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Risk of cardiovascular events in patients receiving *Celecoxib*

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The present study is a meta-analysis for the assesment of cardiovascular (CV) events in patients using Celecoxib. The purpose was to determine the primary CV events defined by Antiplatelet Trialists' Collaboration (APTC) (nonfatal cardiac events, cardiac deaths, cerebrovascular events), for celecoxib compared with non-selective NSAIDs and placebo. 39 studies were selected comprising in one arm 7462 celecoxib patients (200 to 800 mg/day) and 4057 placebo patients, and in another arm 19773 celecoxib patients (the same dose) and 13990 patients treated with nonselective NSAIDs.

Patients were assigned in the following subgroups: (1) users vs nonusers of low-dose aspirin at baseline; (2) celecoxib dosage groups of 200, 400, and 800 mg/day as well as all doses combined; (3) therapeutic indications of osteoarthritis (OA) and rheumatoid arthritis (RA) and the combined subgroup of patients. In addition, analyses were performed for subgroups with or without CV risk factors at baseline (hypertension, diabetes mellitus, hyperlipidemia and history of vascular disease).

In the placebo-controlled arm 23 APTC events were reported in 7462 celecoxib patients and 8 in 4057 placebo patients, with no statistical difference (RR 1.11, p=0.81).

In the nonselective NSAID-controlled arm a total of 57 APTC events were reported among 19773 celecoxib patients and 54 among 13990 control patients also with no statistical significant difference (RR 0.9, p=0.59). Assessment of individual types of CV events indicated a higher risk for myocardial infarction (RR 1.76, p=0.08) and a lower relative risk for stroke (RR 0.51, p=0.09), in the celecoxib group compared with the nonselective NSAIDs.

No significant increase in risk were found in patients with CV risk factors, users or non-users of aspirin, treated with celecoxib compared to placebo or nonselective NSAIDs. In aspirin non-users the CV death rate was lower in the celecoxib group than in the NSAIDs group (p=0.04). No differences were noted between the other subgroup populations (different dosage of celecoxib, RA and OA).

This meta-analysis of more than 41.000 patients, noted no significant increase in CV events in patients using celecoxib, although CV events were higher in patients with CV risk factors (regardless of treatment subgroup).

Limitation: despite the size of the study, most of the trials were of relatively short duration thus not allowing an accurate calculation of absolute risk for long term use of celecoxib. 38 of 39 studies did not exceed 1 year (in comparison with rofecoxib studies VIGOR and APPROVe where CV events where observed, relative to placebo, long after 12 months of drug exposure).

Comment on the paper:
Paola Caramaschi, Domenico Biasi, Marco Colombatti et al – Anti-TNFα therapy in rheumatoid arthritis and autoimmunity. *Rheumatology International* 2006; 26: 209-214