Luis F. Angel, MD

The inventor of the Angel catheter discusses insights learned from participation in the FDA's early feasibility pilot program and his initiatives for the prevention of pulmonary embolism.

How did your device gain entry into the US Food and Drug Administration's (FDA's) early feasibility pilot program?

In Q4 of 2011, the FDA launched a pilot program to allow early clinical evaluation of devices that provided an innovative solution for a problem with a significant clinical impact to provide early proof of concept and safety data without having to go through an extensive, and sometimes unnecessary, program. Initially, the FDA chose eight products for this pilot, and the Angel catheter was selected among them to conduct a limited clinical trial with five patients in the United States.

What makes the Angel device unique among the class of IVC filters?

Clinical data for IVC filters show, although with some limitations, that they are effective in preventing clinically significant pulmonary embolisms (PEs). However, currently approved devices have multiple limitations preventing the early use of these filters in critically ill patients and more importantly, because their retrieval rates are relatively low, they are associated with multiple long-term complications. The Angel catheter provides a solution to these problems with a device that is easily inserted at the bedside—as early as in the emergency room or upon arrival in the intensive care unit—as part of the central venous catheters used for the management of these patients. It can be easily removed later in all patients when the risk of PE is decreased or when anticoagulation is no longer contraindicated. The current technology also offers opportunities for improvement in the diagnosis and management of deep vein thrombosis (DVT) with local therapy.

How would you summarize the design of the current trial toward gaining US approval, and how does it differ from others that are/were not part of the early feasibility program?

The early feasibility program was vital for us to understand not only the requirements for the approval of the device, but more importantly, to better understand how to implement the clinical trial program. Initially, the early feasibility trial was slow and complicated due to requirements for additional radiology tests, making it difficult to consent and evaluate patients. However, the trial provided enough information for us and the FDA to better understand the use of the device, any potential safety issues, and to design a trial that would answer important questions about safety and effectiveness when the device is used in critically ill patients in whom anticoagulation is contraindicated. The learnings from the early feasibility trial allowed us to make modifications to the pivotal trial, and some of these changes have significantly affected enrollment. For example, it took us over 10 months to enroll five patients in the early feasibility study, whereas in the pivotal trial, we enrolled over 145 patients in 8 months.

What are some of the advantages of participation in the early feasibility program? Is there any potential for higher hurdles to achieving approval?

As mentioned before, this is a great opportunity to formally introduce a technology to the FDA and to understand the requirements and their vision of your technology. It also provides the possibility of evaluating early devices in the United States in a research environment that is proven to be the most effective in successfully bringing products for the benefit of our patients. There is obviously a risk in testing an early device, which could present unforeseen safety issues, making any further evaluation more complex.

How would you describe the process of working with the FDA in this program?

The process has been great and having close communication with the agency has allowed them to better understand the technical aspects of our device and the potential benefit that it could bring to many patients at high risk of PE. At the same time, the interaction has provided us with valuable feedback from the agency, allowing us to better understand the requirements for approval and to design our protocols so as to meet these requirements. In the end, this process is very beneficial to both companies trying to innovate here in the United States and for the FDA in learning about future products early in their life cycle.

Has recent press regarding complications as well as increased focus on conservative placement and aggressive retrieval affected the trial planning or enrollment in any way?

We have been aware of this issue for many years, and

(Continued on page 137)

(Continued from page 138)

the systematic review that we published in 2011 about the use of retrievable filters in clinical trials was a clear indication of the problems. Our device in particular addresses this issue, allowing for early placement of filters and retrieval of all our devices. Currently, this is the only device in clinical trials with a 100% retrieval rate.

If all goes well in the trial, when do you anticipate US regulatory approval?

This is difficult to predict; however, if we continue to have positive results in the trial, we anticipate submission to the FDA early in 2016 and possible approval by late Q2 or early Q3 of 2016.

Outside of this program, what other research are you currently undertaking?

Our company is focusing on developing complementary products for the prevention of PE—in particular, in the early diagnosis of DVT and also in the implementation of catheter-related modalities for the treatment of DVTs and massive trapped clots.

If a philanthropic group approached you with $1 million to research a vascular condition or develop a therapy, on what would you spend it?

Obviously, we are very committed to the prevention of clinically significant or fatal PE, where we strongly believe we could have a major impact in decreasing the mortality associated with this condition. There are more patients in the United States dying from PE than from breast, colon, and prostate cancer combined. Measures that look into the early detection, treatment, and prevention of PE may have a huge impact on this disease. ■

Luis F. Angel, MD, is Professor of Medicine, Director of Lung Transplantation, and Director of Interventional Pulmonary, Pulmonary and Critical Care Medicine, University of Texas Health Science Center at San Antonio in San Antonio, Texas. He has disclosed that he is the Chief Medical Officer for BiO2 Medical. Dr. Angel may be reached at (210) 743-2809; langel@bio2medical.com.