PHILIPS

March 2019

Dear Healthcare Provider,

On March 15, FDA posted a Letter to Health Care Providers that indicated their preliminary analysis of the premarket randomized trials associated with approved paclitaxel-coated products used in peripheral arterial disease in the femoropopliteal artery in the U.S. The FDA has identified a potentially concerning signal that stems from five-year data of three trials that showed increased long-term mortality in study subjects treated with paclitaxel-coated products compared with patients treated with uncoated devices.

The Stellarex drug-coated balloon (DCB) was not the subject of any of the three trials with data referenced by FDA. Moreover, at three years, follow-up data from Stellarex studies do not show any such signal.

With our commitment to keeping customers first, we support studies that help ensure the safety of drugs and medical devices used in patients and we will continue to cooperate with the FDA analysis. Stellarex, the only low-dose DCB with already demonstrated durable efficacy,[1] has no mortality signal through 3 years.[2] We are confident in our data and the safety profile of our unique low-dose (2 µg/mm^2) Stellarex DCB.

The following is a recap of the Stellarex safety analysis of patient-level data presented at LINC 2019 during a Drug Eluting Technologies Roundtable on January 22, 2019 by Sean Lyden, MD[2]:

- Stellarex safety analysis was an **independent, 3rd party** integrated analysis of 2,521 (2,351 DCB and 170 PTA) patients from Stellarex 7 studies
- Pooling of more uniform / homogeneous mortality data in patients treated with Stellarex DCB for above-the-knee lesions
- It is one of the largest patient-level data-sets analyzed, which includes one of the largest control group cohorts
- All adverse events across all studies were independently adjudicated by a Clinical Event Committee (CEC)
- The main analysis **pooled only randomized controlled trials (RCTs)** to compare mortality through 3 years between Stellarex DCB and the control (PTA) cohorts
- A separate integrated analysis of mortality rates was presented in patients treated with Stellarex DCBs from all 7 studies

Results:

- Zero device-related deaths reported in over 2,300 clinical study patients treated with Stellarex DCB
- There was no significant difference in mortality demonstrated between Stellarex DCB and PTA mortality through 3 years as well as at each intermediate time-points of year 1 and 2 *(see table on mortality rates in Appendix 1)*
- Results hold true within the clean randomized patient subset (N=589) as well as across the full cohort (N=2,521)
- No statistically significant difference in all-cause, cardiovascular and non-cardiovascular mortality between the groups

These results confirm and reinforce the safety profile of Stellarex DCB in ATK lesions.

PHILIPS

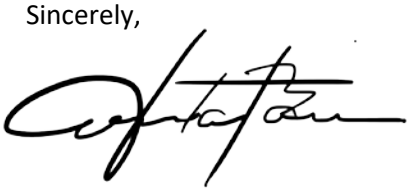
*Data from independent CEC (clinical events committee) adjudication of all events resulting in death across all studies

PHILIPS

While the latest presented patient-level data solidify our confidence in the safety of Stellarex DCB, we are fully committed to continued research on this front through additional analyses, collaborative efforts with regulatory/health authorities, as well with cross-industry research collaboration.

Should you have any questions, please do not hesitate to reach out to the Philips Clinical Team or your local Philips representative.

Sincerely,



Jonathan Batiller
VP of Clinical and Medical Affairs
Philips

PHILIPS

References

1. J. Mathews, ILLUMENATE Pivotal Stellarex DCB IDE Study 2 Year Outcomes, oral presentation. NCVH 2018, New Orleans, LA
2. Lyden S, Long-term safety data from the Stellarex DCB program, oral presentation, LINC Jan 2019

Important Safety Information

Indications for Use: The Stellarex 0.035" OTW drug-coated angioplasty balloon is indicated for percutaneous transluminal angioplasty (PTA), after appropriate vessel preparation of de novo or restenotic lesions up to 180 mm in length in native superficial femoral or popliteal arteries with reference vessel diameters of 4-6 mm. **Contraindications**: Patients with known hypersensitivity to paclitaxel or structurally related compounds and who cannot receive recommended antiplatelet and/or anticoagulation therapy. Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children. Coronary arteries, renal arteries, and supra-aortic/cerebrovascular arteries. Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system.

Please consult product labels and instructions for use for indications, contraindications, hazards, warnings and precautions.
Caution: Federal law restricts this device to sales by or on the order of a physician.

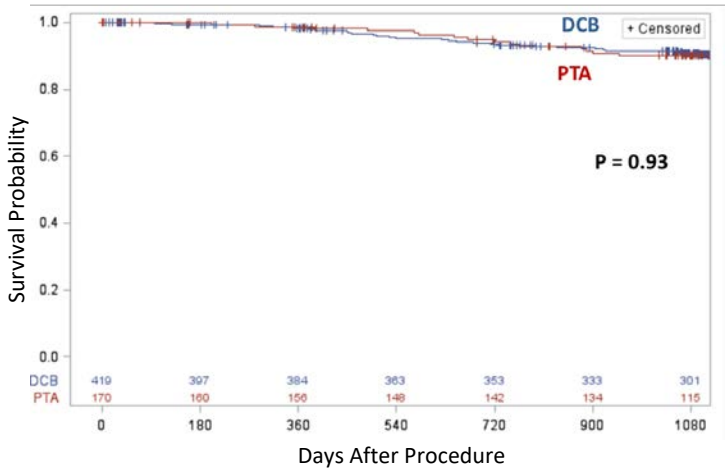
www.stellarexdcb.com

Appendix 1

Mortality for Patients Treated with Stellarex DCB (ATK)[2]

Endpoint	Pooled RCTs		All (Pooled RCTs and non-RCTs)
	DCB KM Estimate (SE) N=419	PTA KM Estimate (SE) N=170	DCB KM Estimate (SE) N=2351
All-Cause Death			
1-year	1.8% (0.7%)	1.3% (0.9%)	2.0% (0.4%)
2-year	6.5% (1.3%)	5.9% (1.9%)	5.5% (0.7%)
3-year	9.3% (1.5%)	9.9% (2.4%)	7.9% (0.9%)
Cardiovascular Death			
1-year	0.5% (0.4%)	0%	0.1% (0.2%)
2-year	1.0% (0.5%)	1.4% (1.0%)	1.3% (0.3%)
3-year	1.9% (0.7%)	2.8% (1.4%)	1.9% (0.5%)
Non-Cardiovascular Death			
1-year	1.3% (0.6%)	1.3% (0.9%)	1.5% (0.3%)
2-year	5.6% (1.1%)	4.6% (1.7%)	4.2% (0.6%)
3-year	7.5% (1.4%)	7.3% (2.1%)	6.1% (0.8%)

Survival: Pooled RCT's All-Cause Mortality through Three Years[2]



No difference in all-cause mortality between Stellarex DCB and PTA through 3 years