

## 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.<sup>11</sup> 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.

## David Ginsburg

Professor of Oncology and Medicine  
Queen's University  
Kingston, Ont.

## References

- Levine M, for the Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. Clinical practice guidelines for the care and treatment of breast cancer: adjuvant systemic therapy for node-positive breast cancer (summary of the 2001 update). *CMAJ* 2001;164(5):644-6.
- Fisher B, Redmond C, Fisher E, Wolmark N. Systemic adjuvant therapy in treatment of primary operable breast cancer: National Surgical Adjuvant Breast and Bowel Project experience. *J Natl Cancer Inst Monogr* 1986;1:35-43.
- Fisher B, Redmond C, Legault-Poisson S, Dimitrov NV, Brown AM, Wickerham DL, et al. Postoperative chemotherapy and tamoxifen compared with tamoxifen alone in the treatment of positive-node breast cancer patients aged 50 years and older with tumors responsive to tamoxifen: results from the National Surgical Adjuvant Breast and Bowel Project B-16. *J Clin Oncol* 1990;8:1005-18.
- Huq AU, Huq MB. Hormonal versus chemohormonal adjuvant therapy in node-positive postmenopausal patients [letter]. *J Clin Oncol* 1990;8:1922.
- Fisher B, Redmond C, and Brown A. Hormonal versus chemohormonal adjuvant therapy in node-positive postmenopausal patients [letter]. *J Clin Oncol* 1990;8:1925-6.
- Castiglione-Gertsch M, Price KN, Nasi ML. Is the addition of adjuvant chemotherapy always necessary in node negative (N-) postmenopausal patients who receive tamoxifen (TAM): first results of IBCSG Trial IX. *Proc Am Clin Oncol* 2000;19:73a.
- Ludwig Breast Cancer Study Group. Randomised trial of chemo-endocrine therapy, endocrine therapy, and mastectomy alone in postmenopausal patients with operable breast cancer and axillary node metastasis. *Lancet* 1990;335:1099-100.
- Wils JA, Bliss JM, Marty M, Coombes G, Fontaine C, Morvan F, et al. Epirubicin plus tamoxifen versus tamoxifen alone in node-positive postmenopausal patients with breast cancer: a randomized trial of the International Collaborative Cancer Group. *J Clin Oncol* 1999;17(7):1988-98.
- Early Breast Cancer Trialists' Collaborative Group. Polychemotherapy for early breast cancer: an overview of the randomized trials. *Lancet* 1998;352:930-42.
- International Breast Cancer Study Group. Effectiveness of adjuvant chemotherapy in combination with tamoxifen for node-positive postmenopausal breast cancer patients. *J Clin Oncol* 1997;15:1385-94.
- Albain K, Green K, Osborne C. Tamoxifen (T) versus cyclophosphamide, adriamycin and 5-FU plus either concurrent or sequential T in postmenopausal receptor (+) node (+) breast cancer: a Southwest Oncology Group Phase III Intergroup trial (SWOG- 8814, INT-0100) [abstract]. *Proc Am Soc Oncol* 1997;16:128a.

## [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.<sup>1</sup> 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 up-

## Table of Contents

dated the results of their trial of anthracycline-containing chemotherapy plus tamoxifen versus tamoxifen alone.<sup>2</sup> 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<sup>3</sup> and we feel that our recommendations were balanced and did not overstate the case.

## Mark Levine

Professor  
Departments of Medicine and Clinical  
Epidemiology and Biostatistics  
McMaster University  
Hamilton, Ont.

## References

- Early Breast Cancer Trialists' Collaborative Group. Polychemotherapy for early breast cancer: an overview of the randomized trials. *Lancet* 1998;352:930-42.
- Albain K, Green S, Ravdin P, et al. Overall survival after cyclophosphamide, adriamycin, 5FU and tamoxifen is superior to tamoxifen alone in postmenopausal receptor positive, node positive breast cancer: new findings from phase 3 Southwest Oncology Group Intergroup Trial S8814 [abstract]. *Proc Am Soc Clin Oncol* 2001;20:94.
- Levine M, for the Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. Clinical practice guidelines for the care and treatment of breast cancer: adjuvant systemic therapy for node-positive breast cancer (summary of the 2001 update). *CMAJ* 2001;164(5):644-6.

## Ammunition against malaria

The recent case series of malaria deaths in Canada illustrates the need for heightened awareness of tropical diseases by Canadian physicians.<sup>1</sup> 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  $\beta$ -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?

**Russell D. MacDonald**

Assistant Professor  
Division of Emergency Medicine  
Faculty of Medicine  
University of Manitoba  
Winnipeg, Man.

**Reference**

1. Kain KC, MacPherson DW, Kelton T, Keystone JS, Mendelson J, MacLean JD. Malaria deaths in visitors to Canada and in Canadian travellers: a case series. *CMAJ* 2001;164(5):654-9.

**[One of the authors responds:]**

We thank Russell MacDonald for his interest in our paper.<sup>1</sup> 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 underserved 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.<sup>2,3</sup> 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.

**Kevin Kain**

Professor  
Division of Infectious Diseases  
Department of Medicine  
University of Toronto  
Toronto, Ont.

**References**

1. Kain KC, MacPherson DW, Kelton T, Keystone JS, Mendelson J, MacLean JD. Malaria deaths in visitors to Canada and in Canadian travellers: a case series. *CMAJ* 2001;164(5):654-9.
2. Tran TH, Day NP, Nguyen HP, Nguyen TH, Tran TH, Pham PL, et al. A controlled trial of artemether or quinine in Vietnamese adults with severe falciparum malaria. *N Engl J Med* 1996; 335(2):76-83.
3. Van Hensbroek MB, Onyiorah E, Jaffar S, Schneider G, Palmer A, Frenkel J, Enwere G, et al. A trial of artemether or quinine in children with cerebral malaria. *N Engl J Med* 1996;335(2): 69-75.

**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.<sup>1</sup> This issue should be discussed when autologous blood transfusion is being considered. Is this a component of the decision aid?

**Alastair Weir**

Family physician (retired)  
Toronto, Ont.

**Reference**

1. Grant FC, Laupacis A, O'Connor AM, Rubens F, Robblee J. Evaluation of a decision aid for patients considering autologous blood donation before open-heart surgery. *CMAJ* 2001;164 (8):1139-44.

**[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.<sup>1</sup> 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.<sup>2</sup> The revised decision aid is available on the Ottawa Health Research Institute Web site ([www.ohri.ca/programs/clinical\\_epidemiology/OHDEC/decision\\_aids.asp](http://www.ohri.ca/programs/clinical_epidemiology/OHDEC/decision_aids.asp)).

**F. Curry Grant**

Associate scientist  
Institute for Clinical Evaluative Sciences  
University of Toronto  
Toronto, Ont.

**Reference**

1. Grant FC, Laupacis A, O'Connor AM, Rubens F, Robblee J. Evaluation of a decision aid for patients considering autologous blood donation before open-heart surgery. *CMAJ* 2001;164(8): 1139-44.
2. Forgie MA, Wells PS, Laupacis A, Fergusson D. Preoperative autologous donation decreases allogeneic transfusion but increases exposure to all red blood cell transfusion. *Arch Intern Med* 1998; 158:610-6.

**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.<sup>1</sup> I have trouble understanding Shortt's position because it is not the law that will determine whether his fears are