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August 9, 2019

Dear colleagues,

Over the past several months, patient safety associated with paclitaxel-coated devices has been at the forefront of a discussion among the FDA, medical device manufacturers, and physicians. Most recently, a public meeting of the FDA's Circulatory System Devices Panel in June resulted in recommendations to address concerns about mortality rates that were published in a meta-analysis of paclitaxel device studies. On August 7th, FDA updated its communication to healthcare providers after reviewing the panel's recommendations.

Updated recommendations to healthcare providers

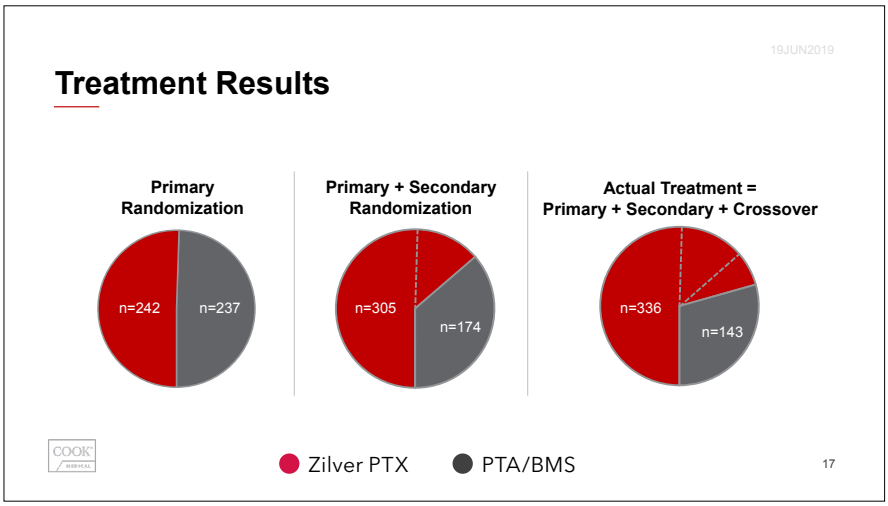
FDA's updated letter outlines new recommendations to healthcare providers who are making treatment decisions about paclitaxel devices. We recommend that healthcare providers follow the FDA guidelines. A full version of the letter is available at www.fda.gov.

We applaud FDA's work in the best interest of patients. Cook is pleased that clinicians and patients will continue to have access to important technologies like Zilver PTX. We will continue to collaborate with FDA, clinicians, industry partners and medical societies to provide the data needed to make informed decisions on treatment options.

Key points related to the Zilver PTX stent

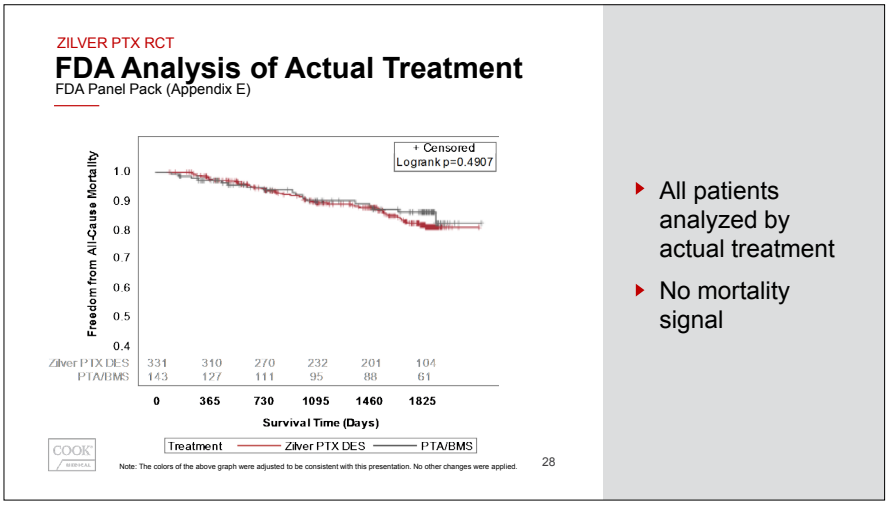
Zilver PTX is the only peripheral drug-eluting stent with five years of clinical data. The Zilver PTX stent has been shown to provide greater than 40% reduction in both restenosis and reintervention through five years. Zilver PTX has shown a sustained clinical benefit for patients suffering from PAD to provide them a better quality of life.

