FOURIER: Discussion of Outcomes in Patients with PAD and History of MI

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2 Pre-Specified High-Risk Subgroups

- Symptomatic PAD: low ABI increases risk for all-cause and CVD mortality
- History of MI: risk of recurrent MI or fatal CHD within 5 years is 17% for men and 21% for women
Key Points: PAD Subgroup

- PAD subgroup was particularly high-risk vs no PAD (HTN, smoking, CKD, diabetes)
- Absolute RR for CV death, MI, or stroke was greater in patients with PAD than for patients without PAD
  - PAD 3.5% vs 1.4% for patients without PAD
  - 4.8% in patients with PAD but no MI/stroke (NNT 21)
- Does profound LDL lowering translate to less claudication, improved QOL, and greater PA tolerance?
Key Points: History of MI Subgroup

• Patients were treated with high/moderate-intensity statin therapy (baseline LDL-C 92 mg/dL).

• Greater benefit from evolocumab + background statin therapy with more recent event, ≥ 2 prior MIs, and presence of multivessel disease → more benefit in the highest risk subgroups

• “The absolute benefit relates chiefly to an individual's absolute risk of such events and to the absolute reduction in LDL cholesterol achieved.” (CTT Collab, 2005)
How Does Intensive LDL Lowering → Even Fewer Events in High Risk Subgroups?

- Is there plaque regression as shown in the GLAGOV trial: more disease, more atheroma regression → fewer CVD events?
- Does PCSK9 inhibition impact inflammatory processes → plaque stabilization?
- Is there an independent role for lower lipoprotein (a) with evolocumab?
Final Questions/Comment

- Why so few women (prior MI 21%, PAD 28%)? Can we discern the benefit achieved with respect to a woman’s risk?
- Will evolocumab + statin therapy show a mortality benefit vs statin therapy alone with longer follow-up?

- These subgroup analyses will help clinicians target use of PCSK9is to the patients who will benefit the most.