Abstract: P5367
Indirect comparison of the safety and efficacy of alirocumab and evolocumab: from a comprehensive meta-analysis of 30 randomized controlled trials

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Background: Alirocumab and evolocumab, two proprotein convertase subtilisin–kexin type 9 inhibitors, have both been associated with improved outcomes in patients with atherosclerotic cardiovascular disease in addition to standard lipid-lowering therapies. However, their comparative safety and efficacy profiles are unknown.

Purpose: To compare the safety and efficacy of alirocumab versus evolocumab.

Methods: We conducted a systematic review and network meta-analysis of placebo-controlled randomized trials available up to November 2018 evaluating the safety and efficacy of alirocumab and evolocumab. We estimated risk ratio and 95% confidence intervals using fixed effect model in a frequentist pairwise and network metanalytic approach. The primary safety endpoints were any adverse events leading to treatment-discontinuation, injection site reaction, systemic allergic reaction, neurocognitive events, ophthalmologic events and new-onset of diabetes mellitus (DM) or worsening of pre-existing DM. The primary efficacy endpoints were all-cause and cardiovascular (CV) death, myocardial infarction (MI) and stroke. This study was registered in PROSPERO (CRD42018090768).

Results: A total of 30 trials, enrolling 59,026 patients were included in this analysis, of whom 13,607 received alirocumab and 17,931 received evolocumab. Mean weighted follow-up time was 2.5 years, with an exposure time of 144,907 patients-years. Eligibility criteria varied significantly across trials evaluating alirocumab and evolocumab. There were no significant differences between alirocumab and evolocumab in terms of safety endpoints, except for injection site reaction with a 27% increased risk of injection site reaction with alirocumab compared to evolocumab (Figure). Compared with evolocumab, alirocumab was associated with a reduction of all-cause death but not CV death. There were no significant differences in MI or stroke between alirocumab and evolocumab.

Conclusion: Alirocumab and evolocumab share a similar safety profile. No significant differences were observed across the efficacy endpoints, except for all-cause death, which may be related to heterogeneity of the studied populations between the two drugs.
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