The Challenges of Bringing Drug Elution to the US Market

Cook Medical Vice President Rob Lyles provides insight on the approval and launch process of Zilver PTX in the United States, as well as next steps in the evolution of drug-eluting therapies.

Now that the device is approved, what's next for Zilver PTX (Cook Medical, Bloomington, IN)?

A lot—we are really excited. The fundamental shift that occurs when drug-eluting technology enters the market is so profound that it can forever change the paradigm going forward. Peripheral drug elution will likely follow a very similar path to that of coronary drug elution. As for Zilver PTX specifically, we anticipate the size range will expand. In the United States, we're working with the FDA to make longer-length Zilver PTX stents a reality.

We will also continue clinical work with the device. Dr. Scheinert just started a trial in Europe that will directly compare Zilver PTX with drug-eluting balloons in a head-to-head fashion. That's an area of great interest for interventionists.

What is the plan for rolling out Zilver PTX?

The rollout will happen in three stages. There is a postapproval study requirement in the United States, so we've decided to move ahead with that first (similar to what we did in Japan), which could involve about 16 to 20 sites. The sites that participated in the clinical trial in the United States will be next because they have the most experience with the product. This will include approximately 30 more sites. Next, we'll continue to the remaining US customers.

Most of the customers in the United States should have availability around the end of this year.

Why will it take a full year to supply the majority of the market?

This is partially because of a commitment to the postapproval study requirement. The other part, which might not be appreciated, is the time it takes to ramp up a revolutionary product such as Zilver PTX. Because we're in such a regulated industry, device manufacturers don't know exactly what the manufacturing requirements are until they receive approval. Once the final requirements are received, the process of ramping up and building out can begin.

We want to be methodical and careful about the way we roll out the device. Even though this technology focuses on ease of use for the operator, we want to make sure that it is used properly. As Zilver PTX is rolled out, training is provided to physician users. This is a technology that will be around for the long-term, and that takes time to implement. Cook has learned over our 50 years of doing business that you must take the time to launch these devices the right way.

Why did the FDA mandate the postapproval study?

Actually, this is pretty common. Most regulators around the world are starting to require some sort of postapproval study. With this type of implantable device, one must go through the proper steps to achieve approval. But once it's released to the market, most regulators want some level of surveillance to monitor longer-term effects or to get an idea of how it is performing in the real world.

In Japan, we performed a fairly large postapproval study (approximately 900 patients), and we were able to enroll that study in just 92 days. Because there was so much enthusiasm for the product, this process went very quickly.

We've heard about market concerns over the cost of drug-eluting stents before the launch. How did Cook address these concerns?

One of Cook's main considerations was to make this technology affordable and cost effective. With the pressures on the health care industry today to deliver bet-

ter outcomes for less cost, part of the innovation of this technology was enabling physicians and hospitals to utilize it at a cost that ensured wide access for patients. Clearly Zilver PTX delivers better outcomes. In terms of price, it's basically in the range of about a 30% premium compared to bare-metal stents, but significantly less than covered stents.

Also, what we're learning from physician experts who are researching the costs associated with reintervention is that Zilver PTX helps offset cost to health care providers, payers, and patients by reducing the need for costly SFA reinterventions. This makes the technology even more attractive from a cost standpoint.

In general, it is a fairly affordable entry into the market. For example, when drug elution was introduced with coronary stenting, those devices cost many times what bare-metal stents did at the time. Zilver PTX is coming in at a much lower entry point, which many believe will drive a lot of market uptake.

What is the next step in the evolution of drug-eluting therapies?

First, Cook is excited about the use of drug elution as the peripheral space absorbs its impact and as physicians start to take full advantage of the technology. We are currently the only company that offers both drug-eluting stents and drug-eluting balloons in the European peripheral market. The next phase is going to be a significant one. Everyone will begin to recognize the importance of the drug effect: if you have the opportunity to use a stent, a drug-eluting stent is likely going to work better than a bare-metal stent; if you have the opportunity to use a drug-eluting balloon, it's likely going to work better than a bare balloon.

But we've got some important questions to answer. To date, there doesn't appear to be good data to support the notion that a drug-eluting balloon performs better than a drug-eluting stent, or even a bare-metal stent. There are two paths to choose from. There's the balloon path and the stent path. Both are critical. There's a time to use balloons, and there's a time to use stents; however, it has not been demonstrated that drug-eluting balloons are powerful enough to cross over and work as well as a stent does. Currently, a long-term drug effect from a scaffold is the best option in the SFA.[1]

Once drug elution is really ingrained in the market, we're going to see a progression similar to what we've seen on the coronary side. Adoption curves for drug-elution technology may go as high as being involved in 80% to 90% of peripheral procedures. The sustained improvement from drug-eluting devices is profound, especially with the growing PAD patient population who need more durable results.[2]

Once drug elution takes hold, it's going to be adopted and penetrate the market. There are many interesting technologies evolving on both the stent side and the drug side. To give a time frame, it will still be at least 3 or 4 years until we see drug-eluting balloons become available due to the regulatory pathway involved in the United States. Bioresorbable technology is even further out—probably 5 to 8 years until it will become available on the US market.

In terms of the practical reality for a physician practicing today, Zilver PTX represents that first move into the drug-eluting world for US peripheral interventionists.

How do you see yourself competing with future technologies such as drug-eluting balloons and bioresorbable devices?

From a timing perspective, the bioresorbable devices are still a long way off. There is also the lingering question of whether it's really going to work or not. The SFA is one of the most hostile pieces of real estate in the arterial system due to the mechanics. There is still a question of whether a bioresorbable scaffold can hold up in that environment.

We're not to the place yet where the implantable device is going away anytime soon, but there's a lot of promise in this field. There's a lot to be done, and there are some technologies even beyond the bioresorbable, which are very promising. ■

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1. Dake MD, Ansel GM, Jaff MR, et al. Paclitaxel-eluting stents show superiority to balloon angioplasty and bare-metal stents in femoropopliteal disease: twelve-month Zilver PTX randomized study results. Circ Cardiovasc Interv. 2011;4:495-504.

2. White CJ, Gray WA. Endovascular therapies for peripheral arterial disease: an evidence-based review. Circulation. 2007;116:2203-2215.