Not all DCBs are the same

New-generation coating technologies can influence safety and effectiveness.

BY PROF. ULF TEICHGRÄBER, MD, WITH EXPERT OPINION BY KOEN DELOOSE, MD

Drug-coated balloons (DCBs) have been shown to be an effective solution to inhibit vessel restenosis and improve clinical outcomes following endovascular revascularization of the femoropopliteal arteries. DCBs were developed to improve patency rates by inhibiting neointimal hyperplasia and smooth muscle cell proliferation without stent implantation. The lack of metal prosthesis, which can cause restenosis, gives more flexibility for future treatment decisions. Since the first DCB was launched in 2001, coating technologies have evolved. The next-generation DCBs, such as luminor (iVascular), have demonstrated the best safety and efficacy outcomes.[1]

The luminor DCB is coated with TransferTech (iVascular), a proprietary coating nanotechnology that is a homogeneous combination of a liquid excipient and microcrystalline paclitaxel with a dose of 3 µg/mm^2. Paclitaxel is a cytotoxic agent that stops the cell cycle in the M phase of the mitotic cycle and irreversibly inhibits arterial smooth muscle cell proliferation. Paclitaxel's unique mechanism of action as well as its highly lipophilic profile makes this drug ideal to treat vessel restenosis in the femoropopliteal segment.[2]

The presence of a liquid excipient plays a central role during the navigation and transfer of paclitaxel into the vessel wall. The excipient needs to be lipophilic in order to retain the paclitaxel on the balloon, but it is also important that it is soluble in water to allow for the paclitaxel to transfer and diffuse through the vessel wall. Ideally, the excipient should have both lipophilic and hydrophilic characteristics. Luminor is the only DCB with an amphiphilic excipient, a water-reduced ester.

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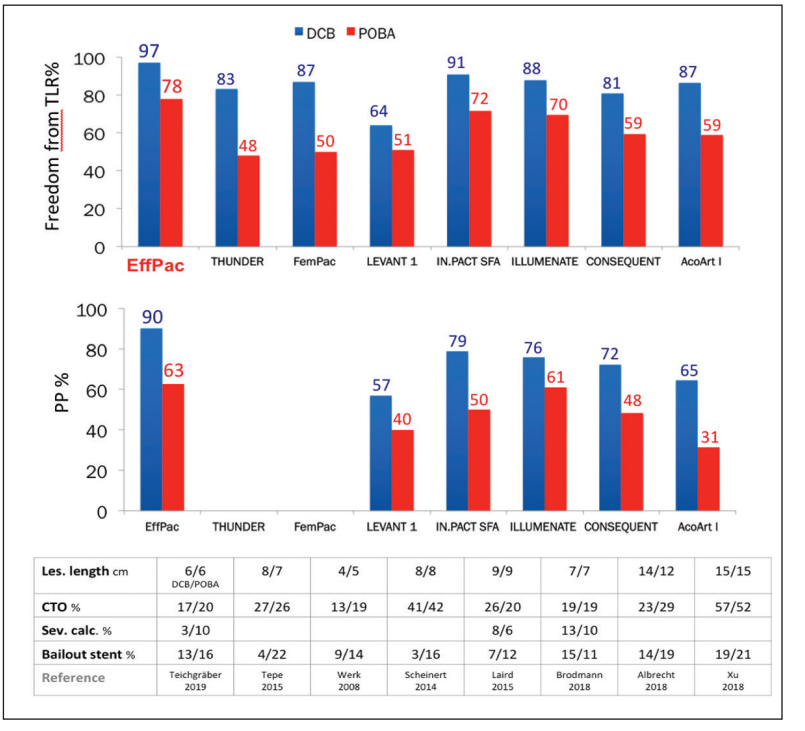
Paclitaxel in a microcrystalline structure, together with the excipient, is spread on the balloon using ultrasound spray pulse. The balloon surface is covered with multiple independent nanodrop layers. This unique and innovative technology provides a flexible coating that adapts to the balloon's movement.



Les. length cm	6/6 DCB/POBA	8/7	4/5	8/8	9/9	7/7	14/12	15/15
CTO %	17/20	27/26	13/19	41/42	26/20	19/19	23/29	57/52
Sev. calc. %	3/10				8/6	13/10		
Bailout stent %	13/16	4/22	9/14	3/16	7/12	15/11	14/19	19/21
Reference	Teichgräber 2019	Tepe 2015	Werk 2008	Scheinert 2014	Laird 2015	Brodmann 2018	Albrecht 2018	Xu 2018

Figure 1. Freedom from TLR and primary patency of similar DCB RCTs at 24-month follow-up.[1]

Most manufacturers of DCBs use paclitaxel because of its mechanism of action and high lipophilicity; however, not all DCBs are equal. Beyond the differences related to the balloon platforms, the luminor technique of impregnation, the physicochemical structure of the paclitaxel, and the drug's combination with the excipient are differentiating elements that influence the clinical effectiveness.

EFFPAC 24-MONTH OUTCOMES

EFFPAC is an investigator-initiated, prospective, multicenter, randomized controlled trial (RCT) aimed to evaluate the safety and efficacy of the luminor DCB for the treatment of stenotic or occlusive lesions (length, ≤ 15 cm) in the superficial femoral artery and popliteal artery compared with noncoated plain old balloon angioplasty (POBA).[1] A total of 171 patients (mean age, 68 years) were enrolled and randomized 1:1 to POBA (n = 86) or luminor (n = 85) at 11 German study centers.

