Patients with previous MI have close to a 50% recurrence for any CVD event or revascularization in year 1 and up to 75% recurrence within 3 years[1]

REDUCTION IN TOTAL CARDIOVASCULAR EVENTS[2]

FROM THE VASCEPA® (icosapent ethyl) CV OUTCOMES TRIAL (REDUCE-IT™)

Presented at the American College of Cardiology, published online March 2019. doi: xxx

- The Food and Drug Administration (FDA) has not reviewed and opined on a supplemental new drug application related to REDUCE-IT. FDA has thus not reviewed the information herein or determined whether to approve VASCEPA for use to reduce the risk of major adverse cardiovascular events in the REDUCE-IT patient population
- As with any cardiovascular outcomes trial result, further REDUCE-IT data assessment and data release could yield additional useful information to inform greater understanding of study outcome
- Overall adverse event (AE) rates were similar across treatment groups:
  - Adverse events (AE) and serious adverse event (SAE) rates leading to study drug discontinuation were similar to placebo
  - A single serious adverse event (SAE) occurred at a frequency of at least 2%, which was pneumonia (2.6% in the VASCEPA group and 2.9% in the placebo group, *P*=0.42)
- These adverse events (AE) occurred in ≥5% of VASCEPA patients and were statistically more frequent with VASCEPA than placebo:
  - Peripheral edema occurred in 6.5% VASCEPA patients versus 5.0% placebo patients
  - Constipation occurred in 5.4% VASCEPA patients versus 3.6% placebo patients
  - Atrial fibrillation occurred in 5.3% VASCEPA patients versus 3.9% placebo patients but heart attack, cardiac arrest and sudden death each decreased in VASCEPA patients

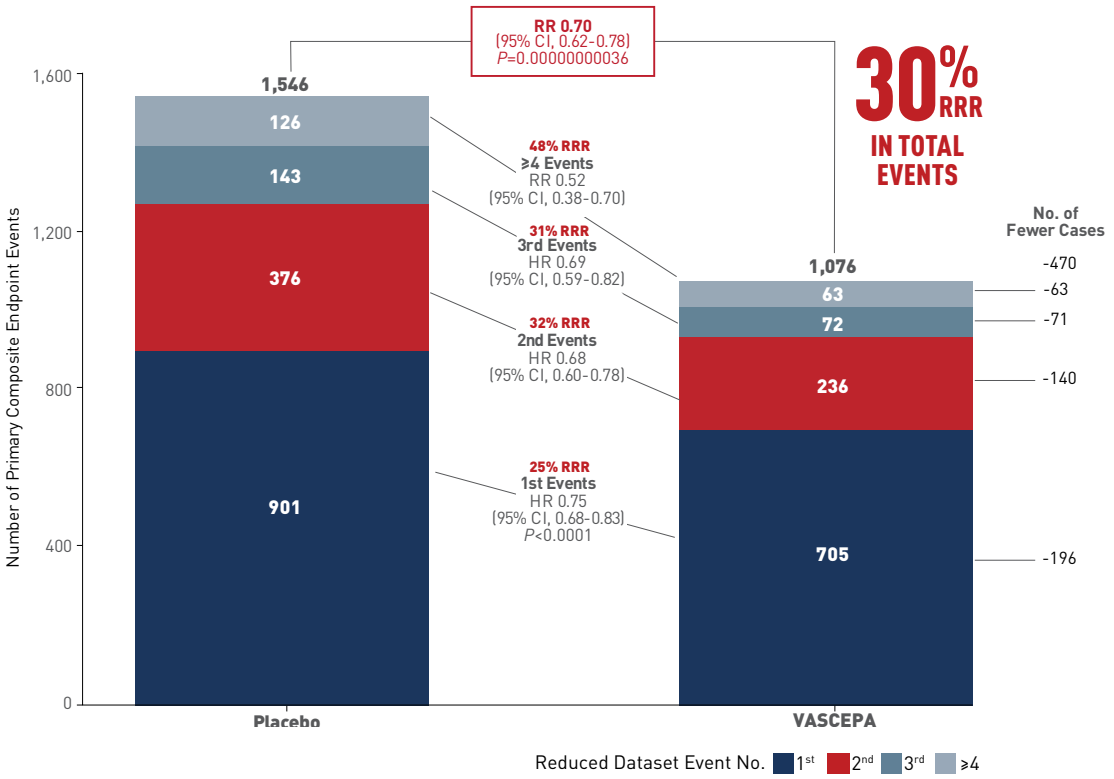
Please see accompanying Important Safety Information and full Prescribing Information for VASCEPA or go to www.vascepahcp.com.

Vascepa®
(icosapent ethyl)

In 8179 statin-treated adults with well-controlled LDL-C (41-100 mg/dL) and CV risk factors including elevated TG (135-499 mg/dL) and either established CVD or diabetes and other CV risk factors[2,3]

VASCEPA SHOWED SIGNIFICANT REDUCTIONS IN **FIRST, SUBSEQUENT, AND TOTAL** CV EVENTS[2]

First and Subsequent Primary Composite Endpoint Events



Adapted from Bhatt DL et al; for REDUCE-IT Investigators. *J Am Coll Cardiol*. In press.

CI=confidence interval; HR=hazard ratio; RR=rate ratio.

Primary composite endpoint was defined as a composite of CV Death, Nonfatal MI, Nonfatal Stroke, Coronary Revascularization, and Unstable Angina Requiring Hospitalization.

