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Provincial drug disparity a roadblock to cancer research

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For the first time, Canada is unable to participate in a key clinical cancer trial because patients are not getting the best known treatment.

Since most provinces don't fund Avastin, a crucial drug in the fight against colorectal cancer, Canadian patients could not join a trial run by the National Cancer Institute in the United States, which is studying what drug is most effective with chemotherapy — Avastin or Erbitux — or if they work best given together.

If effect, if you don't pay, you can't play.

“Not only are we screwing our patients by not offering them the standard of care, the only way we can make advances is by running these clinical trials,” Ralph Wong, a medical oncologist at St. Boniface General Hospital in Winnipeg. “... It makes us look like a Third World country.”

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At a time when provinces are taking a hard fiscal line, saying they will only fund cancer drugs proven to be cost-effective, they are hindering research that would provide the very answers they are seeking — and casting Canada in the role of scientific freeloader.

Used in the U.S. since 2004, Avastin, the trade name for bevacizumab, offers a median of an additional 4.7 months survival to patients with an incurable form of colorectal cancer. But that payoff isn't worth the price for most provinces. Ontario rejected the drug outright. Saskatchewan won't cover it either, although it allows patients to pay for a course of the drug — about $36,000 — while the public system funds the infusion.

On the other hand, Newfoundland and Labrador does pay for Avastin, and the BC Cancer Agency permits some compassionate access to it. At least one Quebec hospital covers it.

The result of this payment hodgepodge is unequal treatment for Canadian patients — and now the unexpected side effect of impaired cancer research.

Canada can't participate in the clinical trial that would confirm whether Avastin should remain part of the standard of care for metastatic colorectal cancer because it does not uniformly provide that care today. Ralph Meyer, director designate of the National Cancer Institute of Canada's clinical trials group, said he knows of no other case where Canada went through the approval process, as it did with Avastin, only to withdraw.

But he predicted that it may happen again, given that some of the newer, more expensive cancer drugs are not uniformly covered across the country.

“There will be instances like this, where at this point in time, we won't be able to participate,” Dr. Meyer said. “Could it potentially compromise certain types of research in Canada? Yes, it can.”

“We find it very concerning and also very disturbing,” added Dr. Wong. “We're supposed to be a First World country.”

Although not a cure, Avastin is part of a new revolution of cancer drugs that works by preventing the growth of new blood vessels, which helps starve tumours, making it harder for cancers to grow.

Clinical trials have shown that patients getting Avastin along with chemotherapy survived a median of 20.3 months, compared with 15.6 months for those receiving chemotherapy alone. Dr. Wong said some patients have dramatic responses to Avastin, literally rising from their death beds. Those who do not respond to the drug discontinue it.

As it is, colorectal cancer is expected to strike 20,000 Canadians this year and kill 8,500, the Canadian Cancer Society says. Malcolm Moore, chairman of the National Cancer Institute of Canada's gastrointestinal cancer disease site, says scientific evidence shows the standard of care for metastatic colorectal cancer patients is Fluorouracil, which is a chemotherapy drug known as 5FU, oxaliplatin — and Avastin.

“The assumption in clinical trials is that that treatment is available,” Dr. Moore said. “The difficulty we've had with some trials is that these drugs are not all available in Canada.”

Dr. Moore said there is no question Avastin is effective. “The issue is an economic one,” he said.

“These drugs are expensive and the reason these drugs are not readily available in Canada is a cost-effectiveness argument.”

That argument holds more sway in some places than others: Canada's biggest cancer centre, Toronto's Princess Margaret Hospital, cannot provide Avastin because it is not funded by the Ontario government, while Newfoundland's Grand Falls-Windsor Cancer Centre can offer it free of charge because that province covers it.

Avastin, said Dr. Kara Laing, clinical chief of the cancer care program for Eastern Health in Newfoundland and Labrador, “has really brought forth this whole issue of disparity and access and how provinces are dealing with it.”

That disparity has excluded Canada from the new randomized trial, which is being run by a group of American cancer doctors whose work is funded through the National Cancer Institute — unlike other trials that are wholly funded by the drug industry. It is a phase III trial, in which drugs are given to large groups of people — in this case 2,300 colorectal cancer patients — to confirm their effectiveness, compare the treatments and monitor side effects.

