



ESC Congress 2019 Highlights

ESC Congress

The ESC Congress is the annual congress of the European Society of Cardiology, the largest medical congress in Europe. It gathers over 30,000 active participants and takes place every year in August/September in a different European city.

This year it was held in Paris from 31 Aug to 4 Sep 2019

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ESC 2019 Dyslipidemia Guidelines says *Lower is Better*

One of the main message of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) Guidelines on dyslipidaemias 2019 is Low-density lipoprotein (LDL) cholesterol levels should be lowered as much as possible to prevent cardiovascular disease, especially in high and very high risk patients.

Cardiovascular disease (CVD) is responsible for millions of death worldwide each year. Clogged arteries, known as atherosclerotic CVD, are the main type of disease. The guidelines provide recommendations on how to modify plasma lipid levels through lifestyle and medication to reduce the risk of atherosclerotic CVD.

The new guidelines was released on August 31 at the ESC Congress 2019 and simultaneously published online in the *European Heart Journal*.

CV Risk Categories	LDL-C Goal recommendation
Very-high-risk patients (10-year risk of CV death >10%)	<ul style="list-style-type: none"> LDL-C reduction of at least 50% from baseline LDL-C goal of < 55 mg/dL
Very high-risk patients who experience a 2 nd vascular event within 2 years while taking maximally tolerated statin therapy	<ul style="list-style-type: none"> LDL-C goal of < 40 mg/dL
High risk (10-year risk for CV death of 5% to 10%)	<ul style="list-style-type: none"> LDL-C reduction of 50% or more from baseline LDL-C goal of < 70 mg/dL
Moderate risk (10-year risk for CV death of 1% to 5%)	<ul style="list-style-type: none"> LDL-C goal of < 100 mg/dL
Low risk (10-year risk for CV death <1%)	<ul style="list-style-type: none"> LDL-C goal of < 116 mg/dL

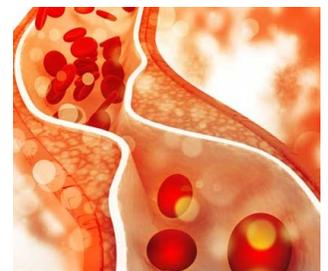
ESC 2019

They have also recommended that patients should be treated aggressively with high-dose statins and with the option of adding Ezetimibe and new class of antidy lipidemic drugs like PCSK9 [proprotein convertase subtilisin/kexin type] inhibitors to achieve these targets.

The guidelines also recommend for the first time the use of new tests to help identify higher-risk patients. These include both coronary artery calcium (CAC)

imaging and biomarker tests like ApoB and Lp(a).

The guidelines also include a recommendation based on the recent REDUCE-IT trial of high-dose eicosapentaenoic acid (EPA) for patients with raised triglycerides (TG).



For full text click link: <https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/>

Coronary Artery Disease

“Ticagrelor is an antiplatelet drug inhibiting the P2Y12 receptor on platelet surface.”

THEMIS trial: Ticagrelor reduce ischemic events in stable coronary patients with diabetes

The combination of Ticagrelor and aspirin reduces ischemic events compared with Aspirin alone in patients with stable coronary artery disease and diabetes.

Patients with diabetes often develop coronary artery disease, with millions of such patients worldwide. Aspirin is generally used to decrease this risk, but cardiovascular events still occur at a high rate.

The THEMIS trial examined whether adding Ticagrelor to Aspirin would reduce the risk of thrombotic events in these patients. The study enrolled 19,220 patients with age 50 years or older, T2DM, and had stable CAD (history of angioplasty, CABG, or angiographic stenosis of 50% or more in at least one coronary artery). Patients with known prior myocardial infarction or stroke were excluded. They were randomly allocated to Ticagrelor versus placebo, both on top of Aspirin.

The incidence of the primary efficacy outcome (composite of CV death, MI, or stroke) was significantly 10% lower in the Ticagrelor group than in the placebo group.

However bleeding events were significantly higher in Ticagrelor group.

It will be interesting to see the fate of Ticagrelor in India after its patent expiry later this year.

NEJM 2019 Sep 1; DOI: 10.1056/NEJMoa1908077

ISAR-REACT 5 trial: Is Prasugrel better than Ticagrelor in ACS

“First Head-to-Head Trial of Newer Antiplatelet Agents.”

Prasugrel is superior to Ticagrelor for reducing ischemic events in patients with acute coronary syndrome and a planned invasive strategy.

In acute coronary syndromes, a dual antiplatelet regimen with a P2Y12 receptor antagonist plus Aspirin is the cornerstone of treatment. Prasugrel and Ticagrelor provide greater, more rapid, and consistent platelet inhibition compared to their predecessor Clopidogrel.

The ISAR-REACT 5 trial was done to test the hypothesis whether Ticagrelor is superi-

or to Prasugrel in reducing the primary composite endpoint of death, MI, or stroke within 12 months in ACS.

4018 patients with ACS were randomly assigned to receive therapy with Prasugrel (loading dose 60 mg & maintenance dose 10 mg/d) or Ticagrelor (LD 180 mg & MD 90 mg BID) on top of aspirin.

