International Heart and Vascular Disease Journal
Volume 6, Number 18, June 2018

Journal of the Cardioprogress Foundation

Congress of the American College of Cardiology: results of clinical trials

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Summary

The 67th annual congress of the American College of Cardiology was held in Orlando (USA) on March 10–12, 2018. It was attended by 18.300 people, including 13.000 professionals and opinion leaders from 137 countries.

Traditionally, new results of large clinical trials that could influence clinical practice, in particular, the ones summarized in this article, generated distinct interest. Data obtained in studies ANNEXA-4, A Cluster-Randomized Trial of Blood-Pressure Reduction in Black Barbershops, CARES, HER2, INDIE-HFpEF, MOMENTUM-3, SECURE, SMART-DATE, STOP PAD, TREAT, TRIUMPH, registers and studies of real practice like ARTEMIS, GWTG-HF, POICE, subanalysis of recently presented major projects CANTOS, CANVAS, COMPASS, CVD-REAL 2, FOURIER were of great importance.

The results of clinical trials presented at the scientific sessions of the American College of Cardiology in 2018 demonstrated new possibilities of antithrombotic therapy, treatment of atherosclerosis, coronary heart disease, cardiac arrhythmias, heart failure and arterial hypertension that will certainly help to optimize the management of patients with common cardiovascular diseases.

Key words

Clinical trials, cardiovascular diseases, congress of the American College of Cardiology.

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The 67th annual congress of the American College of Cardiology was held in Orlando (USA) in the period from 10 till 12 March 2018. It was attended by 18.300 people, including 13.000 professionals and opinion leaders from 137 countries. The exposition consisted of 280 exponents. 375 journalists form 174 mass media covered this major scientific event.

As usually, the point of highest interest consisted in new results of large clinical studies which could influence the clinical practice; in particular, some of these results are given in this article. A significant role belongs also to the data gotten in the ANNEXA-4, A Cluster-Randomized Trial of Blood-Pressure Reduction in Black Barbershops, CARES, HER2, INDIE-HFpEF, MOMENTUM-3, SECURE, SMART-DATE, STOP PAD, TREAT, TRIUMPH, in registers and in practical studies ARTEMIS, GWTG-HF, POICE, subanalyzes of recently presented large projects CANTOS, CANVAS, COMPASS, CVD-REAL 2, FOURIER.

The patients who underwent the myocardium infarction (MI) have a high risk of cardiovascular complications during the subsequent years, despite the modern measures of secondary prevention including intensive statin therapy. Thus, additional treatment is required to decrease this residual risk and to improve the prognosis of these patients.

The long-term efficacy and safety of alicrocumab, a PCSK9 inhibitor that significantly decreases the level of low density lipoproteins (LDL), was evaluated in the ODYSSEY OUTCOMES study. The trial included patients who had underwent acute coronary syndrome (MI or unstable angina) 1–12 months before randomization. All patients received high-intensity statin therapy (atorvastatin 40–80 mg/day or rosuvastatin 20–40 mg/day or the maximum tolerated dose of one of these drugs for 2 weeks), but did not reach the lipid profile target range (LDL level remained ≥70 mg / dl or ≥1.8 mmol/l, and apolipoprotein B level was ≥80 mg / dl). 18.924 patients were randomized for additional subcutaneous administration of alicrocumab (75 or 150 mg 1 time per 2 weeks) or placebo with a median observation time of 2.8 years. The goal of treatment was to achieve a LDL level of 25–50 mg/dL with an acceptable decrease to 15 mg/dL.

The average decrease of LDL level in the alicrocumab group was 62.7% in 4 months time (55.7 mg/dl less compared to placebo) and 54.7% in 48 months time after randomization (48.1 mg/dl lower than for placebo). Alicrocumab treatment was accompanied by a decrease in the incidence of reaching the primary efficacy endpoint (death caused by coronary heart disease — CHD, nonfatal MI, ischemic stroke, or unstable angina requiring hospitalization) by 15% (relative risk — RR 0.85 with 95% confidence interval — CI in the range from 0.78 till 0.93; p = 0.0003; absolute risk reduction — 1.7%). Among the primary endpoint components, coronary artery disease mortality did not significantly decrease (RR 0.92 with 95% CI in the range from 0.76 till 1.11; p = 0.38), in contrast to the non-fatal MI incidence (RR 0.86 with 95% CI in the range from 0.77 to 0.96; p = 0.006), ischemic stroke (RR 0.73 with 95% CI in the range from 0.57 till 0.93; p = 0.01) and unstable angina (RR 0.61 with 95% CI in the range from 0.41 till 0.92; p = 0.02).

