

# Results of the most important clinical trials presented at the Congress of the European Society of Cardiology 2018

## S.G. Kanorskii

Kuban State Medical University, Krasnodar, Russia

## **Author**

Sergey G. Kanorskii, M.D., Ph.D., doctor of sciences, professor, head of the Department of Therapy № 2, Faculty of Advanced Training and Professional Retraining of Specialists, Kuban State Medical University, Krasnodar, Russia.

A report on all five scientific sessions of the Hot Line sessions of the Congress of the European Society of Cardiology 2018 (Munich, Germany), dedicated to the results of new clinical research in cardiology, is presented. Keywords: cardiology, clinical trials, Hot Line sessions.

Conflicts of interest: nothing to declare.

Received: 05.09.2018 Accepted: 26.09.2018

The Congress of the European Society of Cardiology 2018 took place in Munich (Germany) from 25th to 29th of august 2018 with the participation of about 32000 delegates from 156 countries and included 587 scientific sessions. 17 most important clinical trials were selected for 5 Hot Line sessions and were presented for the first time.

## Hot Line session I (august 26, 2018)

12019 patients, who were admitted to hospital for 3-10 days with heart failure and ejection fraction

of the left ventricle <45%, acute respiratory failure, acute exacerbation of chronic obstructive pulmonary disease, ischemic stroke, infectious or inflammatory disease, including rheumatic diseases, with high risk of venous thromboembolism according to IMPROVE risk assessment model (> 4 score or higher or a score of 2 or 3 plus a plasma D-dimer level more than twice upper than normal limit according to the criteria of the local laboratory) took part in double randomized MARINER trial [1]. At hospital discharge, patients were randomized to rivaroxaban (n=6007) or placebo

<sup>\*</sup> Corresponding author. Tel. +79183558281. E-mail: kanorskysg@mail.ru

(n=6012) prescription for 45 days. 10 mg of rivaroxaban was prescribed (with a creatinine clearance  $\geq$ 50 mL/min) with dose adjusted down to 7.5 mg (in those with a creatinine clearance of 30 to less than 50 mL/min) once a day.

The primary outcomes, symptomatic venous thromboembolism (deep vein thrombosis, pulmonary embolism, death from venous thromboembolism), occurred in 0.83% cases in the rivaroxaban group compared with 1.10% of cases in the placebo group (relative risk — RR 0.76 with 95% confidence interval - CI from 0.52 to 1.09; p = 0.14), and symptomatic non-fatal deep vein thrombosis or non-fatal pulmonary embolism occurred in 0.18 % and 0.42 % (RR 0.44 with 95% CI from 0.22 to 0.89; p = 0.023) of patients, respectively. Separate evaluation of the results in accordance with the initial kidney function showed, that the efficiencies of low dose of anticoagulant (7.5 mg / day) and placebo (p = 0.994) are equal. Major bleedings occurred in 0.28% of the rivaroxaban group and 0.15% of patients of the placebo group, small clinically significant bleedings were more common during rivaroxaban treatment (1.42% compared with 0.85%, RR 1.66 with 95 % CI from 1.17 to 2.35; p = 0.004).

Rivaroxaban 45-day after discharge treatment in patients with severe diseases didn't show any significant risk of symptomatic thromboembolism or death from venous thromboembolism decrease compared with placebo.

The **CAMELIA-TIMI 61** [2] study included overweight or obese patients with atherosclerotic cardiovascular disease or multiple cardiovascular risk factors to receive either 10 mg of lorcaserin twice a day (n=5135) (selective agonist of 5-HT2C receptors of serotonin, which regulates appetite, decrease weight in overweight and obese patients) or placebo (n=5083). At 1 year, weight loss of at least 5% had occurred in 38.7% of patients in the lorcaserin group and in 17.4% of patients in the placebo group (odds ratio, 3.01 with 95% CI from 2.74 to 3.30; p<0.001). However, at the end of the trial an average body weight difference in observed patients from lorcaserin and placebo group was about 1.9 kg.

