SFA Trials, Devices, and Decisions

An expert panel provides candid perspectives on issues facing current clinical trials and the regulatory environment, adopting new technologies, and daily decision making in busy peripheral practices.

PANEL

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Gold Standards and Meaningful Evidence

In what ways can the concept of any single gold standard for treating superficial femoral artery (SFA) disease be misleading or counterproductive? In what ways is some standard necessary in evaluating emerging therapeutic options?

Dr. Laird: To begin, I don't believe there is a single, definitive gold standard. The closest thing we currently have to a gold standard is probably stenting for lesions less than 15 cm in length, and this is based on several randomized trials showing that stenting for lesions of those lengths provides better results than balloon angioplasty alone.

The concept of a gold standard procedure for treating SFA disease is misleading because most of the studies that have been conducted looked only at short or medium-length lesions at most, so there are no concrete data regarding what the gold standard is for lesions longer than 15 cm. Whether it will be a drug-eluting stent, drug-coated balloon, or a Viabahn covered stent (Gore & Associates, Flagstaff, AZ), we just don't know. There is no clear answer.

Dr. Dake: It is very difficult to define a gold standard in the SFA because there are so many different subgroups that have been identified, all of which behave differently. Establishing a single gold standard is not as important as knowing how to customize or tailor a procedure based on a number of different considerations. The unique anatomic and individual patient and lesion concerns make it very difficult to truly know what a "gold standard" even means.

Dr. Garcia: One of the other difficult elements is that the type of SFA disease that has been studied toward gaining device approval and what we see in the real world are two different things. What Dr. Dake said is so critical. Every patient we see in the real world, beyond a trial, has anatomy and lesion characteristics that make the case unique—characteristics that may not have the correct "fit" for one trial versus another. We really do tailor our approaches every day, and that's why for the SFA in particular there are so many choices of therapies in this territory without being a "gold standard" per se. Further, the options are often best used in concert with other devices in the same patient who may have several different lesion characteristics that each require a specific approach.

How that translates to establishing a gold standard, I don't know. To Dr. Laird's point, right now we have to believe that lesion sets of 4 cm to 10-15 cm are in the realm of ballooning and stenting. Unless the validity of these options are either proven or disproven in new trials, they constitute the default therapy.

Dr. Ansel: Another issue is that the concept of a gold standard is often misinterpreted by the layperson, by the insurance companies, and by the government as meaning "always the best procedure." We see that in carotids where they are not allowing for a physician to have enough insight to take care of his own patient with alternative therapies, when physician insight and the application of science is what medicine is all about.

I think that whenever we label something a gold standard, we run the risk of people perceiving it as always being the way to treat the patient, and that certainly isn't the way much of the practice of medicine works.

In what instances should randomized controlled trials be undertaken?

Dr. Garcia: Not to bring the gold standard topic back up, but it would be helpful to see randomized trials for many things that we routinely do, so we have an idea of what works best in different scenarios. But for the reasons already discussed, it is very difficult to compare devices in a head-to-head fashion.

One of the great problems in the periphery is that we have this inferred dataset, and we compare the apples of one trial to the oranges of another, and we really get nowhere. The conclusions drawn in this fashion are not meaningful, so it would be nice to have randomized trials among various devices so we can have head-to-head comparisons.

Whether that is absolutely necessary to make a final decision, I don't know. I think registries can give us a lot of signals. We have seen it in the single-arm registry studying the Zilver PTX drug-eluting stent (Cook Medical, Bloomington, IN) in addition to the randomized trial. There is validity to registries as opposed to randomized trials, and I think they do have a big role for what we want to do in the SFA.

Dr. Laird: A poorly designed randomized trial can be even worse than having no trial at all, but I agree, we need more comparative data. We can't answer every question with a randomized trial, but we can certainly design randomized trials that would allow us to compare therapies, like Dr. Garcia mentioned, addressing the questions that clinicians really want answered. For example, can you get as good a result with atherectomy as you can with a stent? Ideally, any such trial would be designed so that it includes real-world patients with real-world lesions—long lesions and occlusions—rather than the cherry-picked short lesions that end up comprising most trials.