All-cause mortality was significantly reduced in alicrocumab group compared with placebo (RR 0.85 with 95% CI in the range from 0.73 till 0.98; p = 0.026; absolute risk reduction — 0.6%), but this indicator did not concern the primary endpoint. Analysis of a subgroup of patients with baseline LDL ≥100 mg / dL showed the greatest benefit of using alicrocumab — it reduced the primary endpoint incidence by 24% (RR 0.76 with 95% CI in the range from 0.65 till 0.87; absolute risk reduction — 3.4%) and all-cause mortality by 29% (RR 0.71 with 95% CI from 0.56 to 0.90; absolute risk reduction — 1.7%). The diabetes incidence, worsening or complications, allergic reactions and neurocognitive disorders in the groups of the PCSK9 inhibitor and placebo did not differ significantly. The patients treated with alicrocumab were more likely to have skin reactions at the injection site (3.8% vs. 2.1% in the placebo group).

Myocardial damage after non-cardiac surgery includes MI and an isolated troponin level increase in the blood that occur during the first 30 days after surgery. Such myocardial damage is independently associated with an increased risk of cardiovascular events and death during the first two years after surgery. Anticoagulant therapy is useful for patients with an increased risk of thrombotic complications, but has not been previously estimated for the prevention of myocardial damage as a result of non-cardiac surgery.

In the randomized MANAGE trial (n = 1754, mean age 70 years), prophylactic efficacy of the direct thrombin inhibitor dabigatran on the vascular complications after non-cardiac surgery was evaluated (110 mg 2 times a day), compared with placebo. Patients who were not taking proton pump inhibitors were randomized to receive omeprazole, 20 mg per day, or placebo (factorial design 2 x 2). The primary composite efficacy endpoint included vascular death, non-fatal MI, non-hemorrhagic stroke, peripheral

arterial thrombosis, amputation, and symptomatic venous thromboembolism. The primary composite safety endpoint included bleeding (life threatening, major or critical organ bleeding). During the 2 years follow-up, 46% of patients in the dabigatran group and 43% of patients in the placebo group stopped the prescribed treatment, mainly at their personal request. The primary efficacy endpoint was registered in 11% of patients randomized to receive dabigatran, and in 15% of the placebo group (RR 0.72 with 95% CI in the range from 0.55 to 0.93; p = 0.012). There was no significant influence of omeprazole on the dabigatran effects in terms of effectiveness (p value for interaction = 0.79). There were no significant differences in the onset of the primary safety endpoint events between the dabigatran and placebo groups (RR 0.92 with 95% CI in the range from 0.55 to 1.53; p = 0.79). Omeprazole had no influence on the safety of dabigatran.

The risk of atrial fibrillation (AF) onset over the age of 55 is more than 1/3, which is associated with a 5-fold increase in the incidence of stroke. If AF is identified, anticoagulant therapy can reduce the risk of stroke by about 65% and mortality by 30%. The clinical value of screening for determining the AF presence is still poorly studied. The aim of the mSToPS study was to determine the effectiveness of this arrhythmia diagnostics by patient self-recording of electrocardiogram in comparison to the usual follow-up of 2655 patients without previously diagnosed AF. The iRhythm Zio device was used for active monitoring at home. The primary endpoint was the number of participants with the newly detected AF in the course of a year. The recurrence of the newly diagnosed AF was 6.3% in the active control group compared to 2.3% of those with standard follow-up (RR 2.8 with 95% CI in the range from 2.1 to 3.7; p <0.0001).

The median of total AF duration in the monitoring group was 0.9%, and the mean duration of the longest AF episode was 185.5 min (92.8% episodes of >5 min, 37.7% episodes of >6 hours). Active monitoring was associated with an increase in the incidence of anticoagulant therapy onset in comparison to the standard follow-up group (5.4% vs 3.4%, p=0.0004). Though, there were no differences in clinical outcomes (stroke, MI, systemic thromboembolism) between the active control group and the standard follow-up group.

The effectiveness of clopidogrel antiplatelet therapy in patients with ACS may decrease due to individual variability of the response to treatment with this drug. The choice of a P2Y12 receptor blocker therapy is usually based on the physician's assessment of the risk of ischemic events on the one side and the risk of uncontrolled bleeding on the other. It has been shown that there are several genes which affect enzymes controlling clopidogrel's antiplatelet efficacy. There has been developed an easy-to-use genetic screening system ST Q3 which is transportable within a medical center and in 70 minutes can provide information on these genes from a blood sample at the bedside of the patient.

The PHARMCLO study was aimed to evaluate a personalized approach to the P2Y12 receptor blocker choice in patients with ACS. The study combined clinical characteristics and genetic data to provide information for the drug choice. Patients from 13 medical centers in Italy who were admitted in hospital because of ACS (n = 888) were randomized for two types of treatment: the standard one which included the prescription of clopidogrel, ticagrelor or prasugrel only on the grounds of patients' clinical characteristics, and the treatment based on the genetic test data (tested on ABCB1, 2C19 * 2, 2C19 * 17). The genetic test results were taken in consideration together with clinical characteristics before the antiplatelet therapy prescription. The primary composite endpoint included MI, stroke, death from cardiovascular causes, or significant bleeding (BARC 3–5).

