

## **Supplemental Material**

Supplemental Table 1. Time Between Screening and Randomization Measurements

Supplemental Table 2. Serious Adverse Events during On- and Off-Treatment

Supplemental Figure 1. Distribution of eGFR at randomization in participants with randomization eGFR  $<30$  mL/min/1.73 m<sup>2</sup>.

**Supplemental Table 1. Time Between Screening and Randomization Measurements**

	<b>Canagliflozin</b>	<b>Placebo</b>	<b>Total</b>
All			
Participants, n	2201	2199	4400
<3 weeks, n (%)	161 (7)	161 (7)	322 (7)
3 to 8 weeks, n (%)	1959 (89)	1950 (89)	3909 (89)
>8 weeks, n (%)	81 (4)	88 (4)	169 (4)
Randomization eGFR <30 mL/min/1.73 m <sup>2</sup>			
Participants, n	84	90	174
<3 weeks, n (%)	4 (5)	3 (3)	7 (4)
3 to 8 weeks, n (%)	74 (88)	80 (89)	154 (89)
>8 weeks, n (%)	6 (7)	7 (8)	13 (7)
Randomization eGFR ≥30 mL/min/1.73 m <sup>2</sup>			
Participants, n	2117	2109	4226
<3 weeks, n (%)	157 (7)	158 (7)	315 (7)
3 to 8 weeks, n (%)	1885 (89)	1870 (89)	3755 (89)
>8 weeks, n (%)	75 (4)	81 (4)	156 (4)

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eGFR, estimated glomerular filtration rate.

**Supplemental Table 2. Serious Adverse Events during On- and Off-Treatment**

	Patients who continued the drug		Patients who discontinued the drug for reasons other than adverse event	
	Canagliflozin	Placebo	Canagliflozin	Placebo
	<i>On-treatment (until post-30 days after the last date of study drug)</i>			
<b>Patients with any SAE, n/N (%)</b>				
Randomization eGFR <30 mL/min/1.73 m <sup>2</sup>	16/51 (31)	22/56 (39)	5/11 (45)	8/17 (47)
Randomization eGFR ≥30 mL/min/1.73 m <sup>2</sup>	466/1605 (29)	474/1483 (32)	89/269 (33)	115/356 (32)
<b>Patients with a SAE per 1000 patient-years</b>				
Randomization eGFR <30 mL/min/1.73 m <sup>2</sup>	119.6	152.6	294.9	325.0
Randomization eGFR ≥30 mL/min/1.73 m <sup>2</sup>	110.8	123.4	255.5	241.3
<b>SAE episodes, n</b>				
Randomization eGFR <30 mL/min/1.73 m <sup>2</sup>	40	45	8	18
Randomization eGFR ≥30 mL/min/1.73 m <sup>2</sup>	875	936	185	272
<b>Days to the last date of drug, mean (SD)</b>				

Randomization eGFR	957.9	940.2	563.0	528.8
<30 mL/min/1.73 m <sup>2</sup>	(228.1)	(246.0)	(370.2)	(316.1)
Randomization eGFR	957.0	946.1	472.9	489.0
≥30 mL/min/1.73 m <sup>2</sup>	(236.3)	(235.5)	(313.8)	(313.3)

***Off-treatment (after 30 days post the last date of study drug)***

**Patients with any SAE, n/N (%)**

Randomization eGFR	2/51 (4)*	0	3/11 (27)	4/17 (24)
<30 mL/min/1.73 m <sup>2</sup>				
Randomization eGFR	10/1605	8/1483	59/269 (22)	96/356
≥30 mL/min/1.73 m <sup>2</sup>	(0.6) <sup>†</sup>	(0.5) <sup>†</sup>		(27)

**Patients with a SAE per 1000 patient-years**

Randomization eGFR	1002.1	0	259.7	189.0
<30 mL/min/1.73 m <sup>2</sup>				
Randomization eGFR	528.8	429.7	157.4	197.6
≥30 mL/min/1.73 m <sup>2</sup>				

**SAE episodes, n**

Randomization eGFR	5	0	8	5
<30 mL/min/1.73 m <sup>2</sup>				
Randomization eGFR	28	12	180	266
≥30 mL/min/1.73 m <sup>2</sup>				

**Days after the last date of drug, mean**

**(SD)**

Randomization eGFR	14.3 (45.1)	3.8 (5.7)	383.5	454.6
<30 mL/min/1.73 m <sup>2</sup>			(312.5)	(308.1)

