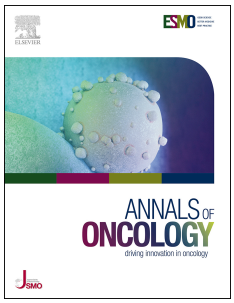

Reply to the Letter to the Editor “Aspirin to Prevent Gastrointestinal Cancer – But Recent Trial Data Don’t Fit” by Jacobsen and colleagues

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Reply to the Letter to the Editor "Aspirin to Prevent Gastrointestinal Cancer – But Recent Trial Data Don't Fit" by Jacobsen and colleagues

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(May 20, 2020)

To the Editor,

Jacobsen and colleagues, in their letter [1] on our meta-analysis of observational studies on aspirin use and the risk of gastrointestinal cancers [2], draw attention to the results of three recently published randomized clinical trials (RCT) in the primary prevention of cardiovascular disease. These were the ASCEND (A Study of Cardiovascular Events in Diabetes) [3], the ASPREE (Aspirin in Reducing Events in the Elderly) [4], and the ARRIVE (Use of Aspirin to Reduce Risk of Initial Vascular Events in patients at moderate risk of cardiovascular disease) [5]. They did not support a protective effect of aspirin on gastrointestinal cancers, as indicated in our meta-analysis.

We did not consider all gastrointestinal cancers together, but various cancer sites separately. Thus, a direct comparison is not possible. However, except for the ASCEND trial which included 484 gastrointestinal cancer cases and had a follow-up of 7.4 years [3], the two other RCTs included a relatively small number of gastrointestinal cancers (121 and 20, respectively) and had a mean follow-up of about 5 years [4, 5]. Therefore, these studies had limited statistical power and were unable to investigate the long-term effects of aspirin. Moreover, the ASPREE study was conducted on an elderly population (over 70 years of age) [4], while the ARRIVE trial was conducted on a low-risk population [5], which are unlikely ideal target populations for the chemo-preventive effect of aspirin.

In addition, the apparent difference between the results of those trials and our meta-analysis may be due to the differences in the aspirin dose, since these RCTs used low-dose aspirin (100 mg/die), while in our meta-analysis a lower risk of colorectal cancer was found for higher aspirin dose.

In a pooled analysis of individual patient data from four RCTs of aspirin for the prevention of cardiovascular disease, with a mean duration of treatment of 6 years, allocation to aspirin reduced the 20-year risk of colorectal cancer (incidence hazard ratio, HR=0.76, 95% confidence interval, CI=0.63-0.94, N=397; mortality HR=0.66, 95% CI=0.52-0.86, N=240) [6]. Another pooled analysis of seven RCTs of aspirin use for 4 years or longer found a HR of death from gastrointestinal cancers in the aspirin group as compared to the control group of 0.46 (95% CI= 0.27-0.77; N=182)

after 5 years of follow-up, and an HR of 0.65 (95% CI=0.54-0.78, N=409) after 20-years [7]. Therefore, our results from observational studies are in broad agreement with most – though not all – findings from RCTs.

Conflict of interest: The authors declare no conflict of interest.

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