During a median follow-up of 3.3 years, the primary safety outcome of major cardiovascular events (a composite of cardiovascular death, myocardial infarction, or stroke) was registered with the frequency of 6.1% in lorcaserin group and 6.2% in the placebo group (RR 0.99 with CI from 0.85 to 1.14; p< 0.001 for «not worse»). Lorcaserin caused previously known side effects—dizziness, fatigue, headache, nausea,

and also an increase in the number of patients with severe hypoglycaemia (p=0.04) and, furthermore, the decrease of diabetes mellitus risk — 8.5% compared with 10.3% (RR 0.81 CI from 0.66 to 0.99) of cases. The risk of pulmonary hypertension development (1.6% compared with 1.0%; p = 0.26) and valvulopathy (1.8% compared with 1.3%; p = 0.24) were not statistically significantly different in the lorcaserin and placebo groups, respectively.

Lorcaserin is the first medication for the reduction in weight with proven efficacy and cardiovascular safety. Lorcaserin contributes to sustained reduction in weight without increasing the incidence of major cardiovascular events compared with placebo in the group of overweight or obese patients with high cardiovascular risk.

Authors of double-blind placebo-controlled multicentral **ARRIVE** [3] trial assessed the efficacy and safety of aspirin among those at moderate estimated risk of a cardiovascular event (20–30% in 10 years) compared with placebo. The investigation included men aged  $\geq 55$  years with  $\geq 2$  and women aged  $\geq 60$  years with  $\geq 3$  risk factors, excluding patients with high risk of gastrointestinal and other types of bleedings or with diabetes mellitus. Patients at moderate risk of coronary heart disease were randomized to aspirin with enteric coating 100 mg daily (n = 6.270) or placebo (n = 6.276).

The primary efficacy outcome — time until first adverse event (cardiovascular death, myocardial infarction, unstable angina, stroke, or transient ischemic attack) occurred in 4.29 % of the aspirin group compared with 4.4 % of the placebo group (RR 0.96 with 95 % CI from 0.81 to 1.13; p = 0.6038). Gastrointestinal bleeding (the primary safety outcome) occurred in 0.97 % of patients of the aspirin group versus 0.46 % in the placebo group (RR 2.11 with 95 % CI from 1.36 to 3.28; p = 0.0007), but most of them weren't severe.

General frequency of adverse outcomes during the ARRIVE trial was lower than expected, which seems to be associated with effective background control of risk factors, which shifted the risk in the observed cohort from moderate to low, hindering the positive effect of aspirin as a medication of primary prevention. Soon after the ASPREE project demonstrated again negative results on aspirin use for primary prevention in the elderly people [4–6].

# Hot Line session II (august 26, 2018)

Randomized **ASCEND** trial [7] aimed to determine whether aspirin administered 100 mg daily is effective

for primary prevention of cardiovascular events in 15.480 patients with diabetes (type II in 94% of cases) compared with placebo.

Primary efficacy outcome (first MI, stroke or transient ischemic attack or vascular death, excluding confirmed intracranial haemorrhage) occurred less frequently in the aspirin group compared with placebo — 8.5% versus 9.6% of cases (RR 0.88 with 95% CI from 0.79 to 0.97; p = 0.01) during extended follow-up of 7.4 years. The key safety outcome (first severe bleeding — intracranial haemorrhage, sightthreatening eye bleeding, gastrointestinal bleeding or any other serious bleeding episode) were more frequent in the aspirin group (4.1%) compared with placebo (3.2%) (RR 1.29 with 95% CI from 1.09 to 1.52; p = 0.003), remarkably, gastrointestinal bleedings were prevalent. There were no significant differences between aspirin group and placebo in accordance to gastrointestinal cancer morbidity (2.0% versus 2.0% — RR 0.99 with 95% CI from 0.80 to 1.24) and other types of cancer (11.6 % and 11.5 %, respectively - RR 1.01 with 95% CI from 0.92 to 1.11), but in order to confirm / eliminate the preventive effect of aspirin, follow-up will continue for many years.

