Immune Therapy for Breast Cancer in 2010—Hype or Hope?

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KEY WORDS
Breast cancer, immunotherapy, cancer vaccine, cytokine, monoclonal antibody

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The application of immunotherapeutic principles to the treatment and prevention of breast cancer has been ongoing for decades. Although cytokines, cancer vaccines, and other host factors have been extensively studied in breast cancer, the therapeutic efficacy of these approaches remains unproven. The recent identification of tumour-specific immunity and of several breast cancer antigens has generated enthusiasm for the application of immune-based therapies. Although monoclonal antibodies, cytokines, and vaccines have all individually shown some promise, and although the immunomodulatory effects of bisphosphonates have taken a front seat in the treatment of breast cancer, it is likely that the best strategy to combat breast cancer will be a multimodality strategy. Clearly, different strategies demonstrate benefit in different patient populations. It may be that the best results will be obtained from vaccines in combination with a variety of antigens, or from vaccine and antibody combinations. Nonspecific and specific immunotherapy combinations may be another potent strategy. The effect of any of the aforementioned strategies in combination with more traditional cancer therapies is another avenue.

Given the mechanisms of immunotherapy, these treatments are most likely to work in the adjuvant setting and not in the setting in which they are usually tested: the heavily treated patient with metastatic breast cancer.

This review assesses modern research and explores whether the hopes for immunotherapy can overcome the hype.

Lymphangitic Metastasis of Recurrent Renal Cell Carcinoma to the Contralateral Lung Causing Lymphangitic Carcinomatosis and Respiratory Symptoms

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KEY WORDS
Renal cell carcinoma, recurrence, lung metastasis, lymphangitic carcinomatosis

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Renal cell carcinoma comprises 80%–85% of kidney malignancies. For early presentations, nephrectomy provides a high cure rate, but patients usually present at advanced stages, leading to poor outcomes. Even for patients without metastatic spread who undergo nephrectomy, metastatic recurrence is frequent. We report the case of a patient who underwent nephrectomy for stage III renal cell carcinoma and who presented 20 months later with respiratory symptoms consistent with pneumonia, influenza, or (less likely) congestive heart failure or a cardiac event. Persistent right pleural effusion on serial chest radiographs despite treatment prompted computed tomography evaluation, which revealed lymphangitic carcinomatosis, a very rare form of renal cell carcinoma metastasis to the lung. This preliminary finding was confirmed by right middle lobe tissue biopsy through bronchoscopy and cytopathology examination.

The Use and Effectiveness of Temozolomide in Children with Central Nervous System Tumours: A Survey from the Canadian Paediatric Brain Tumour Consortium

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KEY WORDS
Temozolomide, children, pediatric, CNS, brain tumour

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Objective: To describe the use of temozolomide (TMZ) in Canadian children treated for brain tumours and to evaluate survival and predictors of survival for children treated with this agent.

Methods: A survey was conducted within the Canadian Paediatric Brain Tumour Consortium (CPBTC), a group of tertiary care centres in pediatric neuro-oncology ($n = 16$) in Canada that are involved in the treatment of children with central nervous system tumours.

Results: In 10 of the 16 participating pediatric oncology centres of the CPBTC, 137 children with brain tumours were treated with TMZ between January 2000 and March 2006. Although 33% of the children were enrolled into a clinical trial, 67% were treated outside open studies. Most patients (72%) received TMZ treatment on recurrence of their brain tumour (first or subsequent). The most commonly administered regimen was single-agent TMZ 150–200 mg/m^2 administered on 5 consecutive days every 28 days. The median duration of TMZ treatment was 141 days (range: 4–1102 days). Response data were provided for 127 of the 137 patients, of whom 6 showed a complete response. Sixteen patients experienced a minor or partial response, 53 had stable disease, and 52 had progressive disease. Of 32 patients alive at last follow-up, 19 had a diagnosis of low-grade glioma.

Conclusions: Temozolomide is used in a variety of pediatric brain tumours, often at the time of recurrence. The lack of insight into clear indications for this agent in pediatric brain tumours—used either alone or in combination therapy—may be a result of suboptimal design of phase I and II studies and a lack of phase III trials in the pediatric brain tumour population.

