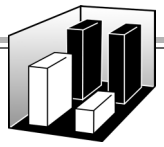
CLINICAL TRIALS REPORT



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# Chemoprevention of FAP with Sulindac

Giardiello FM, Yang VM, Hylind LM, *et al.*: **Primary chemoprevention of familial adenomatous polyposis with sulindac.** *N Engl J Med* 2002, **346:**1054–1059.

**Rating:** •Of importance.

**Introduction:** Both sulindac and celecoxib have been shown to cause regression of adenomatous polyps in individuals with familial adenomatous polyposis (FAP).

**Aims:** This trial was designed to answer the question of whether the development of new adenomas in young people with FAP who are phenotypically normal can be prevented.

**Methods:** Forty-one young subjects with genotypically proven FAP and phenotypically normal colon (*ie*, no polyps at study entry) were randomly assigned to receive daily oral sulindac or placebo. The primary outcome variables were the number and size of polyps at 48 months (or at time of withdrawal from the study) as assessed by sigmoidoscopy to 20 cm from the anal verge.

**Results:** No significant difference in the number or size of polyps was observed in the two groups. Compliance was high in both groups, with no difference in side effects measured. Nevertheless, there was clear evidence of a decrease in prostaglandins in the rectal biopsies of patients in the sulindac group.

**Conclusions:** Standard doses of sulindac did not prevent polyps in subjects who were genotypically affected by FAP but who were phenotypically normal at study entry.

## Editor's comments

This study may have been negative for many reasons, possibly including the following: 1) the mechanism by which sulindac causes regression of established polyps is different than progression; 2) higher dose or longer duration of sulindac administration may be required for an effect on progression; 3) transgenic models suggest that combination therapy is more effective; 4) the study was powered to detect a rather large effect, and a lesser but still clinically significant effect could have been missed; and 5) the relevance of the study to prevention of sporadic polyps in adults is unclear because the involvement of the *APC* gene is considerably more complex and regulated by other parameters.