for the MCP-Mod. MMRM included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Comparison groups	3 mg BI 690517 v 10 mg BI 690517 v 20 mg BI 690517 v Placebo to BI 690517

Number of subjects included in analysis	503
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.0003
Method	MCPMod exponential model fit

Notes:

[7] - Null hypothesis: The dose-response curve is flat across the 3 BI 690517 doses and the placebo.

Exponential model fit assumption: 15% of the maximum effect is achieved at 10 mg.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The difference of adjusted means and 95 % confidence interval were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Comparison groups	20 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	< 0.0001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.421
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.596
upper limit	-0.246

Notes:

[8] - Least Squares Mean of "20 mg BI 690517" - Least Squares Mean of "Placebo to BI 690517".

Primary: Percent change of FMV UACR from baseline to Week 14 based on adjusted median (95% CI) back transformed from MMRM estimate - all patients

End point title	Percent change of FMV UACR from baseline to Week 14 based on adjusted median (95% CI) back transformed from MMRM estimate - all patients

End point description:

Percent change of first morning void (FMV) urine albumine creatinine ratio (UACR) from baseline to Week 14 based on adjusted median (95% confidence interval (CI)) back transformed from mixed models for repeated measures (MMRM) estimate for all patients is presented.
Percent change of FMV UACR= (FMV UACR at Week 14-FMV UACR at baseline)*100/(FMV UACR at baseline).
MMRM included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Full analysis set was used for the analysis of this endpoint.

End point type	Primary

End point timeframe:

The MMRM model is a longitudinal analysis and it incorporated UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period.

End point values	3 mg BI 690517	10 mg BI 690517	20 mg BI 690517	Placebo to BI 690517
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	128	121	121	133
Units: percent change of FMV UACR				
median (confidence interval 95%)	-20.9 (-29.9 to -10.8)	-42.5 (-49.4 to -34.6)	-38.5 (-46.0 to -30.0)	-6.4 (-16.8 to 5.3)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	3 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other[9]
Parameter estimate	Median difference (net)
Point estimate	-15.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.6
upper limit	0

Notes:

[9] - Median of "3 mg BI 690517" - Median of "Placebo to BI 690517"

Statistical analysis title	Statistical analysis 3
Comparison groups	20 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[10]
Parameter estimate	Median difference (net)
Point estimate	-34.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.9
upper limit	-21.8

Notes:

[10] - Median of "10 mg BI 690517" - Median of "Placebo to BI 690517".

Statistical analysis title	Statistical analysis 2
Comparison groups	10 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	Median difference (net)
Point estimate	-38.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-48.3
upper limit	-26.8

Notes:

[11] - Median of "10 mg BI 690517" - Median of "Placebo to BI 690517".

Primary: Change from baseline to Week 14 in the log transformed FMV UACR – patients with background therapy of placebo matching empagliflozin

End point title	Change from baseline to Week 14 in the log transformed FMV UACR – patients with background therapy of placebo matching empagliflozin[12]

End point description:

The adjusted mean change (95% confidence interval) in log transformed first morning void (FMV) urine albumine creatinine ratio (UACR) from baseline at 14 weeks for patients with background therapy of placebo matching empagliflozin in the Run-in period is presented.
The adjusted means and 95 % confidence intervals were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which includes the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

This endpoint is reported for the patients in the full analysis set who received placebo to empagliflozin during the Run-in period and had UACR measurement at baseline and at least one post-baseline UACR measurement while still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Primary

End point timeframe:

The MMRM model is a longitudinal analysis and it incorporated UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period.

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received placebo matching empagliflozin during the Run-in period.

End point values	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	61	59	69
Units: log transformed FMV UACR				
least squares mean (confidence interval 95%)	-0.254 (-0.441 to -0.068)	-0.496 (-0.693 to -0.299)	-0.455 (-0.666 to -0.245)	-0.027 (-0.208 to 0.155)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference of adjusted means and 95 % confidence interval were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment,

background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	= 0.0867
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.227
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.488
upper limit	0.033

Notes:

[13] - Least Squares Mean of "Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517" - Least Squares Mean of "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The difference of adjusted means and 95 % confidence interval were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	= 0.0027
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.429
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.707
upper limit	-0.151

Notes:

[14] - Least Squares Mean of "Treatment period: Placebo to Empa 10 mg + 20 mg BI 6905177" - Least Squares Mean of "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The difference of adjusted means and 95 % confidence interval were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other[15]
P-value	= 0.0007
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.469
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.737
upper limit	-0.201

Notes:

[15] - Least Squares Mean of "Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517" - Least Squares Mean of "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".

Primary: Percent change of FMV UACR from baseline to Week 14 based on adjusted median (95% CI) back transformed from MMRM estimate – patients with background therapy of placebo matching empagliflozin

End point title	Percent change of FMV UACR from baseline to Week 14 based on adjusted median (95% CI) back transformed from MMRM estimate – patients with background therapy of placebo matching empagliflozin[16]

End point description:

Percent change of first morning void (FMV) urine albumine creatinine ratio (UACR) from baseline to Week 14 based on adjusted median (95% confidence interval (CI)) back transformed from mixed models for repeated measures (MMRM) estimate for patients with background therapy of placebo matching empagliflozin in the Run-in period is presented.
Percent change of FMV UACR= (FMV UACR at Week 14-FMV UACR at baseline)*100/(FMV UACR at baseline).
MMRM included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

This endpoint is reported for the patients in the FAS who received placebo to empagliflozin during the Run-in period and had UACR measurement at baseline and at least one post-baseline UACR measurement while still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Primary

End point timeframe:

The MMRM model is a longitudinal analysis and it incorporated UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period.

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received placebo matching empagliflozin during the Run-in period.

End point values	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	61	59	69
Units: percent change of FMV UACR				
median (confidence interval 95%)	-22.4 (-35.6 to -6.5)	-39.1 (-50.0 to -25.8)	-36.6 (-48.6 to -21.7)	-2.6 (-18.8 to 16.8)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[17]
Parameter estimate	Median difference (net)
Point estimate	-20.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.6
upper limit	3.4

Notes:

[17] - Median of "Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517" - median of "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".

