SUPPLEMENTARY DATA

Supplementary Table 1. Association between severe hypoglycaemic events (SHEs) and subsequent major adverse cardiovascular event (MACE) or death outcomes in cardiovascular outcome trials

	Total population or subgroup in trial	MACE/death outcomes	Adj. HR (95% CI)
VADT	All	Cardiovascular mortality	4.04 (1.45-11.28)†
ACCORD	Intensive arm	Annualized mortality	1.41 (1.03-1.93)
	Standard arm	Annualized mortality	2.30 (1.46-3.65)
ADVANCE	All	3-point MACE	2.88 (2.01-4.12)
		Cardiovascular death	2.68 (1.72-4.19)
		All-cause death	2.69 (1.97-3.67)
ORIGIN	All	3-point MACE	1.58 (1.24–2.02)
		Cardiovascular death	1.71 (1.27–2.30)
		All-cause death	1.74 (1.39–2.19)
SAVOR-TIMI 53	All	CV death	1.81 (1.06-2.87)
		Heart failure hospitalisation	2.42 (1.27-4.60)
EXAMINE	All	3-point MACE	1.80 (1.04-2.89)

The time sequence for an SHE after a non-fatal MACE has not been evaluated at all.

ACCORD=Action to Control Cardiovascular Risk in Diabetes; ADVANCE=Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation; EXAMINE=Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care; ORIGIN=Outcome Reduction with an Initial Glargine Intervention; SAVOR-TIMI 53=Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus—Thrombolysis in Myocardial Infarction 53; VADT=Veterans Affairs Diabetes Trial.

SUPPLEMENTARY DATA

Supplementary Table 2. Baseline characteristics for participants with SHEs who had or did not have a CV event (intention-to-treat population)

Age at Randomisation (years) Mean (SD)		Without a CV Event (N=235)	With a CV Event (N=68)
<56 years	Age at Randomisation (years) ¹	(1 - 2 - 7)	(1 2 2)
>=65 years	Mean (SD)	66.9 (8.3)	67.9 (7.7)
>=65 years	<65 years	90 / 231 (39.0%)	19 / 67 (28.4%)
>=70 years Sex Male 150 / 235 (63.8%) 29 / 67 (43.3%) Sex Male 150 / 235 (63.8%) 43 / 68 (63.2%) Female 85 / 235 (36.2%) 25 / 68 (36.8%) Race White 136 / 235 (57.9%) 40 / 68 (58.8%) Asian 59 / 235 (25.1%) 15 / 68 (22.1%) Other 27 / 235 (11.5%) 5 / 68 (74.7%) Diabetes duration 15 years or more 13 / 235 (36.8%) Biabetes therapy at baseline (alone or in combination) Sulfonylurea 110 / 235 (46.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 32 / 68 (71.1%) Mot on Sulfonylurea or Insulin 97 / 235 (31.3%) 1 / 68 (15.9%) Insulin 97 / 235 (31.3%) 1 / 68 (15.9%) Pre-existing vascular disease 234 / 235 (99.6%) 68 / 68 (100.9%) Prior Congestive heart failure 37 / 235 (15.9%) 37 / 68 (48.5%) Prior white 37 / 235 (15.9%) 37 / 68 (48.5%) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 9	>=65 years		48 / 67 (71.6%)
