Title
Re: Vitamin A analogue for breast cancer prevention: a grade of F or incomplete?

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Peer reviewed
We were annoyed by the disparaging title given to the editorial written by S. Piantadosi (1) on our breast cancer prevention trial with fenretinide, which was published in the November 3 issue of the Journal (2). First, we feel that the title is not consistent with the editorial content itself (who gives an F grade to a well designed and conducted study?). In addition, the title is in sharp contradiction with Journal policy to publish only articles of major importance. Our disappointment was increased after learning that, as a result of this title, several media outlets have dismissed our study as being one of poor quality. In the current publicity-dominated era, the choice of this title is at best unscrupulous, if not dictated by reasons that have little to do with science.

It is a shame that the irresistible temptation of adding a sensationalist title has overcome a more reasonable review of our study, while we think we have honestly addressed the limitations of our work in the paper. Contrary to Dr. Piantadosi’s doubts, we had clearly stated in the article that, among the dozen possible interactions, we tested only the one between fenretinide treatment and menopausal status because this interaction has strong biologic support. This support came not only from our previous observations that plasma insulin-like growth factor-I (IGF-I) levels behaved with the same pattern following fenretinide treatment [refs. (27) and (28) of our paper], but also from the well-established notion that premenopausal and postmenopausal breast cancer are different diseases that receive different treatments and have different risk factors, some of which, like body mass index, interact in a qualitative manner with menopausal status [refs. (39–41) of our paper].

Since we believe that biologic plausibility should drive statistics and not vice versa, we feel that leaving this interaction untested would have missed some very important information. It is argued that our study was not powered to test such an interaction. Consistently, we have not recommended treating premenopausal women with fenretinide but simply suggested implementing further studies to address the new hypotheses that are generated by our study. Our prudent attitude is demonstrated by the fact that, in contrast to one reviewer’s advice, we have not pooled contralateral breast cancer and ipsilateral breast cancer events in a single figure. While this combination would have certainly provided more powerful statistical support for the benefit of fenretinide in premenopausal women, such a combined analysis had not been planned before the study was conducted.

The bottom line is that the fenretinide trial is one of the few large cancer prevention trials ever performed and is by far the largest clinical study that tests a retinoid for breast cancer prevention. Awarding an F grade to our pioneering study without any sound scientific argument is arrogant, cynical, and uselessly mortifying for the nearly 3000 women who took part in the study for an average of 8 years, for the many investigators and support personnel who gave their time and effort for such a long period of time, for the reviewers who recommended National Cancer Institute funding for three consecutive periods for a total of 9 years, and last, but not least, for the U.S. and Italian taxpayers and contributors who made the resources available.

We thought it appropriate to submit our paper to the Journal in view of the above-mentioned reasons. We are extremely disappointed by the Journal’s decision to publish our paper alongside this destructive editorial without informing us until the moment of its publication. We are sorry the Journal missed an opportunity to begin a fruitful discussion on the complex issues related to cancer prevention trials.

Both the report on the “Randomized Trial of Fenretinide to Prevent Second Breast Malignancy in Women With Early Breast Cancer” and the accompanying editorial impressed me as thoughtful presentations and discussions of the complex results reported (1,2). Why then the sensationalist title for the editorial? If this title was the one chosen by the editorialists, the Journal should have insisted on a more objective title. If the title was selected by the Journal, then shame on the Journal. Certainly the dismissal by the media of this trial as a poorly done study serves no one well. Doing clinical research is hard enough without our most cited (best?) journal in cancer research resorting to “yellow journalism.”

Frank L. Meyskens, Jr.

REFERENCES


NOTE

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RESPONSE

It’s not often that a favorable editorial gets taken to task by the recipient. I hope that other readers did not miss my points or get them backwards, as

REFERENCES

(1) Piantadosi S. Vitamin A analogue for breast cancer prevention: a grade of F or incom-