Dr. Schneider: One of the interesting things about the randomized trials, both those that have been done and those that are being planned, is that presumably we would have a standard treatment with which to compare our new treatment group, or experimental group. However, when you look at randomized trials, you see that not everybody agrees on what the standard treatment was at the time the trial was initiated. This variability in deciding what is the accepted treatment for comparison could be influenced by the requirements of the regulatory system. It also seems as though the percutaneous transluminal angioplasty (PTA) groups in different trials were handled a variety of ways. For example, early failures were handled differently in each trial. The rate of bailout stenting in different trials seems to have a lot of variability.

As a result, there is some frustration and additional challenge in our daily work. Even when we have a randomized trial, we don't always know exactly what it's telling us because the control group is not something that everyone universally agrees upon.

How do you view industry-sponsored postapproval registries for devices in the SFA? What are their strengths and weaknesses compared to other kinds of clinical studies?

Dr. Schneider: Most registries will not provide the same level of evidence as a randomized trial, but I personally think that they are very useful. Postapproval registries provide a venue to continue to learn more and potentially evaluate lesions that may not have been included in the randomized trials, such as longer lesions, complex lesions, or recurrences.

The registry for the Zilver PTX study is an example that included some real-world elements, such as in-stent restenosis and all kinds of other lesions that wouldn't necessarily work very well in a standard randomized trial. I have the impression that the data from the registry will be important for potential subset analyses for clinicians.

Dr. Laird: I agree. It all comes down to the quality of the registry in terms of how the data are collected and adjudicated, whether there is independent core lab evaluation of the angiograms and duplex ultrasound, etc. We can have a really well done registry in a single-arm study that is incredibly helpful, but there can also be poorly done registries that provide data that are almost meaningless.

Registries are very important, in general, and we have learned a lot from some of the well-done registries over the past several years.

Dr. Dake: Well-designed registries also provide added confidence and security that we know what, if any, untoward side effects might occur at very low frequencies. If we add up every occurrence in a controlled environment, we start to see if a signal emerges. Sometimes, in the original trial, it is unclear whether an infrequent occurrence is something that we needed to worry about being related specifically to the procedure. For example, hypothetically speaking, with a drug-eluting stent in the periphery, the first postapproval registry will allow us to better understand the frequency of any rare hypersensitivity that may exist, something so small that we might not have had a large enough sample size in the first trial to identify such a low-frequency occurrence.

Dr. Ansel: I agree with the others but would add that because cost is often significant; I'd rather see lower numbers of enrolled patients but higher-quality study designs, such as including core lab control, to ensure the data points are very strong. I think we will get a better idea of a signal with the higher quality of data.

What basic elements must an SFA clinical study design include in order to be valid in your eyes?

Dr. Laird: We are increasingly trying to identify the important clinical endpoints. Whenever possible, quality-of-life data would be nice to have as part of these registries. Whether it is just a simple SF-36 or the Walking Impairment questionnaire, those elements can be quite helpful, particularly as we try and convince payers that the therapy we're providing is effective. Treadmill exercise testing to evaluate the response to therapy would be ideal, but a useful compromise is the 6-minute walking test.

Which study design elements do you consider to be red flags for either conflicted or inconclusive data?

Dr. Garcia: I become skeptical whenever a physician touts something they seem to be financially invested in. That is really a big concern. We have seen this time and again, and it just makes many nervous or skeptical about the data. Also, touting a technology with limited to no data is also a challenge to many of us. But as long as the device has a registry that has core lab adjudication, that really raises the level of the benefit we can infer or derive from it. I like registries because they are a bit more real world, but again, the heterogeneity of the patient population really does make them less scientific than the specific question being addressed in the randomized trials. Back to Dr. Schneider's point, the controls vary so much that we do need head-to-head comparisons among devices.

Device Development and the Regulatory and Reimbursement Environment

What are some of the forces affecting SFA device development in the US?

Dr. Ansel: One troubling trend is that some insurers are beginning to not pay for any patient enrolled in an investigational research trial. If this continues or becomes more widespread, it will totally halt our innovation in the United States. If we can't evaluate best patient care by comparing even approved therapies under the typical payer models, then we might as well write off our ability to have any more innovation in the United States.

Dr. Garcia: You hit the nail on the head. If you look at the data coming out on drug-coated balloons, America is no longer leading the way, and I think that is unfortunate.

Dr. Schneider: Yes, I believe we are a half-decade behind now, with no evidence that we will be able to change course and participate once again on the leading edge of development.

