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Letter to the Editor

Correspondence re: S. E. Benner *et al.*, Chemoprevention Strategies for Lung and Upper Aerodigestive Tract Cancer. Cancer Res., *52* (Suppl.): 2758s–2763s, 1992.[1]

In a recent overview article, Benner, Lippman, and Hong (1) discuss chemoprevention strategies for aerodigestive tract cancers. In their discussion on oral leukoplakia some results are presented (Table 1) to support the contention that "Response rates have varied considerably in these trials, especially for β-carotene." However, the data in Table 1 misrepresent the β-carotene references that are mentioned. In fact, if correctly presented, the response rates with β-carotene are reasonably consistent, allowing for small size of the trials. At the very least, they are as consistent as the retinoid data. Specifics of the errors in the table are listed below.

1. Garewal *et al.* (2): This study had 24 evaluable patients (not 17). The overall response rate was 71%; however, the complete response rate was 8% and partial response rate was 63%.

2. Toma *et al.*: The reference quoted is a preliminary report of this trial (3). Subsequently, these authors have reported a 44% response rate for the more mature trial (4).

3. Stich *et al.* (5): Although the response rates quoted in the Benner *et al.* review are correct, it is grossly misleading not to mention that Stich *et al.* report complete response only, in contrast to the other studies. In other words, the 14.8 and 27.5% response rate in their publications must be compared with the complete, rather than overall, response rate of other studies. For example, the complete response rate in the 13-*cis*-retinoic acid study by Hong *et al.* (6) was 8%, which is to be compared with the above numbers from Stich *et al.* and the 8% complete response rate of the study by Garewal *et al.* (2).

4. Stich *et al.* (7): In addition to quoting the wrong dose of β-carotene (correct dose, 180 mg/week), the source of the 0% response rate mentioned in the Benner *et al.* review as being found in this study is a mystery. In fact, this paper reports only on the decrease in micronuclei frequency and some pharmacological issues, but has nothing to do with oral leukoplakia. None of the patients even had leukoplakia. "We did not observe a single case of leukoplakia among 160 male Inuits examined who used smokeless tobacco," says the quoted paper.

A more accurate version of the β-carotene studies quoted in Table 1 of the review article is shown in the table. Clearly these are fewer than the numbers of studies done with the retinoids, the testing of which began nearly three decades ago compared with the more recent β-carotene trials. Additional studies with β-carotene, alone or in combination with other micronutrients, are presently ongoing. The most consistent feature of β-carotene studies has been the lack of toxicity while the most consistent feature of the retinoid trials has been significant toxicity, even when used at extremely low doses, *e.g.*, 0.1–0.2 mg/kg/day of 13-*cis*-retinoic acid (8). In contrast to the interpretation implied in the Benner, Lippman, and Hong review, the early trials with β-carotene have all yielded positive results (*i.e.*, no 0% responses) and are at least as consistent as the retinoid trials.

Table 1 β-Carotene in oral leukoplakia

Author	Ref.	Agent	Dose	Evaluable patients	% of response		
					CR[a]	PR	OR
Garewal *et al.*	2	BC	30 mg/day	24	8	63	71
Toma *et al.*	4	BC	90 mg/day	18	33.3	11.1	44.4
Stich *et al.*	5	BC	180 mg/wk	27	14.8	NS	NS
		BC + Vitamin A	180 mg/wk + 100,000 IU/wk	51	27.5	NS	NS
		Placebo		33	3	NS	NS
Stich *et al.*[b]	7	BC	180 mg/wk	24	Decreased micronuclei		

[a] CR, complete response; PR, partial response; OR, overall response; BC, β-carotene, NS, not stated.

[b] No patient had leukoplakia, hence no response rate can be quoted. Included as a correction of Table 1 in Benner, Lippman, and Hong (1). The end point was reduction in frequency of micronuclei which was observed.

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[1] No reply received.