>=70 years Sex Male 150 / 235 (63.8%) 29 / 67 (43.3%) Sex Male 150 / 235 (63.8%) 43 / 68 (63.2%) Female 85 / 235 (36.2%) 25 / 68 (36.8%) Race White 136 / 235 (57.9%) 40 / 68 (58.8%) Asian 59 / 235 (25.1%) 15 / 68 (22.1%) Other 27 / 235 (11.5%) 5 / 68 (74.7%) Diabetes duration 15 years or more 13 / 235 (36.8%) Biabetes therapy at baseline (alone or in combination) Sulfonylurea 110 / 235 (46.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 30 / 68 (44.1%) Metionmin 177 / 235 (36.8%) 32 / 68 (71.1%) Mot on Sulfonylurea or Insulin 97 / 235 (31.3%) 1 / 68 (15.9%) Insulin 97 / 235 (31.3%) 1 / 68 (15.9%) Pre-existing vascular disease 234 / 235 (99.6%) 68 / 68 (100.9%) Prior Congestive heart failure 37 / 235 (15.9%) 37 / 68 (48.5%) Prior white 37 / 235 (15.9%) 37 / 68 (48.5%) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (69, 7.7) Median (Q1, Q3) 7.3 (69, 9	<70 years	138 / 231 (59.7%)	38 / 67 (56.7%)
Sex Male	>=70 years		29 / 67 (43.3%)
Female 85 / 235 (36.2%) 25 / 68 (36.8%) Race			
Race White	Male	150 / 235 (63.8%)	43 / 68 (63.2%)
White	Female	85 / 235 (36.2%)	25 / 68 (36.8%)
Black Asian 59 (235 (25.5%) 8 / 68 (11.8%) Asian 59 (235 (25.1%) 15 / 68 (22.1%) 10ther 27 / 235 (11.5%) 5 / 68 (7.4%) 127 / 235 (11.5%) 5 / 68 (7.4%) 127 / 235 (11.5%) 5 / 68 (7.4%) 127 / 235 (11.5%) 5 / 68 (7.4%) 127 / 235 (11.5%) 5 / 68 (7.4%) 127 / 235 (11.5%) 5 / 68 (7.4%) 127 / 235 (11.5%) 137 / 68 (42.1%) 137 / 68 (48.5%) 133 / 68 (48.5%) 133 / 68 (48.5%) 133 / 68 (48.5%) 133 / 68 (48.5%) 133 / 68 (48.1%) 137 / 235 (48.8%) 137 / 68 (48.1%) 137 / 235 (48.8%) 14 / 68 (72.1%) 14 / 68 (72.1%) 15 / 68 (11.8%) 15 / 68 (Race		
Asian 59 / 235 (25.1%) 15 / 68 (22.1%) Other 27 / 235 (11.5%) 5 / 68 (7.4%) Duration² of type 2 diabetes (years) Median (Q1, Q3) 14.0 (7.0, 22.0) 13.5 (8.0, 22.5) Diabetes duration 15 years or more 113 / 235 (48.1%) 33 / 68 (48.5%) Diabetes therapy at baseline (alone or in combination) Sulfonylurea 110 / 235 (46.8%) 30 / 68 (44.1%) Metformin 177 / 235 (75.3%) 49 / 68 (72.1%) Thiazolidinedione (includes Pioglitazone) 7 / 225 (3.0%) 1 / 68 (17.5%) Not on Sulfonylurea 97 / 235 (41.3%) 32 / 68 (47.1%) Not on Sulfonylurea or Insulin 97 / 235 (41.3%) 32 / 68 (47.1%) Not on Sulfonylurea or Insulin 33 / 235 (14.0%) 7 / 68 (10.3%) 17 / 68 (10.3%) 17 / 68 (25.0%) 18 / 68 (100.0%) Pre-existing vascular disease 234 / 235 (99.6%) 68 / 68 (100.0%) Prior MI 85 / 235 (36.2%) 33 / 68 (48.5%) 17 / 68 (25.0%) 18 / 68 (44.6%) Qualifying HbA1c (mmol/mol) Median (Q1, Q3) 22 / 235 (9.4%) 3 / 68 (4.4%) Qualifying HbA1c (mmol/mol) Median (Q1, Q3) 7.3 (6.9, 7.7) 7.2 (6.9, 7.7) Median (Q1, Q3) 7.3 (6.9, 7.7) 7.2 (6.9, 7.7) Median (Q1, Q3) 66 / 235 (28.1%) 21 / 68 (30.9%) 7.2 / 7.5% 90 / 235 (38.3%) 29 / 68 (42.6%) 6FR (mL/min/1.73m²) 66 / 60 (54.0, 85.5) 60.0 (47.0, 71.0) Median (Q1, Q3) 66 / 60 (54.0, 85.5) 60 / 60 (47.0, 71.0) Median (Q1, Q3) 7.3 (6.9, 7.7) 7.2 (6.9, 7.7) Median (Q1, Q3) 7.3 (6.9, 7.7) 7.3 (6.9, 7.7) 7.3 (6.9, 7.7) 7.3 (6.9, 7.7) 7.3 (6.9, 7.7) Median (Q1, Q3) 7.3 (6.9, 7.7) 7.3 (6.9,	White	136 / 235 (57.9%)	40 / 68 (58.8%)
