Medtronic News

# Patient-Level Survival Analysis Demonstrates No Link Between Paclitaxel Dose and Mortality in Patients Treated with IN.PACT Admiral DCB

*Data Presented Today at LINC Reiterate Commitment to Patient Safety and Data Transparency*

DUBLIN and LEIPZIG, Germany - January 22, 2019 - Medtronic plc (NYSE:MDT) today announced new data shared on the IN.PACT(TM) Admiral(TM) drug-coated balloon (DCB) in patients with peripheral artery disease (PAD) in the superficial femoral (SFA) and popliteal arteries. Outcomes from the IN.PACT DCB Paclitaxel Safety Analysis, an independent, patient-level survival analysis inclusive of all IN.PACT DCB clinical programs, were presented at the Leipzig Interventional Course (LINC) in Leipzig, Germany. A manuscript detailing outcomes from the IN.PACT DCB Paclitaxel Safety analysis was also accepted and is in press with the *Journal of the American College of Cardiology(JACC)*.

Key data highlights:

- 
- At five years there was no statistically significant difference in all-cause mortality between the DCB and plain balloon angioplasty (PTA) arms (9.3 percent versus 11.2 percent respectively, p=0.399)
- 
- Data found no correlation between paclitaxel dose and long-term survival. Patients treated in the DCB arm were classified by upper, mid, and lower dose ranges. Freedom from all-cause mortality based on Kaplan-Meier estimates was 91.7 percent in the upper range, 90.6 in the mid-range, and 90.0 percent in the lower range (p=0.700).
- 
- Data demonstrated no difference in mean nominal dose of paclitaxel between overall survival in patients treated with DCB (n=1,696) and those who died (n=140). Mean nominal paclitaxel doses were 11,829.8ug +/- 7,347.6ug and 11,419.6ug +/- 7,414.8ug respectively (p=0.529).

Patient-Level Safety Analysis

Dr. Peter Schneider, vascular surgeon, presented data from the IN.PACT Safety analysis. The independent, patient-level analysis evaluated the relationship between nominal dose of paclitaxel and mortality in all 1,837 DCB patients enrolled across the IN.PACT Admiral clinical program, including IN.PACT SFA, IN.PACT SFA Japan, IN.PACT SFA China, and IN.PACT Global. The analysis was independently performed by the Baim Institute for Clinical Research (formerly the Harvard Clinical Research Institute) and led by Gheorghe Doros, Ph.D., professor of Biostatistics, Boston University School of Public Health and director, Statistical Consulting, Baim Institute of Clinical Research.

"This independently adjudicated analysis includes 1,837 patients treated with IN.PACT Admiral and followed long-term," said Dr. Schneider. "In contrast to a recently published summary-level meta-analysis-which included 28 trials with different devices, designs, levels of monitoring, and follow-up periods-the findings from this study showed neither paclitaxel use, nor dose had any effect on mortality at five years."

The analysis evaluated all-cause mortality across IN.PACT studies. This included device- or procedure-related death through five years and paclitaxel-related events through 12 months. Upon review of other endovascular therapies in published literature, it was found that the mortality rates across IN.PACT DCB studies are comparable to or lower than what would be expected in similar patient populations. 1-5 Authors also found no significant difference between nominal dose in those with overall survival through five years. Furthermore, patients who died were older and shared a statistically higher level of co-morbidities at baseline, including coronary artery disease, diabetes, and chronic kidney disease, versus those with higher overall survival rates. Across all studies, results were reviewed and adjudicated by an independent clinical events committee.

"Individual patient data meta-analysis (IPD-MA) offers several advantages over the aggregate data meta-analysis (AD-MA) that

renders it as a more powerful statistical approach, allowing for more thorough and more appropriate analyses," said Dr. Gheorghe Doros. "The advantages are realized by being able to utilize more accurate outcome data, such as time of event and time of drop-out, individual patient covariates, such as paclitaxel dose, patient comorbidities, as well as lesion and procedural characteristics, and more sophisticated statistical models, such as frailty Cox regression and inverse probability of treatment weighting (IPTW)."