Dr. Ansel: And, unfortunately, we are starting to get used to it. It is a phenomenon that has occurred in the last 10 years. If we look back before that, America led the world in medical innovation, and not only is the innovation being made more difficult in the United States, but also the business plan, which is going to drive these companies to innovate, market, and sell their products elsewhere.

Dr. Dake: Before 10 years ago, American companies went overseas to get signals in a pilot phase before embarking on the biggest market that made all the difference in the world, which was the US market. Now the US market is completely flat, and targeting one's entire market outside the US while not even attempting to sell within the US becomes a viable consideration because of the heightened regulatory environment we live in. We are increasingly seeing American technology going overseas, not only for first-in-man testing, but possibly to be exclusively delivered there.

This is an increasing concern given that the gap between the original clinical study and US availability of the device is starting to lengthen and could perhaps never come for certain technologies.

Dr. Ansel: That is an accurate description of what has occurred because before, the first-in-man was done elsewhere, but then the big trials were done in the US, and that is becoming less and less common.

Dr. Garcia: The really frightening prospect in all this is that a valid technology that would help our patients may never be seen in this country, based on a regulatory pathway that costs more than $100 million. When the market is huge in Europe or elsewhere, it basically negates any need to come to the US. That is the sad state of affairs.

Dr. Schneider: We have an amazing system for idea development in the US. However, we are not operating in a vacuum. The development process and the technology itself are a lot more transferrable than ever before. In addition, as middle classes and markets grow outside the US and unmet needs there become more apparent than in the past, the relative value of persisting through the regulatory and payment processes in the US will be less.

What specifically has caused the migration you are seeing?

Dr. Dake: I'm not entirely sure, but I think it's multifactorial and not an easy answer. On the one hand, as we go through a hierarchy of iterations and more complex technologies to deal with our enhanced understanding of the underlying pathology, the new devices are not as simple or as straightforward as a single balloon. We now have combination therapies, hybrids, that require different and at times more extensive considerations and evaluation. But unless the FDA makes a concerted, conscious effort to change the manner in which they evaluate these devices and maintain a pace that reflects what is necessary to approve them in a timely fashion, we run the risk of approval time frames being prolonged to intolerable periods.

Dr. Schneider: We are witnessing a steady deconstruction of our idea-development pathway. While technology has become gradually but steadily more complex, the reasons to approve anything in the US have become fewer and farther between. The pressures to say "no" on the basis of regulations and legal issues have gradually increased. With each "no," the next idea becomes more difficult to finance and develop, no matter how good an idea it may be.

What is particularly discouraging is that the only way to change these things is politically, and individual practitioners do not have much political clout in this setting. We are not

used to thinking of political clout being required in order to achieve scientific ends and medical progress.

Dr. Dake: For every voice like ours, there is a chorus in the ear of politicians, saying the FDA is too lax, that their standards over the years have come down, and they are allowing the use of devices or drugs that are shown to be harmful in the end and, in many people's minds, did not undergo the proper rigor of scrutiny. It is tough for all parties involved.

Dr. Laird: The pendulum swings back and forth, but right now the tolerance of politicians and the American public in general toward having any approved product later be found to cause harm is very low. As a result, there is a very cautious environment at the FDA, on top of which we now have devices combined with drugs that are much more complex to understand and evaluate. Drug-coated balloons are being treated nearly the same as drug-eluting stents in terms of the required preclinical testing, and with the cost of all the testing and trials, it becomes very difficult for companies to bring these products to market in the United States.

Dr. Garcia: Being cautious is not a negative motivation, and at the heart of everything, I believe the FDA truly has the well-being of our patients as its top priority. But, I agree with Dr. Laird that the pendulum of the regulatory process seems to have swung to a very conservative stance. The current environment is keeping American innovation out of the hands of American physicians and scientists, and encouraging the outside US approach for the initial and then concurrent data collection, which makes the US less of a leader.

Is there anything specific you would change about the FDA approval and clearance process?

Dr. Ansel: I would like to see more worldwide cooperation among regulatory agencies. Japan and the FDA are starting to do this to a small extent, but I think that especially in some of the more complex trials in which enrollment is particularly difficult, the ability to be multinational may help dramatically.

