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# **2025 ESC Congress HOT LINE sessions:** key clinical studies

At the 2025 European Congress of Cardiology, the results of 42 international multicenter clinical trials were presented in the HOT LINE sessions. The studies addressed various areas of cardiology, including arterial hypertension, coronary heart disease, atrial fibrillation, lipid-lowering therapy, pharmacotherapy for heart failure, intensive care in cardiology, and healthcare management in cardiology. New texts for five clinical guidelines were also presented. A summary report presents the results of the most interesting studies.
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From August 29 to September 1, 2025, the regular Congress of the European Society of Cardiology was held in Madrid (Spain), combined this year with the World Congress of Cardiology. The main theme of the event was "Global Health: Cardiology Without Borders".

Congress participants reviewed 5 new texts of clinical guidelines:

- for the treatment of valvular heart diseases;
- for the treatment of myocarditis and pericarditis;
- for the treatment of cardiovascular diseases in pregnancy;
- targeted update of the 2019 guidelines for the treatment of dyslipidemia;
- consensus statement on mental health and cardiovascular diseases.

The full texts of these documents are available online at https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines.

The results of 42 specially selected clinical studies were reported for the first time at 10 HOT LINE scientific sessions. The studies were devoted to various areas of cardiology, including the management of patients with cardiac arrhythmias, chronic heart failure, hypertrophic cardiomyopathy, dyslipidemia, arterial hypertension, after myocardial infarction, coronary revascularization, venous thromboembolism, in the perioperative period.

The most interesting studies are summarized below.

The **POTCAST** study involved 1200 patients with a high risk of ventricular arrhythmias — with an implantable cardioverter defibrillator — and with an initial plasma potassium level of 4.3 mmol/l or lower. After randomization in a 1:1 ratio, treatment was administered to increase plasma potassium levels to 4.5–5.0 mmol/l using potassium supplements, a mineralocorticoid receptor antagonist, or both plus dietary advice, or standard care. At a median follow-up of 39.6 months, the composite of the primary endpoint events (documented sustained ventricular tachycardia or corresponding cardioverter-defibrillator shock, unplanned hospitalization for more than 24 hours for arrhythmia or heart failure, or death

from any cause) occurred in 22.7% of patients in the high-normal potassium group compared with 29.2% in the standard care group (p=0.01). The rate of hospitalization for hyperkalemia or hypokalemia was similar in both groups.

The therapeutic efficacy of the cardiac glycoside digitoxin in patients with heart failure and reduced ejection fraction was assessed in the **DIGIT-HF** study. A total of 1,212 patients with New York Heart Association functional class III or IV chronic heart failure with a left ventricular ejection fraction of 40% or less, or functional class II with a left ventricular ejection fraction of 30% or less were randomized in a 1:1 ratio to receive digitoxin (at an initial dose of 0.07 mg once daily) or placebo in addition to drug therapy prescribed in accordance with current clinical guidelines. At a median follow-up of 36 months, the primary endpoint (death from any cause or hospitalization for worsening heart failure) occurred in 39.5% of patients in the digitoxin group and 44.1% in the placebo group (p=0.03), with a trend toward a reduction in mortality (by 14%) in the cardiac glycoside group and a comparable incidence of serious adverse events (4.7% versus 2.8% of cases in the digitoxin and placebo groups, respectively).

Following the completion of the **VICTORIA** study (n=5050), the soluble guanylate cyclase stimulator vericiguat was approved for the treatment of advanced heart failure with reduced ejection fraction and received a Class IIb recommendation in European and North American guidelines. The subsequent VICTOR study (n=6,105) evaluated vericiguat in patients with heart failure with reduced ejection fraction without recent worsening. A pre-specified pooled analysis of patient-level data from the **VICTORIA and VICTOR** studies was conducted to determine the effect of vericiguat on clinical outcomes. Participants in both studies received current background heart failure therapy according to guidelines. The primary endpoint of cardiovascular death or hospitalization for heart failure occurred in 25.9% of 5,579 patients in the vericiguat group and 27.9% of 5,576 patients in the placebo group (p=0.0088), including significant reductions in the risk of cardiovascular death (by 11%; p=0.020) and hospitalization for heart failure (by 8%; p=0.043). Therefore, vericiguat may be used as an additional treatment option for selected patients with heart failure with reduced ejection fraction.

In the **ODYSSEY-HCM** study, the cardiac myosin inhibitor mavacamten, approved for the treatment of adult patients with symptomatic obstructive hypertrophic cardiomyopathy, was evaluated in the non-obstructive form. After randomization, 289 patients received mavacamten (starting dose of 5 mg/day adjusted to a maximum dose of 15 mg/day depending on left ventricular ejection fraction) and 291 received placebo. Over a 48-week follow-up period, there were no significant differences in the two primary endpoints: the mean change in peak oxygen consumption was 0.52 ml/kg/min in the mavacamten group and 0.05 ml/kg/min in the placebo group (p=0.07), and the change in quality of life according to the 23-item Kansas City Cardiomyopathy Questionnaire was 13.1 points versus 10.4 points (p=0.06). In patients with non-obstructive hypertrophic cardiomyopathy, mavacamten did not lead to a significantly greater improvement in peak oxygen consumption or reduction in symptoms compared with placebo.

