

Stellarex: The Next-Generation DCB

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Newer-generation drug-coated balloons (DCBs) with a lower drug load of 2 $\mu\text{g}/\text{mm}^2$ balloon surface have been developed as alternatives to first-generation DCBs featuring up to 50% or 70% higher doses of 3 or 3.5 $\mu\text{g}/\text{mm}^2$.

The performance of a DCB relies on four design elements: drug dose; coating stability to survive handling, insertion, tracking, and lesion crossing; coating balloon adhesion or surface energy to control drug transfer to the arterial wall; and

extent of paclitaxel crystallinity versus amorphous microstructure to control drug residency in the arterial tissue. The balance of these features determines the performance of a DCB, and whether any one feature is more important remains debatable and a matter of further research.

The Stellarex DCB (Spectranetics Corporation) is a next-generation DCB designed to match the aforementioned design goals.

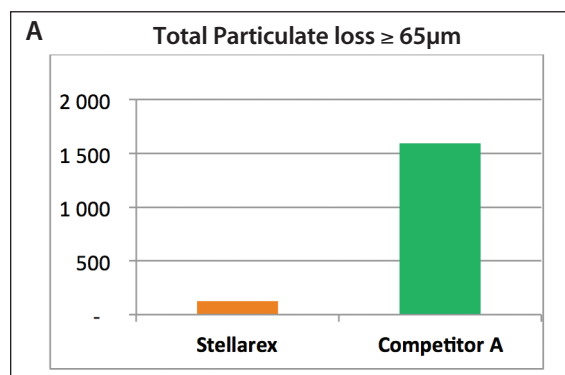


Figure 1. Total particulate loss after balloon inflation in a vessel of room temperature water (A). Photo display of the particulate generated after a balloon is submerged in a vessel of room temperature water, inflated to nominal pressure, and removed from the vessel (B).



THE STELLAREX DCB

Optimal Drug Dose

EnduraCoat technology is characterized by a low dose of $2\mu\text{g}/\text{mm}^2$ of paclitaxel and a polyethylene glycol excipient (an additive largely adopted in pharmaceutical and cosmetic applications). The balloon platform is coated in the unfolded state (partially inflated) and subsequently deflated and folded into the final balloon configuration. This allows most of the drug coating to be protected by the folds as the balloon is tracked to its final destination within the body, allowing for a lower coated dose. A lower drug dose is highly advantageous as it mitigates the downstream effect caused by paclitaxel, while still delivering a highly efficacious treatment to the target lesion.

Coating Stability

High coating stability is the result of extensive drug formulation optimization to enhance performance on the Stellarex-specific balloon material. The ultimate objective was twofold: (1) to obtain excellent drug adherence during balloon preparation and handling, insertion through the introducer, and transit through the vasculature to the target lesion; and (2) to maximize drug release to the vessel wall once the balloon is inflated.

Superior coating stability of Stellarex during preparation, handling, and

manipulation appears evident through qualitative comparisons to competitor DCBs (Figure 1) and through quantitative drug content analysis after handling it in a variety of ways (Figure 2).

The coating stability of Stellarex is confirmed by quantitative particulate testing after tracking the DCB through a vasculature model.¹ This testing supports the notion that Stellarex limits drug particle loss compared to other DCB competitors with the same (and higher) drug dose. In a competitive assessment, Stellarex resulted in up to 50% fewer particles produced during tracking (Figure 3).

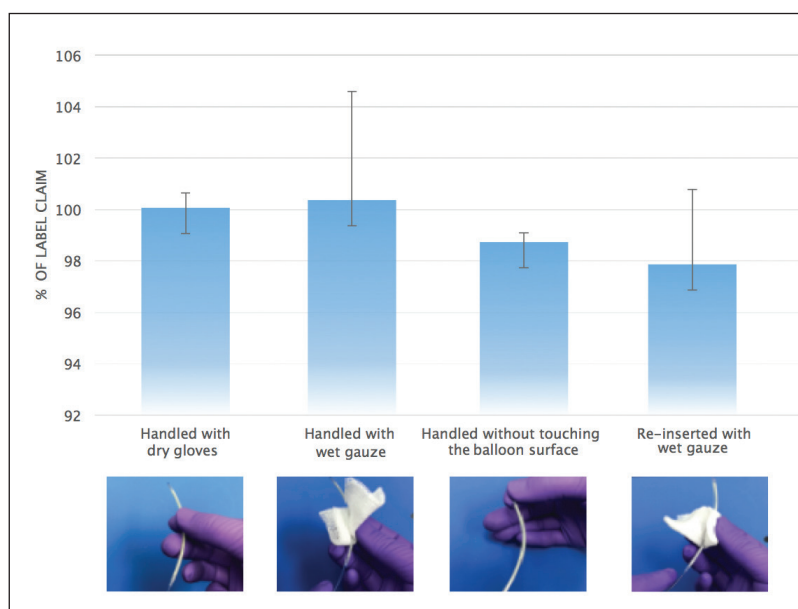


Figure 2. Quantitative drug content analysis after handling it in a variety of ways.