The use of aspirin prevented serious vascular events in people with diabetes and without obvious cardiovascular diseases, but also caused large bleedings, which counteracted the benefits of therapy.

The second part of **ASCEND** project [8] was to estimate the role of omega-3 fatty acid in primary prevention of cardiovascular events in patients with diabetes. The participants (n = 15 480) of the study were randomized to 1 g of omega- 3 fatty acid (group omega-3 of fatty acid) daily and olive oil (placebo group). During extended follow-up of 7.4 years and adherence rate of 76% the primary efficacy outcome, major adverse cardiovascular events (vascular death, myocardial infarction, or stroke or transient ischemic attack), occurred in 8.9% of the omega-3 group compared with 9.2% of the placebo group (RR 0.97 with 95% CI from 0.87 to 1.08; p = 0.55). General major adverse cardiovascular event or revascularization of any arteries was 11.4% versus 11.5% (RR 1.00 with 95% CI from 0.91 to 1.09) and all-cause mortality was 9.7% versus 10.2% (RR 0.95 with 95% CI from 0.86 to 1.05) during omega-3 fatty acids intake versus placebo intake, respectively. There were no significant differences between compared groups in accordance to the frequency of serious side effects.

Despite these data, the results of ongoing VITAL and STRENGTH studies, evaluating the efficacy

of a high dose of omega-3 fatty acids (4 g / day), are expected to be optimistic, as the REDUCE-IT project with the use of high dose of eicosapentaenoic acid has recently completed with a positive result.

The **ART** trial included 3202 patients, who were randomized to bilateral internal thoracic artery (n = 1.548) and one veins versus single internal thoracic artery and two veins (n = 1.554) bypass grafting. During the follow-up the primary endpoint (survival in 10 years) occurred in 329 cases in the group of single internal thoracic artery and in 315 cases in the group of bilateral internal thoracic artery (RR 0.96 with 95% CI from 0.82 to 1.12). There were no differences between groups in accordance to severe cardiovascular events occurrence (death, myocardial infarction, stroke) in 10 years. The results of the study were distorted by the fact, that more than one third of the patients underwent the opposite operation to the one, that was initially prescribed. The outcome of coronary artery bypass grafting using two internal thoracic arteries was significantly influenced by the experience of surgeons—a higher experience was associated with decreased mortality.

According to the authors of the study in 80% of cases coronary artery bypass grafting using two internal thoracic arteries is preferable. However, this technique is associated with high risk of infectious complications in patients with severe obesity or diabetes.

# Hot Line session III (august 27, 2018)

The ATTR-ACT [9] study estimated the effectiveness and safety of tafamidis, new non-steroidal anti-inflammatory drug, which can inhibit amyloidogenesis in patients with transthyretin amyloid cardiomyopathy. 441 patients with family amyloidosis due to pathogenic mutations, and with wild-type of transthyretin amyloid cardiomyopathy, typical changes during the echocardiography study, transthyretin amyloid detection during biopsy and N-terminal pro brain natriuretic peptide plasma concentration > 600 mg/mL, 6-minute walk test distance > 100 meters took part in the study. Patients were randomized in the ratio of 2:1:2 to receive 80 mg of tafamidis daily, 20 mg of tafamidis daily or placebo for 30 months. During the follow-up all-cause death and cardiovascular-related hospitalizations (the primary endpoint) was significantly lower in 264 patients of tafamidis groups compared with 177 patients of the placebo group (p <0.001). Tafamidis significantly reduced total mortality (29.5%) versus 42.9 %) compared with placebo group (RR 0.70 with 95% CI from 0.51 to 0.96; p = 0.0259) and the frequency of cardiovascular-related hospitalizations (RR 0.68 with 95% CI from 0.56 to 0.81; p <0.0001). Tafamidis treatment slowed the decrease in the distance of 6-minute walk test (p <0.001) and the quality of life index according to the Kansas City cardiomy-opathy Questionnaire (p <0.001). The frequency and side effects types were not significantly different in the group of tafamidis versus placebo group. The advantages of tafamidis did not depend on the aetiology of amyloidosis (hereditary or wild-type) and on the dose (20 or 80 mg), but occurred only at the reversible stage of the disease with I or II functional classes of chronic heart failure according to New York Heart Association Functional Classification.