Other Duration² of type 2 diabetes (years) Median (Q1, Q3) Diabetes duration 15 years or more Diabetes therapy at baseline (alone or in combination) Sulfonylurea 110 / 235 (48.1%) 33 / 68 (44.1%) Sulfonylurea 110 / 235 (46.8%) 30 / 68 (44.1%) Thiazolidinedione (includes Pioglitazone) Thiazolidine (includes Pioglitazone) Thiazolidinedione (includes Pioglitazone) Thiazolidinedione (includes Pioglita Pioglitazone) Thiazolidinedione (includes Pioglitazone) Thiazolidinedione (Black	13 / 235 (5.5%)	8 / 68 (11.8%)
Duration	Asian	59 / 235 (25.1%)	15 / 68 (22.1%)
Median (Q1, Q3) 14.0 (7.0, 22.0) 13.5 (8.0, 22.5) 13 (235 (48.1%) 33 /68 (48.5%) 13 /235 (48.1%) 33 /68 (48.5%) 13 /235 (48.1%) 33 /68 (48.5%) 13 /235 (48.1%) 33 /68 (48.5%) 13 /235 (48.1%) 33 /68 (48.5%) 13 /235 (48.8%) 33 /68 (48.5%) 33 /68 (48.5%) 33 /68 (48.5%) 33 /68 (48.5%) 33 /68 (48.5%) 34 /68 (72.1%) 34 /68 (72.1%) 37 /235 (3.0%) 1 /68 (1.5%) 36 /68 (47.1%) 37 /235 (3.0%) 1 /68 (1.5%) 32 /68 (47.1%) 32 /68 (47.1%) 32 /68 (47.1%) 33 /235 (14.0%) 7 /68 (10.3%) 7 /68 (10.3%) 7 /68 (10.3%) 7 /68 (10.3%) 7 /68 (10.3%) 7 /68 (10.3%) 7 /68 (10.3%) 7 /68 (10.0%) 7 /68 (10.3%) 7 /68 (10.0%) 7 /68	Other	27 / 235 (11.5%)	5 / 68 (7.4%)
Diabetes duration 15 years or more Diabetes therapy at baseline (alone or in combination) Sulfonylurea 110 / 235 (46.8%) 30 / 68 (44.1%) Metformin 177 / 235 (75.3%) 1768 (12.1%) Thiazolidinedione (includes Pioglitazone) 177 / 235 (30.9%) 1768 (12.1%) Thiazolidinedione (includes Pioglitazone) 177 / 235 (31.9%) 1768 (10.3%) Not on Sulfonylurea or Insulin 97 / 235 (41.3%) 32 / 68 (47.1%) Not on Sulfonylurea or Insulin 97 / 235 (41.3%) 768 (10.3%) Pre-existing vascular disease 234 / 235 (99.6%) 68 / 68 (100.0%) Prior Congestive heart failure 37 / 235 (35.2%) 33 / 68 (48.5%) Prior MI 85 / 235 (36.2%) 33 / 68 (48.5%) 17 / 68 (25.9%) Current smoking 22 / 235 (9.4%) 3 / 68 (42.5%) Qualifying HbA1c (mmol/mol) Median (Q1, Q3) Qualifying HbA1c categories 47% 66 / 235 (28.1%) 7 - 27.5% 90 / 235 (38.3%) 29 / 68 (42.6%) 27 - 27.5% 90 / 235 (38.3%) 29 / 68 (42.6%) 27 - 27.5% 90 / 235 (38.3%) 29 / 68 (42.6%) 27 - 27.5% 90 / 235 (38.3%) 29 / 68 (42.6%) 26 GR = 60 mL/min/1.73m² Median (Q1, Q3) Me	Duration ² of type 2 diabetes (years)		
