Highlights from the TCT Congress 2019 in San Francisco

Vol. 18, N° 5 - 18 Dec 2019

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In over 30 years of existence, the Transcatheter Cardiovascular Therapeutics (TCT) symposium, the annual scientific meeting of the United States-based Cardiovascular Research Foundation (CRF) has become one of the leading international educational events specialising in interventional cardiology. Focusing on an increasingly wide range of evidence, data and techniques, Prof. Sigmund Silber offers E-Journal readers a review of the key findings from TCT 2019 which took place in late September 2019 in San Francisco, CA, USA.

Topic(s): *Interventional Cardiology;*

Introduction

Electrophysiology and non-invasive investigational methods traditionally play a minor role at TCT, which is dominated by coronary artery and structural heart disease, especially

valvular heart disease which we will look at in the following review of the 2019 meeting.

Coronary artery disease

Onyx ONE

First, the Onyx ONE study: the BioFreedom™ (Biosensors International, Singapore) stent has hitherto been regarded as the gold standard for patients with a high bleeding risk according to the LEADERS FREE study which showed that one month of dual antiplatelet therapy (DAPT) suffices in patients with a high bleeding risk.

The Resolute Onyx™ stent (Medtronic, Minneapolis, MN, USA) with its non-degradable polymer has now challenged the polymer-free BioFreedom. Nearly 2,000 patients with a high bleeding risk were randomised in 84 centres worldwide. With roughly 80% complex lesions, both groups had only one month of DAPT, followed by monotherapy, either with acetylsalicylic acid (ASA) or with a P2Y12 inhibitor. The primary endpoint (a combination of cardiac death, myocardial infarction [MI] or stent thrombosis) was the same in both groups after one year, though I find this relatively high at approximately 17%. The stroke trend was even somewhat higher at 2.1% with the BioFreedom than with the Onyx at 1.3%, but the power for this was insufficient. The bleeding complications were the same. What do we learn from this? The much-vaunted hypothesis that polymer-free is better than durable polymer again was not confirmed here. On the contrary, after one month, MI involving the target vessel occurred significantly more often with the polymer-free BioFreedom at 5.9% than with the durable polymer-coated Onyx at 3.7%. In addition, stents were significantly more successfully implanted with the Onyx than with the rather bulky BioFreedom.

IDEAL-LM

There was another head-to-head stent study, the IDEAL-LM study (LM standing for left main percutaneous coronary intervention [PCI]). The "old" XIENCE (Abbott Vascular, Santa Clara, CA, USA), with a non-degradable polymer, was compared

with the newer SYNERGY™ stent (Boston Scientific, Marlborough, MA, USA) with a degradable polymer. The XIENCE has a cobalt-chromium framework, while the SYNERGY is based on platinum-chromium. Both elute everolimus, but the XIENCE does so "all round" while the SYNERGY does so only on one side into the vessel wall. About 800 patients were included in the study (sponsored by Boston Scientific). The primary endpoint was the combination of overall mortality, MI or ischaemia-driven revascularisation of the target vessel after two years. Non-inferiority of the SYNERGY was achieved but it was extremely close at 88.5% versus 85.3%. Critics said that the tolerance margin was – expressed politely – unusually generous at 7.5%. Just a bit less tolerance and the SYNERGY would be significantly worse than the XIENCE. Importantly, the DAPT duration differed - 12 months with the XIENCE and four months with the SYNERGY. There was therefore a trend to more stent thrombosis with the SYNERGY. The details will have to be examined more closely.

TWILIGHT

Apropos the duration of DAPT, this brings us to the TWILIGHT study. ASA has been on the hit list for years but so far no study has really succeeded. This was the aim of the TWILIGHT study - comparison of DAPT with ASA + ticagrelor versus ticagrelor monotherapy. This study was sponsored by AstraZeneca, which is no surprise. About 7,000 high-risk patients with at least one clinical and one angiographic risk parameter for an increased ischaemic and increased bleeding risk were randomised. The primary aim was the superiority of ticagrelor monotherapy with regard to bleeding complications. However – and this is important – the study enrolled only patients who had tolerated DAPT with ticagrelor during the first three months after stent implantation, i.e., no significant ischaemic or bleeding events had occurred. Patients were randomised three months later, not immediately after PCI in the clinic. The result of the primary endpoint was as expected: significantly fewer bleeding episodes with ticagrelor monotherapy (4%) than when in combination with ASA (7.1%). However, the secondary endpoints of ischaemic events such as death, MI or stroke were exciting: gratifyingly, these were identical at 3.9% each. Can this be applied generally to routine practice? Not really, because 2/3 had acute coronary

syndrome (ACS), where STEMI was excluded, i.e., 1/3 of the patients had stable coronary heart disease (CHD) (now called chronic coronary syndrome [CCS]), but ticagrelor is not licensed for CCS patients, quite apart from the fact that the primary endpoint was no longer significant in these patients.