Dr. Laird: I agree. It seems a little crazy that a company has to spend a ton of money to have a trial in Europe, collect all of that information, and then turn around and repeat the same trial in the United States. There should be a pathway allowing them to use the first set of data. I know they are now able to pool some data between studies in multiple countries, but it could be advantageous to conduct just one uniform trial that includes patients here, in Europe, and Asia, and pool the data rather than having these companies funding multiple trials in different places.

Dr. Garcia: As long as the method and the metrics they are using for outcomes is consistent, I agree. It would be a great use of resources because the worldwide process would begin simultaneously for the company and the technology. However, the way both investigators and regulatory bodies look at certain outcomes may not be the same. There are efforts toward homogeneity though, and the data from major European trials seem to be increasingly consistent with what the US is willing to perform from a study standpoint and further from the regulatory perspective, as well.

Dr. Schneider: It would be fantastic if the FDA's activities were more transparent so that a company in developing a device or a drug could have a little more access to information and understand the reasoning behind the decision making. Decisions regarding specific trial designs—requirements such as number of patients, types of endpoints—seem highly variable, even when similar devices are entering evaluation.

One of the good things going on in the abdominal aortic aneurysm arena is that through a series of major product developments and minor iterations, the FDA and the device manufacturers have developed a more predictable set of requirements that must be met for a product to be approved. The manufacturers know most of what the FDA wants to see, which goes a long way in alleviating the pressures of trying to determine in the early development stages what will ultimately be required. Hopefully, we will see a similar establishment of standards in the noncoronary occlusive arena as well.

Lastly, it would be very helpful for the FDA to know the repercussions of their decisions. For example, a single sentence might add a few million dollars and another year or two to a development effort. When testing requirements and costs are added by the regulatory system, there should be some estimation of the benefit. Sometimes, it appears that the benefit of added tests is negligible while the costs are ever present and right up front. In terms of lab work, bench top testing, preclinical and clinical evaluation, the FDA is requiring more and more rather than less and less. This seems counterintuitive, given the incredible body of scientific knowledge already accumulated in biology, devices, materials, and clinical care. If anything, the more we know, the less we should have to repeat the same steps over and over.

Dr. Dake: I hear that companies feel there is not the predictability in the regulatory response or process that they would like in order to accurately gauge the horizon of what

they must do. The communication is often not as fluid as they might like.

Dr. Schneider: It seems safer on the surface for the regulatory bodies to be conservative. Who among us is against safety? On the other hand, for every extra year that an effective device is held off the market, there are many patients who could have perhaps undergone a better treatment than we currently have to offer. The safest possible automobile is one that doesn't go anywhere. You certainly won't get into an auto accident. However, that is hardly a functional situation. It is better to be safe than sorry, but there needs to be a sense of when it is being taken too far.

Are 510(k) pathways for market clearance proving successful and efficient?

Dr. Laird: The 510(k) process was a necessary pathway to establish. Without it, we would have very few technologies approved for use today. However, over the years, the process has been somewhat capricious in that some devices have been approved for use in patients without any studies or patient data at all, instead based solely on the previous approval of a predicate device. Meanwhile, other 510(k) devices must go through 50-, or 70-, or 100-patient trials.

But although the process has been applied somewhat inconsistently, I think it is a useful pathway, and I hope it doesn't go away. Losing the 510(k) pathway would completely stifle innovation of products that are less complicated than, say, a drug-eluting stent or drug-coated balloon.

Dr. Ansel: I agree. The concern I have is that the 510(k) process will be made almost as stringent as the PMA process. That would add a tremendous amount of cost to getting a device to market. It would be reasonable to look closely at the process again before any decisions are made that would convert it into a more complex pathway, consequently making it harder for a technology to enter the US market.

To what degree does the presence or absence of an FDA-approved indication influence your decision to use an available device?

Dr. Ansel: If I have two equal devices, then I will use the on-label option. The primary reason I do that is I want to give reinforcement to the company that made the investment to get the approval and went through the rigorous process. However, if the devices are unequal and there are data outside the US suggesting that one is superior to the other, I will do what is best for my patient.

Dr. Laird: I completely agree with Dr. Ansel. I have started using more and more devices that have an on-label indication. I try and do my renal cases with an approved renal stent, for the most part, and the same goes for iliac and SFA cases. I don't always stick to that, but I try, and I have tried to reward the companies that have made the investment and gone through the trouble of getting the device on label.