Diabetes therapy at baseline (alone or in combination) 30 / 68 (44.1%) Sulfonylurea 110 / 235 (46.8%) 30 / 68 (44.1%) Metformin 177 / 235 (75.3%) 49 / 68 (72.1%) Thiazolidinedione (includes Pioglitazone) 7 / 235 (30.3%) 1 / 68 (15.5%) Insulin 97 / 235 (41.3%) 32 / 68 (47.1%) Not on Sulfonylurea or Insulin 33 / 235 (14.0%) 7 / 88 (10.3%) Price existing vascular disease 234 / 235 (99.6%) 68 / 68 (100.0%) Prior MI 85 / 235 (36.2%) 33 / 68 (48.5%) Prior congestive heart failure 37 / 235 (15.7%) 17 / 68 (25.0%) Current smoking 22 / 235 (9.4%) 3 / 68 (44.4%) Qualifying HbA1c (mmol/mol) Wedian (Q1, Q3) 56.3 (51.9, 60.7) 55.2 (51.5, 60.1) Median (Q1, Q3) 7.3 (69, 7.7) 7.2 (6.9, 7.7) Qualifying HbA1c categories 7.3 (69, 7.7) 7.2 (6.9, 7.7) 7/2 7.5 (9 90 / 235 (33.6%) 21 / 68 (30.9%) 7 - < 7.5 %	Median (Q1, Q3)	14.0 (7.0, 22.0)	13.5 (8.0, 22.5)
Sulfonylurea 110 / 235 (46.8%) 30 / 68 (44.1%) Metformin 177 / 235 (75.3%) 49 / 68 (72.1%) Thiazolidinedione (includes Pioglitazone) 7 / 235 (3.0%) 1 / 68 (1.5%) Insulin 97 / 235 (41.3%) 32 / 68 (47.1%) 32 / 68 (47.1%) Not on Sulfonylurea or Insulin 97 / 235 (41.3%) 32 / 68 (47.1%) 76 (10.3%) Pre-existing vascular disease 234 / 235 (99.6%) 68 / 68 (100.0%) Prior MI 85 / 235 (36.2%) 33 / 68 (48.5%) Prior Congestive heart failure 37 / 235 (15.7%) 17 / 68 (25.0%) Current smoking 22 / 235 (9.4%) 3 / 68 (44.4%) Qualifying HbA1c (mmol/mol) Median (Q1, Q3) 56.3 (51.9, 60.7) 55.2 (51.5, 60.1) Qualifying HbA1c categories	Diabetes duration 15 years or more	113 / 235 (48.1%)	33 / 68 (48.5%)
Metformin			
Metformin 177 / 235 (75.3%) 49 / 68 (72.1%) Thiazolidinedione (includes Pioglitazone) 7 / 235 (3.0%) 1 / 68 (1.5%) Insulin 97 / 235 (41.3%) 32 / 68 (47.1%) Not on Sulfonylurea or Insulin 33 / 235 (14.0%) 7 / 68 (10.3%) Prior MI 85 / 235 (36.2%) 33 / 68 (48.5%) Prior ongestive heart failure 37 / 235 (15.7%) 17 / 68 (25.0%) Current smoking 22 / 235 (9.4%) 3 / 68 (4.4%) Qualifying HbA1c (mmol/mol) 56.3 (51.9, 60.7) 55.2 (51.5, 60.1) Median (Q1, Q3) 7.3 (6.9, 7.7) 7.2 (6.9, 7.7) Qualifying HbA1c categories 79 / 235 (33.6%) 21 / 68 (30.9%) <7%	Sulfonylurea	110 / 235 (46.8%)	30 / 68 (44.1%)
Insulin	Metformin		
Not on Sulfonylurea or Insulin Pre-existing vascular disease Prior MI St. 234 / 235 (99.6%) St. 68 (100.0%) Prior MI St. 235 (36.2%) St. 33 / 68 (48.5%) Prior congestive heart failure 37 / 235 (15.7%) Prior congestive heart failure 37 / 235 (15.7%) Prior congestive heart failure 22 / 235 (9.4%) Qualifying HbA1c (mmol/mol) Median (Q1, Q3) Qualifying HbA1c (%) Median (Q1, Q3) Qualifying HbA1c categories 7% 66 / 235 (28.1%) 7 - 2 (6.9, 7.7) Qualifying HbA1c categories 66 / 235 (28.1%) 21 / 68 (30.9%) 7 - 47.5% 90 / 235 (33.6%) 18 / 68 (26.5%) >=7.5% 90 / 235 (33.6%) 18 / 68 (26.5%) >=7.5% 90 / 235 (38.3%) 29 / 68 (42.6%) eGFR (mL/min/1.73m²) Median (Q1, Q3) 66.0 (54.0, 85.5) 60.0 (47.0, 71.0) Renal function² eGFR <60 mL/min/1.73m² 154 / 232 (36.6%) 33 / 68 (48.5%) UACR categories 30 g/mol Creatinine 38 / 104 (36.5%) 8 / 26 (30.8%) >=300 g/mol Creatinine 60 / 104 (57.7%) 31 / 26 (50.0%) Systolic blood pressure (mmHg) Mean (SD) Mean (SD) Mean (Q1, Q3) Renal (Q1, Q3) Re	Thiazolidinedione (includes Pioglitazone)	7 / 235 (3.0%)	1 / 68 (1.5%)
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Insulin	97 / 235 (41.3%)	32 / 68 (47.1%)
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Not on Sulfonylurea or Insulin	33 / 235 (14.0%)	
Prior MI Prior Congestive heart failure Prior MI Prior M235 (93.6.%) Prior Congestive heart failure Prior M235 (94.4%) Scale (94.4%)	Pre-existing vascular disease		68 / 68 (100.0%)
$\begin{array}{c} \text{Current smoking} \\ \text{Qualifying HbA1c (mmol/mol)} \\ \text{Median (Q1, Q3)} \\ \text{Median (Partition (Q1, Q3))} \\ \text{Median (Q1, Q3)} \\ Med$	Prior MI		33 / 68 (48.5%)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Prior congestive heart failure	37 / 235 (15.7%)	17 / 68 (25.0%)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Current smoking	22 / 235 (9.4%)	3 / 68 (4.4%)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Qualifying HbA1c (mmol/mol)		
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Median (Q1, Q3)	56.3 (51.9, 60.7)	55.2 (51.5, 60.1)
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Qualifying HbA1c (%)		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Median (Q1, Q3)	7.3 (6.9, 7.7)	7.2 (6.9, 7.7)
7 - <7.5%	Qualifying HbA1c categories		
>=7.5% 90 / 235 (38.3%) 29 / 68 (42.6%) eGFR (mL/min/1.73m²) Median (Q1, Q3) 66.0 (54.0, 85.5) 60.0 (47.0, 71.0) Renal function³ eGFR <60 mL/min/1.73m² 78 / 232 (33.6%) 33 / 68 (48.5%) 6GFR >=60 mL/min/1.73m² 154 / 232 (66.4%) 35 / 68 (51.5%) UACR categories <30 g/mol Creatinine 60 / 104 (57.7%) 13 / 26 (50.0%) 30 - <300 g/mol Creatinine 38 / 104 (36.5%) 8 / 26 (30.8%) >=300 g/mol Creatinine 6 / 104 (5.8%) 5 / 26 (19.2%) Systolic blood pressure (mmHg) Mean (SD) 135.8 (19.1) 140.0 (18.2) Diastolic blood pressure (mmHg) Median (Q1, Q3) 75.2 (11.4) 74.9 (11.5) Body mass index categories <25 kg/m² 48 / 233 (20.6%) 7 / 68 (10.3%) 33 / 68 (48.5%) 30 - <35 kg/m² 88 / 233 (37.8%) 33 / 68 (48.5%) 30 - <35 kg/m² 36 / 233 (15.5%) 13 / 68 (19.1%) Weight (kg) Mean (SD) 81.1 (19.1) 84.7 (20.7) Medications taken at time of randomisation Statins 196 / 235 (83.4%) 61 / 68 (89.7%) ACE inhibitors or angiotensin receptor blockers 185 / 235 (78.7%) 56 / 68 (82.4%)	<7%	66 / 235 (28.1%)	21 / 68 (30.9%)
