Abstract: P5015

Efficacy of lipid lowering therapy beyond statins to prevent cardiovascular events: A meta-analysis

Authors:
I Dykun¹, R Mincu¹, M Totzeck¹, T Rassaf¹, AA Mahabadi¹, ¹University Clinic Essen, West German Heart and Vascular Center, Department of Cardiology and Vascular Medicine - Essen - Germany,

Topic(s):
Coronary Artery Disease – Prevention

Citation:
Background: Lipid lowering therapy is a key cornerstone in secondary prevention of patients with coronary artery disease. However, only a minority of patients with statin therapy reach LDL thresholds as suggested by the ESC. Ezetimibe and proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors allow for reduction in LDL-cholesterol in addition to statin therapy.

Purpose: To perform a meta-analysis of existing trials, evaluating how lipid lowering therapy beyond statins impacts cardiovascular outcome.

Methods: We performed a systematic search using the Pubmed, Cochrane, SCOPUS, and Web of Science databases for studies, evaluating the impact of an intensified lipid lowering therapy via ezetimibe or PCSK-9 inhibitor in addition to statin therapy compared to statin therapy alone. Manuscript and congress presentations, published until 1st of November 2018, were included. We made our search specific and sensitive using Medical Subject Headings terms and free text and considered studies published in English language. Search terms used were "ezetimibe", "evolocumab", "alirocumab", or "bococizumab" and "cardiovascular events".

Results: A total of 100,610 patients from 9 randomized controlled trials (IMPROVE-IT, FOURIER, ODYSSEY Outcomes, SIPRE I, SPIRE II, ODYSSEY LONG TERM, OSLER-1 and OSLER-2, HIJ-PROPER) were included. Treatment with ezetimibe or a PCSK-9 inhibitor was associated with a 18% risk reduction in cardiovascular events (OR [95%CI]: 0.82 [0.75-0.89]). Effect sizes were similar for myocardial infarction (0.84 [0.76-0.92]) and even more pronounced for ischemic stroke (0.77 [0.67-0.83]). In contrast, all-cause mortality was not improved by the intensified lipid lowering therapy (0.94 [0.85-1.05]). No relevant heterogeneity and inconsistency between groups was present in all analyses (detailed data not shown). Comparing efficacy of LDL-reduction and relative risk reduction of cardiovascular events, a linear relationship was observed (figure).

Conclusion: Intensified LDL-lowering therapy with ezetimibe or PCSK-9 inhibitors, in addition to statins, reduces the risk of myocardial infarction and stroke, however, does not impact overall mortality. There is a linear relationship between LDL reduction and cardiovascular risk reduction, confirming the beneficial effects of LDL lowering therapy beyond statins in secondary prevention.

Figure: Correlation of reduction of LDL-cholesterol at one year with relative risk reduction (95% confidence interval) of cardiovascular events in included trials
Efficacy of lipid lowering therapy beyond statins to prevent cardiovascular events: A meta-analysis

Authors:
I Dykun 1, R Mincu 1, M Totzeck 1, T Rassaf 1, AA Mahabadi 1

University Clinic Essen, West German Heart and Vascular Center, Department of Cardiology and Vascular Medicine - Essen - Germany,

Topic(s): Coronary Artery Disease – Prevention

Background: Lipid lowering therapy is a key cornerstone in secondary prevention of patients with coronary artery disease. However, only a minority of patients with statin therapy reach LDL thresholds as suggested by the ESC. Ezetimibe and proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors allow for reduction in LDL-cholesterol in addition to statin therapy.

Purpose: To perform a meta-analysis of existing trials, evaluating how lipid lowering therapy beyond statins impacts cardiovascular outcome.

Methods: We performed a systematic search using the Pubmed, Cochrane, SCOPUS, and Web of Science databases for studies, evaluating the impact of an intensified lipid lowering therapy via ezetimibe or PCSK-9 inhibitor in addition to statin therapy compared to statin therapy alone. Manuscript and congress presentations, published until 1st of November 2018, were included. We made our search specific and sensitive using Medical Subject Headings terms and free text and considered studies published in English language. Search terms used were “ezetimibe”, “evolocumab”, “alirocumab”, or “bococizumab” and “cardiovascular events”.

Results: A total of 100,610 patients from 9 randomized controlled trials (IMPROVE-IT, FOURIER, ODYSSEY Outcomes, SIPRE I, SPIRE II, ODYSSEY LONG TERM, OSLER-1 and OSLER-2, HIJ PROPER) were included. Treatment with ezetimibe or a PCSK-9 inhibitor was associated with a 18% risk reduction in cardiovascular events (OR [95%CI]: 0.82 [0.75–0.89]). Effect sizes were similar for myocardial infarction (0.84 [0.76–0.92]) and even more pronounced for ischemic stroke (0.77 [0.67–0.83]). In contrast, all-cause mortality was not improved by the intensified lipid lowering therapy (0.94 [0.85–1.05]). No relevant heterogeneity and inconsistency between groups was present in all analyses (detailed data not shown).

Comparing efficacy of LDL-reduction and relative risk redaction of cardiovascular events, a linear relationship was observed (figure).

Conclusion: Intensified LDL-lowering therapy with ezetimibe or PCSK-9 inhibitors, in addition to statins, reduces the risk of myocardial infarction and stroke, however, does not impact overall mortality. There is a linear relationship between LDL reduction and cardiovascular risk reduction, confirming the beneficial effects of LDL lowering therapy beyond statins in secondary prevention.

Figure: Correlation of reduction of LDL-cholesterol at one year with relative risk reduction (95% confidence interval) of cardiovascular events in included trials.