Combinations in the treatment of oral premalignancy, and we welcome the opportunity of contributing knowledge, along with that of Dr. Garewal and Dr. Meyskens, to the area of natural agents for the chemoprevention of cancer.

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References


Response

Dr. Scott M. Lippman and Dr. Waun Ki Hong are understandably upset by our comments regarding widespread press coverage of their as yet non-peer reviewed, unpublished study. Much has been said about the implications of this practice by leading academicians and editors of prominent medical journals. We appreciate the considerable effort in their current response to state that their goal was not to discredit beta-carotene, and comments to this effect are contained in the Journal News item "Beta-Carotene Didn't Prevent Cancer: What's Up Doc?" However, this was clearly not the impact of the press coverage. Although accrual to beta-carotene trials may not have dropped, as stated by Smigel and Van Nevel (1) in their response to our letter, we can vouch for the problems created for ongoing and planned studies in the context of the extra effort required by involved investigators to keep participants interested in continuing after they brought in copies of news stories from the national and local press.

In the absence of a hard copy of a peer-reviewed publication, critically analyzing the study in question remains problematic, since we are faced with a moving target consisting of the latest interpretation of an ongoing trial. Testing these agents and concepts is an exciting avenue of clinical investigation with several active or planned local, national, and international studies. We concur with Dr. Lippman and Dr. Hong that no "scientific study attempting to advance knowledge of uncharted areas is problem free." But this emphasis misses the main point of our original letter which is that premature and, therefore necessarily incomplete, dissemination of the results of an ongoing trial must be thoroughly discouraged. Our critique of their study and their response only serve to highlight the problems created by this practice. We invite Dr. Lippman and Dr. Hong to join us, along with most academicians and editors of prominent medical journals, in condemning premature release of information. Their valuable contributions to the field of head and neck cancer management are well known, and such a gesture will only enhance, not detract from, their reputations.

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Reference


Colorectal Cancer Screening

In their otherwise excellent review of colorectal cancer screening, Winawer et al. (1) present in Table 3, for the first time in print, I believe, some of the mortality data from the Memorial Sloan-Kettering Cancer Center-Preventive Medicine Institute-Strang Clinic trial. The data presented are for the patients who had not been examined previously at the clinic. However, as reported previously by Flehinger et al. (2) [reference (17) of Winawer et al.], there were in addition to the original total of 21756 people admitted to this trial, 7168 patients assigned to the study group and 2109 patients assigned to the control group who had previously attended the Preventive Medicine Institute-Strang Clinic at least once before the visit at which they were enrolled in the trial.

As reported in the discussion on screening for colorectal cancer in the book Screening for Gastrointestinal Cancer (3), "There was some discussion over the appropriateness of basing the analysis of the New York study on the initial screen group alone, rather than combining the initial and annual screen group, as this appeared to be a post-

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study decision. A finding of no difference in the annual screen group is of interest because there is a suggestion of more cases being found in the annual screened, than in the control group.”

At the International Union Against Cancer meeting on Screening for Gastrointestinal Cancer held in Göteborg, Sweden, in November 1985, the mortality results for both the annual and the initial study participants were presented. These results did not appear in the report of Flehinger et al. (2) because Dr. Winawer requested they be omitted as they had not been submitted to peer-reviewed publication. To my knowledge, they have still not been submitted for publication. Although in our discussion in 1985, we recognized some of the difficulties with this trial (it was not a randomized trial at all; individuals were assigned depending on the dates they attended the Preventive Medicine Institute-Strang Clinic), we also were strongly of the opinion that the results for the annual participants as well as the initial study participants should be presented. I regret that Winawer et al. chose not to follow this advice and only presented a selective account of mortality in this study, which will undoubtedly leave the false impression in most of their readers’ minds that the trial difference for colorectal cancer mortality merged on being statistically significant. In practice, with the annual study and control participants included, this is not so.

