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Cardiology science in the pandemic era: scientific sessions of American College of Cardiology 2020/World Heart Federation: a virtual experience, March 28–30, 2020

Nauka w erze pandemii — wirtualne sesje naukowe *American College of Cardiology* i *World Heart Federation*, 28–30 marca 2020

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While watching the news on TV at the end of March this year, did you notice snapshots from Chicago where one of the largest convention centers — McCormick Place Convention Center — was turned into an isolation facility with hundreds of beds for COVID-19 (coronavirus disease 2019) infected patients? This was the very facility that was supposed to host the American College of Cardiology's 69th Annual Scientific Session & Expo and the World Heart Federation Congress. The pandemic did not prevent the organizers of this prestigious meeting from presenting to would-be visitors to the "Windy City" the latest results of clinical trials, attractive didactic sessions, enabling participation in poster sessions, and even a virtual walk through the exhibition of pharmaceutical and equipment companies. The whole of this year's congress took place for the first time ever online. We present a selection of the latest clinical trials that we believe deserve to be popularized.

The results of the **VICTORIA (A study of vericiguat in participants with heart failure with reduced ejection fraction)** program on the evaluation of the role of vericiguat in patients with heart failure with reduced ejection fraction (HFrEF) were presented by its principal investigator, Dr. Paul W. Armstrong of the University of Alberta, Canada. The aim of the study was to investigate whether vericiguat, a guanylate cyclase stimulator, will be well tolerated by patients with HFrEF and whether its use will reduce mortality and hospitalization rates due to cardiac decompensation. The study included 5050 persons who underwent randomization and were assigned to two treatment groups (vericiguat or placebo) in a 1:1 ratio. The inclusion criterion was hospitalization due to the deterioration of heart failure in adults within three to six months prior to selection for study participation or the need for extra-hospital use of intravenous diuretics for the same reason within the last three months. Patients taking intravenous inotropic positive drugs, treated with long-acting nitrates, other guanylate cyclase stimulators (e.g. riociguat) or phosphodiesterase inhibitors, or left ventricular assist devices were excluded from the study. More than three-quarters of the randomized patients are male, more than half are European, the average ejection fraction is 28.9 ± 8.3%, the majority are New York Heart Association (NYHA) class II patients, and the average time from the diagnosis of heart failure expressed in years is 4.8 ± 3.4. Scheduled 18 months of observation (from randomization to final visit), included vericiguat treatment lasting an average of 480 days — the median of actual observation time was 10.8 months. The drug tested was applied orally, initially at a dose of 2.5 mg, which in the case of good tolerance was gradually increased to 10 mg. After only three months, the beneficial effects of adding vericiguat to standard heart failure therapy were noticed; this effect lasted until the end of the program. The results of the analyses showed that in the vericiguat group, compared to the placebo group, a significant ($p = 0.019$), 10% reduction in the risk of a composite endpoint in the form of cardiovascular death or hospitalization due to decompensated heart failure was achieved — mainly due to a decrease in the second component frequency. The percentage of adverse events (hypotonia and fainting)

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was similar in the vericiguat and placebo group (9.1 vs. 7.9 and 4.0 vs. 3.5). Finding a new drug for patients with heart failure exacerbations was considered a major success for the sponsor Bayer and Merck as well as for the project sponsors the Duke Clinical Research Institute and Canadian VIGOUR Center [1].

Another important clinical trial was the **VOYAGER PAD** (**Vascular Outcomes Study of ASA Along with Rivaroxaban in Endovascular or Surgical Limb Revascularizations for Peripheral Artery Disease**), which concerned lower limb atherosclerosis patients after revascularization. 6564 patients underwent randomization — in one of the equal-sized arms the participants received 100 mg of acetylsalicylic acid (ASA) and a small dose of rivaroxaban (2 × 2.5 mg per day), and in the other one — ASA and placebo. The aim of the program is to evaluate the effects of treatment and safety of the therapy with the addition of rivaroxaban to the existing pharmacological therapy after interventional treatment of lower limb ischemia. The participants were predominantly male (74%) and their average age was 67 years. Two-thirds were treated using angioplasty with stent implantation, while the rest underwent surgical revascularization. The primary composite endpoint was the incidence of acute lower limb ischemia, the need for limb amputation, myocardial infarction, stroke, or death from cardiovascular causes. Treatment and observation lasted on average 28 months. In the ASA and rivaroxaban arm, compared to the arm without factor Xa inhibitor, a statistically significant decrease of 15% in the frequency of composite endpoints was noted (17.3% vs. 19.9% at p = 0.009). Major bleeding as defined in the TIMI classification or by the International Society on Thrombosis and Haemostasis (ISTH) was considered the main adverse event. When the former one was applied, the difference in the frequency of major bleeding between the arms of the study was not statistically significant (2.65% vs. 1.87%), while according to the ISTH classification, the frequency of bleeding increased in the rivaroxaban group by 42% (5.94% vs. 4.06%, p = 0.007). The study was summarized by the main researcher of the program, Professor Marc P. Bonaca of the University of Colorado School of Medicine (USA), stating that by adding rivaroxaban to the existing treatment strategy after interventions in the peripheral arteries, the risk of acute lower limb ischemia incidence was significantly reduced, and the amount of bleeding — although greater than in the group treated actively — did not translate into a greater amount of irreversible intracranial or fatal bleeding [2].

