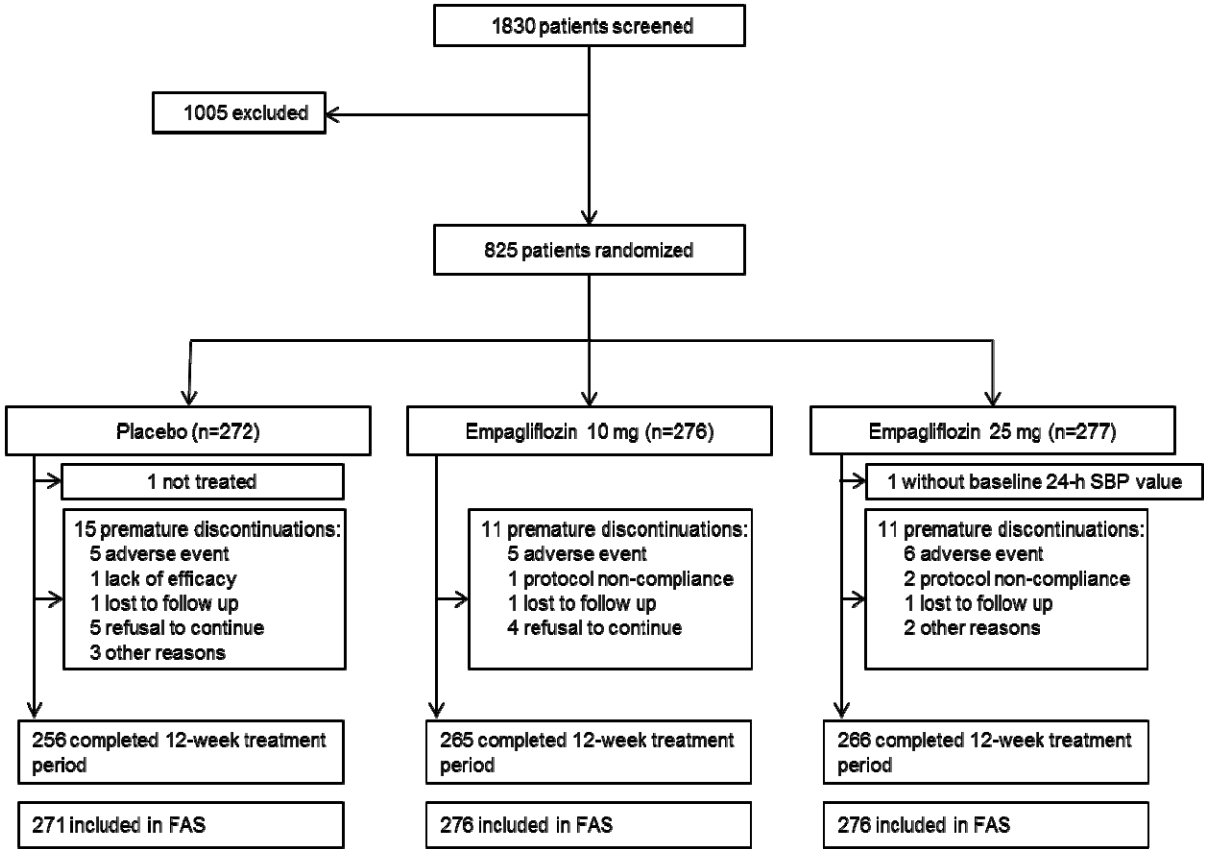
SUPPLEMENTARY DATA

Supplementary Figure 1. *Study flow.*



SUPPLEMENTARY DATA

Supplementary Table 1. *Sensitivity analyses of co-primary and key secondary BP endpoints with different imputation methods.*