Statistical analysis title	Statistical analysis 3
Comparison groups	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other[18]
Parameter estimate	Median difference (net)
Point estimate	-34.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.7
upper limit	-14

Notes:

[18] - Median of "Treatment period: Placebo to Empa 10 mg + 20 mg BI 6905177" - median of "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Median of "Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517" - median of "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517"

Comparison groups	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-37.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.2
upper limit	-18.2

Primary: Change from baseline to Week 14 in the log transformed FMV UACR − patients with background therapy of empagliflozin

End point title	Change from baseline to Week 14 in the log transformed FMV UACR − patients with background therapy of empagliflozin[19]

End point description:

The adjusted mean change (95% confidence interval) in log transformed first morning void (FMV) urine albumine creatinine ratio (UACR) from baseline at 14 weeks for patients with background therapy of empagliflozin in the Run-in period is presented.
The adjusted means and 95 % confidence intervals were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which includes the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

This endpoint is reported for the patients in the FAS who received empagliflozin during the Run-in period and had UACR measurement at baseline and at least one post-baseline UACR measurement while still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Primary

End point timeframe:

The MMRM model is a longitudinal analysis and it incorporated UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period.

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received empagliflozin during the Run-in period.

End point values	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	60	62	64
Units: log transformed FMV UACR				
least squares mean (confidence interval 95%)	-0.210 (-0.366 to -0.055)	-0.614 (-0.783 to -0.445)	-0.516 (-0.675 to -0.357)	-0.112 (-0.264 to 0.040)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference of adjusted means and 95 % confidence interval were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Comparison groups	Treatment period: 10 mg Empa + 3 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[20]
P-value	= 0.3737
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.098
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.316
upper limit	0.119

Notes:

[20] - Least Squares Mean of "Treatment period: 10 mg Empa + 3 mg BI 690517" - Least Squares Mean of "Treatment period: 10 mg Empa + Placebo to BI 690517".

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The difference of adjusted means and 95 % confidence interval were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

Comparison groups	Treatment period: 10 mg Empa + 20 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[21]
P-value	= 0.0004
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.404
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.625
upper limit	-0.184

Notes:

[21] - Least Squares Mean of "Treatment period: 10 mg Empa + 20 mg BI 690517" - Least Squares Mean of "Treatment period: 10 mg Empa + Placebo to BI 690517".

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The difference of adjusted means and 95 % confidence interval were estimated by restricted maximum likelihood-based mixed models for repeated measures ((REML)−based MMRM) which included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as

main effects, as well as random effects of patient.

Comparison groups	Treatment period: 10 mg Empa + 10 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other[22]
P-value	< 0.0001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.502
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	-0.275

Notes:

[22] - Least Squares Mean of "Treatment period: 10 mg Empa + 10 mg BI 690517" - Least Squares Mean of "Treatment period: 10 mg Empa + Placebo to BI 690517".

Primary: Percent change of FMV UACR from baseline to Week 14 based on adjusted median (95% CI) of MMRM estimate – patients with background therapy of empagliflozin

End point title	Percent change of FMV UACR from baseline to Week 14 based on adjusted median (95% CI) of MMRM estimate – patients with background therapy of empagliflozin[23]

End point description:

Percent change of first morning void (FMV) urine albumine creatinine ratio (UACR) from baseline to Week 14 based on adjusted median (95% confidence interval (CI)) back transformed from mixed models for repeated measures (MMRM) estimate for patients with background therapy of empagliflozin in the Run-in period is presented.
Percent change of FMV UACR= (FMV UACR at Week 14-FMV UACR at baseline)*100/(FMV UACR at baseline).
MMRM included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, background medication (empagliflozin or placebo matching empagliflozin) and randomisation stratum as main effects, as well as random effects of patient.

This endpoint is reported for the patients in the FAS who received empagliflozin during the Run-in period and had UACR measurement at baseline and at least one post-baseline UACR measurement while still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Primary

End point timeframe:

The MMRM model is a longitudinal analysis and it incorporated UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period.

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received empagliflozin during the Run-in period.

End point values	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	60	62	64
Units: percent change of FMV UACR				
median (confidence interval 95%)	-19.0 (-30.6 to	-45.9 (-54.3 to	-40.3 (-49.1 to	-10.6 (-23.2 to

-5.4)	-35.9)	-30.0)	4.1)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Treatment period: 10 mg Empa + 3 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[24]
Parameter estimate	Median difference (net)
Point estimate	-9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.1
upper limit	12.7

Notes:

[24] - Median of "Treatment period: 10 mg Empa + 3 mg BI 690517" - median of "Treatment period: 10 mg Empa + Placebo to BI 690517".

Statistical analysis title	Statistical analysis 3
Comparison groups	Treatment period: 10 mg Empa + 20 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[25]
Parameter estimate	Median difference (net)
Point estimate	-33.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.5
upper limit	-16.8

Notes:

[25] - Median of "Treatment period: 10 mg Empa + 20 mg BI 690517" - median of "Treatment period: 10 mg Empa + Placebo to BI 690517".

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Median of "Treatment period: 10 mg Empa + 10 mg BI 690517" - median of "Treatment period: 10 mg Empa + Placebo to BI 690517".	
Comparison groups	Treatment period: 10 mg Empa + 10 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517

Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-39.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.8
upper limit	-24

Secondary: UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - Multiple imputation

End point title	UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - Multiple imputation

End point description:

Number of patients with UACR response I is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
The multiple imputation filled in missing values at Week 14 based on other data observed in the same patient using regression.

This endpoint is reporting statistics for the Full Analysis Set (FAS). FAS included all randomised patients who had at least one baseline measurement of UACR at Week -2, -1, or 0 and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the multiple imputation approach.

End point values	3 mg BI 690517	10 mg BI 690517	20 mg BI 690517	Placebo to BI 690517
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	128	121	121	133
Units: Participants	40	73	66	24

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	3 mg BI 690517 v Placebo to BI 690517

Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other[26]
P-value	= 0.0136 [27]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	3.72

Notes:

[26] - Odds ratio of "3 mg BI 690517" vs. "Placebo to BI 690517".

[27] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	20 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[28]
P-value	= 0 [29]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.09
upper limit	9.71

Notes:

[28] - Odds ratio of "20 mg BI 690517" vs. "Placebo to BI 690517".

[29] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	10 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[30]
P-value	= 0 [31]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.94
upper limit	12.49

Notes:

[30] - Odds ratio of "10 mg BI 690517" vs. "Placebo to BI 690517".

[31] - P-value was rounded to four decimal places.

Secondary: UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - Missing as non−responder

End point title	UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - Missing as non−responder

End point description:

Number of patients with UACR response I is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
The missing as non-responder imputes patients with missing Week 14 data as non-responders.