"In light of recent discussions around the safety of paclitaxel-coated and -eluting technologies, it's now more important than ever for Medtronic and our industry peers to be forthcoming with all our clinical data," said Mark Pacyna, vice president and general manager of the Peripheral business, which is part of the Aortic, Peripheral, and Venous division at Medtronic. "The evidence presented today at LINC underscores our ongoing commitment to patient safety, improved long-term outcomes, and data transparency."

IN.PACT SFA Japan Three-Year Results

New data from the IN.PACT SFA Japan Study were also presented by Osamu Iida, M.D., Kansai Rosai Hospital, Japan. The data demonstrated continued safety, durability, and efficacy compared to PTA at three years. The study enrolled 100 patients across 11 sites in Japan and randomized treatment to either DCB (n=68) PTA (n=32). Results showed a consistently low clinically-driven target lesion revascularization (CD-TLR) rate and high patency rate.

IN.PACT SFA Japan demonstrated a 68.9 percent primary patency in the DCB group compared to 46.9 percent in the PTA group at three years based on Kaplan-Meier estimates (p=0.001). The three-year freedom from CD-TLR rates based on Kaplan-Meier estimates were 84.4 percent in the DCB group compared to 81.3 percent in the PTA group (p=0.451). In IN.PACT SFA Japan, major adverse events were also lower in the DCB group at three years with a rate of 20.9 percent compared to 31.0 percent in the PTA group (p=0.306), with no major target limb amputations in either study arm. The mortality rate was also lower in the DCB arm at 6.0 percent, versus 6.9 percent in the PTA group.

"We stand behind IN.PACT Admiral DCB, which is well supported by evidence from our robust clinical program," said Simona Zannetti, M.D., vice president, Clinical Research, Medical Affairs, and Education, Medtronic Aortic, Peripheral, and Venous. "In line with our commitment to timely data dissemination-and the physicians and patients we serve-it is critical that we continue to review, report, and publish our findings."

In collaboration with leading clinicians, researchers and scientists worldwide, Medtronic offers the broadest range of innovative medical technology for the interventional and surgical treatment of cardiovascular disease and cardiac arrhythmias. The company strives to offer products and services that deliver clinical and economic value to healthcare consumers and providers around the world.

About Medtronic

Medtronic plc (www.medtronic.com), headquartered in Dublin, Ireland, is among the world's largest medical technology, services and solutions companies - alleviating pain, restoring health and extending life for millions of people around the world. Medtronic employs more than 86,000 people worldwide, serving physicians, hospitals and patients in more than 150 countries. The company is focused on collaborating with stakeholders around the world to take healthcare Further, Together.

Any forward-looking statements are subject to risks and uncertainties such as those described in Medtronic's periodic reports on file with the Securities and Exchange Commission. Actual results may differ materially from anticipated results.

-end-

References

1. Caro J, Migliaccio-Walle K, Ishak KJ, Proskorovsky I. The morbidity and mortality following a diagnosis of peripheral arterial disease: long-term follow-up of a large database. BMC Cardiovasc Disord 2005;5:14.
2. Muluk SC, Muluk VS, Kelley ME et al. Outcome events in patients with claudication: a 15-year study in 2777 patients. J Vasc Surg 2001;33:251-7; discussion 257-8.
3. Mueller T, Hinterreiter F, Luft C, Poelz W, Haltmayer M, Dieplinger B. Mortality rates and mortality predictors in patients with symptomatic peripheral artery disease stratified according to age and diabetes. J Vasc Surg 2014;59:1291-9.
4. Jelnes R, Gaardsting O, Hourgaard Jensen K, Baekgaard N, Tonnesen KH, Schroeder T. Fate in intermittent claudication: outcome and risk factors. Br Med J 1986;293:1137-1140.
5. Rantner B, Kollerits B, Pohlhammer J et al. The fate of patients with intermittent claudication in the 21st century revisited - results from the CAVASIC Study. Sci Rep 2017;8:45833.

Contacts:

Julia Baron Fuller
Public Relations
+1-858-692-2001

Ryan Weispfenning
Investor Relations
+1-763-505-4626

---

https://news.medtronic.com/2019-01-22-Patient-Level-Survival-Analysis-Demonstrates-No-Link-Between-Paclitaxel-Dose-and-Mortality-in-Patients-Treated-with-IN-PACT-Admiral-DCB