Regulatory Perspectives on Long-Term EVAR Outcomes

Representatives from FDA discuss how "long term" is defined, the goals of and insights from recent panel discussions, use of real-world registries to explore long-term durability, how follow-up can be achieved in the face of real-world challenges, and the agency's call to action for EVAR implanters.

With Ronald Fairman, MD, and Carmen Gacchina Johnson, PhD

When discussing outcomes and follow-up for devices, what does the agency typically consider "long term"?

The Society for Vascular Surgery reporting standards indicate "short term" includes outcome measures reported within 30 days to 6 months after endovascular aneurysm repair (EVAR).[1] "Mid term" refers to 6 months to 5 years, and "long term" refers to beyond 5 years. With respect to EVAR, the FDA agrees that generally, long term refers to outcomes beyond 5 years.

What is the agency currently considering "long term" for EVAR devices and outcomes in particular, and has this philosophy changed in recent years?

The FDA balances pre- and postmarket data to make safe and effective devices available in the United States in a timely manner. Typically, pivotal studies to evaluate safety and effectiveness of new EVAR devices include primary endpoints evaluated through 1 year and a condition of marketing approval to continue follow-up through at least 5 years. However, valuable clinical experience is often gained postapproval. For example, real-world outcomes captured in registries and claims data may differ from those reported in a controlled clinical study and provide longer-term data.

Additionally, although EVAR technology has advanced since the first devices were FDA approved in 1999 and EVAR continues to be associated with favorable early and mid-term outcomes, improvements in medical care have resulted in an increase in EVAR patient life expectancy, and there are fewer longer-term data available to assess potential late device failure modes.

EVAR has been widely embraced in the United States; approximately 80% of abdominal aortic aneurysms (AAAs) are treated with EVAR.[2] The FDA believes that the following outcomes are important to track in the longer term: aneurysm-related mortality, aortic rupture, reinterventions, sac enlargement, endoleak, and other clinically meaningful EVAR-related events related to variations and iterative changes in graft design. Follow-up imaging is an important factor in assessing these outcomes.

EVAR devices as a device class continue to evolve, and there are limited longer-term data for newer-generation devices. A better understanding of the real-world safety and effectiveness profile of these devices aligns with the FDA's public health mission of ensuring that approved products remain safe and effective. Although our foundational safety and effectiveness standards remain the same, we appreciate the dynamic nature of medical device development and patient needs that guide regulatory decision-making. As patients with cardiovascular disease are living longer and events continue to occur over time, longer-term data collection and evaluation are important. The FDA believes that an improved system of long-term data collection and analysis is in the best interest of patients, physician users, device manufacturers, and hospital systems.

What prompted the agency to put together the recent panel exploring long-term follow-up after EVAR?

Endovascular grafts continue to be an important treatment modality for AAA patients. However, despite significant technologic and treatment advancements, there are limitations in the currently available data to address questions of longer-term performance. An improved long-term postmarket data collection system would allow timely detection of individual device or device class safety signals and potentially guide device improvement and labeling updates.

How would you summarize the goals of these panel discussions and the most important insights the agency gained during them?

The goal of the meeting was to obtain input from key stakeholders on the need for improved postmarket data collection and the outcomes that are most relevant to capture in the real world. Additionally, the FDA sought input on data collection platforms and how to incentivize and optimize real-world data collection. Discussions at the panel meeting led to the following conclusions[3]:

- Endovascular grafts continue to be an essential and important part of the treatment of patients with AAAs.
- All parties, including EVAR device manufacturers, indicated a need for improved postmarket data collection.
- There was consensus that data collection should be through 10 years postprocedure for all-cause mortality, aneurysm-related mortality, aortic rupture, and aortic reintervention. The reintervention endpoint should capture the reason for reintervention and type of reintervention performed.
- The panel recommended collection of key imaging endpoints, including endoleaks, change in aneurysm size, and device patency. Although panel members acknowledged the challenges of collecting imaging data, they emphasized the importance of these studies and encouraged creative approaches to address the imaging endpoint goals.

What do you envision the role of industry should be in ensuring long-term follow-up is conducted? Does the agency have any notable changes that might be required in typical follow-up protocols for pivotal and postmarket approval trials that will result from recent discussions?

The FDA will work collaboratively with key stakeholders (eg, patient representatives, professional societies, industry, existing postmarket data collection infrastructures) to help drive the effort forward. The FDA was encouraged that industry representatives who spoke at the panel meeting expressed support for establishing an improved postmarket long-term data collection system.

How has the FDA's view of the utility of "real-world" registries such as the Vascular Quality Initiative, Medicare database, and similar programs outside of the United States evolved in recent years? How are they best used, and where do these fit into the agency's data hierarchy? How might these registries be employed to further explore long-term durability?