This endpoint is reporting statistics for Full Analysis Set (FAS). FAS included all randomised patients to one of 3 doses of BI 690517 (3mg QD, 10 mg QD or 20 mg QD) or placebo matching BI 690517 who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6, 7 or 8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

End point values	3 mg BI 690517	10 mg BI 690517	20 mg BI 690517	Placebo to BI 690517
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	128	121	121	133
Units: Participants	40	62	57	23

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	3 mg BI 690517 v Placebo to BI 690517

Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other[32]
P-value	= 0.0111 [33]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	3.88

Notes:

[32] - Odds ratio of "3 mg BI 690517" vs. "Placebo to BI 690517".

[33] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	20 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[34]
P-value	= 0 [35]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.88
upper limit	9.44

Notes:

[34] - Odds ratio of "20 mg BI 690517" vs. "Placebo to BI 690517".

[35] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	10 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[36]
P-value	= 0 [37]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.49
upper limit	11.49

Notes:

[36] - Odds ratio of "10 mg BI 690517" vs. "Placebo to BI 690517".

[37] - P-value was rounded to four decimal places.

Secondary: UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 week - all patients - Last observation on treatment carried forward (LOCF)

End point title	UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 week - all patients - Last observation on treatment carried forward (LOCF)

End point description:

Number of patients with UACR response I is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
LOCF uses the last value observed on treatment to substitute all missing values until Week 14.

This endpoint is reporting statistics for Full Analysis Set (FAS). FAS included all randomised patients to one of 3 doses of BI 690517 (3mg QD, 10 mg QD or 20 mg QD) or placebo matching BI 690517 who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6, 7 or 8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the last observation carried forward approach.

End point values	10 mg BI 690517	20 mg BI 690517	Placebo to BI 690517	BI 690517 3 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	121	121	133	128
Units: Participants	67	73	31	45

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	BI 690517 3 mg v Placebo to BI 690517

Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other[38]
P-value	= 0.0348 [39]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	3.09

Notes:

[38] - Odds ratio of "3 mg BI 690517" vs. "Placebo to BI 690517".

[39] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	20 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[40]
P-value	= 0 [41]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.91
upper limit	8.67

Notes:

[40] - Odds ratio of "20 mg BI 690517" vs. "Placebo to BI 690517".

[41] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	10 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[42]
P-value	= 0 [43]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	7.08

Notes:

[42] - Odds ratio of "10 mg BI 690517" vs. "Placebo to BI 690517".

[43] - P-value was rounded to four decimal places.

Secondary: UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - complete case analysis

End point title	UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - complete case analysis

End point description:

Number of patients with UACR response I is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
Complete case analysis used patients with both baseline and Week 14 data available.

All randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who had at least one baseline measurement of UACR at Week -2, -1, or 0 (i.e. Week 6, 7 or 8 of Run-in period) and one post-baseline measurement at Week 12-14 when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

End point values	3 mg BI 690517	10 mg BI 690517	20 mg BI 690517	Placebo to BI 690517
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	124	107	106	127
Units: Participants	40	62	57	23

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	3 mg BI 690517 v Placebo to BI 690517

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	other[44]
P-value	= 0.0111 [45]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	3.88

Notes:

[44] - Odds ratio of "3 mg BI 690517" vs. "Placebo to BI 690517".

[45] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	10 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	other[46]
P-value	= 0 [47]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.49
upper limit	11.49

Notes:

[46] - Odds ratio of "10 mg BI 690517" vs. "Placebo to BI 690517".

[47] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	20 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	233
Analysis specification	Pre-specified
Analysis type	other[48]
P-value	= 0 [49]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.21

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.88
upper limit	9.44

Notes:

[48] - Odds ratio of "20 mg BI 690517" vs. "Placebo to BI 690517".

[49] - P-value was rounded to four decimal places.

Secondary: UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of placebo matching empagliflozin - Multiple imputation

End point title	UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of placebo matching empagliflozin - Multiple imputation[50]

End point description:

Number of patients with UACR response I for patients with background therapy of placebo matching empagliflozin in the Run-in period is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
The multiple imputation filled in missing values at Week 14 based on other data observed in the same patient using regression.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo to BI 690517 who received placebo to empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo to BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the multiple imputation approach.

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received placebo matching empagliflozin during the Run-in period.

End point values	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	61	59	69
Units: Participants	19	31	30	10

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[51]
P-value	= 0.0419 [52]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	5.74

Notes:

[51] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[52] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other[53]
P-value	= 0 [54]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.64
upper limit	14.25

Notes:

[53] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[54] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other[55]
P-value	= 0 [56]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.64
upper limit	14.08

Notes:

[55] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[56] - P-value was rounded to four decimal places.

Secondary: UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of placebo matching empagliflozin - Missing as non−responder

End point title	UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of placebo matching empagliflozin - Missing as non−responder[57]

End point description:

Number of patients with UACR response I for patients with background therapy of placebo matching empagliflozin in the Run-in period is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
The missing as non-responder imputes patients with missing Week 14 data as non-responders.

This endpoint reports statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who received placebo to empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

Notes:

[57] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received placebo matching empagliflozin during the Run-in period.

End point values	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	61	59	69
Units: Participants	19	28	25	9

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[58]
P-value	= 0.0195 [59]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	7.02

Notes:

[58] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[59] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other[60]
P-value	= 0.0001 [61]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.6
upper limit	15.67

Notes:

[60] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[61] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other[62]
P-value	= 0 [63]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.65
upper limit	15.35

Notes:

[62] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[63] - P-value was rounded to four decimal places.

Secondary: UACR response I, defined as decrease of at least 30% absolute change in FMV urine of UACR from treatment period baseline to 14 weeks - background therapy of placebo matching empagliflozin - Last observation on treatment carried forward (LOCF)

End point title	UACR response I, defined as decrease of at least 30% absolute change in FMV urine of UACR from treatment period baseline to 14 weeks - background therapy of placebo matching empagliflozin - Last observation on treatment carried forward (LOCF)[64]

End point description:

Number of patients with UACR response I for patients with background therapy of placebo matching empagliflozin in the Run-in period is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void (FMV) urine of UACR from treatment period baseline to 14 weeks. LOCF uses the last value observed on treatment to substitute all missing values until Week 14.

This endpoint reports statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who received placebo to empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the last observation carried forward approach.

Notes:

[64] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received placebo matching empagliflozin during the Run-in period.

End point values	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	61	59	69
Units: Participants	22	31	32	14

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[65]
P-value	= 0.0767 [66]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	4.42

Notes:

[65] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[66] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other[67]
P-value	= 0.0001 [68]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.69

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.15
upper limit	10.24

Notes:

[67] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[68] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other[69]
P-value	= 0.0003 [70]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.89
upper limit	8.91

Notes:

[69] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[70] - P-value was rounded to four decimal places.

