CX Daily News

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Good day for drug-coated balloons, swirling flow stents and drug-eluting stents at CX

Yesterday's Peripheral Arterial Challenges session saw a host of new developments being presented and a lift for drug-coated balloons (DCBs), swirling flow stents and drug-eluting stents.

Drug-coated balloons are in the ascendancy for moderate length lesions, as is the support for pretreatment for calcified or severe disease by predilation or atherectomy/debulking followed by DCB to discourage restenosis. Yet, the treatment of long lesions remains a challenge for interventionists. Various endovascular approaches such as the use of DCBs, atherectomy followed by drug-coated balloon, sequential stents and the use of a single long stent are being used in the treatment of long lesions, but surgical bypass still has a place for these patients, the voting results showed. Swirling flow in stents is here to stay, as are drug-eluting stents, but costs remain a factor and members of the CX audience also expressed an interest in and are awaiting three- to five-year data for DCB.

The day began by trying to avoid any intervention by exercise, best medical treatment and smoking cessation. Presenters showed that supervised exercise is effective, but costly and that patients do not submit to it.

Vessel preparation before use of DCBs gains further support

A vast majority, 87% of the Charing Cross audience, believes in the idea of pretreating superficial artery lesions before the use of drug-coated balloons. In 2013, just 32% supported the idea of pretreatment, and this number has steadily grown to 43% in 2014 and 77%, last year. Pretreatment of calcified lesions or severe disease can be approached in various ways including by predilatation, atherectomy or debulking.

Speaking on the rationale, evidence and indication for plaque modification before DCB, Erwin Blessing, Heidelberg, Germany, said that it is observed that DCBs work less well in heavily calcified lesions, meaning that there could be improved penetration of drug after lesion preparation or removal.

Then, Stephan Duda, Berlin, Germany, explained that pre-dilatation was important to protect DCB performance, to best assess lesion type and to potentially reduce need for post-dilatation and stenting. It is highly recomended in presence of calcium and in total occlusions, he said.

New data

Subsequently, new data were presented on the use of DCB for increasingly complex patients and lesions. The data included the one-year results from the chronic total occlusion imaging cohort from the IN.PACT Global Study and the two-year gender and diabetic subgroup analyses from the pivotal IN.PACT SFA Trial that used the IN.PACT Admiral DCB (Medtronic) and the 12-month interim IL-LUMENATE Global Study that used the Stellarex DCB (Spectranetics).

New data from the chronic total occlusion imaging cohort of the real-world, IN.PACT Global Study were presented by Gunnar Tepe, Rosenheim, Germany. Chronic total occlusions are typically characterised by calcified plaque, which often result in complete (or nearly complete) obstruction of blood flow through the artery.

As part of the 1,535 patients enrolled across 27 countries in IN.PACT Global Study, 126 patients with an average lesion length of 22.9cm were included in the chronic total occlusion imaging cohort analysis. The primary patency rate was 84.4% and the clinically-driven target lesion revascularisation rate (CD-TLR) was 12.2% at one year. Additional safety and efficacy outcomes included low rates of all-cause mortality (4.3%), thrombosis (4.3%) and no occurrences of major target limb amputation (0%). Previous reports from the IN.PACT Global Study demonstrated effectiveness in complex in-stent restenosis lesions and long lesions in the superficial femoral artery through one year.

"Despite the complexity of these challenging and complex long chronic total occlusion lesions, the outcomes were excellent and remarkably consistent to that of the overall cohort. These results show the effectiveness of the IN.PACT Admiral drug-coated balloon as a primary treatment in this complex lesion subset," concluded Tepe.

IN.PACT SFA Trial investigators sought to better understand the treatment effect of the IN.PACT Admiral DCB compared to balloon angioplasty in females and patients with diabetes, patient populations whose outcomes have historically not fared as well as males and non-diabetic patients, respectively. Peter Schneider, Honolulu, USA, presented outcomes from the IN.PACT SFA Trial gender and diabetes subgroups, which showed superior and durable outcomes for the IN.PACT Admiral DCB compared to balloon angioplasty across both subgroups at two years.

The IN.PACT SFA Trial enrolled 331 patients, 113 of which were women, at 57 sites across Europe and the United States. At two years, females who were treated with the IN.PACT Admiral DCB demonstrated a higher primary patency rate compared to balloon angioplasty arm (76.7% vs. 42.3%, p<0.001). Similarly, women in the IN.PACT Admiral DCB arm had a lower clinically-driven target lesion revascularisation rate compared to the balloon angioplasty arm (13.2% vs. 38.2%, p=0.005). The beneficial treatment effect seen in female patients who were treated with the IN.PACT Admiral DCB was consistent with the male population, who had a primary patency rate of 80.2% in the IN.PACT Admiral DCB arm, compared to 53.7% in the balloon angioplasty arm (p<0.001), and a 6.9% CD-TLR rate

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vs. 23.6% (p=0.002), respectively.