A Comparative Analysis of Monthly Out-of-Pocket Costs for Patients with Breast Cancer as Compared with Other Common Cancers in Ontario, Canada

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KEY WORDS
Breast cancer, out-of-pocket costs, self-administered questionnaire, health care funding

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Background: In Ontario, cancer patients do not have publicly funded comprehensive coverage once care moves outside of the hospital setting. Hence, patients may be required to pay for direct medical costs such as prescription drugs, complementary and alternative medicine (CAM), or home nursing once they are discharged from hospital. Similarly, direct nonmedical costs for home care or personal care have not traditionally been publicly funded for cancer patients. Monthly out-of-pocket costs (OOPC) for Ontario cancer patients have previously been reported, but little detail has been provided on differences based on tumour type.

Methods: Using descriptive statistics and regression analyses, we analyzed an existing cross-sectional study in which a questionnaire was administered to patients in urban and rural cancer clinics in the province of Ontario. The dependent variable was OOPC, analyzed separately for total OOPC (excluding imputed travel costs) and for each of the individual cost categories. Individual cost categories included travel costs, prescription drugs, in-home health care, homemaking services, CAM, vitamins and supplements, family care, accommodations and meals, devices and equipment, and other costs.

Results: Compared with colorectal, lung and, prostate cancer patients combined, breast cancer patients had statistically significant higher total OOPC ($393 vs. $149, travel excluded; $p = 0.02$), "devices" costs ($142 vs. $12, $p = 0.018$), and "family care" costs ($38 vs. $3, $p = 0.01$), and yet they trended toward lower costs for travel ($225 vs. $426, $p = 0.055$) and had significantly lower costs for parking ($32 vs. $53, $p = 0.0198$). Breast cancer patients reported a greater perceived financial burden than did non-breast-cancer patients (31% vs. 17%, $p = 0.0133$). The primary

regression analysis, which used backward stepwise methods, initially tested tumour type, treatment type, treatment duration, marital status, age category, education, income, sex, and insurance coverage. The regression showed that, in addition to tumour type, only income and insurance coverage were statistically significant predictors of expenditure ($R^2 = 0.1051$).

Interpretation: Results show that mean total OOPC, as well as the categorical costs for "devices" and "family care," are greater for patients with breast cancer than for patients with other common cancers combined. The significant difference in mean total OOPC remains true even when controlling for age, education, and income.

These findings highlight differences in the financial burden experienced by cancer patients with various tumour types; compared with patients with other common tumour types, breast cancer patients potentially require a different mix of supportive services. Supportive care programs related to financial burden should consider the likelihood and nature of financial burden when counselling breast cancer patients.

First- and Second-Line Therapy for Metastatic Urothelial Carcinoma of the Bladder

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KEY WORDS
Bladder cancer, first-line therapy, second-line therapy, targeted therapy, chemotherapy, metastasis

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Urothelial cancer of the bladder is the 4th most common malignancy in American men and the 9th most common in women. Although most newly diagnosed tumours are still superficial, up to 25% will initially present with muscle invasion, with half of the affected patients having metastatic disease. Conventional chemotherapy regimens in the neoadjuvant setting—and more particularly platinum-based ones—have shown promising results in the management of locally invasive tumours, but very little improvement has been achieved in the outcomes of patients with advanced or metastatic disease. Almost 90% of those patients will eventually succumb to their cancer.

At the present time, data from randomized phase III trials suggest that systemic cisplatin-based combination chemotherapy remains the only current first-line modality to have shown improved survival in patients with advanced disease, with gemcitabine–cisplatin (GC) showing therapeutic non-inferiority and less toxicity than is seen with methotrexate–vinblastine–doxorubicin–cisplatin (MVAC). Similarly, compared with MVAC, high-dose MVAC (HD-MVAC) has shown significantly improved progression-free survival and better toxicity. To date, however, no phase III trials have compared HD-MVAC and GC head to head. However, in patients deemed unfit to receive cisplatin, gemcitabine–carboplatin or gemcitabine–paclitaxel can be considered. Karnofsky performance status score and the presence of liver or bone metastases have been found to be independent predictors of poor outcome in this patient population.

Patients who recur after first-line therapy have a very poor prognosis. Because of a lack of randomized trials showing benefit over supportive care, most evidence comes from small phase II trials of single agents, combinations of agents, and new targeted therapies. As a result, no standard therapy has been established. Notably, a phase III trial of second-line vinflunine (compared with best supportive care) showed a 23% reduction in risk of death without a decrease in health-related quality of life in platinum-pretreated patients. In patients previously treated with a cisplatin-based first-line therapy and considered platinum-sensitive, with more than 6 months elapsed from last treatment to progression, re-challenge with the same cisplatin regimen remains a viable option if no clinical trial is available. Finally, novel targeted therapies are currently being actively investigated and are sorely needed to further improve the delivery and efficacy of chemotherapy in this group of patients.