Secondary: UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of placebo matching empagliflozin - complete case analysis

End point title	UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of placebo matching empagliflozin - complete case analysis[71]

End point description:

Number of patients with UACR response I for patients with background therapy of placebo matching empagliflozin in the Run-in period is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks. Complete case analysis used patients with both baseline and Week 14 data available.
This endpoint reports statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who had received placebo matching empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (i.e. Week 6, 7 or 8 of Run-in period) and one post-baseline measurement at Week 12-14 when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

Notes:

[71] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received placebo matching empagliflozin during the Run-in period.

End point values	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	56	50	66
Units: Participants	19	28	25	9

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[72]
P-value	= 0.0195 [73]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	7.02

Notes:

[72] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[73] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[74]
P-value	= 0.0001 [75]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.6
upper limit	15.67

Notes:

[74] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[75] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517 v Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	other[76]
P-value	= 0 [77]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.65
upper limit	15.35

Notes:

[76] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[77] - P-value was rounded to four decimal places.

Secondary: UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Multiple imputation

End point title	UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Multiple imputation[78]

End point description:

Number of patients with UACR response I for patients with background therapy of empagliflozin in the Run-in period is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
The multiple imputation filled in missing values at Week 14 based on other data observed in the same patient using regression.

This endpoint reports statistics for all randomised patients to of 3 doses of BI 690517 or placebo matching BI 690517 who received empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 placebo matching BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the multiple imputation approach.

Notes:

[78] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received empagliflozin during the Run-in period.

End point values	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	60	62	64
Units: Participants	21	42	36	14

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 3 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[79]
P-value	= 0.1398 [80]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	4.04

Notes:

[79] - Odds ratio of "Treatment period: 10 mg Empa+ 3 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[80] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of

binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 10 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other[81]
P-value	= 0 [82]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	8.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.73
upper limit	19.02

Notes:

[81] - Odds ratio of "Treatment period: 10 mg Empa + 10 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".

[82] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 20 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[83]
P-value	= 0.0001 [84]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.28
upper limit	10.9

Notes:

[83] - P-value was rounded to four decimal places.

[84] - Odds ratio of "Treatment period: 10 mg Empa + 20 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".

Secondary: UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Missing as non−responder

End point title	UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Missing as non−responder[85]

End point description:

Number of patients with UACR response I for patients with background therapy of empagliflozin in the

Run-in period is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
The missing as non-responder imputes patients with missing Week 14 data as non-responders.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who received empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

Notes:

[85] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received empagliflozin during the Run-in period.

End point values	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	60	62	64
Units: Participants	21	34	32	14

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 3 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[86]
P-value	= 0.1884 [87]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	3.79

Notes:

[86] - Odds ratio of "Treatment period: 10 mg Empa + 3 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[87] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 20 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[88]
P-value	= 0.0003 [89]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	9.94

Notes:

[88] - Odds ratio of "Treatment period: 10 mg Empa + 20 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[89] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 10 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other[90]
P-value	= 0 [91]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.94
upper limit	15.72

Notes:

[90] - Odds ratio of "Treatment period: 10 mg Empa + 10 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[91] - P-value was rounded to four decimal places.

Secondary: UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - complete case analysis

End point title	UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy

	of empagliflozin - complete case analysis[92]

End point description:

Number of patients with UACR response I for patients with background therapy of empagliflozin in the Run-in period is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
Complete case analysis used patients with both baseline and Week 14 data available.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who had received empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (i.e. Week 6, 7 or 8 of Run-in period) and one post-baseline measurement at Week 12-14 when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

Notes:

[92] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received empagliflozin during the Run-in period.

End point values	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	51	56	61
Units: Participants	21	34	32	14

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 3 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other[93]
P-value	= 0.1884 [94]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	3.79

Notes:

[93] - Odds ratio of "Treatment period: 10 mg Empa + 3 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[94] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 10 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other[95]
P-value	= 0 [96]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.94
upper limit	15.72

Notes:

[95] - Odds ratio of "Treatment period: 10 mg Empa + 10 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[96] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 20 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	other[97]
P-value	= 0.0003 [98]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	9.94

Notes:

[97] - Odds ratio of "Treatment period: 10 mg Empa+ 20 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[98] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change

in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients -multiple imputation

End point title	UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients -multiple imputation

End point description:

Number of patients with UACR response II is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 week. The multiple imputation filled in missing values at Week 14 based on other data observed in the same patient using regression.

This endpoint is reporting statistics for the Full Analysis Set (FAS). FAS included all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6, 7 or 8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the multiple imputation approach.

End point values	3 mg BI 690517	10 mg BI 690517	20 mg BI 690517	Placebo to BI 690517
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	128	121	121	133
Units: Participants	68	82	81	46

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	3 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other[99]
P-value	= 0.0024 [100]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.32
upper limit	3.61

Notes:

[99] - Odds ratio of "3 mg BI 690517" vs. "Placebo to BI 690517".

[100] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	20 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[101]
P-value	= 0 [102]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.29
upper limit	6.55

Notes:

[101] - Odds ratio of "20 mg BI 690517" vs. "Placebo to BI 690517".

[102] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	10 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[103]
P-value	= 0 [104]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.39
upper limit	6.86

Notes:

[103] - Odds ratio of "10 mg BI 690517" vs. "Placebo to BI 690517".

[104] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - Missing as non−responder

End point title	UACR response II, defined as decrease of at least 15%

	absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - Missing as non−responder

End point description:

Number of patients with UACR response II is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
The missing as non-responder imputes patients with missing Week 14 data as non-responders.

This endpoint is reporting statistics for the Full Analysis Set (FAS). FAS included all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6, 7 or 8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

End point values	3 mg BI 690517	10 mg BI 690517	20 mg BI 690517	Placebo to BI 690517
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	128	121	121	133
Units: Participants	67	71	70	44

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	3 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other[105]
P-value	= 0.0019 [106]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	3.77

Notes:

[105] - Odds ratio of "3 mg BI 690517" vs. "Placebo to BI 690517".

[106] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	20 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[107]
P-value	= 0 [108]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.12
upper limit	6.35

Notes:

[107] - Odds ratio of "20 mg BI 690517" vs. "Placebo to BI 690517".

[108] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	10 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[109]
P-value	= 0 [110]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	6.59

Notes:

[109] - Odds ratio of "10 mg BI 690517" vs. "Placebo to BI 690517"

[110] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - Last observation on treatment carried forward (LOCF)

End point title	UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - Last observation on treatment carried forward (LOCF)

End point description:

Number of patients with UACR response II is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14

weeks.
LOCF uses the last value observed on treatment to substitute all missing values until Week 14.

