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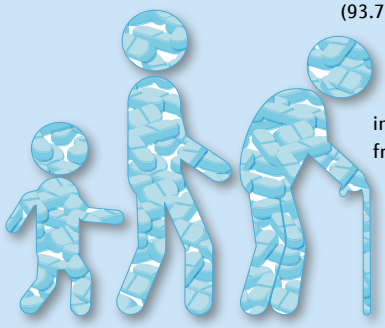
colchicine group than in the placebo group (0.9% versus 0.4%; $P = 0.03$).

The researchers now plan to investigate the use of colchicine for the primary prevention of cardiovascular events in the COLCOT-T2D trial, in which they will enrol 10,000 patients with type 2 diabetes mellitus without known coronary artery disease.

Gregory B. Lim

> low-dose colchicine reduces the risk of ischaemic cardiovascular events

ORIGINAL ARTICLE Tardif, J.-C. et al. Efficacy and safety of low-dose colchicine after myocardial infarction. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1912388 (2019)



Credit: V. Summersby/Springer Nature Limited

(93.7% of the overall cohort). Dapagliflozin-treated patients had significantly greater improvements in symptom frequency and severity, physical function and quality of life than placebo-treated patients. Dapagliflozin reduced the risk of clinical events to a similar extent across the entire range of KCCQ scores at baseline.

Together, these post-hoc analyses indicate that the beneficial effects of dapagliflozin on HF outcomes are independent of age and health status impairment at baseline.

Karina Huynh

ORIGINAL ARTICLES Martinez, F. A. et al. Efficacy and safety of dapagliflozin in heart failure with reduced ejection fraction according to age: insights from DAPA-HF. *Circulation* https://doi.org/10.1161/CIRCULATIONAHA.119.044133 (2019) | Kosiborod, M. N. et al. Effects of dapagliflozin on symptoms, function and quality of life in patients with heart failure and reduced ejection fraction: results from the DAPA-HF trial. *Circulation* https://doi.org/10.1161/CIRCULATIONAHA.119.044138 (2019)

HEART FAILURE

Dissecting the benefits of sacubitril–valsartan for heart failure

New analyses of the PARAGON-HF and PARADIGM-HF trials indicate that sacubitril–valsartan treatment might be beneficial in patients with heart failure with mildly reduced left ventricular ejection fraction (LVEF) for reducing the risk of hospitalizations for heart failure or cardiovascular-related death compared with treatment with a renin–angiotensin system (RAS) inhibitor alone. Moreover, the benefit seems to be greater in women than in men. These findings were presented at the AHA Scientific Sessions 2019.

The pre-specified analysis of the effects of sacubitril–valsartan across the LVEF range combined data from the PARADIGM-HF and PARAGON-HF trials, stratifying patients ($n = 13,195$) according to LVEF. Overall, sacubitril–valsartan reduced the incidence of all heart failure-related outcomes compared with a RAS inhibitor alone. However, the therapeutic effects varied by LVEF. Compared with a RAS inhibitor, the effect of sacubitril–valsartan on the composite outcomes of time to first hospitalization for heart failure or cardiovascular-related death and total hospitalizations for heart failure or cardiovascular-related death declined with increasing LVEF, with the greatest benefits observed in patients with LVEF below the normal range and no benefit in patients at the highest LVEF range. Interestingly, the effect modification by LVEF of sacubitril–valsartan was similar in men and women, but the benefits extended to a higher LVEF in women.

> sacubitril–valsartan treatment might be beneficial in patients with heart failure with mildly reduced left ventricular ejection fraction

Further pre-specified analyses of outcomes according to sex in the PARAGON-HF trial showed that sacubitril–valsartan mediated a greater reduction in the rate of first and recurrent hospitalizations for heart failure or cardiovascular-related death in women than in men (rate ratio (RR) 0.73, 95% CI 0.59–0.90 versus RR 1.03, 95% CI 0.84–1.25, P for interaction = 0.017), driven by a reduction in hospitalizations for heart failure. The investigators provided several potential explanations for this possible sex-related modification of the effect of sacubitril–valsartan but highlight that further studies are needed to understand the mechanisms.

An additional post-hoc analysis of the PARAGON-HF trial on the effects of sacubitril–valsartan in relation to the proximity to hospitalization for heart failure indicated that a recent hospitalization can identify patients at high risk of near-term adverse outcomes. The risk of the primary end point (a composite of total hospitalizations for heart failure or cardiovascular-related death) was inversely and non-linearly associated with the timing from previous hospitalization for heart failure ($P < 0.001$). In addition, the benefits of sacubitril–valsartan seemed to be higher when the treatment was initiated during the high-risk window after hospitalization. Compared with valsartan alone, the absolute risk reductions in the primary end point with sacubitril–valsartan were 6.4%, 4.6% and 3.4% for patients enrolled ≤30 days, 31–90 days and 91–180 days after hospitalization, respectively. By contrast, patients enrolled >180 days after hospitalization or who were never hospitalized had no reductions in risk (P for interaction = 0.050).

Irene Fernández-Ruiz

ORIGINAL ARTICLES Solomon, S. D. et al. Sacubitril/valsartan across the spectrum of ejection fraction in heart failure. *Circulation* https://doi.org/10.1161/CIRCULATIONAHA.119.044586 (2019) | McMurray, J. J. V. et al. Effects of sacubitril-valsartan, versus valsartan, in women compared to men with heart failure and preserved ejection fraction: insights from PARAGON-HF. *Circulation* https://doi.org/10.1161/CIRCULATIONAHA.119.044491 (2019) | Vaduganathan, M. et al. Prior heart failure hospitalization, clinical outcomes, and response to sacubitril/valsartan compared with valsartan in HFpEF. *J. Am. Coll. Cardiol.* https://doi.org/10.1016/j.jacc.2019.11.003 (2019)