WHEN DISTORTED EVIDENCE-BASED MEDICINE LEADS TO OVERTREATMENT

The IMPROVE-IT trial case

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Ezetimibe was an evidence-lacking drug

SEAS trial showed no differences vs placebo in patients with aortic valve stenosis. SHARP trial only compared combination ezetimibe/simvastatin vs placebo in patients with chronic kidney disease. There was scarcity of morbi-mortality data.

IMPROVE-IT trial to fix this situation?

Patients aged ≥ 50 years with LDL-C 50-125 mg/dL (50-100 mg/dL with previous lipid-lowering therapy), hospitalized within the previous ten days for acute coronary syndrome with associated CV risk factors such as diabetes mellitus, previous coronary angiography or percutaneous coronary intervention during the index hospitalization.

ezetimibe 10 mg/simvastatin 40 mg vs placebo/simvastatin 40 mg

A critical appraisal

IMPROVE-IT results are not directly applicable to

• all ACS patients
• primary prevention of cardiovascular disease in high-risk patients
• secondary prevention after atherothrombotic events other than ACS

Enlargement in the search of statistical significance

Statistical significance was inappropriately attained after imputing data to the 11% patients for whom ACS-episode data were lacking

In spite of this

Navarre: population 640,000
4,158 patients received ezetimibe
63.5% ezetimibe without statin
44.8% for primary CV prevention
2.6% for familial hypercholesterolemia
Cost 1.7 million €

The IMPROVE-IT trial does not provide sufficient evidence supporting the use of ezetimibe in combination with a statin for ACS

The FDA advisory committee recommended prohibiting the pharmaceutical company from promoting the addition of ezetimibe to simvastatin to reduce the incidence of cardiovascular events

Overtreatment risk with ezetimibe should be seriously considered and actively managed

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