Dr. Dake: I have as well. But, obviously, if you believe that there are opportunities to help patients with devices that are not approved for the specific indication, that they are truly better and there is justification for it, then I have no problem using the unapproved device.

Dr. Garcia: I too have gone more toward using devices that have an on-label indication for most everything. One of the trickier decisions in this regard is that the company who comes forward first with a new technology sometimes bears the largest cost burden, and the next wave of devices can gain their approvals based on the predicate example set by the first device, which is less costly.

It can also be hard to know which devices are equal or comparable, as we discussed before, due to the lack of comparative data for available technologies. We can do our best to evaluate registry data or single-center data, whether it is US or international, to decide which device to use. But yes, at the end of the day, I am using more of an on-label approach for the SFA, renals, and other peripheral lesions.

Dr. Laird: In addition to wanting to reward the companies that have put forth the resources to gain the on-label indication, we also have the benefit of knowing more about their devices. The data used as a basis for approval are robust and provide a sound background for clinical decision making as compared to devices that have only "biliary" or "tracheobronchial" approval. We simply don't know as much about the off-label devices.

Does reimbursement influence your procedural decision making, or do you simply perform the procedure in the manner and with the devices you prefer and then put in for the billing?

Dr. Schneider: Reimbursement does not affect my clinical decision making.

Dr. Ansel: Exactly right.

Dr. Laird: Agreed.

What are your thoughts on the way SFA interventions are reimbursed? Is it currently a sufficient system, or are there improvements that you would like?

Dr. Ansel: I don't believe the system accurately identifies the degree of complexity in each procedure. Unfortunately, it would be very difficult to accomplish this. A complex procedure may take one of my esteemed colleagues 10 minutes, but for someone who does the procedure far more infrequently, it might take 2 hours to do the same case.

If the system were designed to reimburse the degree of complexity based on the duration of the procedure, it probably would not work for this reason, as well as possibly incentivizing clinicians to work slower or less efficiently. Maybe length of occlusion could be utilized. There are those really complex procedures when you spend a long time and pull a critically ill patient through, and personally, you and the staff are exposed to significant radiation. Certainly, you would desire at that time better reimbursement. I'm not sure how it can be improved upon, so for now, we have to deal with it.

Dr. Laird: You're right though—you could get paid the same for a 4-cm stenosis that you primarily stent as you would a 30-cm occlusion in a limb salvage case, where you spend 2 hours trying to get through the occlusion before stenting it.

What other factors should influence reimbursement rates? Comparative effectiveness? Costs of devices used?

Dr. Garcia: Industry would love for reimbursement to be based on device cost and, more importantly, devices used in an unbundled manner, but I can't imagine that would be the way to go or practical in the current financial environment. Reimbursement should be commensurate with what you do—PTA/stenting or atherectomy/PTA or the like. If you treat a long lesion and it takes a lot of work, whether it is for limb salvage or even just standard treatment of critical claudication, the reimbursement should be commensurate with what you've accomplished—recanalization and therapy for claudication, etc. The overall reimbursement depends on the outcome: an open artery.

I don't believe there needs to be a new code to support whether or not angioplasty was performed, but if it was a lot of work to do that angioplasty, then I think it should be paid for. The problem is there is no way to gauge what we consider "a lot of work," and that's why we have these standards for what we are paid.

Dr. Laird: And, there are not enough comparative data to allow reimbursements to be based on comparative effectiveness. With the heterogeneous patient populations and sets of lesions we treat, it would be really tough to do it that way. I agree it would be nice if there were a better way to reimburse based on time spent and difficulty of the case, rather than focusing on the type of device that is used.

Who decides which stents are on shelves in your facility? Clinicians or purchasing staff?

Dr. Ansel: At our institution, it is a combination of both. The effort is to offer our patients the best technology but to also try to keep the cost of health care as efficient as possible.

Dr. Garcia: I think that is more or less the standard. A lot of people are pushing cost, but clinicians have a fairly big role in what is on the shelf.

Dr. Laird: It's the same here at UC Davis. Everything has to go through a committee, but the committee usually adheres to the recommendations of the physicians.

Dr. Dake: That's exactly the way we do it here, too. There is a value-added committee. No clinicians sit on it, but everything comes through in an application, and there has to be justification by the clinician who submits the request.

