Long-Term Efficacy of Evolocumab in Patients with and without Multi-Vessel Disease
An Analysis from FOURIER and FOURIER-OLE

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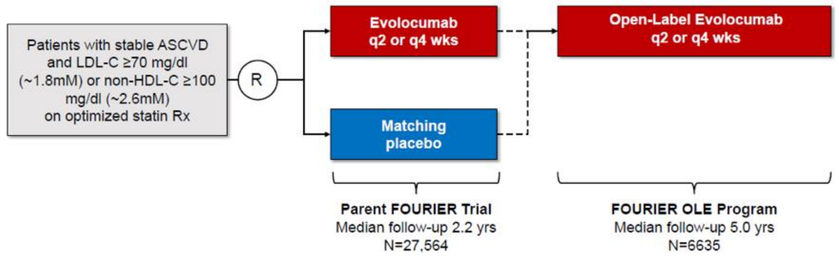
BACKGROUND

- In FOURIER, treatment with evolocumab resulted in greater risk reductions in patients with residual multivessel coronary artery disease (MVD) compared with those without.
- In patients with MVD, the cumulative incidence curves in the evolocumab and placebo arms diverged rapidly
- In contrast, in patients without MVD, the curves only started to diverge near the end of follow-up, with marginal statistical significance after a median follow-up of 2.2 yrs
- Given that the clinical benefit seen with LDL-C lowering grows over time, we hypothesized that the additional follow-up in the FOURIER Open Label Extension (FOURIER-OLE) would allow a more clinically meaningful benefit to emerge in patients without MVD.

OBJECTIVE

To assess the long-term benefits of evolocumab in patients with and without MVD

METHODS



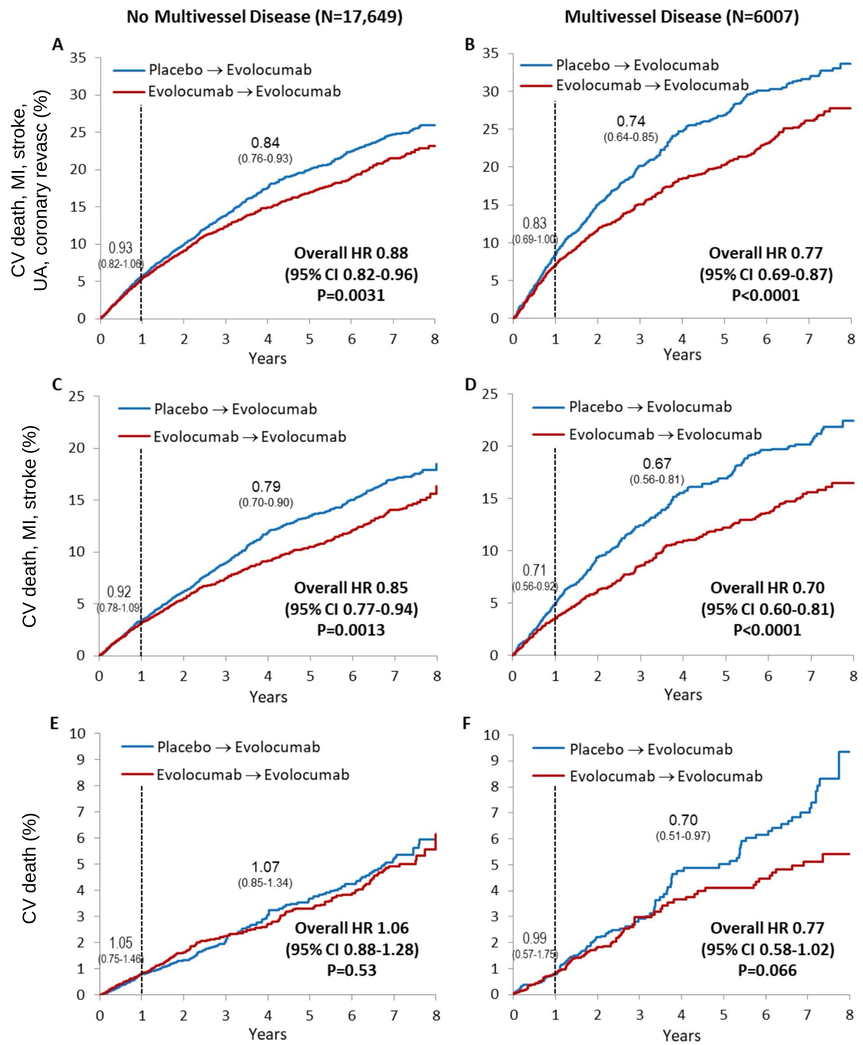
- FOURIER enrolled 27,564 pts with stable ASCVD on optimized statin therapy. Median follow-up was 2.2 (1.8-2.5) yrs.
- 6635 pts who completed FOURIER trial on study drug (either evolocumab or placebo) and were at a participating site in the U.S. and Europe were enrolled in FOURIER-OLE, during which all pts were to receive evolocumab. Median follow-up was an additional 5.0 (4.6-5.1) yrs.
- For this analysis, we included 23,656 pts with CAD who entered FOURIER, 5887 of whom continued in FOURIER-OLE
- Residual MVD was prespecified as ≥40% stenosis in ≥2 large vessels
- Outcomes included: primary endpoint (PEP: CVD, MI, stroke, UA, or coronary revasc), key secondary endpoint (SEP: CVD, MI, stroke), and CV death