- Regarding bleeding:
  - –The rate of treatment-emergent serious adverse events for bleeding was 2.7% in the VASCEPA group versus 2.1% in the placebo group, with a nonsignificant, but trending *P*-value of 0.06
- VASCEPA may not be eligible for reimbursement under government healthcare programs (such as Medicare and Medicaid) and certain commercial plans to reduce the risk of major adverse cardiovascular events in the REDUCE-IT patient population. We encourage you to check that for yourself

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VASCEPA DEMONSTRATED ROBUST RISK REDUCTION **SUSTAINED OVER TIME**[2]

Total and Time to First Primary Composite

No. at Risk*

Placebo	4090	3914	3674	3236	2788	1653
Icosapent Ethyl	4089	3933	3701	3276	2861	1692

*No. at Risk=Number of patients at risk for recurrent events.

Recurrent event analyses for the total primary endpoint events and for the total key secondary endpoint events were conducted using a series of statistical models. These analyses were tertiary or exploratory endpoints; most of the models used were prespecified and one was *post hoc*. Each recurrent event statistical model has inherent strengths and weaknesses, with no single model considered definitive or outperforming the other models, and this is an evolving field of science. Nonetheless, results from the total primary and total key secondary endpoint events analyses are consistent across the various recurrent event statistical models and are also consistent with the original primary and secondary endpoint results. Together, the REDUCE-IT recurrent event analyses and the original primary and key secondary endpoint analyses support the robustness of the clinical benefit of VASCEPA therapy in reducing cardiovascular risk.

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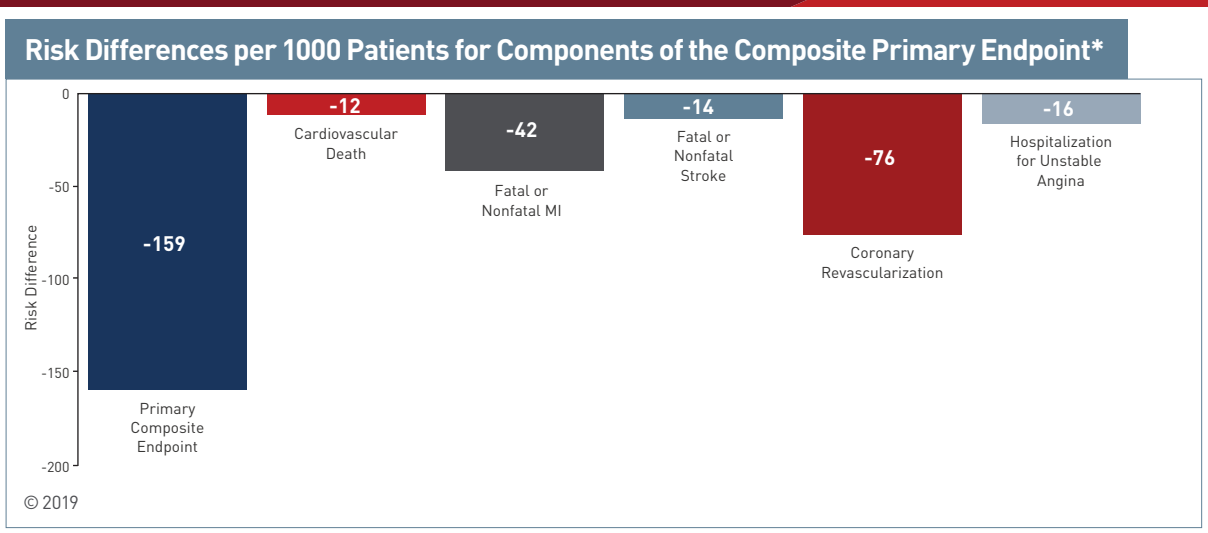
LATEST CV OUTCOMES

159 CV EVENTS WERE PREVENTED FOR EVERY 1000 PATIENTS TREATED FOR 5 YEARS WITH VASCEPA® 4 g/d[2]



*VASCEPA versus placebo.

A pharmacoeconomic analysis is planned to add further context to the study results.

Download the article at **www.vascepahcp.com/JACC**

FDA-APPROVED INDICATION AND LIMITATIONS OF USE FOR VASCEPA[4]

- VASCEPA® (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia
- In patients with severe hypertriglyceridemia, the effect of VASCEPA on cardiovascular mortality or morbidity or on the risk of pancreatitis has not been determined

References: 1. Bansilal S, Castellano JM, Fuster V; Global burden of CVD: focus on secondary prevention of cardiovascular disease. *Int J Cardiol*. 2019;201(suppl 1):S1-S7. **2.** Bhatt DL, Steg PG, Miller M, et al; on behalf of the REDUCE-IT Investigators. Effects of icosapent ethyl on total ischemic events – further insights from REDUCE-IT [published online ahead of print March 18, 2019]. *J Am Coll Cardiol*. doi: xxxxxxxxxxx. Bhatt DL. ACC 2019, New Orleans. **3.** Bhatt DL, Steg PG, Brinton EA, et al. Rationale and design of REDUCE-IT: Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial. *Clin Cardiol*. 2017;40(3):138-148. **4.** VASCEPA [package insert]. Bedminster, NJ: Amarin Pharma, Inc.; 2017.

Please see accompanying Important Safety Information and full Prescribing Information for VASCEPA or go to www.vascepahcp.com.

AMARIN®

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