Roles of Current SFA Devices: Adjunctive, Primary, or Situation-Based?

In which SFA cases do you stent 100% of the time? Which require only ballooning or should not be stented for one reason or another?

Dr. Laird: One hundred percent of the time that I get a suboptimal result with a balloon, I stent. Perhaps with the exception of lesions in the common femoral artery, but otherwise, this is the default option if you have a suboptimal angioplasty result. I stent most lesions that are up to 15 cm in length based on data from the randomized trials.

Dr. Dake: In general, for complete occlusions, if I am not going subintimal and the lesion is more than 3 or 4 cm long, I will place a stent almost 100% of the time.

Dr. Garcia: It's hard for me to say 100%, but I would tend to agree with Drs. Laird and Dake. Most of the time, whether it be up to 10 cm or longer lesions, and most CTOs, we will generally stent those with the proviso that the patient will often be coming back for a second look or for restenosis. Fortunately, we will have upcoming data for alternative therapies, such as atherectomy in these longer lesion subsets with and without adjunctive drug-eluting balloon therapy (DEFINITIVE LE and DEFINITIVE AR), that may afford an equal outcome with an equal or better durability at 12 months and beyond.

Is there any area of the SFA in which you would definitely not place a stent, or any types of patients in particular?

Dr. Garcia: I do not have any stenting restrictions specifically in the SFA itself, but perhaps in the common femoral artery or at the knee. It will be intriguing to see how some of the newer stent technologies perform down there. If we are strictly talking about native vessels, I don't think there is a "no-stent" zone in the SFA. It will be intriguing to see where the alternative therapies such as atherectomy land with their upcoming data as a comparator to the stenting data.

Dr. Laird: I try to avoid long-segment stenting, in particularly small vessels (4 mm or less) in diabetic patients. The restenosis rates are so high in those cases. But, sometimes, it can't be avoided if you can't get a decent result with angioplasty or adjunctive devices.

Is atherectomy ideally used as a standalone therapy, or as part of a combination procedure?

Dr. Garcia: I perform atherectomy as a standalone therapy most of the time, but I have become more liberal with my use of adjunctive therapy, which would be plain old balloon angioplasty. There is probably about a one in three chance the atherectomy procedure will include some adjunctive therapy and, for me, probably a less than 5% chance of stenting at the time of their intervention. It will be interesting to see whether current trials (such as the upcoming DEFINITIVE LE and DEFINITIVE AR) come out with data that are supportive of atherectomy in general, but also to see if we can compare an atherectomy device directly with other treatments for short, medium, and long lesions and see where the cards fall. I think that would be helpful to find out how each option performs in the long-term and ultimately see the potential added benefit for drug-coated balloons to the up front use of atherectomy in this challenging territory.

Dr. Ansel: In the vast majority of atherectomy procedures that we perform, our initial goal is to achieve a standalone result. But, like Dr. Garcia, I will at times touch it up with a balloon at low pressure and only stent it if we have a flow-limiting dissection. From a stenting standpoint, I try to stay away from the ostial SFA lesions because I don't think our results are particularly good there. And, if we get too close, we may actually compromise the profunda, which is a problem with the current technology.

In which situations do you use embolic protection devices during SFA interventions?

Dr. Ansel: We use embolic protection in most of the atherectomy procedures and in any lesions that have thrombus associated with them. At times, when runoff is poor, I utilize embolic protection in complex lesions. This is all off-label and again is the art of physician practice with their patients' best interests, such as complication avoidance, in mind.

Dr. Laird: I agree. I think most if not all people who perform a lot of atherectomy use embolic protection devices as well because there is quite a bit of embolization that occurs, particularly in in-stent restenosis cases, long, complex lesions, or heavily calcified lesions. In certain situations, we will use the Proteus embolic capture balloon (Angioslide, Ltd., Caesarea, Israel) for SFA occlusions or cases where we have done atherectomy.

Dr. Garcia: I tend to agree. Much to the chagrin of the atheroablative technology manufacturers out there, I use a lot more distal protection than they would probably like me to use. I generally like to be proactive about avoiding complications, and whether the atherectomy device aspirates small debris, creates small particles, or is supposed to capture it, I think they all tend to embolize. The question is how many are clinically relevant, and we don't know the answer to that.

