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Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial

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Published: August 26, 2018 • DOI: https://doi.org/10.1016/S0140-6736(18)31924-X •

Summary

Background

The use of aspirin in the primary prevention of cardiovascular events remains controversial. We aimed to assess the efficacy and safety of aspirin versus placebo in patients with a moderate estimated risk of a first cardiovascular event.

Methods

ARRIVE is a randomised, double-blind, placebo-controlled, multicentre study done in seven countries. Eligible patients were aged 55 years (men) or 60 years (women) and older and had an average cardiovascular risk, deemed to be moderate on the basis of the number of specific risk factors. We excluded patients at high risk of gastrointestinal bleeding or other bleeding, or diabetes. Patients were randomly assigned (1:1) with a computer-generated randomisation code to receive enteric-coated aspirin tablets (100 mg) or placebo tablets, once daily. Patients, investigators, and others involved in treatment or data analysis were

masked to treatment allocation. The primary efficacy endpoint was a composite outcome of time to first occurrence of cardiovascular death, myocardial infarction, unstable angina, stroke, or transient ischaemic attack. Safety endpoints were haemorrhagic events and incidence of other adverse events, and were analysed in the intention-to-treat population. This study is registered with ClinicalTrials.gov, number NCT00501059.

Findings

Between July 5, 2007, and Nov 15, 2016, 12 546 patients were enrolled and randomly assigned to receive aspirin (n=6270) or placebo (n=6276) at 501 study sites. Median follow-up was 60 months. In the intention-to-treat analysis, the primary endpoint occurred in 269 (4·29%) patients in the aspirin group versus 281 (4·48%) patients in the placebo group (hazard ratio [HR] 0·96; 95% CI 0·81–1·13; p=0·6038). Gastrointestinal bleeding events (mostly mild) occurred in 61 (0·97%) patients in the aspirin group versus 29 (0·46%) in the placebo group (HR 2·11; 95% CI 1·36–3·28; p=0·0007). The overall incidence rate of serious adverse events was similar in both treatment groups (n=1266 [20·19%] in the aspirin group *vs* n=1311 [20·89%] in the placebo group. The overall incidence of adverse events was similar in both treatment groups (n=5142 [82·01%] *vs* n=5129 [81·72%] in the placebo group). The overall incidence of treatment-related adverse events was low (n=1050 [16·75%] *vs* n=850 [13·54%] in the placebo group; p<0·0001). There were 321 documented deaths in the intention-to-treat population (n=160 [2·55%] *vs* n=161 [2·57%] of 6276 patients in the placebo group).

Interpretation

The event rate was much lower than expected, which is probably reflective of contemporary risk management strategies, making the study more representative of a low-risk population. The role of aspirin in primary prevention among patients at moderate risk could therefore not be addressed. Nonetheless, the findings with respect to aspirin's effects are consistent with those observed in the previously published low-risk primary prevention studies.

Funding

Bayer.

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Article Info

Publication History

Published: August 26, 2018

IDENTIFICATION

DOI: 10.1016/S0140-6736(18)31924-X

ScienceDirect

Access this article on ScienceDirect

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