

## New HF guidelines

### Management of HF

The ESC 2023 Focused Update on HF provided targeted recommendations on new pharmacotherapy.<sup>1</sup> In this update, the use of dapagliflozin or empagliflozin was now also expanded to heart failure with mid-range ejection fraction (HFmrEF, EF 41-49%) and to heart failure with preserved ejection fraction (HFpEF, EF $\geq$ 50%) to reduce the risk of HF hospitalization or cardiovascular (CV) death. As a result, there now is a broad evidence base to consider these gliflozins in all-comer HF patients, regardless of the ejection fraction.<sup>2</sup> At the minimum, both gliflozins reduce HF hospitalizations by about 30% (HR: 0.71; 95% CI: 0.67-0.77). The impact on *all-cause* hospitalizations is dependent on the ejection fraction however, as HF hospitalizations constitute a larger portion in heart failure with reduced ejection fraction (HFrEF, EF $\leq$ 40%), compared to HFmrEF and HFpEF. Also, an intensive strategy was promoted to initiate and rapidly up-titrate evidence-based treatments before discharge and during frequent and careful follow-up visits in the first weeks after an HF hospitalization to reduce the risk of HF rehospitalization or death. Informed by the recent STRONG-HF data, there is nothing to be gained from postponing trial-proven therapies in HF.<sup>3</sup> Conversely, it is crucial to identify patients before discharge and to implement a strategy to both initiate and uptitrate GDMT in as many patients as possible, as rapidly as possible. Particularly with regard to the latter, hospital pharmacists can play a major role, leveraging electronic health records to identify un(der)treated HF patients, working on multidisciplinary inpatient guidelines, and implementing GDMT uptake strategies before and after discharge.

Intravenous (IV) iron supplementation was recommended in symptomatic patients with HFrEF and HFmrEF, who also had documented iron deficiency, to alleviate HF symptoms and improve the quality of life. With less certainty, IV iron supplementation should be considered in symptomatic patients with HFrEF and HFmrEF, and iron deficiency, to reduce the risk of an HF hospitalization.

### Prevention of HF

In patients with both type 2 diabetes and chronic kidney disease *but without HF*, the use of the same two SGLT2 inhibitors was also recommended to reduce the risk of a first HF hospitalization or CV death, based on DAPA-CKD and EMPA-KIDNEY.<sup>4, 5</sup> In the same patient cohort, the use of finerenone was recommended as well, to reduce the risk of a first HF hospitalization.<sup>6</sup>

### Cardiomyopathies

At ESC 2023, the Guidelines for the management of cardiomyopathies were presented as well.<sup>7</sup> Herein, all data were assembled with regard to the diagnosis and treatment of several cardiomyopathy entities, among which transthyretin cardiac amyloidosis and hypertrophic cardiomyopathy. At the very least, this guideline is relevant to hospital pharmacists given that recent trials have now identified effective treatments for these conditions, the transthyretin stabilizer tafamidis and the cardiac myosin ATPase inhibitor mavacamten respectively. In the ATTR-ACT study (n=414), use of tafamidis versus placebo led to more wins, leading to a win ratio of 1.695 (95% CI: 1.255 - 2.289), which coincided with a substantial reduction of mortality (HR: 0.70; 95% CI: 0.51 - 0.96).<sup>8</sup> For mavacamten, we have data from two pivotal trials which showed that it improved functioning and symptom burden to such a degree that 58.9% fewer patients (95% CI: 44.0-73.9%, p<0.001) underwent septal reduction therapy, a therapeutic option in hypertrophic cardiomyopathy reserved for those with intractable symptoms.<sup>9, 10</sup> Importantly, given that CYP219 plays a major role in mavacamten's exposure, patients should be genotyped as per the package insert, to avoid overexposure in poor metabolizers.

## References

1. McDonagh TA, Metra M, Adamo M, et al. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2023 Oct 1;44(37):3627-39.
2. Usman MS, Siddiqi TJ, Anker SD, et al. Effect of SGLT2 Inhibitors on Cardiovascular Outcomes Across Various Patient Populations. *J Am Coll Cardiol*. 2023 Jun 27;81(25):2377-87.
3. Mebazaa A, Davison B, Chioncel O, et al. Safety, tolerability and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial. *Lancet*. 2022 Dec 3;400(10367):1938-52.
4. Heerspink HJL, Stefansson BV, Correa-Rotter R, et al. Dapagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med*. 2020 Oct 8;383(15):1436-46.
5. Herrington WG, Staplin N, Wanner C, et al. Empagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med*. 2023 Jan 12;388(2):117-27.
6. Agarwal R, Filippatos G, Pitt B, et al. Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis. *Eur Heart J*. 2022 Feb 10;43(6):474-84.
7. Arbelo E, Protonotarios A, Gimeno JR, et al. 2023 ESC Guidelines for the management of cardiomyopathies. *Eur Heart J*. 2023 Oct 1;44(37):3503-626.
8. Maurer MS, Schwartz JH, Gundapaneni B, et al. Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy. *N Engl J Med*. 2018 Sep 13;379(11):1007-16.
9. Olivetto I, Oreziak A, Barriales-Villa R, et al. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2020 Sep 12;396(10253):759-69.
10. Desai MY, Owens A, Geske JB, et al. Myosin Inhibition in Patients With Obstructive Hypertrophic Cardiomyopathy Referred for Septal Reduction Therapy. *J Am Coll Cardiol*. 2022 Jul 12;80(2):95-108.