The authors of **COMMANDER HF** [10] trial assumed that rivaroxaban (inhibitor of Xa factor) can decrease production of thrombin and improve outcomes in patients with an episode of decompensated chronic heart failure and coronary artery disease. Patients with II and III functional classes of chronic heart failure and left ventricular ejection fraction  $\geqslant 40\%$ , coronary artery disease and elevated plasma natriuretic peptides, without atrial fibrillation were randomized to rivaroxaban 2.5 mg twice daily (n = 2.507) versus placebo (n = 2.515).

During the median follow-up of 21.1 months the primary efficacy outcome (all-cause mortality, myocardial infarction, or stroke) occurred in 25.0% of the rivaroxaban group compared with 26.2% of the placebo group (RR 0.94 with 95% CI from 0.84 to 1.05; p = 0.27). There were no significant differences in allcause mortality (21.8% versus 22.1%, respectively — RR 0.98 with 95 % CI from 0.87 to 1.10) and myocardial infarction risk (RR 0.83 with 95 % CI from 0.63 to 1.08), but the frequency of stroke was lower in rivaroxaban group (RR 0.66 with CI from 0.47 to 0.95). The primary safety outcome — fatal bleeding or bleeding into a critical space (intracranial, intraspinal, intraocular, pericardial, intraarticular, retroperitoneal, intramuscular) with potential cause of disability, occurred in 0.7% cases in the rivaroxaban group compared with 0.9 % of cases in the placebo group (RR 0.80 with 95 % CI from 0.43 to 1.49; p = 0.484), severe bleedings in 3.3% and 2.0% of cases (RR 1.68 with 95% CI from 1.18 to 2.39; p = 0.003), respectively.

Apparently, antithrombotic drugs cannot improve the prognosis in patients with heart failure without atrial fibrillation, who usually die from a critical reduction in heart's pumping function and ventricular arrhythmia. **MITRA.fr** [11] trial estimated the hypothesis on the outcomes improvement in patients with reduced left ventricular ejection fraction, severe secondary mitral regurgitation and chronic heart failure by the result of percutaneous mitral valve repair. Patients with severe secondary mitral regurgitation (effective regurgitant orifice  $>20~\text{mm}^2$  or regurgitant volume >30~ml per beat), left ventricular ejection fraction of 15–40% and chronic heart failure symptoms were randomized to percutaneous mitral valve repair (n = 152) versus medical therapy (control group) (n = 152).

During 12 months of follow-up, the primary outcome (death or hospitalization for heart failure) occurred in  $54.6\,\%$  and  $51.3\,\%$  of cases (RR  $1.16\,\%$  with  $95\,\%$  CI from 0.73 to 1.84; p = 0.53), all-cause mortality in  $24.3\,\%$  and  $22.4\,\%$  of cases (RR  $1.11\,\%$  with  $95\,\%$  CI from  $0.69\,\%$  to 1.77), hospitalization for heart failure in  $48.7\,\%$  and  $47.4\,\%$  of cases (RR  $1.13\,\%$  with  $95\,\%$  CI from  $0.81\,\%$  to 1.56) in percutaneous mitral valve repair group and control group, respectively.