The results of the accompanying **CIAO-ISCHEMIA** (**Changes in Ischemia and Angina over One year among trial screen failures with no obstructive coronary artery disease on coronary CT angiography**) registry have become an interesting thread in the discussion following the publication of the ISCHEMIA results. This is an observation of the fate of a subgroup that was selected from among candidates for the ISCHEMIA trial, described in more detail in a report on the Scientific Sessions of American Heart Association 2019 [3], and which was composed of individuals who, despite a positive result of a stress test, were not diagnosed with coronary artery stenosis greater than 50% using imaging studies and were ultimately not included in the ISCHEMIA trial. As Dr. Harmony R. Reynolds, reporting on the CIAO study, said, it is a group of patients (usually females) often "sent on their way" by doctors who believe that non-critical coronary artery stenosis is a guarantee of the safe course of ischemic heart disease. A year-long observation of 208 patients (of which 66% were female) included in the CIAO study and 1,079 patients included in the ISCHEMIA trial due to the presence of ≥ 50% stenosis (of which 26% of were female) showed that despite a similar baseline outcome of the stress test, the course of coronary artery disease is even more worrying for the patient and the doctor than in the group of patients with ≥ 50% stenosis in coronary arteries. This is illustrated by the following figures: a higher percentage of patients in the CIAO group experienced recurrent angina pectoris once a week or more often than in the ISCHEMIA group within 12 months of the initial stress test (most often a stress echo test) — 17% vs. 4%, and a lower percentage reported no coronary artery pain within the last month — 41% vs. 62%. Interestingly, in half of the subjects, the follow-up stress echo test after a year showed a normal result, and in 45% — the result was the same as at the beginning of the study. In conclusion, Dr. H.R. Reynolds emphasized that it is important not to underestimate complaints about coronary artery pain, despite being aware of the lack of critical stenosis in these patients, as they are also patients with a significant cardiac risk, although lower than that of classical coronary artery disease [4, 5].

Another report concerns non-obstructive hypertrophic cardiomyopathy. Myokardia Inc. has proposed a new drug. It is a reversible inhibitor of cardiac-specific myosin called mavacamten and tested in **MAVERICK-HCM** (**A phase 2 study of mavacamten in adults with symptomatic non-obstructive hypertrophic cardiomyopathy**), presented by Dr. Carolyn Ho. This study focused on assessing the safety of the new molecule and its impact on biomarkers of high prognostic value: N-terminal pro-B-type natriuretic peptide (NT-proBNP) and troponin I. The percentage of patients with serious adverse events was lower in the actively treated group (10.3%) than in the placebo group (21.1%) — these were mainly episodes of atrial fibrillation/flutter. In 5 out of 39 actively treated patients, the study was discontinued due to a decrease in the left ventricular ejection fraction to ≤ 45% which was defined as a criterion requiring discontinuation of trial participation. The NT-proBNP concentration decreased (p = 0.0005)

after 16 weeks of taking mavacamten compared to the placebo. Similarly, a reduction was observed for troponin I — p = 0.009. Due to the fact that the NT-proBNP concentration so far has been well reflected in the degree of myocardial wall stress, and troponin I indicates myocardial damage, MAVERICK-HCM results suggest that mavacamten provides an innovative and promising treatment option for patients with non-obstructive hypertrophic cardiomyopathy [6].

In conclusion, we would like to mention that the scientific session of this year's edition of ACC/WHF 2020 was attended by the Team of our Department. Among the few Polish works included in the sessions was the presentation of the results of 4 years of cooperation with **ANGIONICA sp. z o.o.**, founded by the researchers of the Lodz University of Technology, the creators of a unique apparatus for measuring skin autofluorescence. As we have observed, the parameters describing autofluorescence induced by compounds involved in skin redox reactions correlate with the probability of sleep apnea both in cardiac patients and in healthy persons. From a practical point of view, the method carries the potential of a screening tool for respiratory distress during sleep. The report was of interest to congress reviewers, who qualified it for the Spotlight on Special Topics session: Innovation and Technology; and the entire study is approved for publication in one of the next issues of the "Cardiology Journal" [7].

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