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Cancer Prevention Research

Letter to the Editor

Allopurinol in Subjects with Colorectal Adenoma—Letter

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With interest, we have read the paper written by Puntoni and colleagues concerning the potential beneficial effects of allopurinol administration on inhibiting biomarkers of oxidative activation in adenomas and normal adjacent mucosa of colon and rectum (1). The authors subsequently speculate that allopurinol may be considered as an inexpensive and (relatively) safe chemopreventive agent. This may especially hold true for those patients with an elevated risk of developing colorectal cancer (CRC).

Patients with inflammatory bowel diseases (IBD) are at increased risk for developing CRC, as this chronic inflammatory process is believed to promote carcinogenesis. The risk for colon cancer decreases when patients with IBD take effective drugs to induce and subsequently maintain remission of disease. In addition, chemoprotective capacities have been ascribed to mesalazine and thiopurine derivatives. Thiopurine therapy (azathioprine or mercaptopurine) is currently the immunosuppressive therapy of choice for maintenance of remission, and its (long-term) use protects against the development of advanced colorectal neoplasia in these patients (2). Unfortunately, a relatively large number of patients fail this thiopurine therapy early, mainly because of the development of adverse events. The occurrence of these toxic effects is, in part, explained by a skewed thiopurine metabolism characterized by largely increased levels of methylated metabolites (6-methylmercaptopurine; MMP). This preferential 6-MMP–generating metabolism can be circumvented by the coadministration of allopurinol alongside adapted, low-dose thiopurines. This combination therapy leads to a significant decrease in 6-MMP levels and consequently avoidance of 6-MMP–associated adverse events (3).

We conclude that allopurinol not only possesses advantageous thiopurine metabolism modulating properties, but may also serve as a (beneficial) chemopreventive agent in patients with IBD. Thus, the reported additional pharmacodynamic effects and the preferable pharmacokinetics of thiopurines together with allopurinol administration may imply that this combination therapy is a more optimal and perhaps novel standard, immunosuppressive therapy for this patient group with IBD. We realize that prospective and controlled studies are warranted to explore the potential beneficial role of prescribing combination therapy of allopurinol and thiopurines to optimize its metabolism and to lower the lifetime risk of developing CRC (in particular patient groups).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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