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IN REPLY: We would like to reply to the letter from Marc Chamberlain regarding our article entitled “Bevacizumab Plus Irinotecan in Recurrent Glioblastoma.” Chamberlain raises a number of important issues and makes many good points.

The first issue was the schedule of irinotecan. We chose a regimen of administration once every 2 weeks with both irinotecan and bevacizumab to limit the toxicity. The regimen of administration once every 3 weeks may be simpler, but the dose of irinotecan will be increased and we did not want to stop the trial because of toxicity. With our experience, the schedule of administration once every 3 weeks for irinotecan and bevacizumab may be as efficacious and tolerable.

The second issue raised by Chamberlain is the use of irinotecan in this regimen. We combined irinotecan with bevacizumab for three reasons. The first reason is that chemotherapy and bevacizumab is more active than bevacizumab alone in most malignancies. The second reason was that irinotecan has a different mechanism of action than temozolomide, so we were trying to limit cross-resistance. The third reason for combining irinotecan with bevacizumab is the experience in colorectal carcinoma and the US Food and Drug Administration approval of irinotecan and bevacizumab. I agree with Chamberlain that alternative cytotoxic chemotherapies may be equally active, and we eagerly await the results of ongoing clinical trials. All of these patients had received temozolomide and radiation therapy, and we hypothesize that irinotecan and bevacizumab would be efficacious in an O⁶-methylguanine-DNA methyltransferase-unfavorable tumor.

The third issue that Chamberlain raises was the pharmacoeconomics of anticancer therapy. We agree that the pharmacoeconomics of cancer care is a contentious issue and needs to be addressed. We feel fortunate that we finally have an active

regimen against recurrent glioblastoma that allows us to worry about pharmacoeconomics.

The final issue raised by Chamberlain was craniotomy site wound dehiscence. We agree that this is a potential problem, and the concurrent administration of antiangiogenic agents and dexamethasone may increase the risk of wound dehiscence. We have had some patients with craniotomy site dehiscence as well as dehiscence of their port-a-cath sites. The issue of wound dehiscence requires extensive patient and provider education, and is one of the potential limitations of this promising therapy.

We appreciate Chamberlain's comments, and hope that the combination of irinotecan and bevacizumab is the beginning of a new wave of therapies for malignant gliomas.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Boost or Not

TO THE EDITOR: We wish to comment on the paper by Bartelink et al¹ reporting a large series of patients treated with wide local excision and radiotherapy, and randomly assigned to receive either standard whole-breast irradiation (50 Gy in 25 fractions) or the same plus a boost of 16 Gy.

The boost may, statistically significantly, reduce the risk of local recurrence in patients older than 50 years, and the proportional reduction may be the same as for younger patients, but the *absolute* reduction in risk of recurrence in these patients is in fact only a few percent (the authors do not provide the exact figures, but this can be seen from the graphs in Fig 3 of the article).

Conversely, the use of a boost results in an increased incidence of moderate to severe fibrosis of approximately 20% (Fig 4 of the article). This obviously influences cosmesis, which is an important consideration for these women as they chose breast-conserving surgery rather than mastectomy.

In summary, only a small percentage of patients age older than 50 years receive any benefit from the boost, whereas a much larger percentage have worse results cosmetically from its use. What benefit there is—a small reduction in local recurrence—in this study has not been shown to translate into an improvement in overall survival.

Although we accept that there might be specific risk factors that could select an individual patient older than 50 years for boost due to an identifiable increased risk of local recurrence, our interpretation of these randomized data is that a boost in patients older than 50 years is certainly not warranted as the routine standard of care.

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