The Zilver PTX Global Registry and RCT

Michael D. Dake, MD, discusses the early experiences in the Zilver PTX randomized trial and the results seen in the larger global registry studying a paclitaxel-eluting stent in the SFA.

How would you briefly describe status of the two components of ongoing study concerning the Cook Medical (Bloomington, IN) Zilver PTX paclitaxel-eluting stent?

Both the global registry, which is composed of 794 patients, and the randomized controlled trial (RCT), which is 480 patients, have been completely enrolled. The RCT, which enrolled patients predominantly in the US, but also in Germany and Japan, is awaiting its 1-year primary endpoint, which should be complete in August 2009. The RCT is a vanguard in this field for several reasons. First, the fact that it is taking place in three countries—one in North America, one in Europe, and another in Asia—is particularly noteworthy. I think that the FDA is showing that it is willing to consider experience outside of the US in the approval process, provided that it is conducted, controlled, and monitored in a manner that is identical to that which is going on in the US.

Another interesting element of the RCT is that failures in the balloon angioplasty control arm will be re-randomized 1:1 to receive a bare-metal stent or a drug-eluting stent. If a significant number of patients require this crossover, we may learn a lot from the comparison of bare-metal and drug-eluting stents in this setting.

The global registry arm, which includes sites in Europe, Russia, Canada, and Korea, is releasing data as it reaches milestones; the most recent update included approximately 324 patients at 12 months, and more than 500 at 6 months.

In what ways do the inclusion criteria for the randomized trial differ from those of the global registry?

The global registry includes essentially all-comers; up to four stents could be placed, in patients with in-stent restenosis could be treated, restenosis after angioplasty, occlusions, and lesions of any length. The lesions included in the RCT had to be less than or equal to 14 cm in length. These lesions could include occlusions, stenoses, or restenosis after previous balloon angioplasty, but with no prior stent placement in the target segment.

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Is there any indication of how the results of the global registry play out if examined for outcomes in the patients that match the criteria for the randomized trial?

Yes, although the data from the RCT will not be available until next summer, we have been able to look at a subgroup of the global registry patients that corresponds to the cohort of patients enrolled in the RCT study—patients who fit the same inclusion criteria (ie, lesions less than or equal to 14 cm long, and were not treated for in-stent restenosis). The 1-year freedom from target lesion revascularization (TLR) rate in this subgroup of the global registry was 95%.

Can these data be compared to previously reported trials as well, or is there too much of an apples-to-oranges effect?

We can look at subgroups of patients from the global registry data who meet the same criteria as the patients included in the FAST, RESILIENT, and ABSOLUTE trials as well. There are about 100 patients in the global registry who fit these criteria, and an apples-to-apples comparison showed that freedom from TLR rates were approximately

10% better at 1 year in patients treated with the Zilver PTX in than what we have seen in the composite of these trials. Of course, these were not the most difficult SFA lesions, but it is interesting to see a basis of comparison with previous and current trials.

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What have the trialists learned from the reports of late stent thrombosis after placement of coronary drug-eluting stents? To what degree is this a concern?

It is a concern, but we still do not know what exactly caused the late stent thromboses in the coronary setting. One of the most significant differences between the coronary trials and the Zilver PTX studies is the absence of a polymer in the latter. If the behavior of the polymer is determined to be one of the reasons for the late stent thrombosis seen in the coronaries, it is conceivable that the Zilver PTX may not encounter the same types of complications. There are reasons to believe that this particular composition, with the absence of a polymer, will have a late result unique from what was previously seen in similar—but by no means identical—drug-eluting stent applications.

What are your thoughts on the differences in the specific drugs that have been studied?

In addition to the previous and ongoing drug-eluting stent trials, we also have the growing global experience with drug-eluting balloons, which has largely been with paclitaxel. Due to its intense protein binding, very high lipophilicity, and long tissue residence time, paclitaxel appears to be well suited for treating peripheral arterial disease via direct delivery to the target site without the use of a polymer. Because of its own unique chemical composition, we have observed that paclitaxel stays around for a long enough time to provide what appears to be a somewhat durable effect. There may be some added benefits if the drug could be delivered over time, but that has yet to be explored. ■

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