The cardiac myosin inhibitor aficamten was compared with metoprolol in patients with obstructive hypertrophic cardiomyopathy in the MAPLE-HCM trial. After randomization, 88 patients received aficamten at a dose of 5 to 20 mg/day plus placebo, and 87 received metoprolol at a dose of 50 to 200 mg/day plus placebo. During 24 weeks of observation, the change in peak oxygen consumption (the primary endpoint) was 1.1 ml/kg/min in the aficamten group and –1.2 ml/kg/min in the metoprolol group (p<0.001). Patients receiving aficamten had significant improvements in New York Heart Association functional class, Kansas City Cardiomyopathy Questionnaire quality of life, left ventricular outflow tract pressure gradient, N-terminal pre-brain natriuretic peptide level, and left atrial volume index compared with patients receiving metoprolol. There were no significant differences in left ventricular mass index or adverse event rates between the two treatment groups.

The open-label, randomized **REBOOT-CNIC** trial compared the results of contemporary treatment (coronary reperfusion and secondary prevention) in patients with ST-segment elevation myocardial infarction and left ventricular ejection fraction greater than 40% with beta-blocker therapy (n=4207) versus no therapy (n=4231). With a median follow-up of 3.7 years, the primary endpoint (a composite of death from any cause, reinfarction, or hospitalization for heart failure) occurred at equal rates (p=0.63) in the

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two groups; there was no difference in the rates of death from any cause, reinfarction, hospitalization for heart failure, or safety outcomes.

The open-label, randomized **BETAMI–DANBLOCK** study included patients with a history of myocardial infarction and a left ventricular ejection fraction of at least 40% who were randomized within 14 days of the event to receive long-term beta-blocker therapy (n=2,783) or no beta-blocker therapy (n=2,791). At a median follow-up of 3.5 years, the combined primary endpoint (death from any cause, myocardial infarction, unplanned coronary revascularization, ischemic stroke, heart failure, or malignant ventricular arrhythmia) occurred in 14.2% of patients in the beta-blocker group and 16.3% in the no-beta-blocker group (p=0.03), with no significant differences in the incidence of individual components or safety parameters between the groups. In this study, in patients with myocardial infarction and a left ventricular ejection fraction of at least 40%, beta-blocker therapy resulted in a reduced risk of death or major adverse cardiovascular events compared with no beta-blocker therapy.

The phase 3 BaxHTN study enrolled patients with sitting systolic blood pressure 140 mmHg to less than 170 mmHg despite treatment with two antihypertensive agents (uncontrolled hypertension) or three or more such agents (resistant hypertension), including a diuretic. After a 2-week placebo run-in period, patients with sitting systolic blood pressure 135 mmHg or greater were randomized to receive the selective aldosterone synthase inhibitor baxdrostat 1 mg (n=264), baxdrostat 2 mg (n=266), or placebo (n=264) once daily. After 12 weeks, the change from baseline in sitting systolic blood pressure (primary endpoint) was -14.5 mmHg. with 1 mg baxdrostat, –15.7 mmHg with 2 mg baxdrostat, and –5.8 mmHg with placebo. The placebo-corrected difference was –8.7 mmHg with 1 mg baxdrostat and –9.8 mmHg with 2 mg baxdrostat (p<0.001 for both comparisons). Potassium levels greater than 6.0 mmol/L were recorded in 2.3% of patients in the 1 mg baxdrostat group, 3.0% in the 2 mg baxdrostat group, and 0.4% in the placebo group. In patients with uncontrolled or resistant hypertension, the addition of baxdrostat to background therapy resulted in a significant reduction in sitting systolic blood pressure after 12 weeks compared with placebo.

Olezarsen is an antisense oligonucleotide that inhibits the synthesis of apolipoprotein C-III, resulting in lower plasma triglyceride levels. The drug was evaluated in the randomized phase 3 Essence–TIMI 73b study in patients with moderate hypertriglyceridemia (triglycerides 150 to 499 mg/dL) and increased cardiovascular risk or severe hypertriglyceridemia (triglycerides ⩾500 mg/dL) who were randomized 1:3 to receive monthly subcutaneous administration of olezarsen 50 mg (n=254), olezarsen 80 mg (n=766), or placebo (n=329). After 6 months of treatment, the mean change in triglyceride levels adjusted for placebo was –58.4% in the olezarsen 50 mg group (p<0.001) and –60.6% in the olezarsen 80 mg group (p<0.001). The incidence of serious adverse events was similar in all study groups.