This endpoint is reporting statistics for Full Analysis Set (FAS). FAS included all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6, 7 or 8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the last observation carried forward approach.

End point values	3 mg BI 690517	10 mg BI 690517	20 mg BI 690517	Placebo to BI 690517
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	128	121	121	133
Units: Participants	67	87	85	53

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	3 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other[111]
P-value	= 0.0418 [112]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	2.74

Notes:

[111] - Odds ratio of "3 mg BI 690517" vs. "Placebo to BI 690517".

[112] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	20 mg BI 690517 v Placebo to BI 690517

Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[113]
P-value	= 0 [114]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.11
upper limit	6.05

Notes:

[113] - Odds ratio of "20 mg BI 690517" vs. "Placebo to BI 690517".

[114] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	10 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[115]
P-value	= 0 [116]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	6.65

Notes:

[115] - Odds ratio of "10 mg BI 690517" vs. "Placebo to BI 690517".

[116] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - complete case analysis

End point title	UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - all patients - complete case analysis

End point description:

Number of patients with UACR response II is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
Complete case analysis used patients with both baseline and Week 14 data available.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who had at least one baseline measurement of UACR at Week -2, -1, or 0 (i.e. Week 6, 7 or 8 of Run-in period) and one post-baseline measurement at Week 12-14 when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

End point values	3 mg BI 690517	10 mg BI 690517	20 mg BI 690517	Placebo to BI 690517
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	124	107	106	127
Units: Participants	67	71	70	44

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	3 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	other[117]
P-value	= 0.0019 [118]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	3.77

Notes:

[117] - Odds ratio of "3 mg BI 690517" vs. "Placebo to BI 690517".

[118] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	20 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	233
Analysis specification	Pre-specified
Analysis type	other[119]
P-value	= 0 [120]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.12
upper limit	6.35

Notes:

[119] - Odds ratio of "20 mg BI 690517" vs. "Placebo to BI 690517".

[120] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	10 mg BI 690517 v Placebo to BI 690517
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	other[121]
P-value	= 0 [122]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	6.59

Notes:

[121] - Odds ratio of "10 mg BI 690517" vs. "Placebo to BI 690517".

[122] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of placebo matching empagliflozin - Multiple imputation

End point title	UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of placebo matching empagliflozin - Multiple imputation[123]

End point description:

Number of patients with UACR response II for patients with background therapy of placebo matching empagliflozin in the Run-in period is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks. The multiple imputation filled in missing values at Week 14 based on other data observed in the same patient using regression.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo to BI 690517 who received placebo to empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo to BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the multiple imputation approach.

Notes:

[123] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received placebo matching empagliflozin during the Run-in period.

End point values	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	61	59	69
Units: Participants	33	35	39	22

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[124]
P-value	= 0.0285 [125]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	4.45

Notes:

[124] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[125] - P-value was rounded to four decimal places.

Statistical analysis title	Statistica analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517

Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other[126]
P-value	= 0.0002 [127]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.97
upper limit	8.72

Notes:

[126] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[127] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other[128]
P-value	= 0.0038 [129]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.41
upper limit	5.96

Notes:

[128] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[129] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of placebo matching empagliflozin - Missing as non−responder

End point title	UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of placebo matching empagliflozin - Missing as non−responder[130]

End point description:

Number of patients with UACR response II for patients with background therapy of placebo matching empagliflozin in the Run-in period is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks. The missing as non-responder imputes patients with missing Week 14 data as non-responders.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who received placebo to empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

Notes:

[130] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received placebo matching empagliflozin during the Run-in period.

End point values	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	61	59	69
Units: Participants	32	32	32	20

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[131]
P-value	= 0.0116 [132]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	5.31

Notes:

[131] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[132] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other[133]
P-value	= 0.0004 [134]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.86
upper limit	8.91

Notes:

[133] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[134] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other[135]
P-value	= 0.0032 [136]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	6.52

Notes:

[135] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[136] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change in FMV urine of UACR from treatment period baseline to 14 weeks - background therapy of placebo matching empagliflozin - Last observation on treatment carried forward (LOCF)

End point title	UACR response II, defined as decrease of at least 15% absolute change in FMV urine of UACR from treatment period

	baseline to 14 weeks - background therapy of placebo matching empagliflozin - Last observation on treatment carried forward (LOCF)[137]

End point description:

Number of patients with UACR response II for patients with background therapy of placebo matching empagliflozin in the Run-in period is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void (FMV) urine of UACR from treatment period baseline to 14 weeks.
LOCF uses the last value observed on treatment to substitute all missing values until Week 14.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who received placebo to empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the last observation carried forward approach.

Notes:

[137] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received placebo matching empagliflozin during the Run-in period.

End point values	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	61	59	69
Units: Participants	28	41	41	25

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[138]
P-value	= 0.4092 [139]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.34

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	2.69

Notes:

[138] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[139] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other[140]
P-value	= 0.0002 [141]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.92
upper limit	8.49

Notes:

[140] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[141] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other[142]
P-value	= 0.0005 [143]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.66

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.77
upper limit	7.58

Notes:

[142] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[143] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Multiple imputation

End point title	UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Multiple imputation[144]

End point description:

Number of patients with UACR response II for patients with background therapy of empagliflozin in the Run-in period is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
The multiple imputation filled in missing values at Week 14 based on other data observed in the same patient using regression.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who received empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the multiple imputation approach.

Notes:

[144] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received empagliflozin during the Run-in period.

End point values	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	60	62	64
Units: Participants	35	47	42	24

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 3 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[145]
P-value	= 0.0348 [146]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	4.43

Notes:

[145] - Odds ratio of "Treatment period: 10 mg Empa + 3 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[146] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 10 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other[147]
P-value	= 0 [148]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.73
upper limit	13.57

Notes:

[147] - Odds ratio of "Treatment period: 10 mg Empa + 10 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[148] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 20 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517

Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[149]
P-value	= 0.0007 [150]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.71
upper limit	7.52

Notes:

[149] - Odds ratio of "Treatment period: 10 mg Empa + 20 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[150] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Missing as non−responder

End point title	UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Missing as non−responder[151]

End point description:

Number of patients with UACR response II for patients with background therapy of empagliflozin in the Run-in period is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
The missing as non-responder imputes patients with missing Week 14 data as non-responders.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who received empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

Notes:

[151] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received empagliflozin during the Run-in period.