Despite the neutral results of this work, it is important to mention, that during the latest COAPT study, the incidence of hospitalization for heart failure and the mortality with percutaneous mitral valve repair were significantly reduced in patients with even more pronounced secondary mitral regurgitation.

The **GLOBAL LEADERS** [12] study included patients undergoing percutaneous coronary intervention with a biolimus A9-eluting stent for stable or unstable coronary disease. Patients were randomized to 75-100 mg/day ticagrelor 90 mg 2 times a day for 1 month, followed by ticagrelor for 23 months (experimental group, n = 7.980) versus standard dual antiplatelet therapy for 12 months (75-100 mg/day of aspirin plus 75 mg/day of clopidogrel for stable coronary disease or 75-100 mg/day of aspirin plus 90 mg of ticagrelor 2 times a day for acute coronary syndrome), followed by aspirin monotherapy for 12 months (control group, n = 7.988). During the next two years, the primary efficacy outcome (all-cause mortality or nonfatal Q-wave myocardial infarction) occurred in 3.81% of the experimental group compared with 4.37% of the control group (RR 0.87 with 95% CI from 0.75 to 1.01; p = 0.073), all-cause mortality in 2.81 % and 3.17 % (RR 0.88 with 95% CI from 0.74 to 1.06; p = 0.18), nonfatal Q-wave myocardial infarction in 1.04% and 1.29% (RR 0.80 with 95% CI from 0.60 to 1.07; p = 0.14) in the experimental and control groups, respectively. The secondary safety outcome (grade 3 or 5 bleeding by the Bleeding Academic Research Consortium criteria) occurred in 2.04% versus 2.12% of cases (RR

0.97 with 95% CI from 0.78 to 1.20; p = 0.77) in the experimental and control groups, respectively.

1 month of ticagrelor and aspirin combination, followed by ticagrelor monotherapy for 23 months was not superior to standard antithrombotic therapy in patients with percutaneous coronary intervention for coronary artery disease.

# Hot Line session IV (august 28, 2018)

The epidemiologic **PURE** study included the follow-up of 9.1 years of 138527 participants of the study (aged 35-70 years) from 50 countries, initially without any cardiovascular diseases. Participants were divided into five groups based on the quality of their diet. A PURE Healthy dietary score was developed based on foods associated with a lower risk of death in previous studies (fruit, vegetables, nuts, legumes, fish, dairy products and unprocessed meat). Each diet had its score based on the consumption quintiles of these protective components of the diet from 1 for the lowest quality to 5 for the highest quality food. The total diet score was defined as the summary of the consumption of seven components of the protective nutrition with a minimum score of 7 and a maximum score of 35. Researchers then compared the risks of cardiovascular disease and death in those with the highest quality diet (18 points or more) with the poorest quality diet (11 points or less).

The highest quality diet compared with the poorest quality diet, was associated with significantly lover risk of mortality (RR 0.75 with 95% CI from 0.68 to 0.83, p-trend in accordance to diet category <0.001) and tendency to lowering of the cardiovascular events (RR 0.91 with 95% CI from 0.81 to 1.02; p-trend in accordance to diet category = 0.0413).

Multiple factors have a positive impact on population's health in high-income countries and, consequently, high quality diet is more common in these countries.

The **FREED** study included patients aged 65 years and older with hyperuricaemia from >7 to ≤ 9 mg/dl and ≥1 cardiovascular risk factor (arterial hypertension, 2 type diabetes mellitus, glomerular filtration rate 30–60 ml/min/1.73m²) or resent cardiovascular events. All patients were recommended to change their lifestyle and were randomized to receive oral febuxostat 10 mg/day with possible dose increase to 40 mg (n=533) or allopurinol 100 mg/day (n=537), if serum uric acid was elevated, which lead to more significant decrease of average serum uric acid level in the first group (4.50 mg/dl versus 6.76 mg/dl;

