Effect of empagliflozin on all-cause hospitalization in EMPA-KIDNEY

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EMPA-KIDNEY
The study of heart and kidney protection with empagliflozin

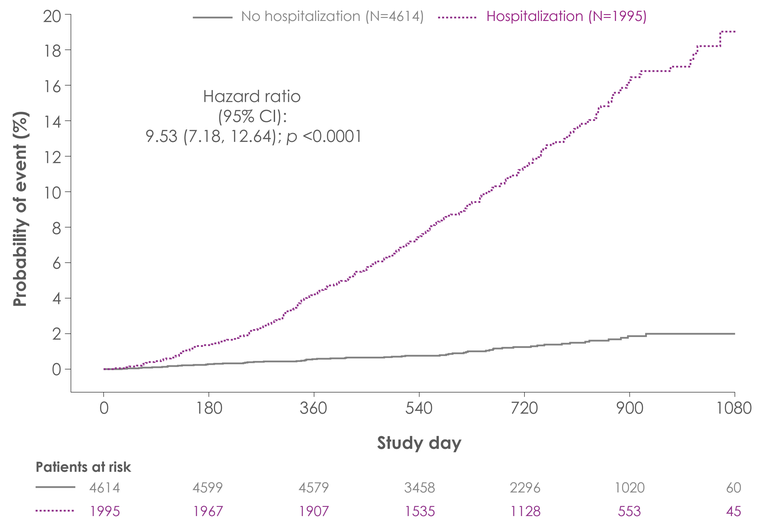
OBJECTIVE

- To examine the burden of all-cause hospitalization (ACH) in chronic kidney disease (CKD), and the effects of empagliflozin on ACH in the EMPA-KIDNEY trial.

METHODS

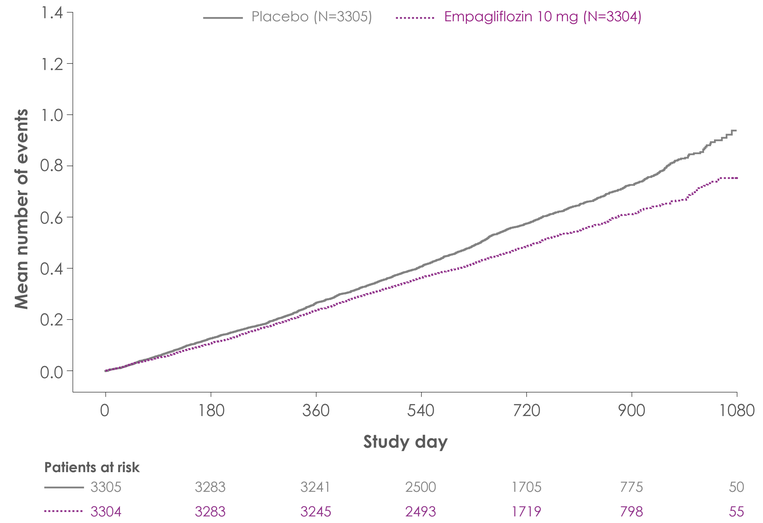
- Inclusion criteria:
  - Estimated glomerular filtration rate (eGFR) of 20 to <45 mL/min/1.73 m^2, or
  - eGFR of 45 to <90 mL/min/1.73 m^2 with a urine albumin-to-creatinine ratio (UACR) ≥200 mg/g.
- Randomized allocation to empagliflozin 10 mg once daily (n=3304) or placebo (n=3305) in addition to standard of care (including a clinically appropriate dose of renin-angiotensin-system inhibitor, where indicated and tolerated).
- Reasons for hospitalization were derived from adverse events (AEs) leading to hospitalization and were assessed by system organ class (SOC). In addition, a user-defined list of kidney and cardiovascular (CV) AEs leading to hospitalizations was used.
  - User-defined categories included multiple events from other surgical and medical procedures SOCs that could be attributed to kidney or CV causes.
  - Re-categorization of these events to the respective user-defined categories (kidney or CV) was warranted to reflect the actual burden of these medical conditions in patients with CKD.

Figure 1. Time to death comparing patients with and without hospitalizations



CI, confidence interval; HR, hazard ratio.

Figure 2. Time to events of ACH



ACH, all-cause hospitalization.

