Correspondance

The Intergroup study appears to be the most significant to date that might justify a recommendation for chemo-endocrine therapy in postmenopausal patients with ER-positive tumours.[11] Unfortunately the full report has not yet been published. It would be useful to know whether there were differential benefits in this study in women aged 50–59, 60–69 and more than 69 years, for making decisions concerning the adjuvant treatment of otherwise healthy people at risk of iatrogenic disease but also at varying risk of developing metastatic disease if not optimally treated.

I should appreciate the authors' views on the use of chemotherapy, particularly in older women with ER-positive tumours, in light of these comments.

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[The author responds:]

David Ginsburg has conducted his own analysis of selected studies. The meta-analysis by the Early Breast Cancer Trialists' Collaborative Group, which included all the trials of chemotherapy plus tamoxifen versus tamoxifen alone in over 9000 postmenopausal women, demonstrated a statistically significant reduction in both breast cancer recurrence and mortality in favour of the combined chemohormonal therapy.[1] Ginsburg points out that some of the trials that compared chemotherapy plus tamoxifen with tamoxifen alone included a small number of patients with estrogen receptor (ER)-negative tumours. Tamoxifen would not be expected to be of benefit in such patients. The implication is that the demonstrated benefit of combination therapy is driven by the effect of chemotherapy in the ER-negative patients. We believe that this is a spurious hypothesis for several reasons. First, the numbers of ER-negative patients were balanced between treatment arms in these trials and these patients comprised a relatively small subgroup. Second, chemotherapy is effective in women with ER-positive tumours as well as ER-negative tumours. Finally, in trials that included only postmenopausal women with ER-positive tumours, a benefit was detected in favour of the addition of chemotherapy to tamoxifen. For example, the Intergroup recently updated the results of their trial of anthracycline-containing chemotherapy plus tamoxifen versus tamoxifen alone.[2] There was a statistically significant improvement in survival in favour of the addition of chemotherapy to tamoxifen.

We agree with Ginsburg that there were very few patients over 70 years of age in the trials of adjuvant chemotherapy. We alluded to this in our guideline[3] and we feel that our recommendations were balanced and did not overstate the case.

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Ammunition against malaria

The recent case series of malaria deaths in Canada illustrates the need for heightened awareness of tropical diseases by Canadian physicians.[1] I was recently involved in caring for a patient who died of malaria shortly after returning from Kenya. Unfortunately, the patient had not taken antimalarial prophylaxis.

While I was in Africa I had the opportunity to see the use of 2 powerful antimalarial agents, dihydroartemisinin and β-artemeter. Studies have shown that these drugs are highly effective plasmodicides, even in multidrug-resistant malaria. The World

Health Organization has listed these agents on their essential drug list in recognition of their activity against malaria. Is there any indication that they will be available in Canada on an "emergency release" basis in the near future?

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Reference

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[One of the authors responds:]

We thank Russell MacDonald for his interest in our paper.[1] As he points out, artemisinin derivatives are potent antimalarials that result in faster parasite and fever clearance times than any other class of antimalarials. The use of artemisinin-based suppositories represents a breakthrough in the management of severe and complicated malaria in medically underserviced areas of the developing world.

Unfortunately, unlike standard treatments such as parenteral quinine (currently the treatment of choice for severe malaria in Canada), artemisinin-based drugs have not been shown to decrease the mortality associated with severe malaria.[2,3] Furthermore, most of the compounds currently in use have not gone through the formal safety and toxicity testing generally required by drug regulatory authorities in order for them to be licensed for use in developed countries. In addition, until recently these drugs were not generally produced using good manufacturing practices. However, a number of these derivatives are now made using good manufacturing practices and I posed MacDonald's question regarding their availability to the Health Protection Branch. Although there was some interest, they indicated that at present there are no plans to make these agents available in Canada.

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Weighing the risks and benefits of autologous blood donation

In their article on the use of a decision aid for patients considering autologous blood donation before open-heart surgery, Curry Grant and colleagues did not mention storage time for blood.[1] This issue should be discussed when autologous blood transfusion is being considered. Is this a component of the decision aid?

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Reference

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[One of the authors responds:]

We agree with Alastair Weir that the storage time of self-donated blood should be discussed with patients considering donating their blood. Self-donated blood has a shorter shelf life than volunteer-donated blood (35 v. 42 days) because of differences in processing methods. We have added the shelf life of self-donated blood to our revised decision aid.[1] The short storage time may contribute indirectly to the increased risk of having a transfusion of either type of blood in patients who have donated their own blood, because there may not be adequate time in some patients for regeneration of red blood cells before surgery. With each unit of blood transfused, whether self-donated or volunteer-donated, there is a small risk of human error resulting in a transfusion reaction and a very small risk of bacterial contamination of the blood. Patients who are considering donating their own blood before surgery should weigh the reduced risk of viral transmission against the increased risk of human error and bacterial contamination owing to the greater average number of units transfused.[2] The revised decision aid is available on the Ottawa Health Research Institute Web site (www.ohri.ca/programs/clinical_epidemiology/OHDEC/decision_aids.asp).

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Alberta's Bill 11

In a recent commentary, Samuel Shortt expressed the fear that Alberta's Bill 11 will lead to the destruction of Canadian medicare, increased privatization and the entry of American health care providers into the Canadian market.[1] I have trouble understanding Shortt's position because it is not the law that will determine whether his fears are