ISAR-REACT 5

So – do we now stop ASA in all patients after NSTEMI who have tolerated aspirin + ticagrelor well for three months? We could consider this if it had not been for ISAR-REACT 5: I have already reported on this from the ESC in Paris. You will recall that one year after ACS the primary efficacy endpoint (MI, stroke, death) was significantly better for prasugrel at 6.9% than for ticagrelor at 9.3%. Major bleeding episodes did not differ significantly. TWILIGHT should really be repeated now with prasugrel, but prasugrel is now generic - so no company is interested.

RUC-4

What really impressed me among the antithrombotic substances is a new drug named RUC-4, which has been tested for the first time in humans. An injection of less than 1 ml is given subcutaneously, which immediately produces 80% inhibition of platelet aggregation and at the same time also inhibits fibrinogen. Patients after MI could always carry this injection and have it injected by an emergency physician if reinfarction is suspected, or perhaps even inject themselves as they are already familiar with their individual infarct symptoms. Fortunately, the duration of action is short, but it should last until they reach hospital. We will hopefully hear a lot more about RUC-4.

PROTECT III

Apropos high-risk patients with PCI, the results of the PROTECT III study were presented for the first time. This was a post-marketing observational study conducted in the USA in about 900 patients to date who had protected PCI with the Impella® pump (Abiomed, Danvers, MA, USA) in two different strengths. This confirmed that the pump protects not only the

heart but also the kidneys during PCI, because acute renal failure occurred significantly less often, probably due to protection of renal perfusion.

Structural heart disease

As regards the mitral and tricuspid valves, there was nothing very new. A lot of studies are currently ongoing, and their results are hotly anticipated.

SCOPE I

There was a real sensation with the TAVI valves - the SCOPE I study. This was a head-to-head comparison between the self-expanding ACURATE neo™ nitinol valve (Boston Scientific) versus the balloon-expandable SAPIEN 3 cobalt-chromium valve (Edwards Lifesciences, Irvine, CA, USA). The aim was the non-inferiority of the ACURATE neo valve, so logically Boston Scientific was the sponsor, now called the "funder". About 700 patients were randomised. Echocardiography yielded better haemodynamic results for the ACURATE neo valve; the rate of new pacemaker implantations was the same in both groups at 10%. The primary endpoint was a combination of many different complication parameters. This was markedly higher for the ACURATE neo at 23.7% than for the SAPIEN 3 at 16.5%, so the aim was not reached, i.e., the SAPIEN 3 is better than the ACURATE neo valve. In addition, the procedure time and contrast agent volume were significantly greater with the ACURATE neo valve, with a significantly greater incidence of renal failure. One could now argue that a first-generation valve was here compared with a third-generation valve, which is not fair, but this was known from the start – so why are such studies performed? There is now the improved ACURATE neo 2 valve; we await the randomised results with this new valve.

Conclusion

In Onyx ONE, the Onyx coronary stent with its non-degradable polymer was non-inferior to the polymer-free BioFreedom drug-eluting stent (DES) in patients with high bleeding risk and a DAPT duration of one month only. IDEAL-LM compared the

XIENCE DES with its non-degradable polymer to the SYNERGY DES with its degradable polymer in patients with left main PCI. The non-inferiority of the SYNERGY was reached. TWILIGHT compared ticagrelor monotherapy versus DAPT (ASA + ticagrelor). Enrolling only patients having tolerated this DAPT well for three months, the primary endpoint of the monotherapy was reached. SCOPE I compared two different TAVI valves, the self-expanding ACURATE neo versus the balloon expandable SAPIEN 3. The non-inferiority of the ACURATE neo valve, however, was not reached.

Notes to editor

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The author has no conflicts of interest to declare.