The optimal duration of anticoagulation after venous thromboembolism in patients with a transient precipitating event (e.g., surgery, trauma, or immobilization) and concomitant persistent risk factors has not been determined. In the randomized HI-PRO study, patients with VTE following a transient trigger, at least 1 persistent risk factor, and receiving anticoagulation for at least 3 months were randomized to receive apixaban 2.5 mg twice daily (n=300) or placebo (n=300) for 12 months. During the follow-up period, the primary efficacy endpoint (first symptomatic recurrence of VTE) occurred in 1.3% of patients in the apixaban group and 10.0% in the placebo group (p<0.001). The primary safety endpoint (first major bleeding event according to the International Society on Thrombosis and Haemostasis criteria) occurred with comparable frequency: major bleeding occurred in 1 patient in the apixaban group and in no patients in the placebo group, minor clinically significant bleeding was observed in 4.8% of patients in the apixaban group and in 1.7% in the placebo group (p=0.06). Rare fatal outcomes were not associated with cardiovascular or hemorrhagic causes.

The **AQUATIC** study included patients with chronic coronary syndrome who had a stent implanted more than 6 months before inclusion in the study, had a high atherothrombotic risk and received continuous oral anticoagulant therapy. After randomization, once-daily aspirin 100 mg (n=433) or placebo (n=439) was administered in addition to anticoagulants. The study was terminated early on the recommendation of an independent data and safety monitoring board after a median follow-up of 2.2 years due to excess death from any cause in the aspirin group. The primary efficacy endpoint (a composite of cardiovas-

cular death, myocardial infarction, stroke, systemic embolism, coronary revascularization, or acute limb ischemia) occurred in 16.9% of patients in the aspirin group and in 12.1% in the placebo group (p=0.02), and death from any cause occurred in 13.4% versus 8.4% of cases, respectively (p=0.01). The key safety indicator (major bleeding) was recorded in 10.2% of patients in the aspirin group and in 3.4% in the placebo group (p<0.001).

The **NEO-MINDSET** study enrolled patients after successful percutaneous coronary intervention for acute coronary syndromes who were randomized within the first 4 days of hospitalization to stop aspirin and then receive monotherapy with a potent P2Y12 inhibitor (ticagrelor or prasugrel) (n=1712) or dual antiplatelet therapy (aspirin and a potent P2Y12 inhibitor) (n=1698) for 12 months. During this follow-up period, the primary end point events (death from any cause, myocardial infarction, stroke, or urgent revascularization) occurred in 7.0% of patients in the monotherapy group and 5.5% in the dual antiplatelet therapy group (p=0.11 for noninferiority). Major or clinically relevant non-major bleeding occurred in 2.0% of patients in the monotherapy group and 4.9% of patients in the dual antiplatelet therapy group, and stent thrombosis occurred in 12 and 4 patients in the matched groups, respectively. Among patients who underwent successful percutaneous coronary intervention for acute coronary syndrome, monotherapy with a potent P2Y12 receptor inhibitor was non-inferior to dual antiplatelet therapy in preventing the combined risk of death and ischemic events at 12 months.

The **TARGET-FIRST** trial included patients who had successfully undergone complete coronary revascularization with implantation of advanced drug-eluting stents within 7 days of myocardial infarction and who completed 1 month of dual antiplatelet therapy without ischemic complications or major bleeding. After randomization, patients were assigned to receive either P2Y12 receptor inhibitor monotherapy (n=961) or dual antiplatelet therapy (n=981) for 11 months. During follow-up, the primary composite endpoint (death from any cause, myocardial infarction, stent thrombosis, stroke, or major bleeding type 3 or 5 according to the Bleeding Academic Research Consortium definition) occurred in 2.1% of patients in the P2Y12 receptor inhibitor monotherapy group and 2.2% of patients in the dual antiplatelet therapy group (p=0.02 for noninferiority). The primary secondary endpoint (Bleeding Academic Research Consortium type 2, 3, or 5 bleeding) occurred in 2.6% of patients in the P2Y12 receptor inhibitor monotherapy group and 5.6% in the dual antiplatelet therapy group (p=0.002 for superiority). Stent thrombosis was rare and its incidence was similar in both groups.

In this open-label, registry-based, cardiothoracic surgery center-based clinical trial, TACSI, patients undergoing coronary artery bypass grafting for acute coronary syndrome were randomized to receive ticagrelor and aspirin (n=1104) or aspirin alone (n=1097) for 1 year. During this follow-up period, the combined primary endpoint event (death, myocardial infarction, stroke, or repeat revascularization) occurred in 4.8% of patients in the ticagrelor plus aspirin group and 4.6% in the aspirin alone group (p=0.77). The key secondary endpoint was all adverse clinical outcomes, defined as the primary endpoint events plus major bleeding, and its incidence was 9.1% of cases in the ticagrelor plus aspirin group versus 6.4% in the aspirin alone group. Major bleeding occurred in 4.9% of patients in the ticagrelor plus aspirin group and 2.0% in the aspirin alone group. In patients undergoing coronary artery bypass grafting for acute coronary syndrome, adding ticagrelor to aspirin does not reduce the risk of death, myocardial infarction, stroke, or repeat coronary revascularization compared with aspirin alone for 1 year.

The next congress of the European Society of Cardiology is scheduled to be held in Munich, Germany, from 28 to 31 August 2026.

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