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TOOLS FOR PRACTICE

PEER PATIENTS EXPERIENCE EVIDENCE RESEARCH

PCSK9 Inhibitors: Cardiovascular prevention panacea or pricey pokes?

CLINICAL QUESTION

Are PCSK9 inhibitors (evolocumab, alirocumab) effective in preventing cardiovascular events?

BOTTOM LINE

When added to statins for secondary cardiovascular disease prevention, PCSK9 inhibitors reduce the risk of cardiovascular events by a relative 15-25% over placebo at 2-5 years. One new randomized, controlled trial (RCT) in patients without a prior stroke or myocardial infarction but known atherosclerotic disease (example: coronary revascularization history) or high-risk diabetes (example: ≥ 10 years duration) showed similar results. Two of 3 RCTs also showed a relative 15% reduction in overall mortality.

EVIDENCE

- Results statistically significant unless mentioned otherwise. All are industry sponsored RCTs.
- Patients with previous history of cardiovascular disease and on maximum tolerated statin dose:
    - FOURIER:[1] Evolocumab versus placebo, 27564 patients, median follow-up 2.2 years.
        - Cardiovascular events: 9.8% versus 11% (placebo); relative reduction ~15%; number needed to treat (NNT)=67.

        - All-cause mortality: No difference.
    - ODYSSEY OUTCOMES:[2] Alirocumab versus placebo, 18924 patients, median follow-up 2.8 years.
        - Cardiovascular events: 9.5% versus 11% (placebo); relative reduction ~15%; NNT=63.
        - All-cause mortality: 3.5% versus 4.1% (placebo); relative reduction ~15%; NNT=167.
- Patients on lipid-lowering therapy (87% statin) with no prior myocardial infarction or stroke but coronary, cerebrovascular, or peripheral artery disease (examples: Prior coronary revascularization, transient ischemic attack, ankle brachial index < 0.85), or high-risk diabetes (example ≥10 years duration):
    - VESALIUS-CV:[3] Evolocumab versus placebo, 12257 patients, median follow-up 4.6 years:
        - Cardiovascular events (death from cardiovascular disease, non-fatal myocardial infarction or stroke): 5.5% versus 7.2% (placebo); relative reduction ~25%; (NNT)=59.
        - All-cause mortality: 7.9% versus 9.7% (placebo); ~20% relative reduction; NNT=56.
- Adverse effects: Did not differ significantly between groups in any RCT.

CONTEXT

- PCSK9 inhibitors are approved as adjuncts to standard care to reduce cardiovascular events in adults with atherosclerotic cardiovascular disease.[4]
- Administered as biweekly or monthly subcutaneous injections.[4]
- Cost ~$7500 per year.[5] In higher cardiovascular risk patients with no previous cardiovascular event, it would cost ~$2,000,000 to treat 56 persons for 4.6 years to prevent one death or cardiovascular event.

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