I use distal embolic protection in thrombotic lesions, recently occluded grafts, and heavily calcified arteries that can shower debris. These are all particularly useful settings for using distal protection. Regardless of whether or not I've used atheroablation or balloon and stenting, I have seen a ton of thrombus in layered grafts that we've ballooned, and it goes downstream.

Up Next?

Drug-Eluting Stents and Drug-Coated Balloons

An FDA panel is scheduled for mid-October to review the data from the Zilver PTX randomized trial to make a recommendation regarding FDA approval. How do you think the data from these studies will translate into real-world practice if the device is approved?

Dr. Ansel: I think this may very well represent a paradigm shift, as we saw in the coronary vessels. We have been modestly successful with bare-metal stents, and the Zilver PTX data show proof of concept that coating these stents with drugs can have a durable, improved effect over bare-metal stents and angioplasty.

Dr. Garcia: The data are very compelling for two reasons. The first is they did the study very well, and they all have to be commended. It is not only a proof of concept, it really was the first time we had a good, meaningful dataset come forward on a fairly conservative peak systolic velocity as a metric for restenosis. Their metric was only a 2.0 PSVR, and they did very well.

The other intriguing part was that this stent was also durable out to 2 years, which is a benefit previous studies, such as the Schillinger study, had not been able to show. It is a remarkably good study with remarkably good outcomes, and whether or not it is a paradigm shift, I think it certainly elevates balloon and stent to a different degree.

The question will be, how do the data translate? I know there will be a registry for a longer lesion subset (greater than 54 mm). That is the crux of why we do what we do in the SFA. It's not just the short lesions, but also the longer ones, and how it will play out when we begin to apply this technology to real-world patients.

The longer registry at 2.5 PSVR really did show some benefit and it has some pretty good working numbers, and I'm sure Drs. Dake and Ansel can speak specifically to that. But I think it's a great study; it's a remarkably good set of data.

Dr. Dake: What everyone wants to see now is what happens when it gets into a more general, nonstudy environment and all hands have a chance to experience it. Will the technology still have the same results in longer lesions, in restenotic lesions, and in other areas that weren't strictly within the confines of the randomized trial?

But it is fair to say that we are probably entering an era in which we have to consider that a drug-eluting stent may soon be the new standard in stents, depending on the cost associated with it. If the DES were priced comparably, I certainly think it would be tough to find reasons why not to use it because there is a signal that seems to be quite clear.

Dr. Laird: While I agree with my colleagues that the results of the Zilver PTX trial look promising, and that it will be nice to have the availability of drug-eluting stents for femoropopliteal lesions, it is too early to put the nail in the coffin of bare-nitinol stents in the SFA. For one, the patency benefit of Zilver PTX over bare-nitinol stents appears to be modest, and we do not yet know what these devices will cost and whether the benefit will warrant the cost differential. Also, SFA bare-nitinol stents continue to improve. There are excellent data with the LifeStent (Bard Peripheral Vascular, Tempe, AZ) and the newer Supera stent (IDev Technologies, Inc., Webster, TX). Gore & Associates also has a unique ePTFE-coated nitinol stent (the Tigris stent) that will be entering trials in the near future.

If drug-eluting stents gain an FDA indication, how will clinicians decide when to use a DES versus a bare-metal stent? How will you decide this in your own practices?

Dr. Ansel: For me, the question will be when not to use a drug-eluting stent. If you have something that performs better, I think you have to use whatever is the best potential outcome to your patient. We will likely have three approved SFA stenting devices on the market soon—LifeStent, Viabahn, and if the FDA approves it, Zilver PTX. Many other registries have been completed or are currently in follow-up that will have further data on bare-metal stents, but now I think it's up to them to conduct a trial comparing Zilver PTX to their stent to prove their bare-metal option is equivalent or better.

The other element of the Zilver PTX trial that certainly seems to be of interest to people involves the patterns of restenosis, which appear to be much more focal in the drug-eluting stents. If that holds up, it really is a paradigm shift. If we can get away from diffuse in-stent restenosis, which is terribly hard to treat, toward a more focal restenotic area, which should at least theoretically be much easier to treat, that will change how we approach these patients.

ZILVER PTX UPDATE

Just before this issue went to press, an FDA Circulatory System Devices Panel of the Medical Devices Advisory Committee reviewed data regarding the safety and efficacy of Cook Medical's Zilver PTX drug-eluting stent in the SFA and voted unanimously to recommend approval of the device. For more information on the panel meeting and its specific recommendation, please see the expanded coverage in our News section, beginning on page 12.