Real-world evidence (RWE) can be leveraged to bring new products to market, evaluate the safety and effectiveness of existing products for new uses, and assess the continued performance and safety of products on the market. In 2021, the FDA issued a report, "Examples of Real-World Evidence (RWE) Used in Medical Device Regulatory Decisions," which illustrates the wide range of RWE examples used in regulatory decisions.[4] We have also issued guidance to clarify how we evaluate RWE submitted to the FDA.[5] These documents explain how real-world registries may serve as appropriate infrastructures to obtain data for pre- and postmarket regulatory review. RWE may be submitted from United States and non–United States data sources.

There are infrastructures already capturing data on EVAR outcomes, which were discussed at the November 2021 Circulatory System Devices Panel of the Medical Devices Advisory Committee meeting.[6] Strengths and limitations of individual data sources should be systematically evaluated, and the FDA recommends that improvements for long-term data collection be discussed during the new data collection system planning stage.

Ensuring follow-up compliance can be challenging for a variety of reasons, from the patient, physician, and the facility perspectives. What are the agency's views on how to achieve the necessary follow-up given real-world daily challenges of cost, data entry and management, and effective patient tracking/communications?

Despite device labeling and medical professional society recommendations, follow-up annual imaging surveillance noncompliance is approximately 60%, with notable gaps at 3 to 4 years post-EVAR. The FDA agrees with the panel's recommendation that stakeholders should work together to improve follow-up imaging compliance and provide incentives for real-world data collection participation. We also agree with the following recommendations from panelists:

- The system should provide value to patients and participating health systems.

- A tiered data collection approach may be considered by individual health systems to facilitate their participation.
- The FDA should encourage data sharing and active participation among stakeholders.
- Input from patients and patient advocacy groups should be considered in the design of real-world data collection platforms.

Does the FDA have a call to action for EVAR implanters regarding the follow-up of AAA devices based on recent discussions?

There is uniform agreement among the FDA and key stakeholders that high-quality, long-term EVAR data collection is warranted. In addition to focused clinical outcomes, the challenges and logistics of obtaining long-term imaging follow-up require further clarity.

The FDA encourages implanters to have preoperative conversations with EVAR patients, emphasizing the importance of lifelong follow-up and the risks of not obtaining regular follow-up. The FDA will engage with industry to consider development of a shared decision-making tool to enhance the preoperative discussion of treatment options. We believe implanting physicians should also stay engaged with patients after EVAR to ensure appropriate follow-up.

In alignment with these comments, the FDA recently issued a letter to health care professionals to impress upon physicians and other health care professionals the importance of EVAR patient follow-up.[7] ■

1. Chaikof EL, Blankensteijn JD, Harris PL, et al. Reporting standards for endovascular aortic aneurysm repair. J Vasc Surg. 2002;35:1048-1060. doi: 10.1067/mva.2002.123763
2. Schanzer A, Greenberg RK, Hevelone N, et al. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. Circulation. 2011;123:2848-2855. doi: 10.1161/CIRCULATIONAHA.110.014902
3. US Food and Drug Administration. 24 hour summary of the Circulatory System Devices Panel meeting November 3, 2021. Accessed February 28, 2022. https://www.fda.gov/media/154009/download
4. US Food and Drug Administration; Center for Devices and Radiological Health. Examples of real-world evidence (RWE) used in medical device regulatory decisions. Accessed February 28, 2022. https://www.fda.gov/media/146258/download
5. US Food and Drug Administration. Use of real-world evidence to support regulatory decision-making for medical devices: guidance for industry and Food and Drug Administration staff. Accessed February 28, 2022. https://www.fda.gov/media/99447/download
6. US Food and Drug Administration. November 2-3, 2021: Circulatory System Devices Panel of the Medical Devices Advisory Committee meeting announcement. Accessed March 7, 2022. https://www.fda.gov/advisory-committees/advisory-committee-calendar/november-2-3-2021-circulatory-system-devices-panel-medical-devices-advisory-committee-meeting
7. US Food and Drug Administration. FDA advisory panel recommendations on lifelong surveillance and long-term postmarket data collection for patients with AAA endovascular aortic repair—letter to health care providers. Accessed February 28, 2022. https://www.fda.gov/medical-devices/letters-health-care-providers/fda-advisory-panel-recommendations-lifelong-surveillance-and-long-term-postmarket-data-collection

Ronald Fairman, MD
Medical Officer, Vascular and Endovascular Devices Team (VEDT)
Division of Circulatory Support, Structural and Vascular Devices
Office of Cardiovascular Devices
Office of Product Evaluation and Quality
CDRH, US Food and Drug Administration
Silver Spring, Maryland
ronald.fairman@fda.hhs.gov
Disclosures: None.

Carmen Gacchina Johnson, PhD
Assistant Director, Vascular and Endovascular Devices Team (VEDT)
Division of Circulatory Support, Structural and Vascular Devices
Office of Cardiovascular Devices
Office of Product Evaluation and Quality
CDRH, US Food and Drug Administration
Silver Spring, Maryland
carmen.gacchina@fda.hhs.gov
Disclosures: None.