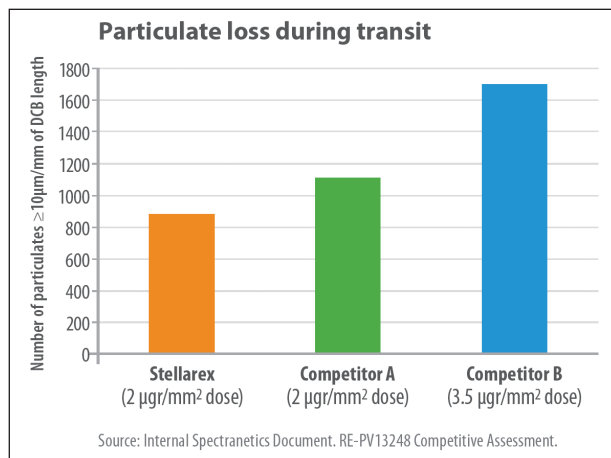


Figure 3. Particulate competitive assessment.

Drug Tissue Transfer and Residency

Stellarex achieves the optimal balance between coating stability and drug transfer to tissue by balancing the ratio of amorphous to crystalline paclitaxel on the balloon surface. In general, amorphous paclitaxel tends to be more durable, whereas crystalline paclitaxel delivers the best therapeutic effect.

The crystalline form of paclitaxel on the Stellarex DCB allows efficient transfer of the drug to vessel tissue. Entrenching paclitaxel into the vessel tissue is of utmost importance; the healing response of a vessel after injury caused during balloon expansion lasts up to 28 days. With Stellarex, a high dose of paclitaxel remains in the tissue for the duration of the healing process (Figure 4). This prevents scar tissue from forming in the vessel during this critical period, thereby preventing restenosis.

Clinical Performance

Initial results from the ILLUMENATE first-in-human trial (the first of a multitude of Stellarex trials) support the notion that a well-designed low-dose DCB can result in high clinical performance similar to, or better than, the best performing DCBs of higher dose and equal dose, as measured in primary patency rates of about 90% and 80% at 1 and 2 years, respectively, in patients with symptoms of claudication and rest pain due to femoropopliteal disease.²

CONCLUSION

DCB technologies are evolving toward an optimized balance between minimal drug load, minimal down-

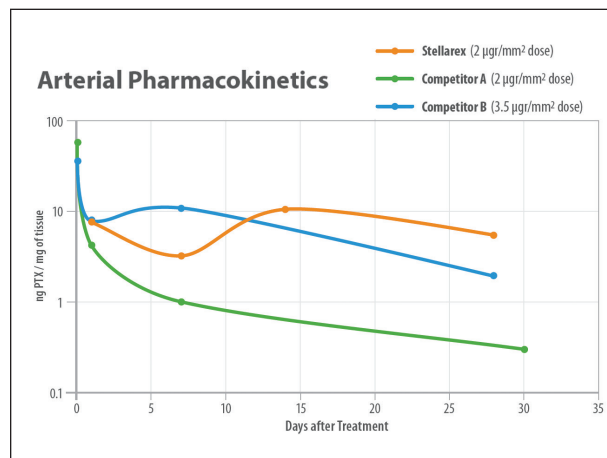


Figure 4. Sustained drug transfer and tissue residency at 28 days is similar to a DCB with ~75% higher dose (3.5 µg/mm²). Superimposed pharmacokinetics curve from different data sets.³⁻⁵

stream loss, and maximal tissue transfer. Particulate loss may lead to potentially relevant clinical implications in specific clinical and anatomical settings, which justify continuous research efforts to enhance DCB process efficiency. Confirmed by a series of bench, preclinical, and clinical evidence, Stellarex represents an important step ahead toward this goal. ■

1. Spectranetics Corporation. Internal data on file. RE-PV13248.

2. Schroeder H, Meyer DR, Lux B, et al. Two-year results of a low-dose drug-coated balloon for revascularization of the femoropopliteal artery: outcomes from the ILLUMENATE first-in-human study. *Catheter Cardiovasc Interv*. 2015;86:278-286.

3. Spectranetics Corporation. Internal data on file. D029433.

4. Yazdani SK, Pacheco E, Nakano M, et al. Vascular, downstream, and pharmacokinetic responses to treatment with a low dose drug-coated balloon in a swine femoral artery model. *Catheter Cardiovasc Interv*. 2014;83:132-140.

5. Melder R. Presented at: EuroPCR; May 15-18, 2012; Paris: France.

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