Exploring the Effects of the Paclitaxel Pause

Dr. Secemsky discusses patient perspectives, recent study findings, and the evolving peripheral market.

With Eric A. Secemsky, MD, MSc, RPVI, FACC, FAHA, FSCAI, FSVM

After the 2018 *Journal of the American Heart Association* (*JAHA*) meta-analysis suggesting an early mortality signal in peripheral artery disease patients treated with paclitaxel-coated products,[1] 2019 was a year defined by the exploration of this signal, largely amidst a "pause" in paclitaxel use. The FDA first issued a safety warning in March 2019, then conducted extensive hearings in June of that year, followed by formal recommendations in August 2019, which limited the use of the devices and suggesting changes to informed consent. After numerous independent trials, industry-backed examinations, and regulatory analyses, the FDA's pause on paclitaxel use was lifted in July 2023.

Do you still field questions from patients about the safety of the procedures? How do you address these if so?

I really never received many questions about the safety of paclitaxel devices from my patients. During our shared decision-making discussions, I try to be exhaustive about the specifics of the peripheral procedures and the devices we use with the patient, and that probably helped. I think since the FDA revised its stance and any messaging about potential harm with these devices has been removed, it has made the overall discussion with patients easier for other practitioners.

Are we yet able to see some of the real-world clinical effects of the period during which paclitaxel products were unavailable?

We recently published an analysis that found an observed increased risk of amputation or death among Medicare beneficiaries during the period that followed the change in labeling of paclitaxel in early 2019.[2] This was also compounded by the COVID-19 pandemic. Medicare patients treated prior to 2019 seemed to fare better, and it's hard not to presume that at least part of this was due to the lack of availability of paclitaxel-coated devices, although we cannot conclude causality. It will be interesting if we see this trend reverses over the next few years as these devices are again being commonly used during peripheral intervention.

As someone who serves on advisory boards and as a principal investigator for industry-funded trials, what is your impression of industry's view on paclitaxel in 2025 and beyond?

The pause seemed to advance the budding enthusiasm for sirolimus delivery devices, which have not yet been approved for use in the lower extremities in the United States but are available in other markets.

I think paclitaxel will continue to have an important role in peripheral interventional devices, but it is also exciting to see a new drug-coating formulation in investigation so that we can bring our patients options with their care.

Has the pause affected this paradigm in a material way, or are the trajectories of these agents relatively independent in the long run? At this point, do you think the competition and ultimately the clinical decisions will come down to efficacy alone?

I think the pause fueled innovation, both among start-up companies and among larger established medical device companies. Innovation is always welcome, and if there is a way to improve the patency, improve the cost, or develop devices for vascular beds without

many options, this is a win. Right now, we are still understanding if sirolimus-coated balloons can compete with paclitaxel-coated balloons in regard to efficacy and safety. Both SELUTION SFA Japan and SIRONA studies have suggested sirolimus-coated balloons can perform at least as well as a paclitaxel-coated balloons, and possibly superiorly.[3,4] The next big questions are whether this will hold in a United States investigational device exemption (IDE) trial, whether there is a role for these devices in the below-the-knee vasculature, and whether cost and reimbursement issues will challenge market adoption. Irrespective of this, more treatment options will be a win for the vascular field and help advance the care of our patients.

Beyond the concerns of early mortality, which appear to have been adequately addressed to regulators and at least the majority of operators, are there other concerns related to paclitaxel that need yet be addressed?

I think one issue that is often raised is distal particulate embolization and slow flow. I find this is more discussed outside the United States, where more paclitaxel devices are available, including those used for below-the-knee treatment and chronic limb-threatening ischemia. Newer preparations of paclitaxel-coated balloons seem to have less particulate matter embolization, but this could be another advantage of sirolimus-coated balloons. However, it is not clear how critical this is for patient outcomes, particularly claudicants without tissue loss. I think we need to first better define the clinical impact of slow flow prior to thinking about this for device selection.

Are there any patient subsets, clinical factors, or anatomic factors in which you still have some concern about the use of paclitaxel?

Our group's paper examining the safety of paclitaxel-coated devices in real-world practice (SAFE-PAD) followed the publication of the *JAHA* meta-analysis by only weeks. It provided a near–real-time assessment of the safety of these devices and was used to guide the decision to keep these devices available on the market.[5] The long-term follow-up of SAFE-PAD was recently presented at JET 2025 and again confirms that safety of paclitaxel across many patient and clinical subsets.

With the caveat that it will be situationally dependent, do you think the fact that the concerns regarding paclitaxel safety were ultimately alleviated will affect how any future findings are approached?

I really hope so. Our group helped design and lead the SAFE-PAD study, which was a public-private collaboration to evaluate the safety of paclitaxel devices in United States patients utilizing real-world data.[6] This template has been used for several other device concerns (ie, SAFE-AAA for aortic endovascular aneurysm repair devices, SAFE-IVC for inferior vena cava filters). If there is a positive of the paclitaxel safety concern, we now have a better pathway for using real-world evidence to support our postmarket approval device safety evaluation and address any future concerns that may arise with medical devices. This is hopefully reassuring to all stakeholders, from regulators to clinicians and patients. ■

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