	Placebo	Empagliflozin 10 mg	Empagliflozin 25 mg
Difference vs. placebo in adjusted mean (SE) change in mean 24-h SBP (mmHg) at week 12			
ANCOVA, FAS (OC-H), n*	234	242	232
Change from baseline in mean 24-h SBP at week 12, mmHg	0.53 (0.55)	-3.31 (0.54)	-4.42 (0.55)
Difference vs. placebo, mmHg		-3.84 (0.77)	-4.95 (0.77)
95% CI		(-5.36, -2.33)	(-6.47, -3.43)
ANCOVA, FAS (OC-IR), n*	248	258	256
Change from baseline in mean 24-h SBP at week 12, mmHg	0.24 (0.54)	-3.32 (0.53)	-4.46 (0.53)
Difference vs. placebo, mmHg		-3.57 (0.75)	-4.70 (0.75)
95% CI		(-5.04, -2.09)	(-6.17, -3.23)
Difference vs. placebo in adjusted mean (SE) change in mean 24-h DBP (mmHg) at week 12			
ANCOVA, FAS (OC-H), n*	234	242	232
Change from baseline in mean 24-h DBP at week 12, mmHg	0.33 (0.33)	-1.13 (0.32)	-1.68 (0.33)
Difference vs. placebo, mmHg		-1.46 (0.46)	-2.02 (0.46)
95% CI		(-2.36, -0.55)	(-2.92, -1.11)
ANCOVA, FAS (OC-IR), n*	248	258	256
Change from baseline in 24-h DBP at week 12, mmHg	0.17 (0.32)	-1.04 (0.31)	-1.76 (0.31)

Difference vs. placebo, mmHg		-1.21 (0.44)	-1.93 (0.44)
95% CI		(-2.08, -0.33)	(-2.80, -1.06)

Data are adjusted mean (SE). ANCOVA model includes baseline mean 24-h SBP or DBP and baseline HbA1c as linear covariates and baseline eGFR (MDRD), geographical region, number of antihypertensive medications and treatment as fixed effects. OC-H, observed cases excluding values after rescue and values following a change in antihypertensive therapy; OC-IR, observed cases including values after rescue. *Number of analyzed patients.

Supplementary Table 2. *Changes in fasting plasma glucose.*

	Placebo (n=271)	**Empagliflozin 10 mg (n=276)**	**Empagliflozin 25 mg (n=276)**
Fasting plasma glucose (FPG)			
FPG at week 12, mmol/L	9.28 (0.15)	7.87 (0.10)	7.68 (0.10)
Change from baseline, mmol/L	0.40 (0.10)	-0.92 (0.10)	-1.28 (0.10)
Difference vs. placebo		-1.32 (0.15)	-1.68 (0.14)
95% CI		(-1.60, -1.03)	(-1.96, -1.39)
p-value		<0.001	<0.001

Data are adjusted mean (SE). ANCOVA in FAS (last observation carried forward).

SUPPLEMENTARY DATA

Supplementary Table 3. *Sensitivity analyses of primary HbA_{1c} endpoint with different imputation methods.*

	Placebo	Empagliflozin 10 mg	Empagliflozin 25 mg
Difference vs. placebo in adjusted mean (SE) change in HbA_{1c} at week 12			
MMRM, FAS (OC), n*	257	266	261
Change from baseline in HbA_{1c} at week 12, % [mmol/mol]	0.03 (0.04) [0.3 (0.4)]	-0.62 (0.04) [-6.8 (0.4)]	-0.67 (0.04) [-7.3 (0.4)]
Difference vs. placebo, % [mmol/mol]		-0.66 (0.05) [-7.2 (0.5)]	-0.70 (0.05) [-7.7 (0.5)]
95% CI		(-0.76, -0.55) [-8.3, -6.0]	(-0.80, -0.60) [-8.7, -6.6]
MMRM, FAS (OC-IR), n*	264	273	272
Change from baseline in HbA_{1c} at week 12, % [mmol/mol]	0.01 (0.04) [0.1 (0.4)]	-0.62 (0.04) [-6.8 (0.4)]	-0.64 (0.04) [-7.0 (0.4)]
Difference vs. placebo, % [mmol/mol]		-0.63 (0.05) [-6.9 (0.5)]	-0.64 (0.05) [-7.0 (0.5)]
95% CI		(-0.73, -0.52) [-8.0, -5.7]	(-0.75, -0.54) [-8.2, -5.9]

Data are adjusted mean (SE). MMRM model includes baseline HbA_{1c} as a linear covariate, baseline eGFR (MDRD), geographical region, number of antihypertensive medications, treatment, visit and visit by treatment interaction as fixed effects, and subject as a random effect. OC, observed cases excluding values after rescue; OC-IR, observed cases including values after rescue; MMRM, mixed model repeated measures. *Number of analyzed patients.

