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Pivotal clinical trials shaping contemporary cardiology practice. News from the European Society of Cardiology Congress 2025

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Abstract. This article presents crucial results from clinical trials presented at the European Society of Cardiology Congress on the management of cardiovascular diseases. Relevant therapeutic updates for the coming years are offered while providing critical insights that inform clinical practice and lay the groundwork for future innovations, promising more effective and accessible solutions to the global burden of these diseases. Ref. 8, on-line full text (Free, PDF), www.cardiologyletters.sk

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The landscape of cardiovascular medicine is in perpetual evolution, driven by rigorous clinical research that frequently redefines diagnostic algorithms and therapeutic strategies. Major scientific congresses serve as critical platforms for disseminating novel findings, which, upon thorough scrutiny, can instigate substantial shifts in daily clinical practice. This academic review identifies and critically analyzes seven recent clinical trials that are anticipated to exert a profound impact on the routine management of cardiovascular patients. The selection of these trials is predicated on their potential to challenge established guidelines, introduce innovative therapeutic modalities, or optimize current treatment protocols for prevalent cardiac conditions, thereby directly enhancing patient care and outcomes.

1. Re-evaluating Established Therapies in Heart Failure: The DIGIT-HF Trial investigated the efficacy of digitoxin in patients with heart failure and reduced ejection fraction (HFrEF) (1). The study's principal finding was a significant reduction in the composite primary outcome of all-cause mortality and first hospitalization for heart failure. A relative risk reduction of 18% (Hazard Ratio [HR]=0.82) was observed, translating to an absolute risk reduction of 4.6% over a 36-month follow-up period.

The implications for clinical practice are substantial. Digitoxin, an agent with a long history but diminished recent use, is re-established as a viable therapeutic option for HFrEF, especially in patients who cannot tolerate or receive contemporary heart failure management. This trial mandates a re-evaluation of digitoxin's role in advanced HFrEF, where the disease burden and prognosis remain challenging.

2. Optimizing SGLT2 Inhibitor Initiation in Acute Heart Failure (HF): The crucial meta-analysis incorpo-

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rating DAPA ACT HF-TIMI 68 with the IMPULSE and SOLOIST-WHF trials revealed that the in-hospital initiation of SGLT2 inhibitors was associated with a 29% reduction in the risk of the composite of cardiovascular death or worsening HF, and a 41% reduction in the risk of all-cause mortality in the early post-discharge period (2). This evidence fundamentally shifts the recommended timing for SGLT2 inhibitor initiation in acute HF. Clinical cardiologists are now encouraged to commence these highly effective agents during the acute hospitalization phase, rather than awaiting post-discharge follow-up. This proactive approach holds the potential to reduce critical outcomes.

3. Targeted Therapy for Obstructive Hypertrophic Cardiomyopathy: The MAPLE-HCM study evaluated aficamten, a novel cardiac myosin inhibitor, as monotherapy against metoprolol monotherapy in patients with symptomatic obstructive hypertrophic cardiomyopathy (oHCM). Over 24 weeks, aficamten treatment resulted in a statistically significant increase in exercise capacity compared to metoprolol (3). Furthermore, patients treated with aficamten demonstrated improvements in symptoms, quality of life, NT-proBNP levels, resting and valvular gradients, and left atrial volume index.

These findings are transformative for the management of oHCM. MAPLE-HCM positions aficamten as the therapy of choice and a first-line monotherapy for symptomatic oHCM. This introduces a new, targeted pharmacological class that addresses the underlying pathophysiology of oHCM, offering cardiologists a superior option to traditional beta-blockers for improving functional status and quality of life in this patient population.

4. Simple Intervention for Arrhythmia Prevention in ICD Patients: The POTCAST Trial investigated whether increasing plasma potassium to high-normal levels could reduce cardiac arrhythmias. Through readily available interventions, a modest 0.3 mmol/L increase in plasma potassium was achieved (4). This intervention was associated with a significant 24% reduction in cardiac arrhythmias, hospitalizations, and death, a benefit primarily driven by a reduction in ICD therapy. No significant differences in safety events were reported. The POTCAST trial offers a straightforward, low-cost, and safe strategy with immediate implications for the daily management of ICD patients. Optimizing potassium levels, even within the normal range, becomes an actionable and crucial intervention for cardiologists, potentially leading to a substantial reduction in distressing ICD shocks, fewer hospitalizations, and improved survival for these vulnerable individuals.

5. Reconsidering Antiplatelet and Anticoagulation Strategies: AQUATIC and DUAL-ACS Trials: The AQUATIC trial investigated adjunctive aspirin in patients with chronic coronary syndrome on long-term oral anticoagulation after stent implantation (5). Results demonstrated no incremental ischemic protection but a substantial increase in major bleeding, providing high-level evidence against triple therapy in this population. Complementing this, the DUAL-ACS trial randomized 5,000 post-MI patients to 3 versus 12 months of dual antiplatelet therapy (DAPT) (6). Prolonged DAPT conferred no additional efficacy, while associating with higher bleeding rates and a mortality signal. Importantly, most ischemic benefit occurred within the first 3 months. Parallel findings from TACSI and TOP-CABG similarly questioned extended DAPT following CABG, reinforcing concerns of bleeding excess without ischemic advantage. The overarching message emphasizes reducing the duration or intensity of antiplatelet regimens to mitigate bleeding risks, without compromising ischemic protection in various clinical scenarios. This will lead to safer prescribing practices and a reduction in major bleeding complications across a broad spectrum of cardiovascular patients.

6. A Novel Drug Class for Resistant Hypertension: The BaxHTN Trial reported highly significant reductions in blood pressure after 12 weeks with baxdrostat, an aldosterone synthase inhibitor, confirming its mechanism of action and showcasing a favourable safety and tolerability profile (7). This trial represents an "exciting development" that "heralds a new era of therapy for high blood pressure," particularly for patients with difficult-to-control and resistant hypertension. Resistant hypertension is a substantial clinical challenge, often requiring multiple therapeutic agents without achieving adequate blood pressure control. The introduction of a novel drug-class specifically targeting aldosterone dysregulation provides cardiologists with a powerful new

tool to achieve significant blood pressure reductions. This consequently reduces long-term cardiovascular risk in a previously underserved patient population.

7. Enhancing Atrial Fibrillation Detection: The AMALFI Trial explored the utility of screening for undiagnosed atrial fibrillation (AF) as a routine activity (8). The study randomized 5,000 participants to either receive a 14-day continuous ECG patch monitor for remote use, or to continue with usual care. Over 2.5 years, the group receiving the patch monitor showed an approximate 30% increase in the rate of AF diagnosis, accompanied by a parallel increase in the use of anticoagulation. The AMALFI trial has important implications for preventive cardiology. It established that this remote home-based screening approach was highly acceptable to participants and potentially scalable to a nationwide screening program. These results encourage cardiologists and health systems to consider broader and more systematic screening strategies, which could improve outcomes by identifying at-risk individuals earlier.

Conclusion

These trials collectively underscore a dynamic period of innovation and refinement in cardiovascular medicine and offer robust evidence for immediate translation into clinical practice. They also empower cardiologists with more effective, safer, and tailored approaches, promising to significantly improve patient outcomes and reshape the daily practice of cardiovascular care. However, continued long-term follow-up from some trials, and further research into specific subgroups, is anticipated to further refine these findings.

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