Why "competition"?

Most clinical trials are sponsored by pharmaceutical firms. For example, in 2005, our Institutional Review Board at McGill University received 42 oncology studies, of which 30 were industry-sponsored submissions. Sponsoring companies are usually interested in conducting trials with narrow inclusion criteria. These "fastidious" trials (defined as "using homogeneous groups, reducing or eliminating ambiguity" [3]) are designed to examine the use of a specific therapy in a carefully controlled environment, leaving little doubt that any observed efficacy directly relates to the tested product. This aim is sensible, and expected by regulatory authorities, but it leads to a trial milieu that may not reflect the general practice of oncology. "Pragmatic" trials—defined as those that "would incorporate heterogeneity, occasional or frequent ambiguity, and other 'messy' aspects of clinical practice" [3] are more relevant to actual oncology practice, but are less commonly conducted. The protocols for fastidious trials usually contain an exclusion clause with wording along the following lines: "Concomitant employment of other experimental therapies during the course of the clinical trial is prohibited" [3].

Inherently, a paradox is evident. The cancer community believes that research into palliation and symptom control deserves a high priority [4] and that that research should commence with the onset of a symptom (for example, as soon as a weight-losing patient with lung cancer presents with disease). However, the same patient cannot go on a symptom control trial if enrolled in a chemotherapy study, because participation in another clinical trial is proscribed. Consequently, late in the course of illness, a small coterie of exhausted patients with profound weight loss may now be asked if they wish to consider enlisting in a cachexia trial. But is this trial hierarchy logical?

Exclusion of patients from participation in two simultaneous trials is usually justified for these reasons:

- Regulatory authorities will not permit simultaneous trials.
- Participation in two trials will present confounding information that will make it impossible for the pharmaceutical firm to properly study the efficacy of the drug or drug and radiotherapy combination of interest and to accurately assign adverse reactions.

These excellent reasons fail to take note of certain confounding facts. Many patients with advanced cancer are using a variety of untested combinations of diet, supplements, vitamins, herbs, naturopathic products, yoga, and so on [5]. Pharmaceutical trials have not usually controlled for these widespread potential confounders. Moreover, the populations at risk for cancer tend to be older, and they often have comorbid conditions—notably diabetes, hypertension, cardiovascular disease, and chronic obstructive pulmonary disease. Patients with these disorders are thus receiving a wide variety of drugs that could affect disease activity [6–8] and certainly may interfere with drug metabolism. Information on these agents and their relevance usually does not appear in study reports.

Excluding careful clinical research observations on agents aimed at helping control symptoms, while ignoring the chaotic, uncontrolled potential effects of alternative and non-cancer-related therapies on drug and radiotherapy response is therefore illogical. From a statistical point of view, patients who are also engaged in a symptom control trial can be readily stratified, although trials may then need to be larger.

We worship at the "evidence based" altar. Many of our symptom control trials are lightly regarded because of small patient enrolment and high dropout rates from death and increasing frailty. Here are some examples from two recent studies published by leaders in the anorexia–cachexia field:

- Fearon and colleagues [9] recently reported on the efficacy of two doses of an omega-3 fatty acid on pancreatic cancer–induced cachexia. A robust effect was not found, only a favourable trend at the level of a 2-g dose of eicosapentaenoic acid. The mean weight loss on trial entrance was 18%, and the dropout rate among these profoundly ill patients was approximately 50% over 8 weeks.
- The recent article by Strasser *et al.* [10] on cannabinoid use in combating anorexia had a 32% dropout rate in 8 weeks; the study population had a mean weight loss of 11.9% upon enrolment.

We will not advance cachexia research until we can invite people with early weight loss to consider trial participation.

OBLIGATION TO DEVELOPING COUNTRIES

Recent advances have come at a cost—a cost passed on to the health system, or now, frequently, to the patient as governments lag in picking up the tab for non-curative, extraordinarily expensive therapies that may modestly prolong survival for a select group of patients. To paraphrase the Etruscan general Pyrrhus' comment on winning a battle with the Romans at great cost to his army, "A few more pharmaceutical advances like cetuximab and our cancer care system is bankrupt."

The costs of new anticancer agents create major dilemmas in Canada. What about resource-poor countries such as those of the African continent? Those countries will never be able to pay for drugs like bevacizumab or cetuximab. Do we have an ethical