PRESS RELEASE

ASN Contact: Christine Feheley
(202) 640-4638 | cfeheley@asn-online.org

STUDY ESTIMATES THE LIFETIME BENEFIT OF COMBINATION THERAPY IN PATIENTS WITH KIDNEY DISEASE WITHOUT DIABETES

Combining medications is expected to substantially prolong patients' survival free of kidney failure.

Highlights

- A recent analysis of clinical trial data estimates that treatment with the combination of angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers (ACE inhibitors/ARBs) and sodium-glucose cotransporter-2 (SGLT2) inhibitors can substantially increase the lifetime survival free of kidney failure for patients with albuminuric chronic kidney disease without diabetes.
- A 50-year-old-patient treated with this combination may experience about 7 additional years free of kidney failure and death compared with a patient not treated with these agents.

Washington, DC (November 22, 2022) — New research in *CJASN* highlights the potential to lower the burden of chronic kidney disease (CKD) complications by delaying or even preventing kidney failure and premature death if currently available treatments are appropriately utilized—specifically, offering patients combination therapy of angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers (ACE inhibitors/ARBs) and sodium-glucose cotransporter-2 (SGLT2) inhibitors.

About half of patients with CKD do not have diabetes but experience high rates of kidney failure and early death. These patients are typically treated with ACE inhibitors/ARBs, when presented with albuminuria (a sign of kidney disease in which a person has too much of the protein albumin in the urine). The SGLT2 inhibitor dapagliflozin, which is designed to lower blood sugar levels, has been shown to have kidney- and heart-protective effects in patients with CKD (with and without diabetes).

Priya Vart, PhD (University Medical Center Groningen, in the Netherlands) and his colleagues conducted a study to estimate lifetime survival free of kidney failure for patients with albuminuric CKD without diabetes treated with the combination therapy of ACE inhibitors/ARB and SGLT2 inhibitors relative to patients not treated.

The study used estimates from clinical trials of the effect of treatment with ACE inhibitors/ARBs (ramipril/benazepril) (in 690 patients) and SGLT2 inhibitors (dapagliflozin)

(in 1,398 patients) compared with placebo to derive the indirect estimate of the effect of combination therapy vs. no treatment. Using this effect, investigators estimated the treatment effect of combination therapy among patients with albuminuric CKD without diabetes in the DAPA-CKD trial (697 patients) and projected kidney failure–free and overall survival for those treated and not treated with combination therapy. The primary outcome was a composite of doubling of serum creatinine (a marker of kidney dysfunction), kidney failure, or death.

Combination therapy with ACE inhibitors/ARBs and SGLT2 inhibitors was associated with a 65% lower risk of the primary outcome compared with no treatment. For a 50-year-old-patient, the estimated survival free from the primary outcome was 17.0 years with the combination therapy and 9.6 years with no treatment with any of these agents, corresponding to a gain in eventfree survival of 7.4 years. Even when assuming that the effect of combination therapy is not completely additive and that treatment adherence and efficacy may wane over time, there was a gain in eventfree survival of 5.3 to 5.8 years.

“The present study provides estimates of treatment benefit expressed in extra years free from the disease or death that is easy to understand for patients, clinicians, and policy makers. This may facilitate risk communication in clinical management, increase uptake of these therapies in clinical practice, and inform decision making by policy makers and payers,” the authors wrote.

An accompanying editorial notes that the findings also provide a tool for advocacy efforts to improve access to and coverage for kidney-protective medicines, especially SGLT2 inhibitors, which are currently cost prohibitive to many.

Additional study authors include Muthiah Vaduganathan, MD; Niels Jongs, PhD; Giuseppe Remuzzi, MD; David C. Wheeler, MD; Fan Fan Hou, PhD; Finnian McCausland, MD; Glenn M. Chertow, MD; and Hiddo J.L. Heerspink, PhD.

Disclosures: G.M. Chertow reports consultancy agreements with Akebia, Ardelyx, AstraZeneca, Cricket, DiaMedica, Gilead, Miromatrix, Reata, Sanifit, Unicycive, and Vertex; ownership interest in Ardelyx, CloudCath, Durect, DxNow, Eliaz Therapeutics, Outset, Physiowave, PuraCath, and Renibus; research funding from Amgen, NIDDK, and NIAID; stock options in Ardelyx, CloudCath, Durect, and Miromatrix; was on advisory board for Reata Pharmaceuticals, Ardelyx, Baxter, CloudCath, Cricket, DiaMedica, Durect, and Miromatrix; steering committee for Akebia, AstraZeneca, Gilead, Sanifit, and Vertex; serving on the Satellite Healthcare Board of Directors and as Co-Editor of *Brenner & Rector’s The Kidney* (Elsevier); and DSMB service for NIDDK, Angion, Bayer, Gilead, Mineralys, Palladio, and ReCor.
H.J.L. Heerspink reports ongoing consultancy agreements with AstraZeneca, Bayer, Boehringer Ingelheim, CSL Behring, Chinook, Dimerix, Eli-Lilly, Gilead, GoldFinch, Janssen, Merck, Novo Nordisk, and Travere Pharmaceuticals; research funding from