End point values	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	60	62	64
Units: Participants	35	39	38	24

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 3 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[152]
P-value	= 0.0578 [153]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	4.14

Notes:

[152] - Odds ratio of "Treatment period: 10 mg Empa + 3 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[153] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 20 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[154]
P-value	= 0.0022 [155]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.54
upper limit	7.16

Notes:

[154] - Odds ratio of "Treatment period: 10 mg Empa + 20 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[155] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation

stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 10 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other[156]
P-value	= 0.0001 [157]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.23
upper limit	11.78

Notes:

[156] - Odds ratio of "Treatment period: 10 mg Empa + 10 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[157] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of placebo matching empagliflozin - complete case analysis

End point title	UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks -patients with background therapy of placebo matching empagliflozin - complete case analysis[158]

End point description:

Number of patients with UACR response II for patients with background therapy of placebo matching empagliflozin in the Run-in period is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks. Complete case analysis used patients with both baseline and Week 14 data available.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who had received placebo matching empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (i.e. Week 6, 7 or 8 of Run-in period) and one post-baseline measurement at Week 12-14 when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

Notes:

[158] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received placebo matching empagliflozin during the Run-in period.

End point values	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	56	50	66
Units: Participants	32	32	32	20

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[159]
P-value	= 0.0116 [160]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	5.31

Notes:

[159] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[160] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[161]
P-value	= 0.0004 [162]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.86
upper limit	8.91

Notes:

[161] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[162] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517 v Treatment period: Placebo to Empa 10 mg+Placebo to BI 690517
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	other[163]
P-value	= 0.0032 [164]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	6.52

Notes:

[163] - Odds ratio of "Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517" vs. "Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517".
[164] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - complete case analysis

End point title	UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - complete case analysis[165]

End point description:

Number of patients with UACR response II for patients with background therapy of empagliflozin in the Run-in period is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
Complete case analysis used patients with both baseline and Week 14 data available.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who had received empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (i.e. Week 6, 7 or 8 of Run-in period) and post-baseline measurement at Week 12-14 when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

At baseline (Week 6,7 or 8 of the Run-in period) and at Week 12-14 of the Treatment Period.

Notes:

[165] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received empagliflozin during the Run-in period.

End point values	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	51	56	61
Units: Participants	35	39	38	24

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 3 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other[166]
P-value	= 0.0578 [167]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	4.14

Notes:

[166] - Odds ratio of "Treatment period: 10 mg Empa + 3 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".

[167] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 20 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	other[168]
P-value	= 0.0022 [169]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.32

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.54
upper limit	7.16

Notes:

[168] - Odds ratio of "Treatment period: 10 mg Empa + 20 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[169] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 10 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other[170]
P-value	= 0.0001 [171]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.23
upper limit	11.78

Notes:

[170] - Odds ratio of "Treatment period: 10 mg Empa + 10 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[171] - P-value was rounded to four decimal places.

Secondary: UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Last observation on treatment carried forward

End point title	UACR response I, defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Last observation on treatment carried forward[172]

End point description:

Number of patients with UACR response I for patients with background therapy of empagliflozin in the Run-in period is reported. UACR response I was defined as decrease of at least 30% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
Last observation on treatment carried forward (LOCF) uses the last value observed on treatment to substitute all missing values until Week 14.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who received empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the last observation carried forward approach.

Notes:

[172] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received empagliflozin during the Run-in period.

End point values	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	60	62	64
Units: Participants	23	36	41	17

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 3 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[173]
P-value	= 0.214 [174]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	3.46

Notes:

[173] - Odds ratio of "Treatment period: 10 mg Empa + 3 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[174] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 20 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517

Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[175]
P-value	= 0 [176]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.52
upper limit	11.71

Notes:

[175] - Odds ratio of "Treatment period: 10 mg Empa + 20 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[176] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 10 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other[177]
P-value	= 0.0003 [178]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.93
upper limit	8.85

Notes:

[177] - Odds ratio of "Treatment period: 10 mg Empa + 10 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[178] - P-value was rounded to four decimal places.

Secondary: UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Last observation on treatment carried forward

End point title	UACR response II, defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks - patients with background therapy of empagliflozin - Last observation on treatment carried forward[179]

End point description:

Number of patients with UACR response II for patients with background therapy of empagliflozin in the Run-in period is reported. UACR response II was defined as decrease of at least 15% absolute change in First Morning Void urine of UACR from treatment period baseline to 14 weeks.
Last observation on treatment carried forward (LOCF) uses the last value observed on treatment to substitute all missing values until Week 12-14.

This endpoint is reporting statistics for all randomised patients to one of 3 doses of BI 690517 or placebo matching BI 690517 who received empagliflozin during the Run-in Period and who had at least one baseline measurement of UACR at Week -2, -1, or 0 (Week 6,7,8 of the Run-in Period) and at least one post-baseline measurement when patients were still on treatment with BI 690517 or placebo matching BI 690517.

End point type	Secondary

End point timeframe:

UACR measurements from baseline (Week 6,7 or 8 of the Run-in period) and Week 6, Week 10 and Week 12-14 of Treatment period were used for the last observation carried forward approach.

Notes:

[179] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics only for the patients who received empagliflozin during the Run-in period.

End point values	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	60	62	64
Units: Participants	39	46	44	28

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 3 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other[180]
P-value	= 0.0342 [181]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	4.44

Notes:

[180] - Odds ratio of "Treatment period: 10 mg Empa + 3 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[181] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 20 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[182]
P-value	= 0.0023 [183]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.52
upper limit	6.73

Notes:

[182] - Odds ratio of "Treatment period: 10 mg Empa + 20 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[183] - P-value was rounded to four decimal places.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The odds ratio, 95% confidence interval, and p-value were calculated based on logistic regression of binary outcome adjusting for treatment, and stratification factors as covariates. Randomisation stratification was used, which is based on estimated glomerular filtration rate (eGFR) and urine albumin creatinine ratio (UACR) levels at screening.

Comparison groups	Treatment period: 10 mg Empa + 10 mg BI 690517 v Treatment period: 10 mg Empa + Placebo to BI 690517
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other[184]
P-value	= 0.0003 [185]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.93
upper limit	9.24

Notes:

[184] - Odds ratio of "Treatment period: 10 mg Empa + 10 mg BI 690517" vs. "Treatment period: 10 mg Empa + Placebo to BI 690517".
[185] - P-value was rounded to four decimal places.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first study drug administration in the treatment period until end of the residual effect period (i.e. 7 days for empagliflozin and BI 690517), up to 15 weeks.

Adverse event reporting additional description:

Adverse events were planned in the protocol and statistical analysis plan to be reported for the treated set.
Treated Set (TS): This patient set included all patients who received at least one dose of BI 690517 or placebo matching BI 690517.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Treatment period: 10 mg Empa + 3 mg BI 690517

Reporting group description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 3 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 3 mg BI 690517 and 10 mg empagliflozin for 14 weeks.