Among patients with diabetes, those treated with an IN.PACT Admiral DCB had significantly higher rates of primary patency (73.3% vs.45.8%, p<0.001) and CD-TLR (10.7% vs. 29.4%, p=0.010) compared to balloon angioplasty. Similarly, in the non-diabetes subgroup, the IN.PACT Admiral DCB arm showed consistent and significant improvements in primary patency (82.5% vs. 54.5%, p<0.001) and CD-TLR (8.1% vs. 27.3%, p=0.002).

Twelve-month interim ILLUMENATE Global Study data show 84.7% primary patency rate

Thomas Zeller, Bad Krozingen, Germany, presented 12-month interim data from the ILLUMENATE Global Study. The ILLUMENATE Global Study is a prospective, multicentre, single-arm study designed to assess the clinical performance of the Stellarex drug-coated balloon (Spectranetics) in the superficial femoral and popliteal arteries.

According to Zeller, interim results from the first 153 of 371 patients enrolled demonstrate a primary patency rate at 12 months of 84.7%. These results are consistent with the results of the ILLUMENATE First-In-Human Study, validating the early results of the Stellarex DCB.

The ILLUMENATE Global Study is being conducted with angiographic and duplex ultrasound core lab assessments, as well as an independent clinical events committee (CEC) to adjudicate adverse events. Key interim results, fully core lab and CEC adjudicated from the first 153 patients (174 lesions) at 365 days include an 84.7% primary patency rate and a 91% freedom from clinically driven target lesion revascularisation rate (CD-TLR). Further, 84% of patients experienced an improvement in their walking distance score.

"The 12-month interim results of the ILLUMENATE Global Study demonstrate consistency with the promising results observed in the previously published ILLUMENATE First-In-Human Study," said Zeller, global principal investigator of the ILLUMENATE Global Study. "Overall, these interim results compare well with the highest DCB patency rates reported in comparable studies with similar patient populations, but with a lower level of drug concentration," he added.

New pre-clinical data presented by Renu Virmani, Gaithersburg, USA, demonstrated that IN.PACT Admiral DCB's coating demonstrates sustained paclitaxel in tissue over time, facilitating an extended retention of drug in tissue available for a sustained antirestenotic effect (read more on page 20).

Swirling flow

Peter Gaines, Sheffield, UK, made the case for why inducing swirling flow improves the outcomes from endovascular procedures. "Blood flow is naturally not laminar, but swirling. Veryan's biomimetic stent, Biomimimcs 3D, is capable of inducing swirling flow. [In] The MIMICS randomised trial, primary patency significantly improved with a helical stent rather than a straight stent," he said.

Gunnar Tepe

Thomas Zeller

Gaines then said that the principal driver for cost, the clinically-driven target lesion revascularisation rate, was reduced by implanting a helical stent. In comparing the results obtained with the helical stent, with those obtained by contemporary drug-eluting studies and Supera (Abbott), Gaines showed that the patency at 12 months and clinically-driven target lesion revascularisation rate at 24 months, as obtained with the helical stent is comparable to the results achieved with drug-eluting technologies.

ZILVER PTX

Michael Dake, Stanford, USA, then presented on the five-year results of ZILVER PTX showing the value of stent drug elution. ZILVER PTX is a prospective, multinational, randomised controlled trial that evaluated the durability of a paclitaxel-coated drug-eluting stent in patients with superficial femoral artery lesions. Outcomes reported here compare the results obtained with Zilver PTX (Cook Medical) vs. standard care, consisting of percutaneous transluminal angioplasty and provisional bare metal stent placement, as well as the direct comparison of provisional drug-eluting stents versus provisional bare metal stent placement.

The five-year results showed that the reduction in reintervention and restenosis for patients treated with the drug-eluting stents was greater than 40% compared to standard care and to bare metal stents. This included a five-year freedom from target lesion revascularisation rate of 83.1% for the drug-eluting stents compared to 67.6% for standard care (p<0.01). The clinical benefit with the drug-eluting stents was also superior to standard care (79.8% vs. 59.3%, p<0.01). The five-year primary patency rate for provisional drug-eluting stent was 72.4% compared to 53% for provisional bare metal stenting (p=0.03). Clinical benefit with provisional drug-eluting stents was also superior to provisional bare metal stents (81.8% vs. 63.8%, p=0.02).

"The data also demonstrate the long-term benefit of drug-eluting stents use over bare metal stent placement. Therefore, as one of the largest randomised controlled trials of an endovascular device to treat patients with femoropopliteal artery disease, and the first to provide five-year follow-up, ZILVER PTX provides long-term data and insights regarding the durability of endovascular therapies of the femoropopliteal arteries for patients suffering from claudication or critical limb ischaemia," said Dake.