However, surprisingly the primary composite endpoint occurred in 9.3% of patients in the Ticagrelor group and 6.9% in Prasugrel group (HR 1.36; p = 0.006).

Thus, Ticagrelor was not superior to Prasugrel. There was no difference in bleeding risk, the primary safety outcome.

It will be interesting to know how this finding will affect the guideline for ACS management. As of now, Prasugrel scores over Ticagrelor in such patient group.



NEJM 2019 Sep 1; DOI: 10.1056/NEJMoa1908973

PARAGON HF trial: No significant advantage to Sacubitril/Valsartan in HFpEF

Sacubitril/valsartan, inhibits the renin-angiotensin system and augments endogenous vasoactive peptide systems and has shown to reduce morbidity and mortality in Heart Failure patients with reduced Ejection Fraction (HFrEF, EF<40%) in the PARADIGM-HF trial.

It has a class I guideline recommendation for the treatment of HFrEF.

Currently there is no evidence-based medicines for Heart Failure with preserved Ejection Fraction (HFpEF).

PARAGON-HF was designed to test the hypothesis that Sacubitril/Valsartan would im-

prove outcomes in HFpEF (EF>50%).

4822 patients with HFpEF were randomly assigned to receive Sacubitril/Valsartan or the ARB valsartan for up to 57 months.

The primary endpoint was a composite of total (first and recurrent) heart failure hospitalizations and CV death.

The rate ratio for the primary endpoint was 0.87 (95% CI 0.75–1.01; $p = 0.059$). This reduction was just short of statistical significance and was driven by a decline in heart failure hospitalization with no effect on CV death or all-cause mortality.

However, significant primary-endpoint reduction observed in women, who made up about 52% of sample, and in those with a below-median left ventricular ejection fraction (LVEF) of 45% to 57%, which is classified as mid-range LVEF.

Sacubitril/Valsartan, as of now remain as first line agent for HFrEF (EF<40%). However, for HFpEF (EF>50%) evidence is insignificant.

NEJM 2019 Sep 1; DOI: 10.1056/NEJMoa1908655

Heart Failure

“Sacubitril/Valsartan, is considered as first line agent for the management of HFrEF (i.e. LVEF <40%)”

DAPA HF trial: Diabetic drug offers new approach to Heart Failure treatment

Treatment with the sodium-glucose cotransporter 2 (SGLT2) inhibitor Dapagliflozin reduced risk for worsening HF and CV death when added to standard therapy in patients with HFrEF, regardless of diabetes status, according to results of the DAPA-HF trial.

The trial enrolled 4,744 patients with HFrEF and randomly allocated to either Dapagliflozin 10 mg once daily or matching placebo.

Primary endpoint was the

composite of a first episode of worsening HF or death from CV causes.

There was a significant 26% reduction in the primary outcome with Dapagliflozin vs placebo (HR 0.74; $p=0.00001$).

In addition, Dapagliflozin reduced the risk for all-cause death by 17%.

What really paradigm-shifting was that there appears to be a significant benefit in the non-diabetic patients with HFrEF too.

These results suggest that Dapagliflozin offers a new approach to the treatment of patients with HFrEF.



The exact mechanism of action for HF benefit by SGLT2i is unknown. However, the postulated early effect is through diuretic action.

“Dapagliflozin is a SGLT2 inhibitor used for T2DM. It helps to improve glycemic control by inhibiting glucose resorption in the kidney and causing glucose excretion through urine”

JACC 2019 Sep 1; presented at ESC Congress 2019

Dyslipidemia

Evolocumab, is a human monoclonal antibodies directed against PCSK9.

It lowers LDL-C levels by inhibiting PCSK9, increasing the number of LDL receptors on the hepatocyte surface, thereby resulting in lower LDL-C plasma concentrations

EVOPACS trial: Early Evolocumab is beneficial in ACS patients

While guidelines recommend in-hospital initiation of high-intensity statin therapy in patients with acute coronary syndromes (ACS), low-density lipoprotein cholesterol (LDL-C) target levels are frequently not attained.

Adding the PCSK9 inhibitor Evolocumab to high-intensity statin therapy in the very high-risk setting of ACS safely lowers LDL-C, according to the EVOPACS trial.

Study enrolled 308 patients within 24 hours of an ST-segment myocardial infarction (STEMI) or within 72 hours of a non-ST-elevation (NSTEMI)-ACS and randomly assigned them to evolocumab injection, 420 mg every 4 weeks, or placebo, both with atorvastatin, 40 mg/day.



The primary endpoint of percentage change in LDL-C from baseline to 8 weeks was 77.1% (mean, 139 mg/dL to 31 mg/dL) among patients receiving Evolocumab and 35.4% (mean, 132 mg/dL to 80 mg/dL) in those receiving placebo ($P < 0.001$).

Overall, 95.7% of patients in the Evolocumab group reached an LDL-C target of <70 mg/dL at 8 weeks.

An LDL-C of less than 55 mg/dL — a new target in the updated 2019 ESC lipid guidelines — was achieved by 90.1% patients in Evolocumab group vs 10.7% in placebo group.

This was a needed first study to show that evolocumab can be administered acutely in ACS patients.

None of the PCSK9 inhibitor class drug has been approved in India yet.

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