Cancer-treatment toxicity: can nutrition help?

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During the past decade, the risk of cancer death decreased every year by 0.01–0.02%—a diagnosis of, for example, lung cancer in 2008 yielded a lower risk of dying of that cancer than the same diagnosis in 2007. If we consider the improvements in understanding cancer metabolism in the same time period and the increasing costs of cancer patient management,¹ this rate of improvement can seem disappointing.² The ability of cancer cells to develop evasive resistance to antitumour therapies is the major factor involved in the suboptimal response rate of patients with cancer.³ However, treatment-associated toxicity also has a considerable role because it limits the delivery of adequate doses of chemotherapy, targeted therapies and radiotherapy, and might impede the completion of the antitumour schedule. Thus, any clinical strategy of treating patients with cancer should be considered alongside an approach that targets cancer-therapy-related toxicity.² Unfortunately, as recently discussed by Charles S. Cleeland and coauthors in their Perspectives article (Reducing the toxicity of cancer therapy: recognizing needs, taking action. *Nat. Rev. Clin. Oncol.* **9**, 471–478; 2012),⁴ toxicity remains an underestimated issue in the management of patients with cancer. Indeed, toxicity is rarely the focus of clinical investigations since, historically, clinicians have been more concerned with cure than toxicity. Thus, there is a paucity of effective therapies. We agree that the agenda set forward by Cleeland *et al.*⁴ (that is, increasing recognition, improving care and promoting research) should be a priority for researchers, clinicians and funding agencies. Nevertheless, major breakthroughs in medicine might come not from the discovery new drugs, but from the more efficient delivery of therapies already available. Thus, implementing strategies that are documented to prevent cancer-therapy toxicity is important.

The clinical relevance of maintaining or restoring nutritional status in patients

with cancer is now supported by robust evidence.⁵ Quality of life is a key outcome measure in oncology, and consistent evidence show that malnutrition impinges on quality of life,⁶ which, in turn, is ameliorated by nutritional intervention.⁷ Beyond this, nutrition remains a potent inducer of metabolic responses. Exploiting this evidence, extreme nutritional stress—short-term fasting—has been tested with positive results in animal models of treatment-related toxicity in cancer, but translation into clinical practice might require necessary adaptations, including deprivation of selective nutrients rather than aspecific reduction in caloric intake.⁸ However, recent data demonstrate that nutritional status and, in particular, muscle mass are key determinants of cancer-therapy-related toxicity. Muscle depletion reduces survival of patients with cancer, even in the presence of excessive body weight.⁹ This negative clinical outcome predominantly results from the greater incidence of dose-limiting toxicity in muscle-depleted patients.¹⁰ Intensive nutritional intervention maintains energy levels and protein intake during active therapy and reduces toxicity,¹¹ which might enable patients to stay on, and complete, their treatment schedule. Indeed, early provision of nutritional support to meet protein and energy requirements contributed to completion of treatment schedule in a study of patients with upper gastrointestinal cancer,¹² whereas supplementation with fish oil increased the number of chemotherapy cycles received by patients with non-small-cell lung cancer.¹³ Finally, the use of immune-enhancing nutrients to metabolically prime patients undergoing elective surgery for gastrointestinal tumours has been shown to reduce postoperative complications.¹⁴

Nutritional intervention seems more effective in preventing, rather than treating, cancer-treatment-related toxicity. Thus, effective strategies to cure toxicity are also needed. Indeed, the integration of different expertise within a comprehensive approach

to treating patients with cancer-related toxicity should yield significant clinical benefits¹⁵ at a fraction of the cost required to develop and test a new drug.

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Competing interests

A. Laviano declares an association with the following companies: Baxter, Danone Research, Fresenius Kabi and Nestlé Health Science. F. Rossi Fanelli declares an association with Fresenius Kabi. See the article online for full details of the relationships. A. Molino declares no competing interests.

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