

## **What were the eicosapentaenoic acid (EPA) levels reached in REDUCE-IT® and how did EPA levels impact the cardiovascular risk reduction seen?**

The cardiovascular benefit observed in REDUCE-IT® is specific to the administered 4g/day of VASCEPA® (icosapent ethyl), which is reflected in the resultant high achieved serum EPA levels. In the REDUCE-IT study, the baseline median serum EPA was 26.1 µg/mL, while at one year the median serum EPA level had increased to 144.0 µg/mL with icosapent ethyl.<sup>1,2</sup> Moreover, substantial REDUCE-IT efficacy was increasingly observed in patients with EPA >100 µg/mL, suggesting that both dose and achieved levels of EPA matter.

For purposes of perspective, this achieved or on-study median serum EPA level in REDUCE-IT was well above that observed for the vast majority of patients in the STRENGTH study, who had a median baseline plasma EPA of 21.0 µg/mL and an on-study median of 89.6 µg/mL at one year (note: plasma and serum lipid levels are similar, but not identical). In STRENGTH,<sup>3</sup> the on-study median level of EPA was lower than the baseline EPA level reported in JELIS, a large Japanese cardiovascular outcomes study conducted with a pure, stable, prescription EPA formulation.<sup>4,5</sup>

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<sup>1</sup> Bhatt DL, Miller M, Steg G, Brinton EA, Jacobson TA, Ketchum SB, Juliano RA, Jiao L, Doyle RT, Copland C, Dunbar RL, Granowitz C, MD, PhD, Martens FM, Budoff M, Nelson JR, Mason RP, Libby P, Ridker P, Tardif J-C, Ballantyne CM, on behalf of the REDUCE-IT Investigators. EPA levels and cardiovascular outcomes in the Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial. Presented at the American College of Cardiology 2020 annual meeting (virtual).

<sup>2</sup> Pisaniello AD, Nicholls SJ, Ballantyne CM, Bhatt DL, Wong ND. Eicosapentaenoic acid: atheroprotective properties and the reduction of atherosclerotic cardiovascular disease events. *EMJ*. 2020;5:29-36.

<sup>3</sup> Nicholls SJ, Lincoff AM, Garcia M, et al. Effect of High-Dose Omega-3 Fatty Acids vs Corn Oil on Major Adverse Cardiovascular Events in Patients at High Cardiovascular Risk: The STRENGTH Randomized Clinical Trial. *JAMA*. 2020 Nov 15:e2022258. doi: 10.1001/jama.2020.22258. Epub ahead of print. PMID: 33190147; PMCID: PMC7667577.

<sup>4</sup> Yokoyama M, Origasa H, Matsuzaki M, et al.; Japan EPA lipid intervention study (JELIS) Investigators. Effects of eicosapentaenoic acid on major coronary events in hypercholesterolaemic patients (JELIS): a randomised open-label, blinded endpoint analysis. *Lancet*. 2007;369(9567):1090-8.

<sup>5</sup> Itakura H, Yokoyama M, Matsuzaki M, et al.; JELIS Investigators. Relationships between plasma fatty acid composition and coronary artery disease. *J Atheroscler Thromb*. 2011;18(2):99-107.