Alan Venook, principal investigator of the trial, who is based in San Francisco, said it really comes down to one key question: Does the combination of Erbitux, Avastin and chemotherapy work better than chemotherapy and one of those drugs alone?

Canada will not be part of the answer, and its inability to provide the expected 200 to 230 participants means American researchers will need about six months longer to gather patients; the first set of study results are expected in the spring of 2008.

“I don't mean to weigh into politics, but it is surprising that Canada wouldn't reflect the standard of care,” said Dr. Venook, professor of clinical medicine at the University of California. “My instinct is that Avastin, in particular, may be the biggest impact agent we have and not using it is questionable.”

Dr. Meyer said the National Cancer Institute of Canada was so keen to participate in the trial that it approached the U.S.-based Cancer Therapy Evaluation Program, which funds Dr. Venook's group, to see if it could provide Avastin to patients who would be participating.

Failing there, Derek Jonker, chairman of the colorectal cancer working group for the National Cancer Institute of Canada, tried to get Avastin from Roche Canada. The drug company declined.

“One obvious reason Roche would not support this study is that it is a head-to-head comparison with a drug [Erbitux] not currently standard in this setting,” said Dr. Jonker, a medical oncologist at the Ottawa Hospital Regional Cancer Centre, specializing in gastrointestinal cancer.

“... The U.S. intergroup [Dr. Venook's group], in which Canada is a participant, has a responsibility to ask the questions that the pharmaceutical industry can't or won't ask.”

Such a trial, he said, could only harm Roche's business; he said it was naive to expect any company to support research that could damage their own product — and that, in any case, funding was really the government's job.

But Sabrina Paiva, national manager of product and corporate communications for Roche Canada, said the company's reason for not participating was that it could not sanction a trial in which some patients are not receiving Avastin, the standard of care. One group is getting only Erbitux and chemotherapy.

“That was really our issue with it,” Ms. Paiva said.

Erbitux, however, is a promising drug. While it is not part of the current, standard treatment for metastatic colorectal cancer, it has shown results: This month, Erbitux, which targets a protein called the epidermal growth factor receptor, was found for the first time to extend the lives of colorectal cancer patients; the details will be released early next year at a medical meeting.

Bristol-Myers Squibb Canada decided not to launch Erbitux, which it distributes and licenses, after it failed to agree on a price with the federal Patented Medicine Prices Review Board, which regulates the price of patented medicines to ensure they are not excessive.

The drug has been prescribed in Canada for certain types of colorectal cancer patients for whom other treatments have failed, or to which they have become resistant. But the only way doctors can obtain Erbitux is under Health Canada's special-access program, in which patients with serious or life-threatening conditions can get unlicensed drugs when conventional therapies fail or are unavailable — as long as no licensed alternative is available.

So far, from April 28th, 2004, to Oct. 3, 2006, that program was granted 116 requests for Erbitux, says Health Canada spokesman Alastair Sinclair. Such requests would no doubt increase if the drug proved effective in its head-to-head competition with Avastin.

“Avastin is very effective but it has some downside because it causes bleeding and wound healing problems in a subset of patients,” Dr. Venook said. “It may not make sense to use Avastin if you're contemplating doing a big operation in a patient. It will be very helpful to know if you get a similar bang for your buck from Erbitux.”

What Dr. Venook finds distressing is that provincial governments want to see if the science shows whether they should fund Erbitux or Avastin — yet Canadian patients can't take part in the studies.

“They're saying, ‘You get the data and you come back to us,' but we're not going to participate in the research,” he said.

If it turns out that the best regimen of all is Erbitux and Avastin, mixed with chemotherapy, that would create a new standard of care — one that would cost $12,000 (U.S.) a month in the United States, said Richard Goldberg, chairman of the gastrointestinal cancer committee for the Cancer and Leukemia Group B (CALGB), the group sponsoring the trial. And that could create more problems for health-care systems already struggling with costly, new cancer drugs.

“It becomes a very troubling issue,” Dr. Goldberg said. “If you can't afford the best treatment, then what's the point?”

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