SUPPLEMENTARY DATA

Supplementary Table 4. *Laboratory measurements.*

	Placebo		Empagliflozin 10 mg		Empagliflozin 25 mg	
	Baseline	**Change from baseline***	**Baseline**	**Change from baseline***	**Baseline**	**Change from baseline***
Hematocrit †	0.42 (0.03)		0.41 (0.03)		0.41 (0.04)	
At last value on treatment		0.00 (0.02)		0.03 (0.02)		0.02 (0.02)
At follow-up		0.00 (0.02)		0.02 (0.02)		0.01 (0.02)
eGFR, ml/min/1.73m^2 (MDRD)†	84.47 (17.06)		83.01 (16.43)		83.97 (17.85)	
At last value on treatment		-0.27 (9.18)		-0.20 (8.99)		-2.60 (9.98)
At follow-up		-0.82 (9.62)		3.06 (10.05)		2.75 (9.71)
Uric acid, µmol/Ll†	347.37 (82.73)		341.85 (81.78)		338.27 (79.52)	
At last value on treatment		-8.17 (43.68)		-41.21 (58.47)		-38.46 (58.51)
At follow-up		-0.54 (48.18)		-10.49 (55.58)		-20.86 (50.99)
Electrolytes, mmol/L‡§						
Sodium	141 (2)	0 (2)	141 (2)	0 (2)	141 (2)	1 (2)
Potassium	4.2 (0.3)	0.0 (0.3)	4.2 (0.3)	0.0 (0.3)	4.2 (0.3)	0.0 (0.3)
Calcium	2.4 (0.1)	0.0 (0.1)	2.5 (0.1)	0.0 (0.1)	2.4 (0.1)	0.0 (0.1)

Magnesium	0.9 (0.1)	0.0 (0.1)	0.9 (0.1)	0.1 (0.1)	0.9 (0.1)	0.1 (0.1)
Phosphate	1.2 (0.1)	0.0 (0.1)	1.2 (0.1)	0.0 (0.1)	1.2 (0.1)	0.0 (0.1)

Data are mean (SD). *Change from baseline at last value on treatment (all parameters) and at follow-up (hematocrit, eGFR, and uric acid). †Patients in the FAS who had a follow-up visit 10–21 days after last intake of trial medication (n=238 for placebo, n=241 for empagliflozin 10 mg and n=244 for empagliflozin 25 mg). ‡Patients who received ≥1 dose of randomized study drug. §Normalized to a standard reference range.

SUPPLEMENTARY DATA

Supplementary Table 5. *Lipid measurements.*

	Placebo		Empagliflozin 10 mg		Empagliflozin 25 mg	
	Baseline	**Change from baseline at week 12**	**Baseline**	**Change from baseline at week 12**	**Baseline**	**Change from baseline at week 12**
Total cholesterol, mmol/L	4.68 (0.06)	0.05 (0.04)	4.65 (0.07)	0.10 (0.04)	4.66 (0.06)	0.20 (0.04)
Difference vs. placebo				0.04 (0.06)		0.15 (0.06)
p-value				0.474		0.013
HDL cholesterol, mmol/L	1.24 (0.02)	0.01 (0.01)	1.27 (0.02)	0.03 (0.01)	1.25 (0.02)	0.03 (0.01)
Difference vs. placebo				0.02 (0.01)		0.02 (0.01)
p-value				0.113		0.091
LDL cholesterol, mmol/L	2.57 (0.06)	0.01 (0.03)	2.52 (0.06)	0.08 (0.03)	2.55 (0.05)	0.17 (0.03)
Difference vs. placebo				0.06 (0.05)		0.16 (0.05)
p-value				0.192		<0.001
Triglycerides, mmol/L	1.93 (0.07)	0.11 (0.06)	1.95 (0.09)	-0.03 (0.06)	1.93 (0.07)	0.03 (0.06)
Difference vs. placebo				-0.13 (0.08)		-0.08 (0.08)
p-value				0.112		0.337

Baseline data are mean (SE) and change from baseline data are adjusted mean (SE) based on ANCOVA (LOCF-IR) in all patients receiving ≥1 dose of study medication.

SUPPLEMENTARY DATA

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SUPPLEMENTARY DATA

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