p <0.001). During 36 months of therapy, the primary endpoint (death, caused by renal or cardiovascular disease; new or recurrent cerebrovascular event ischemic or haemorrhagic stroke or transient ischemic attack; new or recurrent non-fatal myocardial infarction, unstable angina; cardiovascular-related hospitalization; atherosclerotic disease, that needs treatment, including aortic aneurism or dissection or arteriosclerosis obliterans; kidney failure, detected by microalbuminuria or moderate proteinuria. progression of albuminuria or proteinuria, a twofold increase of plasma creatinine, development of kidney failure, or kidney death; atrial fibrillation; death from any other cause) occurred with the frequency of 23.3% in the febuxostat group compared with 28.7% in the control group (RR 0.75 with 95% CI from 0.59 to 0.95; p = 0.017), kidney failure occurred in 16.2% compared with 20.5% of cases (RR 0.745 with 95% CI from 0.562 to 0.987; p = 0.04), death, cerebrovascular event or non-fatal coronary event in 4.3 % compared with 4.9 % of cases (RR 0.861 with 95 % CI from 0.492 to 1.506; p = 0.60), respectively.

There was the J-shaped relationship between the development of clinical outcomes and the plasma uric acid level, the lowest risk of the primary endpoint events was observed at the plasma uric acid rate of > 5 to  $\leq$  6 mg/dL. Therefore, more pronounced decrease in the uric acid level during the febuxostat treatment compared with allopurinol treatment cannot be considered as an advantage.

The safety and effectiveness of smaller than 3 mm in diameter coronary vessels angioplasty with the balloon, covered by lipophilic medication paclitaxel was estimated during BASKET-SMALL 2 trial [14]. Patients with prescribed percutaneous coronary intervention were randomized to angioplasty with drug-coated balloons (n=382) or second-generation drug-eluting stents (n = 376). Dual antiplatelet therapy was performed in accordance with current guidelines. After 12 months the occurrence of primary endpoint (major adverse cardiac events — death from cardiac events, nonfatal myocardial infarction, and target vessel revascularization) occurred in 7.5% of cases in drug-coated balloons group and in 7.3% of cases in the versus drug-eluting stents group (RR 0.97 with 95% CI from 0.58 to 1.64; p = 0.9180). Probable or definite stent thrombosis occurred in 0.8% versus 1.1% of cases (RR 0.73 with 95% CI from 0.16 to 3.26) and major bleeding occurred in 1.1% versus 2.4% of cases (RR 0.73 with 95% CI from 0.16 to 3.26) in the paclitaxel-coated

balloons group and drug-eluting stents group, respectively.

The results of the study showed, that the use of paclitaxel-coated balloons can be the alternative for second-generation drug-eluting stents in the treatment of blocked arteries with small diameter.

The **VERDICT** trial estimated the hypothesis on the help of early (within 12 hours after first symptoms) invasive therapy and revascularization in patients with non–ST-segment elevation acute coronary syndrome.

Patients with acute coronary syndrome, ischemic changes on the electrocardiogram and biomarkers of myocardium necrosis received dual antiplatelet therapy, fondaparinux, beta-blockers and were randomized to early invasive therapy (n = 1.075) versus standard invasive therapy hours (n = 1.072). 32% of patients did not have coronary artery disease. Over a median follow-up time of 4.3 years, the primary endpoint (all-cause death, non-fatal recurrent myocardial infarction and heart failure or refractory myocardial ischemia) occurred in 27.5% of participants in the early group and 29.5% in the standard care group (RR 0.92 with 95% CI from 0.78 to 1.08; p = 0.29). According to pre-planned subanalysis the reduction in primary endpoint events occurred in a subgroup of patients with a GRACE score >140 (RR 0.81 with 95% CI from 0.67 to 1.00).

Among patients with non-ST-segment elevation acute coronary syndrome, early invasive therapy did not decrease the risk of all-cause death, non-fatal recurrent myocardial infarction and hospitalization for heart failure or refractory myocardial ischemia, however, among high-risk patients with GRACE score >140 early therapy seems to be reasonable.

