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Late-Breaking REDUCE Trial Data Demonstrate Non-inferiority of 3 vs 12 months Dual Antiplatelet Therapy in Acute Coronary Syndrome Patients treated with the COMBO™ Stent

One-year results from the REDUCE trial reported at TCT 2017

Denver, USA, November 1, 2017 – OrbusNeich has reported results from the REDUCE trial today in the Late-Breaking Clinical Trial session at the 29th annual Transcatheter Cardiovascular Therapeutics (TCT) scientific symposium, providing fresh insights into the optimal treatment of patients with acute coronary syndrome (ACS) using the COMBO Dual Therapy Stent.

REDUCE is a physician-initiated, prospective, multicenter, randomized study, designed to demonstrate non-inferiority of a strategy of short-term (three months) dual antiplatelet therapy (DAPT) as compared to standard 12-month DAPT in patients with ACS treated with a COMBO stent. The trial found no difference in the primary endpoint between three and 12 months DAPT (8.2% vs. 8.4%, $P_{noninferiority}<0.001$; $P_{superiority}=0.88$) in the intent to treat (ITT) population. COMBO is the only stent with prospective randomized controlled trial-based evidence, to support such a strategy in an ACS population.[1]

The optimal duration of DAPT in ACS patients treated with DES is still under debate. The potential benefits of long-term DAPT in avoiding thrombotic complications may be counterbalanced by a higher risk of major bleeding complications. Per U.S. and European guidelines, DAPT is typically continued for at least 12 months following percutaneous coronary intervention (PCI) with drug-eluting stents (DES) or bare metal stents, primarily based on the CURE trial that was conducted 20 years ago, and the use of first generation DES. Therefore, REDUCE provided an opportunity to explore different DAPT regimens and a new generation stent.

“The REDUCE trial shows that among ACS patients treated with a COMBO stent, three months of DAPT is non-inferior to 12 months of DAPT, and this is consistent for all pre-specified subgroups,” said Harry Suryapranata, MD, PhD, Professor of Interventional Cardiology at Radboud University Medical Center in Nijmegen, The Netherlands, and one of the Principal Investigators who presented the data at TCT. “Therefore, this strategy could be considered if needed, even in an ACS population. Future larger trials are needed to further investigate and confirm the safety of short-term DAPT regimen in ACS patients, particularly, in the era of new adenosine diphosphate (ADP) antagonists and new generation DES.”

The overall incidence of the primary endpoint event (a composite of all-cause mortality, myocardial infarction, stent thrombosis, stroke, target vessel revascularization, moderate and major bleeding (BARC II, III or V)) was low at 8.3% in comparison to the original estimate of 12% based on contemporary trials. Furthermore, the results were consistent across all subgroups (age, gender, STEMI vs non-STEMI, geographic region and diabetes) without any significant statistical interaction. A pre-specified landmark analysis of the primary outcome from 3 months (i.e. the intended deviation

of antiplatelet therapy between the groups) out to 360 days did not reveal significant differences either.
Among the secondary endpoints, major bleeding rates were similar among the treatment arms (2.5% vs. 3.0%, P=0.54), with non-significantly different rates of overall mortality (1.9% vs. 0.8%, P=0.07), cardiac mortality (1.1% vs. 0.4%, P=0.13), and definite/probable ST (1.2 % vs. 0.4%, P=0.08), although the study was not powered to assess these individual endpoints.

COMBO was the world's first dual therapy stent, and since its launch in 2013 has become a key product within OrbusNeich's extensive portfolio of unique products that have changed the lives of patients and their families around the world.

About the REDUCE Trial
The REDUCE study [NCT02118870] was conducted in 36 hospitals in Europe and Asia, enrolling a total of 1496 ACS patients, who were successfully treated with a COMBO stent. Patients were randomized during index hospitalization (before discharge), in a 1:1 ratio, to either 3-month DAPT or to 12-month DAPT. The protocol defined primary clinical endpoint of the REDUCE study was a composite of all-cause mortality, all myocardial infarction, stent thrombosis, stroke, target vessel revascularization, and moderate or severe bleeding (BARC II, III or V) within 360 days post randomization. Clinical follow-ups were scheduled at 3 months, 6 months and 1 year and will continue out to 2 years post randomization.

About the COMBO Dual Therapy Stent
COMBO is the world's first and only dual therapy stent designed to repair vessel injury and regenerate endothelium, fostering natural, true vessel healing. It does this by accelerating endothelial coverage and controlling neo-intimal proliferation. This is done through a combination of the proven endothelial progenitor cell (EPC) capture technology and a sirolimus drug elution, delivered from a bioresorbable polymer that is completely degraded within 90 days. OrbusNeich's patented EPC capture technology promotes the accelerated natural healing of the vessel wall after the implantation of blood-contact devices such as stents. The technology consists of an antibody surface coating that captures EPCs circulating in the blood to the device to form an endothelial layer that provides protection against thrombosis and modulates restenosis.

About OrbusNeich – Pioneers in life-changing technologies
OrbusNeich is a global pioneer in the provision of life-changing vascular solutions and offers an extensive portfolio of products that set industry benchmarks in vascular intervention. Current products are the world's first dual therapy stents, the COMBO Plus and COMBO Dual Therapy Stents, together with stents and balloons marketed under the names of Azule™, Scoreflex™, Sapphire™ II, Sapphire™ II PRO and Sapphire™ II NC, as well as products to treat peripheral artery disease: the Jade™ and Scoreflex™ PTA balloons. OrbusNeich is headquartered in Hong Kong and has operations in Shenzhen, China; Fort Lauderdale, Florida, USA; Hoevelaken, The Netherlands; and Tokyo, Japan. OrbusNeich supplies medical devices to physicians in more than 60 countries. For more information, visit www.OrbusNeich.com

Reference
1. Suryapranata H, De Luca G. REDUCE: A Randomized Trial of 3-Month vs 12-Month DAPT After Implantation of a Bioabsorbable Polymer-Based Metallic DES with a Luminal CD34+Antibody Coating in Patients with ACS. Late-breaking oral presentation at the 29th annual Transcatheter Cardiovascular Therapeutics scientific symposium, November 1, 2017.

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