

Kidney and Cardiovascular Effects of Canagliflozin According to Age and Sex in the CREDENCE Trial

Tae Won Yi	1
Brendan Smyth	1,2,3
Amy Kang	1,4
Kathryn Page Cardoza ...	
Gian Luca Di Tanna	1
Clare Arnott	1,5
Carol Pollock	6,7
Rajiv Agarwal	8
George Bakris	9
Christopher P. Cannon	10,11
David M. Charytan	12
Dick de Zeeuw	13
Hiddo J.L. Heerspink	1,13
Adeera Levin	14
Bruce Neal	1,15,16
David C. Wheeler	1,17
Hong Zheng	18
Bernard Zinman	19
Kenneth W. Mahaffey	20
Vlado Perkovic	1,7
Meg J Jardine	1,2,21

and

CREDENCE Trial Investigators

Affiliations

1. The George Institute for Global Health, University of New South Wales, Sydney, New South Wales, Australia
2. NHMRC Clinical Trials Centre, University of Sydney, Sydney, New South Wales, Australia
3. Department of Renal Medicine, St George Hospital, Sydney, New South Wales, Australia
4. Department of Renal Medicine, Prince of Wales Hospital, Sydney, New South Wales, Australia
5. Department of Cardiology, Royal Prince Alfred Hospital, Sydney Medical School, Sydney, New South Wales, Australia
6. Kolling Institute of Medical Research, Sydney Medical School, University of Sydney, Sydney, New South Wales, Australia
7. Royal North Shore Hospital, Sydney, New South Wales, Australia
8. Indiana University School of Medicine and VA Medical Center, Indianapolis, IN, USA
9. Department of Medicine, University of Chicago Medicine, Chicago, IL, USA
10. Cardiovascular Division, Brigham and Women's Hospital, Boston, MA, USA
11. Baim Institute for Clinical Research, Boston, MA, USA
12. Nephrology Division, New York University Langone Medical Center, New York University School of Medicine, New York, NY, USA
13. Department of Clinical Pharmacy and Pharmacology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands
14. Division of Nephrology, University of British Columbia, Vancouver, British Columbia, Canada
15. The Charles Perkins Centre, University of Sydney, Sydney, New South Wales, Australia
16. Imperial College London, London, United Kingdom
17. Department of Renal Medicine, University College London Medical School, London, United Kingdom
18. Renal Division of Peking University First Hospital, Beijing, China
19. Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, University of Toronto, Toronto, Canada
20. Department of Medicine, Stanford Center for Clinical Research, Stanford University School of Medicine, Stanford, CA, USA
21. Concord Repatriation General Hospital, Sydney, New South Wales, Australia

Kidney and Cardiovascular Effects of Canagliflozin According to Age and Sex in the CREDENCE Trial

Background

Canagliflozin reduces the incidence of kidney and cardiovascular events in people with type 2 diabetes and chronic kidney disease (CKD). We assessed the effects of canagliflozin according to age and sex in a randomized, placebo-controlled trial.

Methods

The CREDENCE study randomized participants with type 2 diabetes and albuminuric CKD. The effects of canagliflozin on the primary outcome (a composite of kidney failure, a doubling of the serum creatinine level, or death from kidney or cardiovascular causes), and secondary outcomes were evaluated by age at baseline (<60, 60-69, and ≥ 70 years) and sex using Cox regression models.

Results

Of the 4401 participants, 33.5%, 42.1%, and 24.4% were <60, 60-69, and ≥ 70 years of age at baseline, respectively; 33.9% were female. Canagliflozin reduced the risk of the primary outcome (HR 0.70, 95% confidence interval 0.59 to 0.82; $P < 0.001$) and key secondary outcomes. Effects were similar within each age group, and by sex (Figure 1A,B). The effect of canagliflozin on safety outcomes was consistent among age groups and by sex, including volume depletion, hypoglycemia and adverse events leading to drug withdrawal (all $P_{\text{interaction}} \geq 0.1$).

Conclusion

Canagliflozin reduces the risk of kidney and cardiovascular events in people with type 2 diabetes and CKD with consistent effects and no differences in safety outcomes across subgroups defined by age and sex.