$\begin{array}{c} {\rm eGFR\ (mL/min/1.73m^2)} \\ {\rm Median\ (Q1,Q3)} \\ {\rm Renal\ function^3} \\ {\rm eGFR\ <60\ mL/min/1.73m^2} \\ {\rm eGFR\ >=60\ mL/min/1.73m^2} \\ {\rm VACR\ categories} \\ {\rm <30\ g/mol\ Creatinine} \\ {\rm >30\ g/mol\ Creatinine} \\ {\rm >20\ g/mol\ Crea$	7 - <7.5%	79 / 235 (33.6%)	18 / 68 (26.5%)
eGFR (mL/min/1.73m²) Median (Q1, Q3) Renal function³ eGFR <60 mL/min/1.73m² 154 / 232 (33.6%) GFR >=60 mL/min/1.73m² 154 / 232 (66.4%) 35 / 68 (51.5%) UACR categories 30 g/mol Creatinine 30 g/mol Creatinine 38 / 104 (36.5%) 37 / 26 (30.8%) 38 / 26 (30.8%) 39 / 30 g/mol Creatinine 40 / 104 (5.8%) 50 / 26 (19.2%) Systolic blood pressure (mmHg) Mean (SD) 135.8 (19.1) 140.0 (18.2) Diastolic blood pressure (mmHg) Median (Q1, Q3) Median (Q1, Q3) Total (1.4) Total (1.5) Total	>=7.5%	90 / 235 (38.3%)	29 / 68 (42.6%)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	eGFR (mL/min/1.73m ²)		
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Median (Q1, Q3)	66.0 (54.0, 85.5)	60.0 (47.0, 71.0)
eGFR >=60 mL/min/1.73m² 154 / 232 (66.4%) 35 / 68 (51.5%) UACR categories <30 g/mol Creatinine 60 / 104 (57.7%) 13 / 26 (50.0%) 30 - <300 g/mol Creatinine 38 / 104 (36.5%) 8 / 26 (30.8%) >=300 g/mol Creatinine 6 / 104 (5.8%) 5 / 26 (19.2%) Systolic blood pressure (mmHg) Mean (SD) 135.8 (19.1) 140.0 (18.2) Diastolic blood pressure (mmHg) Median (Q1, Q3) 75.2 (11.4) 74.9 (11.5) Body mass index categories <25 kg/m² 48 / 233 (20.6%) 7 / 68 (10.3%) 25 - <30 kg/m² 88 / 233 (37.8%) 33 / 68 (48.5%) 30 - <35 kg/m² 88 / 233 (15.5%) 15 / 68 (22.1%) >=35 kg/m² 36 / 233 (15.5%) 13 / 68 (19.1%) Weight (kg) Mean (SD) 81.1 (19.1) 84.7 (20.7) Medications taken at time of randomisation Statins 196 / 235 (83.4%) 61 / 68 (89.7%) ACE inhibitors or angiotensin receptor blockers 185 / 235 (78.7%) 56 / 68 (82.4%)	Renal function ³		
$\begin{array}{llllllllllllllllllllllllllllllllllll$	eGFR <60 mL/min/1.73m ²	78 / 232 (33.6%)	33 / 68 (48.5%)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	$eGFR >= 60 \text{ mL/min}/1.73\text{m}^2$	154 / 232 (66.4%)	35 / 68 (51.5%)
$30 - <300 \text{ g/mol Creatinine} \qquad 38 / 104 (36.5\%) \qquad 8 / 26 (30.8\%) \\ >=300 \text{ g/mol Creatinine} \qquad 6 / 104 (5.8\%) \qquad 5 / 26 (19.2\%) \\ \text{Systolic blood pressure (mmHg)} \qquad \qquad$	UACR categories		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	<30 g/mol Creatinine	60 / 104 (57.7%)	13 / 26 (50.0%)