Reporting group title	Treatment period: 10 mg Empa + 20 mg BI 690517

Reporting group description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 20 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 20 mg BI 690517 and 10 mg empagliflozin for 14 weeks.

Reporting group title	Treatment period: 10 mg Empa + 10 mg BI 690517

Reporting group description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 10 milligrams (mg) of BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received 10 mg BI 690517 and 10 mg empagliflozin for 14 weeks.

Reporting group title	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517

Reporting group description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 20 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 20 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Reporting group title	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517

Reporting group description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 10 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 10 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Reporting group title	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517

Reporting group description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received 3 mg of BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received 3 mg BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Reporting group title	Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517

Reporting group description:

This arm includes patients who received placebo matching empagliflozin (Empa) 10 milligrams (mg) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received placebo matching BI 690517 once daily (QD) orally in combination with placebo matching empagliflozin 10 mg QD orally. Patients received placebo matching BI 690517 and placebo matching empagliflozin 10 mg for 14 weeks.

Reporting group title	Treatment period: 10 mg Empa + Placebo to BI 690517

Reporting group description:

This arm includes patients who received 10 mg of empagliflozin (Empa) during the run-in period and met the eligibility criteria to enter the treatment period. In the treatment period patients received placebo matching BI 690517 once daily (QD) orally in combination with 10 mg of empagliflozin QD orally. Patients received placebo matching BI 690517 and 10 mg empagliflozin for 14 weeks.

Serious adverse events	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 76 (5.26%)	5 / 74 (6.76%)	7 / 73 (9.59%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	0 / 73 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Transitional cell carcinoma metastatic			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Aortic thrombosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Coeliac artery occlusion			

subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Phlebitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	0 / 73 (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			
Sudden death			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Pleural effusion			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Injury, poisoning and procedural complications			
Haematuria traumatic			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Cardiac disorders			
Cardiac failure			

subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	0 / 73 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Coronary artery disease			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Hypertensive heart disease			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracardiac thrombus			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Dizziness			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			

subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Syncope			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Thrombosis mesenteric vessel			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	0 / 73 (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			
Acute kidney injury			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal segmental glomerulosclerosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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

Renal artery stenosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage urinary tract			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Renal mass			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcapsular renal haematoma			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	2 / 73 (2.74%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glucocorticoid deficiency			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	0 / 73 (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			
Abscess soft tissue			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	0 / 73 (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
COVID-19			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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

Dengue fever			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Diverticulitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	0 / 73 (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
Erysipelas			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Pneumonia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	0 / 73 (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
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	0 / 73 (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
Hyperkalaemia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic syndrome			
subjects affected / exposed	0 / 76 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
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	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 72 (8.33%)	4 / 71 (5.63%)	3 / 70 (4.29%)
number of deaths (all causes)	1	1	0

number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Transitional cell carcinoma metastatic			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Vascular disorders			
Aortic thrombosis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 71 (0.00%)	0 / 70 (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
Coeliac artery occlusion			
subjects affected / exposed	1 / 72 (1.39%)	0 / 71 (0.00%)	0 / 70 (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
Phlebitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	0 / 72 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory, thoracic and mediastinal disorders			

Acute respiratory failure			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Pleural effusion			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Pulmonary oedema			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Injury, poisoning and procedural complications			
Haematuria traumatic			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Coronary artery disease			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypertensive heart disease			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Intracardiac thrombus			
subjects affected / exposed	1 / 72 (1.39%)	0 / 71 (0.00%)	0 / 70 (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
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 72 (1.39%)	0 / 71 (0.00%)	0 / 70 (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
Dizziness			
subjects affected / exposed	1 / 72 (1.39%)	0 / 71 (0.00%)	0 / 70 (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
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 72 (0.00%)	1 / 71 (1.41%)	0 / 70 (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
Syncope			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 72 (1.39%)	0 / 71 (0.00%)	0 / 70 (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
Pancreatitis acute			
subjects affected / exposed	1 / 72 (1.39%)	0 / 71 (0.00%)	0 / 70 (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

Thrombosis mesenteric vessel			
subjects affected / exposed	1 / 72 (1.39%)	0 / 71 (0.00%)	0 / 70 (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
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 72 (2.78%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal segmental glomerulosclerosis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Renal artery stenosis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Haemorrhage urinary tract			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Renal mass			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Subcapsular renal haematoma			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	2 / 72 (2.78%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glucocorticoid deficiency			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Infections and infestations			
Abscess soft tissue			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
COVID-19			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Dengue fever			
subjects affected / exposed	0 / 72 (0.00%)	1 / 71 (1.41%)	0 / 70 (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
Diverticulitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Erysipelas			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Pneumonia			
subjects affected / exposed	0 / 72 (0.00%)	1 / 71 (1.41%)	0 / 70 (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

Pyelonephritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Sepsis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 71 (1.41%)	0 / 70 (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
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Urinary tract infection			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 72 (1.39%)	0 / 71 (0.00%)	0 / 70 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Hypoglycaemia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Hyperkalaemia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Hypercalcaemia			

subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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
Hyponatraemia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 71 (0.00%)	0 / 70 (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
Metabolic syndrome			
subjects affected / exposed	0 / 72 (0.00%)	0 / 71 (0.00%)	0 / 70 (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

Serious adverse events	Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 73 (4.11%)	7 / 74 (9.46%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 73 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma metastatic			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic thrombosis			

subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coeliac artery occlusion			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (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			
Sudden death			
subjects affected / exposed	0 / 73 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 73 (1.37%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 73 (1.37%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Haematuria traumatic			

subjects affected / exposed	1 / 73 (1.37%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 73 (1.37%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 73 (1.37%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive heart disease			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracardiac thrombus			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (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			
Cerebral infarction			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			

subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 73 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis mesenteric vessel			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (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			
Diabetic foot			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (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			
Acute kidney injury			
subjects affected / exposed	1 / 73 (1.37%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Focal segmental glomerulosclerosis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage urinary tract			
subjects affected / exposed	1 / 73 (1.37%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal mass			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcapsular renal haematoma			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 73 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glucocorticoid deficiency			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (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			
Abscess soft tissue			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

COVID-19			
subjects affected / exposed	0 / 73 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 73 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 73 (1.37%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 73 (1.37%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic syndrome			
subjects affected / exposed	0 / 73 (0.00%)	0 / 74 (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: 5 %