The primary endpoint was late lumen loss (LLL) at 6 months. Secondary endpoints were patency rate, target lesion revascularization (TLR), quality of life assessed with the Walking Impairment Questionnaire and EuroQoL five dimensions, change in Rutherford class and ankle-brachial index, major and minor amputation rate for index limb, number of bailouts, and all-cause mortality.[1]

Baseline characteristics were typical for patients with peripheral artery disease (PAD) in both groups. Most patients had severe claudication and a mean lesion length of approximately 6 cm. The total occlusion rate was 20.2% in the luminor arm versus 25.6% in the POBA arm. Calcification was mild to moderate in both arms. Vessel preparation via predilatation was performed in 100% of luminor cases and 98.8% of POBA cases.[1]

> "The innovative coating technology is not only superior in patency, LLL, and TLR but also in demonstrating better safety outcomes.

After 6 months, LLL measured a mean of 0.14 mm (95% CI, -0.38–0.67) in the luminor group compared with 1.06 mm (95% CI, 0.54–1.59) in the POBA group ($P < .001$).[1]

At 24-month follow-up, the freedom from TLR rate was 97.2% for the luminor arm versus 78% for the POBA arm ($P = .001$). Primary patency was greater in the luminor arm than in the POBA arm (90.2% vs 62.70%; $P = .0004$). The freedom from TLR and primary patency outcomes are the highest compared with other clinical trials (Figure 1).[1]

Expert opinion on paclitaxel

By Koen Deloose, MD

It is always crucial to focus on our patients' safety, especially with the current ongoing debate about the potential safety signal for increased long-term mortality with paclitaxel-coated devices. Official statements from varying global authorities stress that there is no class effect for DCBs. Every DCB needs to be investigated individually, with its own patient-level data. The luminor, with its TransferTech coating nanotechnology, showed superb efficacy and safety at 24 months in the EFFPAC study.

> "The luminor, with its very specific TransferTech coating nanotechnology, showed superb efficacy and safety at 24 months in the EFFPAC study.

Furthermore, profound analysis of the luminor data is supported by a data safety monitoring board, and a clinical event committee is planned. Additionally, the upcoming TINTIN trial will provide more data on luminor and its use for even more complex lesions in combination with the iVolution stent (iVascular). Patient safety, alongside outstanding efficacy, is our top priority, and data like those from EFFPAC will contribute to more clarification in this critical time for endovascular PAD therapies. A blind stop in using all paclitaxel-eluting devices would be short-sighted and not testify to a clear view of the endovascular evolutions in PAD treatment.

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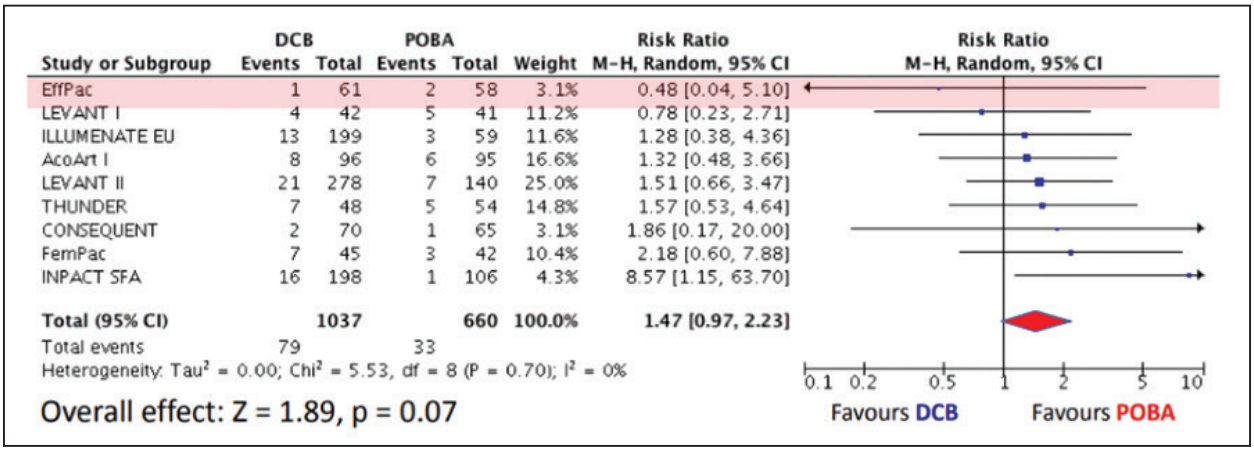

Figure 2. All-cause mortality in DCB RCTs at 24-month follow-up.[1]

EFFPAC also included an all-cause mortality analysis at 24 months that showed the risk ratio (RR) for all-cause mortality with the luminor versus POBA was 0.48 (95% CI, 0.04–5.10) (Figure 2), which makes it one of the few trials to demonstrate a RR < 1 at 2 years.[1] This outcome suggests device design may play a role in the safety risk signal related to paclitaxel recently reported.[3]

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The luminor paclitaxel-coated balloon catheter was found to be highly clinically effective in inhibiting restenosis compared with POBA; these results allow for direct comparison to other RCTs. EFFPAC demonstrated no increased risk of death, and the efficacy results were the highest among RCTs after 24 months. The innovative coating technology is not only superior in patency, LLL, and TLR but also in demonstrating better safety outcomes. ■

1. Teichgräber U. EFFPAC trial: effectiveness of luminor DCB vs. POBA in the SFA: 24-month safety and efficacy outcomes. Presented at: EuroPCR 2019: May 21–24, 2019; Paris, France.
2. Afari ME, Granada JF. Mechanisms of action in drug-coated balloons. Endovasc Today. 2012;11:53-58.
3. Katsanos K, Spiliopoulos S, Kitrou P, et al. Risk of death following application of paclitaxel-coated balloons and stents in the femoropopliteal artery of the leg: a systemic review and meta-analysis of randomized controlled trials. J Am Heart Assoc. 2018;7:e011245.

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