$\begin{array}{c} \text{Systolic blood pressure (mmHg)} \\ \text{Mean (SD)} & 135.8 \ (19.1) & 140.0 \ (18.2) \\ \text{Diastolic blood pressure (mmHg)} \\ \text{Median (Q1, Q3)} & 75.2 \ (11.4) & 74.9 \ (11.5) \\ \text{Body mass index categories} \\ <25 \ \text{kg/m}^2 & 48 \ / \ 233 \ (20.6\%) & 7 \ / \ 68 \ (10.3\%) \\ 25 \ - \ <30 \ \text{kg/m}^2 & 88 \ / \ 233 \ (37.8\%) & 33 \ / \ 68 \ (48.5\%) \\ 30 \ - \ <35 \ \text{kg/m}^2 & 61 \ / \ 233 \ (26.2\%) & 15 \ / \ 68 \ (22.1\%) \\ >= 35 \ \text{kg/m}^2 & 36 \ / \ 233 \ (15.5\%) & 13 \ / \ 68 \ (19.1\%) \\ \text{Weight (kg)} \\ \text{Mean (SD)} & 81.1 \ (19.1) & 84.7 \ (20.7) \\ \text{Medications taken at time of randomisation} \\ \text{Statins} & 196 \ / \ 235 \ (83.4\%) & 61 \ / \ 68 \ (89.7\%) \\ \text{ACE inhibitors or angiotensin receptor blockers} & 185 \ / \ 235 \ (78.7\%) & 56 \ / \ 68 \ (82.4\%) \\ \end{array}$	30 - <300 g/mol Creatinine	38 / 104 (36.5%)	8 / 26 (30.8%)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	>=300 g/mol Creatinine	6 / 104 (5.8%)	5 / 26 (19.2%)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Systolic blood pressure (mmHg)		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Mean (SD)	135.8 (19.1)	140.0 (18.2)
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Diastolic blood pressure (mmHg)		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Median (Q1, Q3)	75.2 (11.4)	74.9 (11.5)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Body mass index categories		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$<25 \text{ kg/m}^2$	48 / 233 (20.6%)	7 / 68 (10.3%)
$\begin{array}{llllllllllllllllllllllllllllllllllll$		•	33 / 68 (48.5%)
>=35 kg/m ² Weight (kg) Mean (SD) Medications taken at time of randomisation Statins 196 / 235 (83.4%) ACE inhibitors or angiotensin receptor blockers 36 / 233 (15.5%) 81.1 (19.1) 84.7 (20.7) 84.7 (20.7) 61 / 68 (89.7%) 56 / 68 (82.4%)	$30 - <35 \text{ kg/m}^2$		· · ·
		36 / 233 (15.5%)	, ,
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$, ,	. ,
		81.1 (19.1)	84.7 (20.7)
Statins 196 / 235 (83.4%) 61 / 68 (89.7%) ACE inhibitors or angiotensin receptor blockers 185 / 235 (78.7%) 56 / 68 (82.4%)	· · ·	` '	` '
ACE inhibitors or angiotensin receptor blockers 185 / 235 (78.7%) 56 / 68 (82.4%)		196 / 235 (83.4%)	61 / 68 (89.7%)
			· · ·
Diureucs 105 / 255 (45.8%) 41 / 68 (60.3%)	Diuretics	103 / 235 (43.8%)	41 / 68 (60.3%)

SUPPLEMENTARY DATA

	Without a CV Event (N=235)	With a CV Event (N=68)
Calcium channel blockers	84 / 235 (35.7%)	25 / 68 (36.8%)
Beta blockers	144 / 235 (61.3%)	50 / 68 (73.5%)
Aspirin	192 / 235 (81.7%)	53 / 68 (77.9%)
Other platelet antagonists	54 / 235 (23.0%)	23 / 68 (33.8%)

^{1:} Age is missing among patients enrolled in Lithuania because the entire birth date including year was not available.
2: Duration = (year of randomisation - year of diagnosis) + 1.
3: MDRD formula was used to calculate the eGFR. Site reported values are presented in the table.