The other aspect of the trial which the article by Flehinger et al. (2) emphasized is that, in practice, the participation in the fecal occult blood testing by the subjects included in the annual screen group was far superior to the participation by those included in the initial screen group. Similarly, the participation by the annual study and annual control groups of patients in proctosigmoidoscopy was far superior to the participation by the initial study and initial control groups [Figs. 1 and 2 of Flehinger et al. (2)]. It seems, at least in part, possible that the almost statistically significant difference in colorectal cancer for the initial study participants compared with the initial control participants is a chance finding and should not be interpreted as indicating a benefit of colorectal cancer screening using the fecal occult blood test in addition to proctosigmoidoscopy.

I call upon Winawer et al. to publish, either in the Journal of the National Cancer Institute or another journal, as soon as possible, the full mortality results of this trial so that all scientists are in a position to judge these results for themselves, not just those who were fortunate in attending the International Union Against Cancer meeting on Screening for Gastrointestinal Cancer.

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References


(2) FLEHINGER BJ, HERBERT E, WINAWER SJ, ET AL.: Screening for colorectal cancer with fecal occult blood test and sigmoidoscopy: Preliminary report of the colon project of Memorial Sloan-Kettering Cancer Center and PMI-Strang Clinic. In Screening for Gastrointestinal Cancer (Chamberlain J, Miller AB, eds). Toronto: Huber, 1988, pp 9–16

(3) Discussion on screening for colorectal cancer. In Screening for Gastrointestinal Cancer (Chamberlain J, Miller AB, eds). Toronto: Huber, 1988, p 53

Response

In reference to our discussion of mortality results of a clinical trial conducted at the Memorial Sloan-Kettering Cancer Center and Preventive Medicine Institute-Strang Clinic in the recently published review of colorectal cancer screening (1), Dr. Anthony B. Miller has urged us to combine the experiences in initial and annual subjects rather than a selective analysis of initial subjects only. We welcome the opportunity to discuss more fully the Memorial Sloan-Kettering Cancer Center-Preventive Medicine Institute-Strang Clinic trial.

The objectives and design features of the Memorial Sloan-Kettering Cancer Center-Preventive Medicine Institute-Strang Clinic trial, as described in previous publications, were to evaluate the feasibility and effectiveness of stool occult blood testing in conjunction with rigid sigmoidoscopy in the setting of a comprehensive preventive medical examination that routinely offered sigmoidoscopy (2-4). As stated in the review, patients over 40 years of age who presented at the clinic were assigned to either the study group or the control group on the basis of date of enrollment. There was no opportunity for selection bias or manipulation by patients or physicians in the assignment to either group. A total of 21 756 patients were enrolled consecutively in the Preventive Medicine Institute-Strang Clinic during the years 1975-1979. The evaluation of feasibility was limited to annual patients who had been examined previously by digital rectal examination and sigmoidoscopy, on one or more scheduled visits, at the Preventive Medicine Institute-Strang Clinic. This group of annual patients ultimately comprised a cohort of 7168 patients, who were assigned to receive Hemoccult slides, and a control group of 2109 subjects. Subsequent to the demonstration of feasibility, an independent experimental cohort of new, initial subjects, without previous visits and sigmoidoscopic examinations at the Preventive Medicine Institute-Strang Clinic, were enrolled and then assigned to study and control groups.

Of the cohort of initial subjects who were examined for the first time at the Preventive Medicine Institute-Strang Clinic, 5806 were given Hemoccult slides in addition to rigid sigmoidoscopy, and 6673 received only sigmoidoscopy. The study and control groups were comparable with respect to distribution by age, gender, family history of colorectal cancer, and personal history of cancer in general or colorectal polyps. In their first examination, 95% of the initial subjects received rigid sigmoidoscopic examinations and 80% of study subjects submitted slides. Subsequently, there was a rapid decline in participation; 80% of patients failed to return after 1 year and 84% failed to return after 2 years. When the methods and procedures for ensuring follow-up visits were intensified, adherence was