OPTUMRx®

Repatha™ (evolocumab) – FOURIER study results

- On March 17, 2017, the Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk (FOURIER) study was published in the *New England Journal of Medicine*. The addition of Amgen's Repatha (evolocumab) to optimized statin therapy significantly reduced rates of major adverse cardiovascular (CV) events in patients with clinically evident atherosclerotic cardiovascular disease (CVD).

- Repatha is a proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor indicated for the following:

    - As an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic CVD, who require additional lowering of low density lipoprotein cholesterol (LDL-C)
    - An adjunct to diet and other LDL-lowering therapies (eg, statins, ezetimibe, LDL apheresis) for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C

- Praluent™ (alirocumab) was the first PCSK9 inhibitor approved in July 2015. Aside from HoFH, Praluent has the same indications as Repatha. Repatha was approved in August 2015.

    - CV outcomes studies for Praluent are underway. Results are anticipated in late 2017.

- FOURIER was a randomized, double-blind, placebo-controlled, multinational clinical trial of 27,564 patients with atherosclerotic CVD and LDL-C levels ≥ 70 mg/dL who were receiving statin therapy. Patients received Repatha (140 mg every 2 weeks or 420 mg monthly) or placebo as subcutaneous injections. The primary efficacy end point was the composite of CV death, myocardial infarction (MI), stroke, hospitalization for unstable angina, or coronary revascularization. The key secondary efficacy end point was the composite of CV death, MI, or stroke. The median duration of follow-up was 2.2 years

    - Relative to placebo, Repatha significantly reduced the risk of the primary end point (1,344 patients [9.8%] vs. 1,563 patients [11.3%]; HR, 0.85; 95% CI: 0.79, 0.92; $p < 0.001$) and the key secondary end point (816 [5.9%] vs. 1013 [7.4%]; HR, 0.80; 95% CI: 0.73, 0.88; $p < 0.001$).
    - The magnitude of the risk reduction for the primary end point tended to increase over time, from 12% (95% CI: 3, 20) in the first year to 19% (95% CI: 11, 27) beyond the first year. The risk reduction for the secondary end point increased from 16% (95% CI: 4, 26) in the first year to 25% (95% CI: 15, 34) beyond the first year.
    - In terms of individual outcomes, Repatha had no observed effect on CV mortality, hospitalization for unstable angina, CV death or hospitalization for worsening heart failure, or death from any cause.
    - Patients in the Repatha group had lower rates of MI (3.4% vs. 4.6%; HR 0.73, 95% CI: 0.65, 0.82; $p < 0.001$), stroke (1.5% vs. 1.9%; HR 0.79, 95% CI: 0.66, 0.95; $p < 0.01$), coronary revascularization (5.5% vs. 7.0%; HR 0.78, 95% CI: 0.71, 0.86; $p < 0.001$), and ischemic stroke or transient ischemic attack (1.7% vs. 2.1%; HR 0.77, 95% CI: 0.65, 0.92; $p = 0.003$).

- At 48 weeks, the mean % reduction in LDL-C levels with Repatha vs. placebo was 59%, from a median baseline value of 92 mg/dL to 30 mg/dL ($p < 0.001$). The reduction in LDL-C levels was maintained over time.

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- There was no significant difference in adverse events between the groups (including new-onset diabetes and neurocognitive events), with the exception of injection-site reactions, which were more common with Repatha (2.1% vs. 1.6%).

- Amgen plans to offer additional contracting options in the U.S. to payers willing to remove access barriers. These options include one that offers a refund of the cost of Repatha for all of their eligible patients who have a heart attack or stroke. In addition, Amgen will continue to offer innovative contracts that provide reasonable budget predictability to help address budget impact concerns raised by payers.