The CX audience also heard presentations on how radial strength and stent design can overcome calcified lesions (Peter Goverde, Antwerp, Belgium) and the value of polymer release and paclitaxel combination with drug-eluting stents (Juan Granada, Orangeburg, USA).

For long lesions a subintimal stent can be useful in bailout situations

Delegates heard various endovascular technologies being employed to meet the challenges in treating long peripheral arterial disease lesions. Lesions longer than 15cm, which are often calcified, can offer significant challenges for the endovascular interventionist. After hearing about various treatment options such as drug-coated balloons, atherectomy plus drug-coated balloon, the sequential use of stents, use of a single long stent and subintimal stenting to treat these lesions, a majority of the CX audience voted that the best strategy for the treatment of more than 25cm femoropopliteal lesions is bypass. Interestingly, 60% of those polled voted in favour of the surgical option for long lesions. Fifteen per cent voted in favour of employing drug-coated balloons for provisional stenting and 12% backed the use of vessel preparation followed by drug-coated balloon.

Michael Jaff, Boston, USA, presented on long lesion femoropoliteal artery treatment with drug-coated balloons. "Real-world atherosclerotic peripheral artery stenoses and occlusions are challenging given that they are longer, more diffuse, and often include significant calcification. Nitinol self-expanding stents, with or without drug coating, have classically been studied in lesions shorter than 15cm. The risk with longer lesions, often requiring multiple overlapping stents extending into the distal superficial femoral and/or proximal popliteal artery is stent fracture, which in certain situations, results in greater in-stent restenosis," he noted.

Jaff highlighted that drug-coated balloons have offered an important advance as a strategy for endovascular treatment of peripheral artery disease, but noted that knowledge of the utility of these devices in lesions longer than 15cm is limited.

"The IN.PACT SFA long lesion cohort, presented at EuroPCR 2015 included 164 lesions. In this report, the mean lesion length was 26.4+8.6cm. All patients were treated with the IN.PACT Admiral DCB, and the cohort included 60% chronic total occlusions. The

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Early data from venous stent trials "very promising"

Two presentations yesterday in the Venous Challenges Main Programme session have demonstrated the value of dedicated venous stents, with interim results from two studies in patients with symptomatic iliofemoral venous outflow obstruction showing symptom improvement 12-months post stent placement.

Data from the VIRTUS and VIVO-EU trials were reported.

Feasibility data from the VIRTUS study were presented for the first time at Charing Cross yesterday by Lowell Kabnick (NewYork, USA). Kabnick maintained that based on the feasibility data, dedicated venous stents are necessary as the early results are very promising, with 12-month primary patency >90%. He added that safety and efficacy results appear to be superior to published literature.

According to Kabnick, the Vici Venous stent (Veniti) has a high crush resistance, a closed cell design, end-to-end shape and strength 9F delivery system. The Vici Venous stent is available in lengths 60, 90 and 120mm and diameters 12, 14 and 16mm.

The objective of the trial is to assess the safety and effectiveness of the Vici Venous stent in achieving patency of target venous lesion through 12 months post stent placement. Safety is determined by major adverse events at 30 days and effectiveness by primary patency at 12 months. The prospective, multicentre, single arm non-randomised trial is being conducted at up to 45 sites worldwide. The trial will enrol 200 patients with clinically significant chronic non-malignant obstruction of the iliofemoral venous segment.

Yesterday, Kabnick presented 12-month post stent placement data from the feasibility cohort of the first 30 patients treated with the device. He reported that lesion stenosis is calculated by venogram as mandated by the US Food and Drug Administration (FDA) and ≥50% stenosis is required for patient inclusion.

According to Kabnick, the feasibility data show 85.2% lesion stenosis pre-procedure as determined by IVUS, and 1.8% lesion stenosis post procedure as determined by IVUS. Additionally, there was only one patient with >50% stenosis at 12 months post stent placement.

Lowell Kabnick on the podium

In terms of the primary safety endpoint at 30-days post stent placement, Kabnick reported that there were no composite major adverse events.

As it relates to published trials, he explained that the VIRTUS feasibility cohort seems to be better or equal to published effectiveness and safety of iliofemoral venous stenting.

Looking at 12-month status post stent placement, Kabnick added that 85% of the population showed symptomatic improvement (VCSS ≥2) and 59% had substantial symptomatic improvement (VCSS ≥4). Further, he stated that univariate analysis of predictors of substantial symptomatic improvement show that "there was no significant difference, however, minimum lumen diameter by Venogram (substantial improvement: 2.4±2.2; no substantial improvement: 5.5±4.5; p=0.075) may approach statistical significance with further look".