After 12 months, 50.7% of patients from the standard treatment group received clopidogrel, 8.4% received prasugrel, 32.7% received ticagrelor, and 8.2% did not received any P2Y12 receptor inhibitor. In the genetic test group, 43.3% of patients received clopidogrel, 7.6% received prasugrel, 42.6% received ticagrelor, and 6.5% did not receive any P2Y12 receptor inhibitor. The primary endpoint was registered in 15.9% of patients from the pharmacogenomics group and in 25.9% of patients from the standard treatment group (RR 0.58 with 95% CI in the range from 0.43 till 0.078; p <0.001), which was mainly due to a decrease in the non-fatal myocardial infarction incidence (RR 0.42 with 95% CI in the range from 0.25 till 0.70). Among those treated with clopidogrel, the primary endpoint was reached 32% less frequently in the pharmacogenomics group compared to the control group (RR 0.68, 95% CI in the range from 0.47 till 0.97; p = 0.03).

The realization of genotyping for the choice of antiplatelet therapy in ACS is possible in actual practice and leads to changes in the drug administration regimen. The personalized choice of anti-platelet

therapy can lead to a clinically significant reduction in the incidence of ischemic and hemorrhagic complications. It is necessary to confirm these data about genotype-based antiplatelet therapy in future studies and to clarify the economic efficiency of genotyping in a complex situation of providing medical care in ACS, when the test cannot be delegated to any centralized genetic laboratory because of the lack of time.

The incidence of sudden cardiac death (SCD) after MI is higher in patients with low left ventricular ejection fraction (LVEF). Implantable cardioverter-defibrillators (ICDs) are not introduced into the body of patients during the first 40–90 days after the date of myocardial infarction, depending on the revascularization method and several other reasons. First, large randomized clinical trials did not demonstrate that ICD implantation during this period could lead to a long-term mortality reduction. Secondly, in many cases LVEF improves in the course of the following months after MI. Thirdly, there is a competing risk of death from other causes that cannot be prevented by ICD.

The task of the multicenter randomized VEST study was to answer the question about the possibility of reducing the SCD risk by the usage of a wearable cardioverter-defibrillator (WCD) during the first period after MI (up to 90 days) in patients with reduced LVEF.

Patients who had recently underwent myocardial infarction, with LV EF ⩽35% and an adequate drug therapy, were randomized in a 2: 1 ratio for usage or non-usage of WCD on hospital discharge. The primary endpoint was SCD in the course of 3 months; the secondary endpoint was death from any other cause and non-fatal outcomes. During a mean observation period of 84.3 ± 15.6 days, no significant differences were shown in the primary endpoint incidence between the WCD group (n = 1524) and the control group (n = 778) — 1.6% vs 2.4% (p = 0.18). There were also no significant differences in the association with the causes of death and nonfatal outcomes between the two groups. However, the overall mortality was significantly lower in the WCD group (3.1% compared to 4.9% in the control group, p = 0.04). Among the side effects of the NCD usage, there were skin manifestations in the form of rash and itching, more likely on chest region.

The results of clinical trials presented at the scientific sessions of the American College of Cardiology in 2018 demonstrated new possibilities of antithrombotic therapy, treatment of atherosclerosis, coronary heart disease, cardiac arrhythmias, heart failure and arterial hypertension that will certainly help to optimize the management of patients with common cardiovascular diseases.

More information about the scientific event held in March 2018 in Orlando is presented on the official website http://www.acc.org/acc2018

Conflict of interest: None declared.

References

1. Steg P., Szarek M., Bhatt D. et al. Cardiovascular Outcomes with Alirocumab After Acute Coronary Syndrome: Results of the ODYSSEY Outcomes Trial. ACC Scientific Sessions, March 10, 2018, Orlando, Florida. https://www.medscape.com/cardiology
2. Kumbhan D.J. Management of Myocardial Injury After Noncardiac Surgery — MANAGE. ACC Scientific Sessions, March 11, 2018, Orlando, Florida. https://www.medscape.com/cardiology
3. Steinhubl S.R., Waalen J., Edwards A. et al. A Digital End-to-End, Nationwide, Pragmatic Trial of Screening for Undiagnosed Atrial Fibrillation Within a Health Insurance System Using a Self-Applied ECG Patch: Primary Results of the mHealth Screening to Prevent Strokes (mSToPS) Trial. ACC Scientific Sessions, March 10, 2018, Orlando, Florida. https://www.medscape.com/cardiology
4. Notarangelo F.M., Maglietta G., Bevilacqua P. et al. Pharmacogenomic Approach to Selecting Antiplatelet Therapy in Acute Coronary Syndromes: PHARMCLO trial. J Am Coll Cardiol. 2018 Feb 24. pii: S0735–1097 (18) 33306–0. doi: 10.1016/j.jacc.2018.02.029. [Epub ahead of print]
5. Olgin J.E., Pletcher M., Vittinghoff E. et al. Efficacy of a Wearable Cardioverter-Defibrillator after Myocardial Infarction: Results of the Vest Prevention of Early Sudden Death Trial (VEST). ACC Scientific Sessions, March 10, 2018, Orlando, Florida. https://www.medscape.com/cardiology