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Title

Canagliflozin Improves Cardiovascular and Renal Outcomes Across Broad Geographic

Regions: Results from CREDENCE

Background

Diabetes is the most common cause of kidney disease in people requiring renal

replacement therapy (RRT). RRT is projected to dramatically increase globally, with the

greatest increase in Asia. CREDENCE showed canagliflozin reduces kidney and

cardiovascular (CV) events in individuals with type 2 diabetes (T2DM) and chronic kidney

disease (CKD).

Methods

We explored canagliflozin efficacy across geographic regions. A Cox proportional-hazards model was used to analyze the primary outcome (composite of end-stage kidney disease [dialysis, transplantation, or a sustained eGFR of <15 mL/min/1.73 m^2], a doubling of the serum creatinine, or death from renal or CV causes).

Results

A total of 4401 participants were enrolled across North America (n=1182, 27%), Central and South America (n=941, 21%), Eastern Europe (n=947, 21%), Western Europe (n=421, 10%), Asia (n=749, 17%), and Other (n=161, 4%). Placebo event rates ranged widely, with 32 and 77 events/1000 patient-years in Western Europe and Asia, respectively. Canagliflozin consistently reduced the risk of the primary outcome in all geographic regions (see Figure, previously reported data on race also included).

Conclusions

Event rates varied two-fold across regions and needs further study. Canagliflozin reduces the risk of kidney and CV events in all geographic regions.

	Canagliflozin no. of patients/total no.	Placebo	Canagliflozin events/1000 patient-years	Placebo	Hazard Ratio (95% CI)	P value for interaction
Overall	245/2202	340/2199	43.2	61.2	0.70 (0.59, 0.82)	
Region						0.39
North America	82/574	99/608	53.9	61.0	0.84 (0.63, 1.13)	
Central/ South America	49/476	75/465	42.6	69.8	0.61 (0.43, 0.88)	
Western Europe	15/226	17/195	23.9	31.8	0.73 (0.36, 1.47)	
Eastern Europe	52/483	63/464	40.7	51.9	0.76 (0.53, 1.11)	
Asia	41/364	69/385	46.7	77.2	0.59 (0.40, 0.87)	
Other	6/79	17/82	28.1	80.5	0.40 (0.15, 1.02)	
Race						0.91
White	153/1487	206/1444	39.0	55.2	0.70 (0.57, 0.86)	
Black or African American	18/112	19/112	60.5	64.4	0.82 (0.43, 1.59)	
Asian	49/425	76/452	47.0	70.4	0.66 (0.46, 0.95)	
Other	25/178	39/191	60.9	87.7	0.71 (0.43, 1.18)	

0.25   0.5 Canagliflozin better   1   1.5 Placebo better