Kabnick concluded stating, "In terms of the feasibility trial, dedicated venous stents are necessary and the early results are very promising. Twelve-month primary patency rates in the feasibility cohort are >90%."

Later in the session, Gerard O'Sullivan (Galway, Ireland) presented interim results from a European study of the Zilver Vena Venous Stent (VIVO-EU). He reported that stent placement resulted in a greater than 100% luminal diameter improvement at procedure.

VIVO-EU, a prospective, non-randomised, multicentre study, is intended to evaluate the Zilver Vena stent (Cook Medical) in the treatment of symptomatic iliofemoral venous outflow obstruction. Patients participating in the study are followed after their procedure to monitor complication rates and improvement of symptoms.

The Zilver Vena Venous Stent, CE marked in 2010, is a self-expanding nitinol stent available in 14 and 16mm diameters and 60, 100, and 140mm lengths. The stent is intended for use in the iliofemoral veins for the treatment of symptomatic venous outflow obstruction.

The study has reached full enrolment, with final follow-up anticipated in summer 2016. Thirty-five patients with symptomatic iliofemoral outflow obstruction (ie., CEAP "C" ≥3 or VCSS pain score ≥ 2) were enrolled into the study. Consistent with this patient population, the patients in this study had predominantly left-sided lesions (94%).

In terms of major adverse events, O'Sullivan reported a clinically-driven reintervention for occlusion at 155 days post-procedure and a symptomatic pulmonary embolism one day post-procedure, categorised as possibly related to the study procedure and managed by a change in medication. No additional clinical sequelae was reported.

He explained that at procedure, Zilver Vena stent placement resulted in a more than two-fold improvement in the vessel minimum lumen diameter. Available clinical, data, O'Sullivan said, "suggest that stent placement corresponds to improved clinical symptoms as measured by VCSS, VDS, CIVIQ, and CEAP 'C', suggesting that the Zilver Venous stent is beneficial to patients".

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primary patency rate was a surprising 90.1%, with a CD-TLR rate of only 6%. Of note, 40% of patients required a bailout stent.

This is in contrast to another series presented in 2015 by Micari *et al* using the same DCB. In this series of 105 lesions where the mean lesion length was 25.1+7.9cm, the primary patency rate was 83.5%. However, the bail out stent rate was only 10.5%. Zeller *et al* published a series comparing DCB vs. the Zilver PTX drug-eluting stent where the mean lesion length was around 19.5cm. The DCB in this series was the IN.PACT Admiral DCB, and the bailout stent rate was 18.3%. In this long lesion comparative trial, there was no significant difference in primary patency between the DCB (23.9%) and drug-eluting stent (30.4%).

"There is little doubt that DCB will continue to have a major role in superficial fermoral artery/popliteal artery endovascular intervention, and as we expand our trials to evaluate their role in more complex, long peripheral artery disease lesions, we will gain a greater understanding of the effects on patency, clinical outcomes, and cost-effectiveness," he said.

Then, Luis Mariano Palena, Abano Terme, Italy, presented on subintimal stent use for critical limb ischaemia and biphasic wave forms.

Amman Bolia, Leicester, UK, who devised the subintimal angioplasty technique with his colleagues in 1988, stood up to comment that when he performs subintimal angioplasty, also known as the Bolia technique, he ensures that he gets good haemodynamic flow in order to achieve good patency. Further, he referred to a study from Oslo that showed, that a like a bypass graft, the subintimal channel is a new channel and needs surveillance as it may develop a stenosis, which can be treated before occluding. "The point I am making is that the channel needs surveillance. Most importantly, if you put in a stent and it develops a stenosis or an occlusion, you have really ruined that case, whereas plain subintimal angioplasty is repeatable, and many times over," Bolia said. In reponse to chairman Roger Greenhalgh who asked whether Bolia would put a stent in after a subintimal angioplasty procedure, the latter clarified that the only situation in which he would do that was if there was a haemodynamic problem, a recoil, which occurred in about 1% of cases."

Sequential stents for long lesions

Donald L Jacobs, St Louis, USA, noted that multiple stents being placed in the superficial femoral artery has been identified as a risk factor for decreased patency in several studies and that stent overlap has been noted to be a factor in precipitation of stent fractures, both being associated with recurrent symptoms and decreased patency.

"Single long stents have been demonstrated to have some improved patency compared to multiple overlapping stents as far as stent fractures are concerned and single long stents have shown a trend to increased patency over multiple overlapping stents in controlled studies but the difference is not statistically significant (Durability 200 Protégé stent trial, Medtronic)," Jacobs said.

He further reported that it has been long accepted that the longer the stented segment, the lower the patency. "However, it has been reported that the stented length of the vessel does not correlate to patency of Supera stents (Abbott) in several studies. This combined with the finding of a near complete absence of fractures with the Supera stent would indicate that multiple stent use with the Supera may have less impact on patency.