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The Future of Antiproliferative Therapies for Endovascular Interventions

Translational findings from the Ranger Paclitaxel-Coated Balloon data.

BY RENU VIRMANI, MD, FACC

Significant advancements have been made in the field of drug-eluting therapies for peripheral applications. Unlike the coronary vasculature, where atherosclerotic calcification is more predominately encountered, more aggressive (medial) calcification is often observed in the peripheral arteries, elevating the need for further technological advancements to treat this aggressive disease.

Next-generation DCBs, such as the Ranger Paclitaxel-Coated Balloon, are demonstrating a balance of high levels of neointimal inhibition beyond 90 days comparable to higher-dosed technologies, while also providing fewer physiologically significant histological findings in the downstream vessel beds.

DESIGN CONSIDERATIONS FOR DRUG-ELUTING THERAPIES

The biological process of restenosis occurs well beyond the first 90 to 180 days in humans (Figure 1), whereas in juvenile animals it is observed at 30 days in normal arteries. Therefore, it is important to have long-term release of the drug. The longer the drug is released, the more durable the results will be. The argument over required drug dose has been ongoing for the past several years. Many experts in the medical community believe that higher loading doses of a drug lead to increasingly superior outcomes. Personally, I am not of that opinion. The ideal design considerations should maximize neointimal inhibition by maintaining therapeutic tissue levels over a

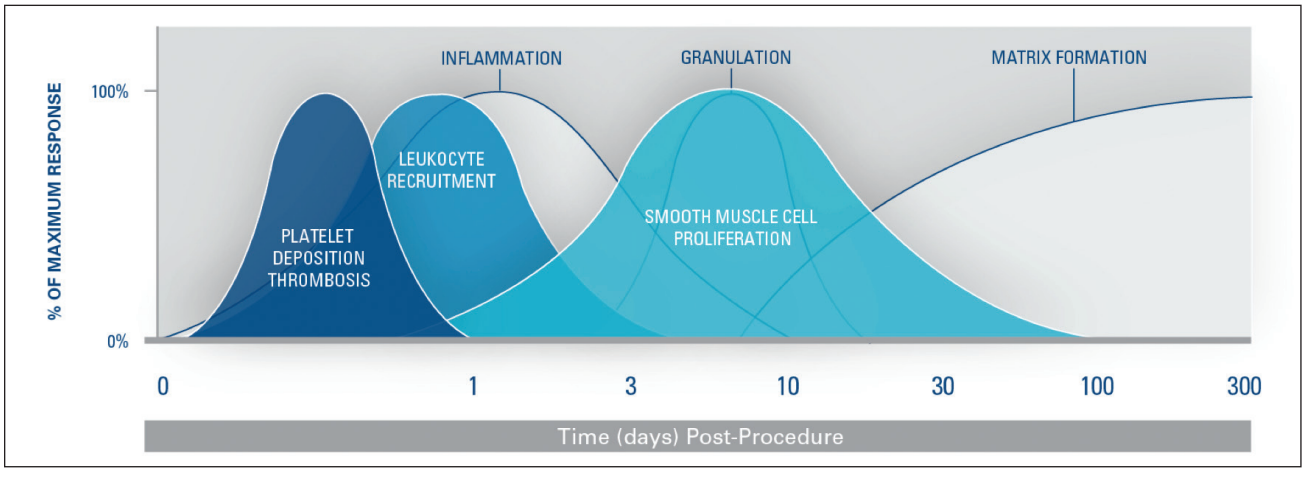

Figure 1. The biology of restenosis.

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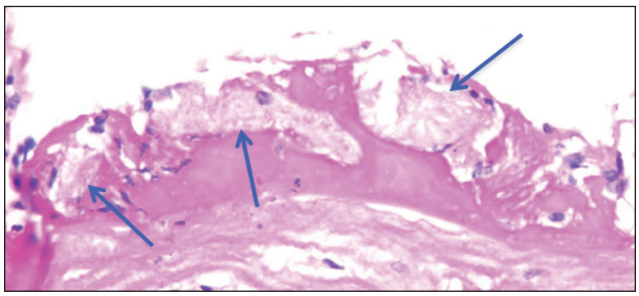

Figure 2. Crystalline material continues to be present in the arterial wall at 90 days.

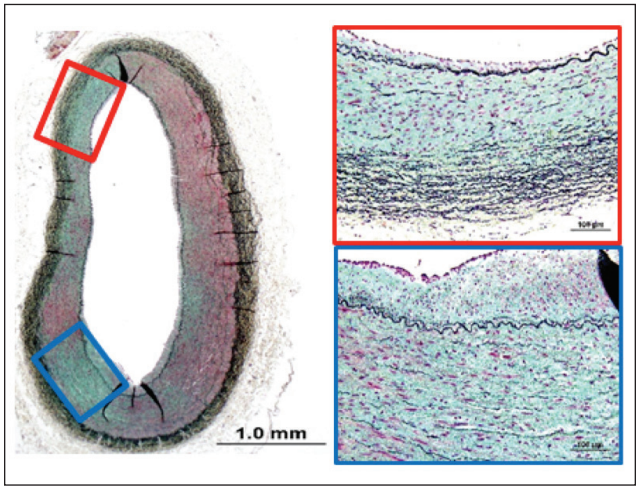

Figure 3. Biologic effects of paclitaxel are associated with loss of smooth muscle cells with replacement by proteoglycans as have been confirmed in multiple sections at 90 days in porcine femoral arteries with minimal neointimal thickening.

long time, while ensuring adequate healing and minimizing particulate loss downstream.

TRANSLATIONAL FINDINGS

Ranger Pharmacokinetics 90-Day Data From the CVPath Institute

Research has shown that next-generation drug-coated balloons (DCBs), such as the Ranger Paclitaxel-Coated Balloon (Boston Scientific Corporation), are demonstrating a balance of high levels of neointimal inhibition beyond 90 days (Figure 2) comparable to higher-dosed technologies, while also providing fewer physiologically significant histological findings in the downstream vessel beds.

We have seen a range of effects in porcine arteries, especially in the superficial femoral artery. We have looked for biologic effects at 7, 30, and 90 days. In the femoral artery, we see loss of smooth muscle cells, which range from involving half the vessel wall to transmural—the whole vessel wall shows us changes and, to a large extent, even circumferentially.

We have also observed sustained effects thus far up to 90 days. It seems that the Ranger DCB is effective in its mission to reduce smooth muscle cells in the arterial wall with replacement by proteoglycans and collagen matrix (Figure 3). ■

Renu Virmani, MD, FACC
President
CVPath Institute, Inc.
Gaithersburg, Maryland
rvirmani@cvpath.org
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