# Hot Line session V (August 28, 2018)

High-sensitivity troponin measurements allow to use lower thresholds of this marker for the diagnosis of myocardial infarction, but it is not known whether it improves clinical outcomes. The **High-STEACS** [15] study included patients presenting to the emergency department with suspected acute coronary syndrome in Scotland. Hospitals were randomized for early (n=5) and 6 month later high-sensitivity troponin test (n=5) together with the gender-specific diagnostic threshold of  $99^{th}$  percentile (34 ng/l for men and 16 ng / l for women) in healthy population.

Among a total of 48.282 of observed patients, 10.360 (21%) had troponin I concentration higher than  $99^{th}$  percentile of diagnostic threshold, identified with standard or high-sensitivity troponin test. 17% of

patients were reclassified in the myocardial infarction group by the results of high-sensitivity test, which wasn't diagnosed by standard analysis, and only one-third of reclassified patients were diagnosed with myocardial infarction. The primary outcome (myocardial infarction or cardiovascular death) was registered in 15% of reclassified patients on the stage of test validation and in 12% on the stage of test realization within 1 year (adjusted realization chances ratio against the validation stage 1.10 with 95% CI from 0.75 to 1.61; p = 0.620).

Reclassified patients with high-sensitivity troponin I test after negative results of standard test have the same possibility of myocardial infarction and cardiovascular death during the next year.

Clinically stable patients with infectious endocarditis with aortic and/or mitral valve lesion, caused by streptococcus, Enterococcus faecalis, Staphylococcus aureus, or coagulase negative staphylococci, who underwent intravenous antibiotic therapy for more than 10 days, took part in the **POET** trial. Patients with stable condition (absence of fever, normalization of C-reactive protein level, absence of an abscess or other reasons for surgical intervention according to transesophageal echocardiography) were randomized to oral antibiotic therapy (n = 201), in 80% of cases on outpatient basis, with a median duration of 17 days (interquartile range from 14 to 25) or intravenous antibiotic therapy at the hospital (n = 199) with median duration of 19 days (interquartile range from 14 to 25). Patients from the group of oral antibiotic therapy had physical examination every 3-4 days to assess their condition, determine plasma levels of medications. During the follow-up pf 6 months, the primary outcome (all-cause death, unplanned cardiac surgery, embolic events, or relapse of bacteraemia with the primary pathogen) occurred in 9.0% of the oral administration group compared with 12.1% of the intravenous administration group (p = 0.40; satisfying the «not worse» criterion).

Switching to oral antibiotic therapy in stable patients with infective endocarditis can significantly reduce the duration of hospital stay and reduce the risk of new nosocomial infection. To reproduce the results of the POET study in practice, strict adherence of patient selection criteria and monitoring is required.

The slowing of aortic dilation in patients with Marfan syndrome is the important target during beta-blockers, angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers treatment. Patients aged from 6 to 40 years, who underwent be-

ta-blockers treatment in case of good tolerance (more than half of the patients), took part in the **AIMS** study. Patients were randomized to 150-300 mg of irbesartan once daily depending on body weight (n=104) or placebo (n=88).

Aortic diameter was assessed using transthoracic echocardiography at baseline and at yearly intervals for up to 5 years. While aortas in both groups continued to enlarge, researchers noted the rate of dilatation was slower in the irbesartan group compared with the placebo group (0.53 mm versus 0.74 mm per year, respectively; p = 0.030). The rate of adverse events, including the need for cardiac surgery to replace the aortic root was similar across the two groups. Irbesartan is well-tolerated by children, which makes it possible to use this medication for potentially delaying the need for elective surgery.

The next Congress of the European Society of Cardiology will be held on August 31st-September  $4^{th}$  2019 in Paris (France).

