

SESSION 5: LOCALIZED/ADJUVANT COLORECTAL CANCER

The Role of Aspirin in Adjuvant Therapy of CRC

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Spiraea is a genus of shrubs in which salicylic acid can be extracted that has been used to alleviate headaches, pain, and fevers since ancient times. Since the isolation of salicylic acid and then formulation of acetylsalicylic acid (aspirin), the beneficial health effects of aspirin have been increasingly realized, including in cancer prevention and possibly treatment. Aspirin, as well as NSAIDs, have been extensively studied as a chemoprevention for colorectal cancer leading to 20-40% reduction in incidence and colorectal cancer mortality.^{1,2,3,4} Over the past decade, prospective observational studies have demonstrated associations between aspirin usage and improved outcomes in colorectal cancer survivors. In a study from the Nurse's Health Study and Health Professional Follow-up Study, aspirin use was associated with a 29% improvement in colorectal cancer-specific mortality (hazard ratio [HR] 0.71, 95% confidence interval [CI] 0.53-0.95) and 21% improvement in overall mortality (HR 0.79, 95% CI 0.65-0.97).⁵ The association was stronger with increasing dosage per week and appeared limited to those patients whose tumors expressed COX-2. The mechanism of aspirin's antineoplastic effect is likely varied, with substantial evidence supporting both COX-dependent and COX-independent mechanisms.⁶ There are increasing studies seeking to determine the molecular phenotype of colorectal cancers most likely to benefit from aspirin or COX-2 inhibitors. In addition to COX-2 expression, PIK3CA has been reported, with mixed results. In one study of stage I-III colorectal cancer, patients who were regular aspirin users and whose tumors had a PIK3CA mutation had 82% improvement in colorectal cancer mortality (HR 0.18, 95% CI 0.06-0.61) while no association was seen with aspirin usage in patients with wildtype PIK3CA.⁷ However, a recent study using a cohort from the Moffitt Cancer Center and Royal Melbourne Hospital did not demonstrate an interaction by PIK3CA mutational status and aspirin usage.⁸ There are currently multiple ongoing randomized studies in colorectal cancer patients and survivors to test the added benefit of aspirin, celecoxib or other NSAIDs in addition to standard therapy for nonmetastatic colorectal cancer, with results expected in the next several years.

¹ Flossmann E, Rothwell PM. *Lancet* 2007;**369**:1603–13

² Thun et al. *J Natl Cancer Inst* 2007;**99**:608–15

³ Chan et al. *Gastroenterology* 2008;**134**:21–8

⁴ Chan, et al. *JAMA* 2005;**294**:914–23

⁵ Chan et al *JAMA*. 2009;302(6):649-658.

⁶ Chan et al. *Cancer Prev Res* February 2012 5; 164

⁷ Liao X et al. *N Engl J Med* 2012;367:1596-1606

⁸ Kothari et al *Acta Oncologica* 2015, 54, 487-492.