AstraZeneca, Novo Nordisk and Janssen research support (grant funding directed to employer); lecture fees from AstraZeneca; speakers bureau for AstraZeneca; and funding/honoraria and consulting fees for steering committee membership and/or advisory board participation from Abbvie, AstraZeneca, Bayer, Boehringer Ingelheim, Chinook, CSL Pharma, Dimerix, Gliead, GoldFinsch, Janssen, Fresenius, Merck, MundiPharma, Mitsubishi Tanabe, Novo Nordisk, and Travere Pharmaceuticals.
F.F. Hou is a member of the DAPA-CKD study executive committee and is a study investigator. She reports personal fees from AbbVie, consultancy agreements with AstraZeneca, and honoraria from AstraZeneca.
F. McCausland reports consultancy agreements with GlaxoSmithKline; research grants from National Institute of Health (NDDK), Fifth Eye, Advanced Instruments, and Satellite Healthcare; and research funding paid to institution from Advanced Medical and Fifth Eye.
G. Remuzzi reports employment with Mario Negri Institute for Pharmacological Research; speaker honorarium/travel reimbursements from Alnylam, Alexion Pharmaceuticals Inc, Janssen Pharmaceutical, BioCryst Pharmaceuticals, Akebia Therapeutics, Silence Therapeutics, and Novartis - no personal remuneration is accepted, compensations are paid to his institution for research and educational activities; honoraria from Alnylam, Alexion Pharmaceuticals Inc, Janssen Pharmaceutical, Akebia Therapeutics, Catalyst Biosciences, Silence Therapeutics, and Novartis; and serving as a member of numerous editorial boards of scientific medical journals.
M. Vaduganathan reports consultancy agreements with American Regent, Amgen, AstraZeneca, Bayer AG, Baxter Healthcare, Boehringer Ingelheim, Cytokinetics, Lexicon Pharmaceuticals, Novartis, Pharmacosmos, Relypsa, Roche Diagnostics, Sanofi, and Tricog Health; research funding from American Regent, Amgen, AstraZeneca, Bayer AG, Boehringer Ingelheim, Roche Diagnostics, Novartis, Galmed, Occlutech, and Impulse Dynamics; speakers bureau for AstraZeneca, Novartis, and Roche Diagnostics; research grant support or served on advisory boards for American Regent, Amgen, AstraZeneca, Bayer AG, Baxter Healthcare, Boehringer Ingelheim, Cytokinetics, Lexicon Pharmaceuticals, Relypsa, and Roche Diagnostics; speaker engagements with Novartis and Roche Diagnostics; and participates on clinical endpoint committees for studies sponsored by Galmed and Novartis.
P. Vart is an Editor for *Clinical Kidney Journal*.
D.C. Wheeler reports consultancy agreements with Astellas, AstraZeneca, Bayer, Boehringer Ingelheim, Janssen, Napp, Mundipharma, Merck Sharp and Dohme, GlaxoSmithKline, Gilead, Tricida, Vifor Fesenius, and Zydus; honoraria from Amgen, Astellas, AstraZeneca, Bayer, Boehringer Ingelhiem, Gilead, GlaxoSmithKline, Janssen, Mundipharma, Merck Sharp and Dohme, Napp, Reata, Pharmacosmos, Tricida, Vifor Fresenius, and Zidus; an advisory or leadership role for AstraZeneca; speakers bureau for Amgen, AstraZeneca, Astellas, Janssen, Mundipharma, Napp, Merck Sharp and Dohme, and Vifor Fresenius; and serving as an Honorary Professorial Fellow, George Institute for Global Health.
The remaining author has nothing to disclose.

The article, titled “Estimated Lifetime Benefit of Combined RAAS and SGLT2 Inhibitor Therapy in Patients with Albuminuric CKD without Diabetes,” will appear online at http://cjasn.asnjournals.org/ on November 22, 2022, doi: 10.2215/CJN.08900722.

The editorial, titled “Toward Guideline-Directed Medical Therapy in Nephrology—Lifetime Benefit of RAAS and SGLT2 Inhibition in Nondiabetic Kidney Disease,” will appear online at http://cjasn.asnjournals.org/ on November 22, 2022, doi: 10.2215/CJN.12401022.

About ASN

Since 1966, ASN has been leading the fight to prevent, treat, and cure kidney diseases throughout the world by educating health professionals and scientists, advancing research and innovation, communicating new knowledge, and advocating for the highest quality care for patients. ASN has more than 20,000 members representing 132 countries. For more information, visit www.asn-online.org and follow us on Facebook, Twitter, LinkedIn, and Instagram.

# # #