#### Conflict of Interest: None declared.

### References

- Spyropoulos A.C., Ageno W., Albers G.W., Elliott C.G., Halperin J.L., Hiatt W.R., et al. Rivaroxaban for Thromboprophylaxis after Hospitalization for Medical Illness. N Engl J Med 2018;379 (12): 1118–27.
- Bohula E.A., Wiviott S.D., McGuire D.K., Inzucchi S.E., Kuder J., Im K., et al. Cardiovascular Safety of Lorcaserin in Overweight or Obese Patients. N Engl J Med 2018;379 (12): 1107–17.
- Gaziano J.M., Brotons C., Coppolecchia R., Cricelli C., Darius H., Gorelick P.B., et al. Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial. Lancet 2018;392 (10152): 1036–46.
- McNeil J.J., Wolfe R., Woods R.L., Tonkin A.M., Donnan G.A., Nelson M.R., et al. Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly. N Engl J Med 2018 Sep 16. [Epub ahead of print].
- McNeil J.J., Woods R.L., Nelson M.R., Reid C.M., Kirpach B., Wolfe R., et al. Effect of Aspirin on Disability-free Survival in the Healthy Elderly.N Engl J Med 2018 Sep 16. [Epub ahead of print].
- McNeil J.J., Nelson M.R., Woods R.L., Lockery J.E., Wolfe R., Reid C.M., et al. Effect of Aspirin on All-Cause Mortality in the

- Healthy Elderly. N Engl J Med 2018 Sep 16. [Epub ahead of print].
- ASCEND Study Collaborative Group. Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus. N Engl J Med 2018 Aug 26. [Epub ahead of print].
- ASCEND Study Collaborative Group. Effects of n-3 Fatty Acid Supplements in Diabetes Mellitus. N Engl J Med 2018 Aug 26. [Epub ahead of print].
- Maurer M.S., Schwartz J.H., Gundapaneni B., Elliott P.M., Merlini G., Waddington-Cruz M., et al. Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy. N Engl J Med 2018;379 (11): 1007–16.
- 10. Zannad F., Anker S.D., Byra W.M., Cleland J.G.F., Fu M., Gheorghiade M., et al. Rivaroxaban in Patients with Heart Failure, Sinus Rhythm, and Coronary Disease. N Engl J Med 2018 Aug 27. [Epub ahead of print].
- Obadia J.F., Messika-Zeitoun D., Leurent G., lung B., Bonnet G., Piriou N., et al. Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation. N Engl J Med 2018 Aug 27. [Epub ahead of print].
- 12. Vranckx P., Valgimigli M., Jüni P., Hamm C., Steg P.G., Heg D., et al. Ticagrelor plus aspirin for 1 month, followed by ticagrelor monotherapy for 23 months vs aspirin plus clopidogrel or ticagrelor for 12 months, followed by aspirin monotherapy for 12 months after implantation of a drug-eluting stent: a multicentre, open-label, randomised superiority trial. Lancet 2018;392 (10151): 940-9.
- White W.B., Saag K.G., Becker M.A., Borer J.S., Gorelick P.B., Whelton A., et al. Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout. N Engl J Med 2018;378 (13): 1200–10.
- Jeger R.V., Farah A., Ohlow M.A., Mangner N., Möbius-Winkler S., Leibundgut G., et al. Drug-coated balloons for small coronary artery disease (BASKET-SMALL 2): an open-label randomised non-inferiority trial. Lancet 2018;392 (10150): 849-56.
- 15. Shah A.S.V., Anand A., Strachan F.E., Ferry A.V., Lee K.K., Chapman A.R., et al. High-sensitivity troponin in the evaluation of patients with suspected acute coronary syndrome: a stepped-wedge, cluster-randomised controlled trial. Lancet 2018;392 (10151): 919–28.
- Iversen K., Ihlemann N., Gill S.U., Madsen T., Elming H., Jensen K.T., et al. Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis. N Engl J Med 2018 Aug 28. [Epub ahead of print].