APERTO DCB "promising" for central venous stenosis in haemodialysis patients

In a Q&A with *LINC Today*, Michael Lichtenberg, angiologist at Klinikum Hochsauerland GmbH, Arnsberg, Germany, discussed the APERTO® OTW (over-the-wire) drug coated balloon (DCB) currently being trialled in haemodialysis patients with central venous stenosis (CVS) in a bid to improve patency of arteriovenous fistulas (AVFs).

In September 2020 the prospective observational multicentre trial APERTO CVS[1] began recruiting its targeted 80 dialysis patients diagnosed with CVS or restenosis at four centres in Germany and two in Switzerland. Its first results will emerge next year.

What is the rationale behind the APERTO CVS study?

There are now millions of people worldwide receiving replacement renal dialysis and this number has been projected to double by 2030[2]. We currently have more than 100,000 patients on haemodialysis in Germany, with a disease incidence of 2% per year. These numbers are rising due to an increase in patients with cardiovascular disease, especially those who have diabetes and who are smokers.

Most of these patients rely on AVFs. The real problem with these after standard balloon angioplasty is that there is a very high rate of CVS and repeated restenosis in a very short time – it can happen in a matter of weeks or months (about 70–80% recurrence at six months follow-up).

Of course, stenting could be an option, but the problem is that stents also tend to develop restenosis and occlusion too, and treatment to reopen a stent is more challenging than reopening a native vessel that you have just ballooned. Stenting may also not always be suitable due to the stenosis position. Restenotic lesions are characterised by fibroblastic proliferation within the venous intima, therefore it makes complete sense to use a device with an antiproliferative effect such as paclitaxel, reducing the risk of restenosis and prolonging time of freedom from reintervention for patients and avoiding the potential risks of stenting.

> "APERTO OTW is the first high-pressure DCB specifically designed for the management of AVF stenosis."
>
> **Michael Lichtenberg**

There have been a number of promising studies[3] which looked at using paclitaxel DCBs to prevent CVS, but it was felt that larger studies were needed. Paclitaxel is a very good option for preventing stenosis and restenosis, but not every DCB is effective; it depends on the coating technology used. Recently published results of APERTO OTW RCT[4], which showed safety and efficacy of the APERTO OTW in treating native AVF lesions compared to treatment with high pressure balloon alone, gave us some evidence for the efficacy of APERTO OTW in other vein lesions and has encouraged us to study the safety and efficacy of the device in the CVS population.

What makes the APERTO OTW particularly innovative for meeting the challenges of AVF CVS?

APERTO OTW is the first high-pressure DCB specifically designed for the management of AVF stenosis. The device uses paclitaxel as an antiproliferative and anti-inflammatory substance to prevent

Continued on page 5

Continued from page 4

restenosis in AVFs, but also uses a unique non-crystalline stable coating technology called SAFEPAX®, an ammonia salt excipient with the lowest reported drug wash-off rate during the procedure, which helps ensure paclitaxel is delivered to the target lesion. The coating is homogenous and elastic, reducing the risk of microembolism. This coating matrix is patented by Cardionovum GmbH, a German Company with headquarters in Bonn specialised in manufacturing innovative drug coating technologies, including DCBs and drug-eluting stents (DESs). The device is designed with a short shaft on one side which makes the handling easier (40 cm for AVF, and 80 cm for the 9 and 10 mm, which are frequently used for treatment of the CVS).

> "Paclitaxel may have a major role to play in preventing restenosis of central veins in patients on haemodialysis."
>
> **Michael Lichtenberg**

What is the design of the APERTO CVS study?

Previous experiences with paclitaxel DCBs[3] used for CVS treatment reported encouraging results with significant reduction of intervention-free period compared to standard percutaneous angioplasty and an increase of primary patency duration compared to historical data. But these were limited in the number of patients and device size.

For this reason, we decided to plan a prospective, observational, single arm study with 80 patients with CVS or restenosis to be treated with APERTO OTW and to be followed up every three months, evaluating CVS symptoms occurrence and the need for reintervention.

We have recruited six patients so far. The inclusion criteria stipulate that dialysis patients must be undergoing endovascular angioplasty due to clinically symptomatic stenosis (de novo or restenosis) of the central veins with significant (>50%) stenosis and diameter. The target lesion must consist of one or more lesions with a target lesion length of less than or equal to 100 mm. So not every patient fits, but we wanted to find a well-defined patient group as this will make evaluation easier afterwards. We have chosen high volume centres to recruit the patients, all of them very experienced in treating CVS.

I am looking forward to seeing the data come through. We can then compare the patency outcomes with those of other devices that have trial data published.

The primary endpoint of the study is the clinically assessed intervention-free period at six months, defined as dialysis access circuit with no need for clinically driven target lesion repeat intervention for symptom recurrence. We are hoping to show a longer intervention-free period for patients treated with APERTO OTW, compared to available clinical data related to standard angioplasty efficacy. We plan to present first results of the primary endpoint in mid-2022.

What is your take home message?

I personally believe, based on initial experience[5], that paclitaxel may have a major role to play in preventing restenosis of central veins in patients on dialysis. The APERTO OTW balloon gives us the opportunity and the options to effectively prevent repeated reinterventions, improving quality of life and survival for patients with AVFs. Repeatedly having to treat restenosis means that eventually you lose the fistula, and the patient must have another created and then one day they are left with no more options. The more you can prolong the life of the fistula, the more you can do for your patients.

There are not many studies yet on using this technology but carrying out more research like our study will give us the evidence we need.

References

1. APERTO CVS PMCF Study (APERTO CVS). ClinicalTrials.gov. https://www.clinicaltrials.gov/ct2/show/NCT04514406 (accessed Jan 2021).
2. Liyanage T, Ninomiya T, Jha V et al. Worldwide Access to treatment for end stage kidney disease: a systematic review. Lancet. 2015 May 16;385(9981):1975–82.
3. Karnabatidis D, Kitrou P. Drug eluting balloons for resistant arteriovenous dialysis access stenosis. J Vasc Access. 2017;18(1):S88-S91.
4. Yin Y, Shi Y, Cui T et al. Efficacy and safety of paclitaxel-coated balloon angioplasty for dysfunctional arteriovenous fistulas: a multicentre randomised controlled trial. Am J Kidney Dis. 2021 Jan 5:S0272-6386(20)31202-6.
5. Tozzi M, Franchin M, Savio D et al. Drug-coated balloon angioplasty in failing haemodialysis arteriovenous shunts: 12-month outcomes in 200 patients from the APERTO Italian Registry. J Vasc Access. 2019;20(6):733–9.