Trial Design: To obtain FDA approval of the Zilver PTX stent, Cook performed a randomized controlled trial (RCT) comparing treatment with a Zilver PTX stent to treatment with PTA. Understanding the **unique trial design of the RCT is important when reviewing the mortality analysis**. The

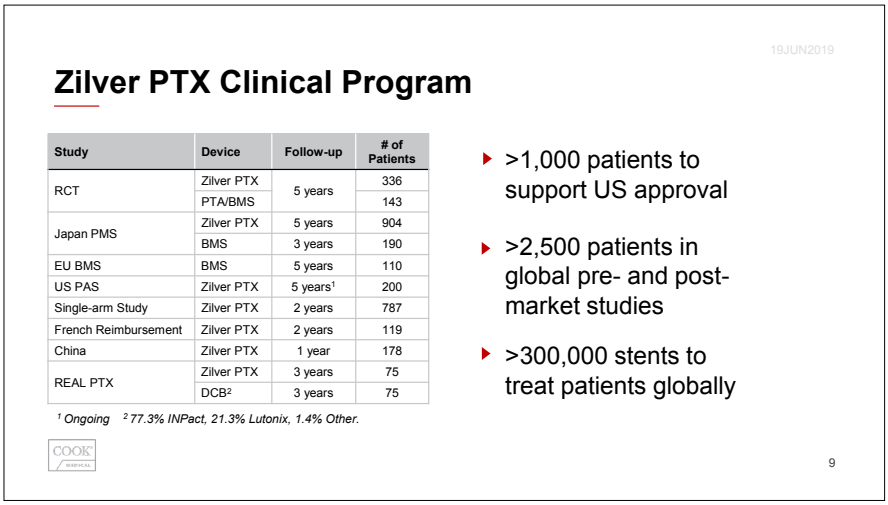


RCT included a primary and secondary randomization, as well as an opportunity for patients in the PTA arm to cross over to treatment with Zilver PTX after experiencing a reintervention in the first 12 months. As a result of this trial design, 40% of patients who were initially assigned to the PTA arm were subsequently treated with Zilver PTX. In total, 70% of the patients enrolled in this trial received a Zilver PTX stent.

Treatment analysis: To appropriately analyze the role of paclitaxel on mortality, it is important to compare all patients who were treated with Zilver PTX to those treated only with non-drug-eluting devices. When comparing patients treated with Zilver PTX to patients treated with angioplasty or bare-metal stents, our randomized trial data and real-world post-market studies showed no difference in mortality rates.[1] In FDA's analysis of all patients actually treated with Zilver PTX compared to patients who did not receive Zilver PTX, there was no significant difference between the two groups.



Clinical program: Cook started researching and developing paclitaxel-coated technologies more than 25 years ago. Over that time, we continued to develop a clinical program to evaluate our Zilver PTX technology in a broad patient population, including patients at high risk of restenosis and reintervention, with co-morbidities that are inclusive and representative of real-world patient populations.



Predictors of mortality: Cook performed a covariate analysis of Zilver PTX to better understand the factors associated with patient mortality. Treatment with Zilver PTX and paclitaxel dose were not predictors of mortality. However, co-morbidities common in PAD patients, such as age, tissue loss, congestive heart failure, renal disease, and diabetes, were associated with mortality.

We are committed to serving patients and clinicians.
Cook continues to analyze Zilver PTX clinical trial data, and we have gathered additional data on patients who did not initially complete the study. We will provide updates as additional information becomes available. We are also collaborating with FDA and industry partners to continually improve data collection and data analysis methods. We are committed to providing physicians and patients what they need to make informed decisions on treatment options, and we will continue to fight this disease to improve the quality of life for PAD patients.

If you have questions about Zilver PTX, please contact us at zilverptx@cookmedical.com, and a member of our team will respond within 24 hours. You can also visit cookmedical.com/newsroom for additional information.

Sincerely,

Aaron Lottes, Ph.D.
Director, Regulatory Science
Cook Research, Inc.

Mark Breedlove
Vice President, Vascular Division
Cook Medical

1 Zilver ® PTX®Drug-ElutingPeripheral Stent: Circulatory SystemsDevice Panel Meeting. FDA Web site. https://www.fda.gov/advisory-committees/advisory-committee-calendar/june-19-20-2019-circulatory-system-devices-panel-medical-devices-advisory-committee-meeting. Accessed August 9, 2019.