RESULTS

- In the placebo group, hospitalized participants were more likely to be older, White, have a history of CV disease, lower blood pressure, lower eGFR, and higher N-terminal pro B-type natriuretic peptide compared with non-hospitalized participants.
- In the placebo group, 1035 participants had 1895 total hospitalizations, and in the empagliflozin group, 960 participants had 1611 total hospitalizations.
- The estimated mortality rate after first hospitalization in participants with ≥1 ACH was 12% after 1 year and 18% after 2 years.
- Most common reasons for ACH were infections and infestations, surgical and medical procedures, cardiac disorders, kidney and urinary disorders, and investigations.

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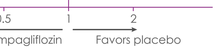
Figure 3. Time to total hospitalization (first and recurrent) in key subgroups

	Empagliflozin 10 mg n with event/N analyzed	Placebo n with event/N analyzed	HR (95% CI)	Interaction p-value
Overall	1611/3304	1895/3305	0.86 (0.78, 0.95)	
Baseline Diabetes Status				
Non-diabetic	655/1779	781/1790	0.86 (0.74, 0.99)	0.9867
Diabetic	956/1525	1114/1515	0.86 (0.75, 0.98)	
Baseline eGFR (CKD-EPI) [mL/min/1.73 m^2]				
<30	716/1131	821/1151	0.88 (0.75, 1.03)	
≥30 to <45	646/1467	793/1461	0.81 (0.69, 0.94)	0.6268
≥45	249/706	281/693	0.91 (0.72, 1.14)	
Baseline UACR [mg/g]				
Normal (<30)	326/665	410/663	0.80 (0.65, 0.99)	
Microalbuminuria (≥30 to ≤300)	451/927	563/937	0.83 (0.69, 0.99)	0.3641 (trend test)
Macroalbuminuria (>300)	834/1712	922/1705	0.89 (0.78, 1.02)	



CI, confidence interval; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration formula; eGFR, estimated glomerular filtration rate; HR, hazard ratio; UACR, urine albumin-to-creatinine ratio.

Figure 4. Causes of hospitalization by SOC and by user-defined AEs

	Empagliflozin 10 mg n with event/N analyzed	Placebo n with event/N analyzed	HR (95% CI)	Interaction p-value
Kidney				
SOC	137/3304	164/3305	0.81 (0.63, 1.02)	0.0783
User-defined	214/3304	257/3305	0.81 (0.66, 0.98)	0.0305
CV				
SOC	186/3304	206/3305	0.83 (0.67, 1.03)	0.0870
User-defined	307/3304	369/3305	0.77 (0.65, 0.91)	0.0021
Metabolic				
SOC	90/3304	105/3305	0.81 (0.61, 1.08)	0.1481

AEs, adverse events; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; SOC, system organ class.

CONCLUSION

- Treatment with empagliflozin significantly reduced risk of ACH in patients with CKD, including ACHs attributed to kidney, CV, or metabolic conditions.

Poster 0047: Presented at the World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease (WCIRDC), Universal City, CA, USA, December 7–9, 2023.
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Disclosures
AU, **EP**, and **ARM** are employees of Boehringer Ingelheim (BI). **ND** reported grants from Amgen, AstraZeneca, BI, Cytokinetics, and Vifor, and personal fees from Bayer, Bristol Myers Squibb, Merck, Novartis, and SC Pharmaceuticals. **SN** reported receiving personal fees from ACI clinical, AstraZeneca, Bayer, BI/Eli Lilly, GlaxoSmithKline, Intercept, Vertex, and Vifor.

Acknowledgments
The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors received no direct compensation related to the development of the poster. Editorial and graphical support provided by Envision Pharma Group was funded by BI. BI was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations. The EMPA-KIDNEY trial was initiated, designed, and conducted by the University of Oxford in collaboration with a Steering Committee of experts and BI. The presented analyses were initiated and conducted by BI independently from the EMPA-KIDNEY Collaborative Group. This publication was developed by BI representatives and independent collaborators based on the EMPA-KIDNEY original database. EMPA-KIDNEY was coordinated by the MRC Population Health Research Unit at the University of Oxford, which is part of the Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU), Nuffield Department of Population Health. We thank the participants, the local site staff, regional coordinating center staff, the central coordinating center at the University of Oxford, and all members of the EMPA-KIDNEY Steering Committee.