Dr. Garcia: I agree with Dr. Ansel. I think this will be the next big step, and it is a remarkable step for us when it comes to research. Now, like we had in the coronaries, we can have the Palmaz-device equivalent of what people will use as a comparator. Whether it ends up being a drug-coated balloon, drug-eluting stent, or atheroablative therapy in whatever form, it will now have to go against this metric that people want to say is the best. And it may very well end up being this drug-eluting stent or perhaps another technology based on the head-to-head comparison.

Looking ahead at other devices currently being evaluated, do you see the role of drug-coated balloons being primary or adjunctive, or is too early to tell?

Dr. Dake: There will definitely be a role for drug-coated balloons, but I think it's too early to tell exactly what it will be. The studies to date have shown a definite positive signal in relatively short lesions, but as is the case with the drug-eluting stent, the real question with drug-coated balloons is what happens in longer lesions, hard-to-treat areas, and total occlusions. We also don't know how often we will need a supplemental stent or another device to take care of recoil in the vessel, which is one of the known limitations of balloon angioplasty.

Dr. Schneider: I agree with Dr. Dake—we don't know if its role will be primary. It certainly could become a primary therapy. In addition, there is a high likelihood that drug-coated balloons will also have a role as an adjunctive tool because there are so many situations in which they might be useful, such as focal recurrences, in-stent restenosis, or in conjunction with other technologies like atherectomy. This might be applied in patients who have a high risk of recurrence based on past performance, in which a particular intervention might be used followed by a drug-coated balloon as an adjunct.

Dr. Ansel: I agree with Dr. Schneider and think the question is not unlike when we consider surgery versus endovascular repair. For some reason, we act like there is an all or none dynamic to this. But what we learn when we get more experience is which patients are optimized for particular therapies, be they drug-coated balloons or drug-eluting stents, for a unique set of reasons. There will be a learning process and fodder for research projects as we go down the road.

Dr. Garcia: I wish we had a better answer than we just don't know, but that is the case for now. One can envision, as everyone is describing here, that this could be potentially be more of an adjunctive option. One could also envision that it could be the primary modality to treat restenosis more focally if it does occur in the short, medium, or long lesions, and to get a better sense of how it works in those short, medium, and long lesions.

Dr. Laird: I suspect that drug-coated balloons will be used in both ways. If the trials are successful, the technology will be approved for primary use as an alternative to balloon angioplasty. But I would envision that they would likely be used after atherectomy by the advocates of atherectomy until we have definitive proof one way or the other about that strategy. There will still be a lot of stenting for suboptimal balloon angioplasty results, and the same will likely be the case when we can't get a decent result with a drug-eluting balloon.

Although we have already learned from the trials that we can leave behind a suboptimal balloon angioplasty result with a drug-coated balloon and still end up with a pretty good long-term result, I think many physicians will need to be retrained in terms of how to deal with suboptimal or less than ideal angiographic results after angioplasty with a drug-eluting balloon. We will need to fight the urge to stent to achieve a cosmetically perfect result in every case.

When do you anticipate drug-coated balloon availability in the US?

Dr. Garcia: I don't think it will be before 2014 or 2015.

Dr. Schneider: I would say 3 years at the earliest. I assume there will be around a year to enroll, a year to follow the patients, and a year to work through the regulatory and reimbursement processes. But, it could be longer.

Dr. Laird: The Lutonix trial (Lutonix, Maple Grove, MN) has already enrolled a significant number of patients, and they are making great progress. But I agree that even with the most favorable scenarios, we probably will not see drug-coated balloons available in the US until 2014, and that would likely only be for SFA and popliteal use. There is not yet a trial in the US for below-knee drug-coated balloon use, and it will be a while before that happens.

Dr. Garcia: One of the tough parts of this, as we've touched on earlier, is that America really has not led in this whole process. It's really bothersome to me.

Overall though, I think the process of treating the SFA will continue to be a work in progress. But, technologies will not have multiple shots at gaining acceptance. There will be the opportunity to establish effectiveness as a primary option, followed by a shot at playing an adjunctive or niche role. In the SFA, there is often the opportunity for each to play an important part in a patient's overall course of therapy. ■