DISCLOSURES

FOURIER and FOURIER-OLE studies were funded by research grants from Amgen Inc. DJM has no disclosures. The TIMI Study Group has received institutional grant support through the Brigham and Women's Hospital from: Abbott, Amgen, Anthos Therapeutics, ARCA Biopharma, AstraZeneca, Boehringer Ingelheim, Daiichi-Sankyo, Ionis, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Roche, Saghmos Therapeutics, Siemens Healthcare Diagnostics, Softcell Medical Limited, Verve Therapeutics, and Zora Biosciences.

RESULTS

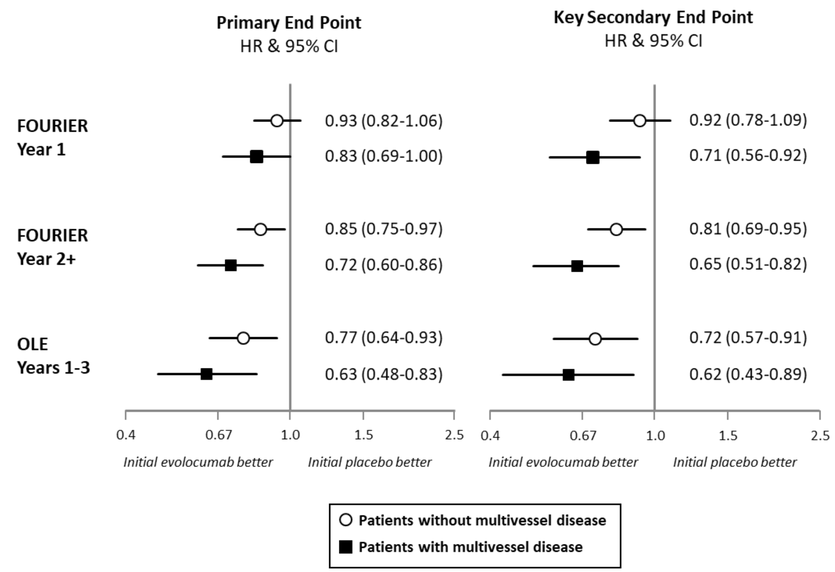
Figure 1. Effect of Initial Allocation to Evolocumab vs Placebo by MVD



- Initial allocation to evolocumab reduced the risk of the PEP and key SEP in both MVD and no MVD subgroups
- However, there was earlier divergence of the curves in MVD such that the risk reduction was roughly double that in no MVD (PEP: 23% vs 12%; SEP: 30% vs 15%) (P interactions 0.070 & 0.038, respectively)
- For CV death, the HRs were 0.77 (0.58-1.02) in MVD vs. 1.06 (0.88-1.28) (P interaction 0.06). In those with MVD, initial allocation to evolocumab reduced the risk of CV death by 30% after the 1st year.

RESULTS

Figure 2. Effect of Initial Allocation to Evolocumab by Time Period and MVD



- There were lag and legacy effects both in patients with and without MVD
- MVD patients had 17% and 29% risk reductions in the PEP and key SEP by end of FOURIER Year 1
- Benefit grew in Year 2 of FOURIER and in the 1st 3 years of the OLE, resulting in risk reductions of 37% and 38% for the PEP and key SEP, respectively
- In patients without MVD, the risk reductions were <10% in Year 1.
- However, like in MVD, the benefit grew in Year 2 of FOURIER and in the 1st 3 years of the OLE eventually resulting in risk reductions of 23% and 28% for the PEP and key SEP, respectively

CONCLUSIONS

- **Evolocumab reduced the risk of major adverse cardiovascular events in both the MVD and no MVD subgroups**
- **MACE reduction in patients without MVD needed longer to become apparent, though the benefit grew over time such that this group still achieved a significant reduction in MACE**
- **Patients with MVD also had a reduction in CV death in later years**
- **Early and aggressive lowering of LDL-C with evolocumab should be initiated in patients with and without MVD**