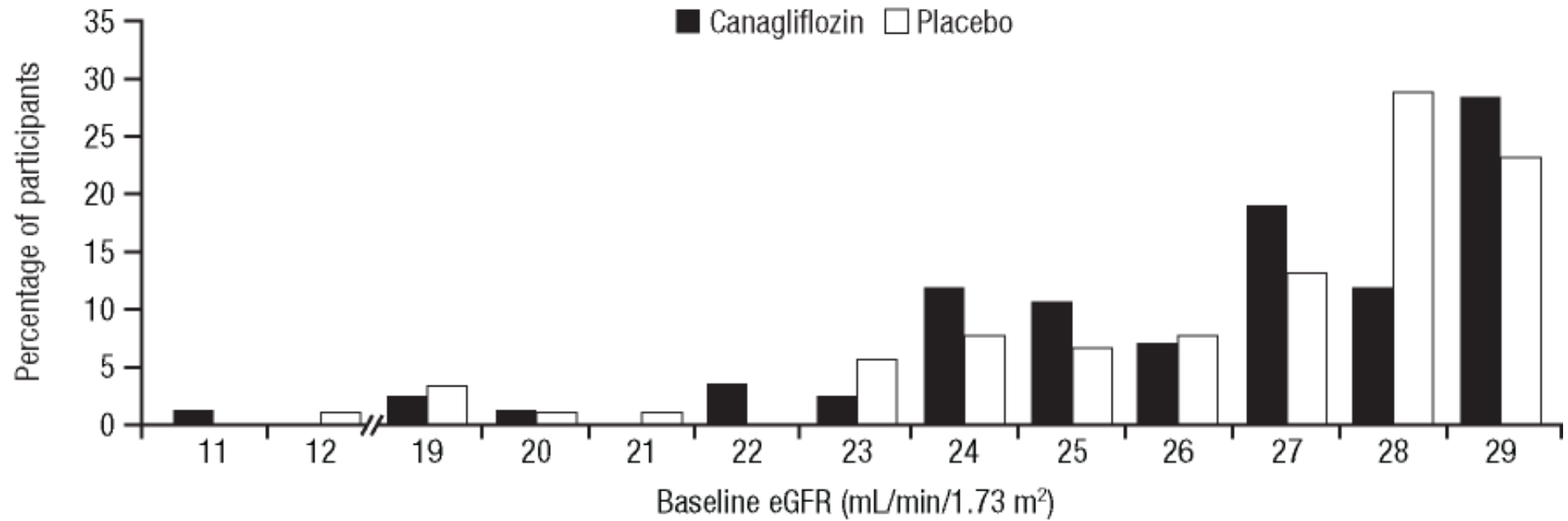
Randomization eGFR	4.3 (12.9)	4.6 (16.5)	508.9	498.5
≥30 mL/min/1.73 m <sup>2</sup>			(313.8)	(338.4)
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<b>Total (on- and off-treatment)</b>				
<b>Patients with any SAE, n/N (%)</b>				
Randomization eGFR <30	17/51 (33)	22/56	6/11 (55)	9/17 (53)
mL/min/1.73 m <sup>2</sup>		(39)		
Randomization eGFR ≥30	468/1605	476/1483	117/269	157/356
mL/min/1.73 m <sup>2</sup>	(29)	(32)	(43)	(44)
<b>Patients with a SAE per 1000 patient-years</b>				
Randomization eGFR <30	125.4	152.2	210.7	196.8
mL/min/1.73 m <sup>2</sup>				
Randomization eGFR ≥30	110.9	123.4	162.0	163.3
mL/min/1.73 m <sup>2</sup>				
<b>SAE episodes, n</b>				
Randomization eGFR <30	45	45	16	23
mL/min/1.73 m <sup>2</sup>				
Randomization eGFR ≥30	903	948	366	539
mL/min/1.73 m <sup>2</sup>				
<b>Days during follow-up, mean (SD)</b>				
Randomization eGFR <30	971.2	943.1	945.5	982.5
mL/min/1.73 m <sup>2</sup>	(213.7)	(246.8)	(396.7)	(215.5)
Randomization eGFR ≥30	960.3	949.7	980.8	986.5
mL/min/1.73 m <sup>2</sup>	(235.1)	(234.9)	(259.1)	(257.8)
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SAE, serious adverse event; eGFR, estimated glomerular filtration rate; SD, standard deviation.

\*2 patients with eGFR  $<30$  mL/min/1.73 m<sup>2</sup> in the canagliflozin arm stopped the drug due to a fatal SAE.

†10 and 8 patients with eGFR  $\geq 30$  mL/min/1.73 m<sup>2</sup> in the canagliflozin and placebo arms, respectively, stopped the drug due to a fatal SAE.

**Supplemental Figure 1. Distribution of eGFR at randomization in participants with randomization eGFR <30 mL/min/1.73 m<sup>2</sup>.**



eGFR, estimated glomerular filtration rate.