Non-serious adverse events	Treatment period: 10 mg Empa + 3 mg BI 690517	Treatment period: 10 mg Empa + 20 mg BI 690517	Treatment period: 10 mg Empa + 10 mg BI 690517
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 76 (14.47%)	19 / 74 (25.68%)	20 / 73 (27.40%)
Investigations			
Cortisol decreased			
subjects affected / exposed	2 / 76 (2.63%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences (all)	2	0	1
Glomerular filtration rate decreased			
subjects affected / exposed	4 / 76 (5.26%)	7 / 74 (9.46%)	8 / 73 (10.96%)
occurrences (all)	4	7	8
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 76 (0.00%)	2 / 74 (2.70%)	4 / 73 (5.48%)
occurrences (all)	0	2	4
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 76 (1.32%)	4 / 74 (5.41%)	1 / 73 (1.37%)
occurrences (all)	1	4	1
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	5 / 76 (6.58%)	7 / 74 (9.46%)	11 / 73 (15.07%)
occurrences (all)	5	7	11

Non-serious adverse events	Treatment period: Placebo to Empa 10 mg + 20 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 10 mg BI 690517	Treatment period: Placebo to Empa 10 mg + 3 mg BI 690517
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 72 (34.72%)	16 / 71 (22.54%)	15 / 70 (21.43%)
Investigations			
Cortisol decreased			
subjects affected / exposed	2 / 72 (2.78%)	4 / 71 (5.63%)	3 / 70 (4.29%)
occurrences (all)	2	4	3
Glomerular filtration rate decreased			
subjects affected / exposed	6 / 72 (8.33%)	7 / 71 (9.86%)	1 / 70 (1.43%)
occurrences (all)	6	7	1
Vascular disorders			

Hypotension subjects affected / exposed occurrences (all)	0 / 72 (0.00%) 0	0 / 71 (0.00%) 0	1 / 70 (1.43%) 1
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 72 (4.17%) 5	1 / 71 (1.41%) 1	2 / 70 (2.86%) 2
Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all)	17 / 72 (23.61%) 20	7 / 71 (9.86%) 8	8 / 70 (11.43%) 8

Non-serious adverse events	Treatment period: Placebo to Empa 10 mg + Placebo to BI 690517	Treatment period: 10 mg Empa + Placebo to BI 690517	
Total subjects affected by non-serious adverse events subjects affected / exposed	9 / 73 (12.33%)	13 / 74 (17.57%)	
Investigations Cortisol decreased subjects affected / exposed occurrences (all)	0 / 73 (0.00%) 0	1 / 74 (1.35%) 1	
Glomerular filtration rate decreased subjects affected / exposed occurrences (all)	3 / 73 (4.11%) 4	2 / 74 (2.70%) 2	
Vascular disorders Hypotension subjects affected / exposed occurrences (all)	0 / 73 (0.00%) 0	1 / 74 (1.35%) 1	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 73 (2.74%) 2	4 / 74 (5.41%) 5	
Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all)	4 / 73 (5.48%) 6	5 / 74 (6.76%) 10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 October 2021	Global protocol amendment 1 included the following changes in the protocol. The screening period was extended from 14 to 21 days to allow for any allowed repetition of screening procedures. The Flowchart was changed to detect and mitigate the potential risk of adrenal insufficiency by addition of extensive serum and urine cortisol sampling and addition of an adrenocorticotropic hormone (ACTH) challenge test (on an as-needed basis based on cortisol levels); serum cortisol was added to the list of hormones to be tested in safety laboratory parameters. The Flowchart was changed to allow pre-screening for urine albumin creatinine ratio (UACR) and estimated Glomerular Filtration Rate (eGFR) subject to pre-screening informed consent. Legal adult age (according to local legislation) as part of the inclusion criteria was added on top of 18+ years of age. Patients who needed to or wished to continue the intake of restricted medications or any drug considered likely to interfere with the safe conduct of the trial were excluded. An exclusionary criterion regarding intake biotin or related preparations was introduced. Patients who had taken Vitamin B7, Vitamin H, or coenzyme-R at doses ≥5 mg/day (including food supplements) within 72 h of Visit 1 or who planned to take above dosesof biotin during the trial were excluded. The original cut off value of increase in serum cortisol of 200 nmol/L at 30 min postinjection was modified to absolute cortisol value of <18 µg/dL (496.6 nmol/L) at 30 min (± 5 min) after injection of ACTH at Visit 1 to follow the Cosyntropin label and relevant United States (US) guidelines. Any clinically relevant abnormal laboratory value was expanded to specifically include a serum cortisol level <5 µg/dL (138.0 nmol/L) at Visit 1 or until first randomization to exclude those patients at greater risk of adrenal insufficiency.
25 October 2021	Global protocol amendment 1 continued: Added requirements for discontinuation of trial treatment (BI 690517/placebo) in patients who develop Cushing's syndrome, adrenal insufficiency (including cortisol level <18 µg/dL 30 min (±5 min) after ACTH application), or cortisol levels <3 µg/dL (82.8 nmol/L) at any point in the trial should. Added requirement to permanently discontinue patients who permanently discontinue empagliflozin/placebo during the randomised run-in period due to any reason. Adrenal insufficiency and Cushing's syndrome were added as an AESI to the protocol. Requirements for ACTH challenge tests during the study and at the end of treatment were added. The shipment of trial medication from the site to the patient's home was allowed to support regular visits performed at the patient's home specified by the Flowchart. Management of eGFR decrease was specified. Management of serum cortisol decrease was specified.
30 March 2022	Global protocol amendment 2 included the following changes. Flowchart was modified to remove 24-hour urine sample at EOT for patients who discontinue prematurely before initiation of treatment with BI 690517/placebo. Inclusion criteria on chronic kidney disease as baseline condition was simplified to include patients with any kind of diagnosed chronic kidney disease according to Investigator's opinion and that diagnosis of chronic kidney disease (CKD) could be reached by standard clinical method and no biopsy was required. An additional criterion mandating screening of patients before the second randomization to treatment period was added to exclude patients with known hepatic cirrhosis (Child Pugh A, B or C), or other liver disease causing impaired liver function according to investigator's judgement. An additional criterion was added to exclude those patients with CKD in whom no benefit to treatment with BI 690517 was expected due to underlying causes of CKD attributed to either of the following: CKD secondary due to malignancy (e.g. Cast-Nephropathy, AL-amyloidosis), CKD secondary to infectious disease (e.g. Hepatitis-/HIV-associated), autosomal-dominant polycystic kidney disease. Clarification was provided regarding unblinding status at last patient last visit primary endpoint snapshot. Methotrexate was added to the restricted medications list.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported