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A VAST INJUSTICE

Investigation into the Ministry of Health and Long-Term Care's decision-making concerning the funding of Avastin for colorectal cancer patients

OMBUDSMAN REPORT • André Marin, Ombudsman Of Ontario • September 2009

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"A Vast Injustice"

André Marin
Ombudsman of Ontario
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Overview

1 In Ontario this year, an estimated 8,100 people will be diagnosed with colorectal cancer, and approximately 3,300 will die as a result of this implacable disease. Historically, the prognosis was dismal for individuals with the metastatic form of this illness. However, the advent of new cancer-fighting drugs has brought hope for those who in the past would have faced a certain and imminent death. While individuals respond differently to chemotherapy regimens, many have been able to extend their lives considerably as a result of these new treatments. But these drugs do not come cheap. Many carry very high price tags, reflective of the considerable investments made by manufacturers in their development. Today, approximately 2.8 million of Ontario's citizens receive $3.8 billion worth of drug benefits from Ontario's Public Drug Programs annually. In the past few years, the province has spent over $53 million funding cancer drugs that are designed to assist colorectal cancer sufferers.

2 The Ministry of Health and Long-Term Care is tasked with the considerable responsibility of deciding where to spend precious health care dollars. Its funding decisions have direct and profound impact on the lives of many Ontarians. In the case of new drugs, the Ministry is charged with considering the clinical evidence and the economic implications of approving public funding. It must weigh the potential costs against the medical benefits, and balance the needs of Ontarians as patients, consumers and taxpayers.

3 In September 2005, Health Canada approved the drug Avastin for marketing and sale in Canada for the initial "first-line" treatment of patients with metastatic colorectal cancer. Avastin works by inhibiting the growth of blood vessels supplying tumours. This may shrink tumours, stop their growth, and generally increase the rate of overall patient survival. At the time Avastin was approved federally, it was noted that clinical studies using the drug in combination with other chemotherapy had shown a statistically significant increase in median overall patient survival of 4.7 months.

4 The cost of Avastin varies depending on patient weight and usually costs $1,500 to $2,000 per treatment. The number of treatments that must be administered depends on individual response. In clinical studies, patients were given Avastin until their disease progressed. Ontario initially rejected the manufacturer's request to have Avastin included as a publicly funded cancer drug under the New Drug Funding

Program. While Ontario oncologists specializing in the treatment of colorectal cancer began calling for Avastin to be used as a matter of standard patient care in December 2005, in January 2006, an advisory committee recommended that the Ministry reject funding of the drug because it was not cost-effective when the increased life expectancy it offered was weighed against its exorbitant price.

5 In 2007 and 2008, new information about further clinical studies using Avastin became available. Patients in these studies experienced median progression-free survival of over 11 months, reinforcing the effectiveness of Avastin in helping to combat the spread of colorectal cancer. By the spring of 2008, Ontario was under increasing pressure to reconsider its position on Avastin. Four provinces were already providing public funding for the drug, and stakeholders were lobbying the Ministry to reverse its decision, including oncologists specializing in colorectal cancer, who continued to support administration of Avastin as a matter of standard clinical practice. In April 2008, Cancer Care Ontario presented recommendations to the Ministry addressed at improving treatment and patient outcomes for patients with metastatic colorectal cancer. One of the key recommendations was that the province fund Avastin.

6 By early May 2008, the Ministry had begun a formal assessment of the costs associated with funding Avastin. Cost-conscious officials had also started to negotiate with the drug's manufacturer in an attempt to gain some price concessions. Discussions proceeded rapidly after that point and by June 4, 2008, a deal had been struck with the manufacturer to provide Avastin at a discount. On July 2, 2008, the Ministry publicly announced that it would fund three new cancer drugs, including Avastin. However, the Ministry failed to publicly emphasize that the funding was limited. Avastin would be provided for 12 treatment cycles (about six months of treatments) with patients having the opportunity to obtain a maximum of four additional treatments (covering another two months) provided they could demonstrate that their condition remained stable.

7 Despite a statutory requirement that decisions to fund drugs be made openly, the Ministry's communications about the funding limit applying to Avastin not only lacked transparency but at times were blatantly misleading. When questioned about the treatment cap, Ministry officials provided a variety of explanations. It was suggested that there was insufficient evidence to support funding beyond the 16th treatment cycle based on patient benefit, and that the restriction was in line with scientific and clinical evidence as well as how Avastin was used in other jurisdictions. But in reality there was no clinical support for cutting off Avastin treatment at the 16th cycle when patients were still responding well to the drug.

Oncologists in Ontario and other jurisdictions continued to recommend the use of Avastin until the patient's disease progressed. In addition, at that time, no other province that was funding Avastin imposed an absolute limit on the number of treatments available. While there was some attempt on the part of Ministry officials to justify the decision based on clinical evidence, it became apparent during our investigation that the restriction of funding to a maximum of 16 cycles was essentially a cost containment measure. The Ministry had compared the expense of providing treatment up to 12, 16 and 23 cycles (until disease progression) and decided that the additional expense necessary to allow for open-ended funding was simply not cost-effective. At 16 cycles, the total incremental annual cost of funding Avastin for Ontarians was estimated at $16.7 million a year, while funding to disease progression was predicted as being in the $25.4-million range, which proved too steep for the Ministry.

8 Unfortunately, the end result of the Ministry's qualified funding of Avastin is that desperate patients who have responded well to the drug are faced with the unconscionable choice of having to either give up the treatment against medical advice once they hit the 16-cycle point or to try to come up with the cash in order to continue. Given the significant costs associated with Avastin treatments, this means that many must forgo the life-sustaining drug. There is even concern among some medical professionals that if Avastin is stopped prematurely before it has reached its maximum benefit, it may result in a negative rebound, actually accelerating the course of the disease.

9 My investigation revealed that patients reaching the public spending limit for Avastin treatments are at the mercy of an arbitrary funding rule, which disregards the individual needs of medical consumers as well as the ethical obligations of their physicians. Oncologists throughout Ontario are being forced to be the government's grim messengers, telling their patients that they can no longer access publicly funded Avastin despite the fact that continued treatment with the drug represents their best chance of continued survival. While the Ministry is satisfied that its decision to cap Avastin funding at 16 cycles balances the needs of the statistical majority of Ontarians afflicted with metastatic colorectal cancer, it ignores the actual experience of real cancer sufferers, who currently face an unjustified obstacle to recommended treatment.

10 As Ombudsman, it is not my role to substitute my own opinions regarding health care priorities for that of the Ministry. But it is squarely within my mandate to consider whether the drug funding decisions that are reached by the Ministry are reasonable, supportable and credible. In the case of Avastin, the Ministry has

created an arbitrary and artificial barrier to patient access to Avastin, which is not supported by medical evidence. While a funding decision may be influenced by economic factors, any limit placed on the duration of funding that impacts patient treatment should reflect sound clinical practice. In the case of Avastin, the funding limit runs directly counter to the accepted standards of medical care. As a result of my investigation, I am of the opinion that the Ministry acted unreasonably and wrongly in limiting public funding of Avastin, and in failing to openly and honestly discuss the basis for this restriction. In addition, I have found that despite the Ministry's focus on fiscal considerations, it has failed to properly monitor the actual costs associated with its funding decision.

11 I have made four recommendations to address my concerns, including that the Ministry should, on an expedited basis, extend patient eligibility for funding for first-line treatment using Avastin beyond the current 16-cycle treatment limit in individual cases until disease progression is evident based on medical assessment, and reimburse those patients who have paid out of their own pockets to continue their life-sustaining treatment with Avastin. I have also recommended that the Ministry ensure that decisions concerning funding of new drugs, including a summary of financial and medical considerations relied on in reaching those decisions, are publicly posted. In addition, I have recommended that the Ministry centrally monitor the number of patients receiving drugs under the New Drug Funding Program, the duration of treatment and the expenses associated with the funding. Finally, I have asked that the Ministry to report back to my Office at quarterly intervals on its progress in implementing my recommendations.

12 In response to my recommendations, the Ministry was not prepared to revisit its position with respect to the 16-cycle cap on Avastin treatments. While it did undertake to work with Cancer Care Ontario on a compassionate review policy for oncology products, in the interim, cancer patients were offered little relief. The Ministry suggested that patients could apply under the current compassionate review policy, which does not generally apply to cancer drugs, to extend Avastin treatments beyond 16 cycles. Unfortunately, given the limitations associated with the application of that policy, it is unclear how it would be of any practical assistance to most colorectal cancer sufferers facing the Avastin treatment cutoff.

13 The Ministry was also unwilling to compensate those who have incurred substantial expense in order to continue their treatment with Avastin beyond the point when public funding is available.

14 The Ministry did commit to posting a detailed rationale concerning its decision to

fund Avastin. In addition, with respect to monitoring of drug expenditures under the New Drug Funding Program, the Ministry noted that it would discuss this with Cancer Care Ontario and that it had requested that Avastin's manufacturer do an analysis. Finally, the Ministry undertook to report back to me on its progress with respect to the initiatives that it was prepared to undertake at six-month intervals.

15 While the Ministry has agreed to take some actions to address concerns I have identified regarding the decision-making around the funding of Avastin for colorectal cancer patient sufferers, it has not committed to taking the effective and immediate steps I believe are necessary to ameliorate the hardships of those faced with the prospect of having to end successful treatment with Avastin because of the Ministry's overriding concern with cost containment.

16 The Ministry is entitled to consider financial expense in deciding whether to fund costly cancer treatments. However, once a decision is made to fund a drug, the duration of public funding should be consistent with the prevailing medical evidence. In the case of Avastin, the funding limit flies in the face of the acceptable standard of oncology practice in this province and beyond. The steps that the Ministry is proposing to take in response to my recommendations do not provide a remedy for those featured in this report, nor is it clear to what extent they will benefit metastatic colorectal cancer sufferers in future. Instead of a workable solution, supported by sound medical practice, the Ministry's retention of the Avastin treatment cap continues to perpetuate a vast injustice.

Investigative process

17 On May 19, 2009, MPP Joyce Savoline contacted my Office on behalf of her constituent, Robert Anderson, a senior suffering from metastatic colorectal cancer. Mr. Anderson's cancer had stopped progressing as a result of a treatment regimen that included Avastin. Unfortunately, Mr. Anderson had just received his 16th and last publicly funded treatment, and found himself in a very difficult situation. Although the treatments with Avastin were helping to prolong his life, and despite the fact that his oncologist urged him to continue with them, he was not in a position to pay out of his own pocket, at a cost of $1,750 per treatment. Mr. Anderson could not understand why the Ministry would limit his access to Avastin when it continued to be effective in holding his cancer in abeyance.

18 After receiving Mr. Anderson's complaint, we conducted preliminary inquiries in an effort to try to discover the rationale behind the Ministry's decision to cap public funding of Avastin. However, the Ministry was unable to provide any concrete scientific or clinical evidence to justify the 16-treatment limit. Accordingly, on June 3, 2009, I notified the Ministry of my intent to pursue an investigation into whether it had reached an informed and reasonable decision in limiting funding of Avastin to 16 treatments regardless of patient response. The investigation was assigned to our Special Ombudsman Response Team (SORT).

19 After the investigation was announced publicly, we received another 31 complaints concerning access to Avastin, 17 from individuals directly affected by the Ministry's treatment cap.

20 Three SORT investigators and two Early Resolution Officers conducted the investigation. We received and reviewed documentation from the Ministry, Cancer Care Ontario and Hoffman La-Roche Limited, the manufacturer of Avastin. SORT also undertook extensive research into how other Canadian jurisdictions deal with the funding of the drug.

21 The investigation team conducted more than 65 interviews, including with Ministry and Cancer Care Ontario officials, stakeholders, officials from other jurisdictions, and 12 Ontario oncologists, including the Head of the Gastrointestinal Disease Site Group at Cancer Care Ontario. The Access Navigator assisting Mr. Anderson in his attempt to find alternative sources of funding and his private insurers were also contacted. The complainant and other individuals affected by the Ministry's decision to limit funding of Avastin were also interviewed in depth. Given the nature of this investigation, many of the witness interviews were conducted over the telephone.

22 In order to ensure accuracy and investigative efficiency, it is SORT's practice to record interviews with witness consent. The recordings are then usually transcribed and form part of the record of the investigation. Most of the interviews in this investigation were recorded and transcribed, and in fact, we encounter few cases when this has ever presented a problem. This investigation proved to be the exception, with senior Ministry and Cancer Care Ontario officials refusing to have their interviews recorded.

23 Generally we received good co-operation from the Ministry throughout the investigation.

A Brief History of Funding for New Cancer Drugs

24 Cancer is an insidious disease that threatens the lives of thousands of Ontarians each year. However, advances in medical pharmacology have resulted in some individuals being given the chance of recovery or at least an opportunity to prolong or improve the quality of their lives. The problem is that many of the new intravenous cancer drugs come with a very high price tag.

25 Historically in Ontario, the availability of chemotherapy drugs for cancer patients depended on whether an individual hospital or dedicated cancer centre could accommodate the therapy through its own operating budget, or whether a patient could satisfy the requirements of the Ontario Health Insurance Plan's out-of-country program and obtain treatment outside of Ontario. This eventually led to an inequality of access to chemotherapy for Ontarians. In the early 1990s, as a result of increasing concern about many aspects of the cancer care system, the Ministry began to engage stakeholders in consultation. A Provincial Cancer Network was established and in April 1994, the Systemic Therapy Working Group recommended that a managed systemic therapy program be established and that all cancer-specific and supportive care drugs be administered and funded through a single agency.[1]

26 In 1997, Cancer Care Ontario was formally launched and funded by the provincial government to conduct programs of research, diagnosis and treatment of cancer, and to act as the Ministry's primary advisor on cancer care in the province. That same year, the Ministry approved the creation of the provincial New Drug Funding Program to ensure that Ontarians would have equal access to intravenous drugs. Under this program, the Ministry was responsible for deciding whether to fund cancer-fighting drugs on the recommendation of Cancer Care Ontario.

27 Between 1997 and 2006, the cost of funding drugs in Ontario rose exponentially, increasing by more than 140%, to the point where the province was spending $3.4 billion annually on its drug benefit program.[2] In April 2006, in an effort to ensure better access to drugs, greater value for taxpayers, promotion of the appropriate use

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[1] Ontario, Ministry of Health, Life to Gain: A Cancer Strategy for Ontario (Toronto: Queen's Printer 1994).
[2] Ontario, Legislative Assembly, *Official Report of Debates (Hansard),* (13 April 2006) at 1350 (Hon. George Smitherman).

of medications, investment in innovative health system research and strengthened transparency and accountability in the public drug system, the government introduced Bill 102, the *Transparent Drug System for Patients Act, 2006*.[3] In commenting on the bill, the then Minister of Health and Long-Term Care remarked:

> This bill is the cornerstone of our government's comprehensive plan to reform Ontario's drug system, to transform it into something more efficient, more transparent and more accountable, to change it into a system that patients can understand and can trust.
>
> The case for change is strong. The sad reality is that our drug system has been failing us. That's strong language, but it's true. Our drug system hasn't been serving patients as well as it should, it hasn't been serving taxpayers, and it hasn't been serving the professionals who work within it each and every day.
>
> Equally troubling, the escalating costs of our drug system are threatening its very sustainability…
>
> Our reforms are destined to give patients better access to drugs, and better access to drugs also means getting better value for taxpayers' money…
>
> Improving patient access also means getting drugs to them faster and more efficiently. We need to make the drug review system more efficient and more transparent. That too is a key part of our plan.[4]

28 By October 1, 2006, amendments to the *Ontario Drug Benefit Act* issued in by the *Transparent Drug System for Patients Act* came into force. Among the amendments was the introduction of the following set of guiding principles for the public drug system:

1. The public drug system aims to meet the needs of Ontarians, as patients, consumers and taxpayers.
2. The public drug system aims to involve consumers and patients in a meaningful way.

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[3] Bill 102, *An Act to amend the Drug Interchangeability and Dispensing Fee Act and the Ontario Drug Benefit Act*, 2d Sess., 38th Leg., Ontario, 2006 (assented to 20 June 2006), S.O. 2006, c. 14.
[4] *Supra* note 2 at 1340.

3. The public drug system aims to operate transparently to the extent possible for all persons with an interest in the system, including, without being limited to, patients, health care practitioners, consumers, manufacturers, wholesalers and pharmacies.
4. The public drug system aims to consistently achieve value-for-money and ensure the best use of resources at every level of the system.
5. Funding decisions for drugs are to be made on the best clinical and economic evidence available, and will be openly communicated in as timely a manner as possible.[5]

29 In order to enhance accountability and transparency, under the amendments, the Minister is now required to publish the details of the drug review process on the Ministry website. An Executive Officer was also established with responsibility for the administration of all of Ontario's public drug programs, and the express authority to negotiate agreements with drug manufacturers concerning drug benefit prices. Currently, the Ontario public drug programs provide benefits to approximately 2.8 million Ontarians each year and account for $3.8 billion in drug benefits spending annually.

30 Under the New Drug Funding Program, the Executive Officer has the authority to make funding decisions with respect to newer intravenous cancer fighting drugs, which are typically administered in hospitals and cancer care facilities. As of May 13, 2009, the Ministry estimated that it had invested $410 million over the last three fiscal years for intravenous cancer drugs under the New Drug Funding Program and that the cost of cancer drugs had increased on average by 35% over the same period.

31 Approval of new intravenous cancer drugs for public drug program funding involves a multi-stage process, which begins at the federal level.

Getting to 'Yes': The Process for New Drug Approval

32 In order for a drug to be marketed and sold in Canada, it must first obtain Health Canada approval. Health Canada evaluates drugs on the basis of safety and

[5] *Ontario Drug Benefit Act*, R.S.O. 1990, c. O.10, s. 0.1.

efficacy. If a drug is approved, Health Canada will issue a Notice of Compliance followed by a Drug Identification Number. The federal review process can take one to two years, depending on the nature of the product.

33 Since March 2007, every province except Quebec requires that cancer drugs be screened by the Joint Oncology Drug Review, an interim cross-jurisdictional review pilot process, based on Ontario's review process for cancer drugs. The Joint Oncology Drug Review makes recommendations relating to funding to the participating jurisdictions. In Ontario, submissions for cancer drug funding coverage are considered by the Committee to Evaluate Drugs, (formerly known as the Drug Quality and Therapeutics Committee), an independent advisory group responsible for reviewing and evaluating clinical evidence, scientific data and cost-effectiveness of drug products and then making recommendations to the Ministry of Health and Long-Term Care.[6]

34 Manufacturers' submissions concerning new cancer drugs are initially reviewed by a subcommittee, which was established in Ontario in early 2005, that is comprised of members of the Committee to Evaluate Drugs, and experts from Cancer Care Ontario. The Subcommittee considers the clinical efficacy and safety, the standard of care, and the cost effectiveness of the drug (i.e. whether it provides good value for money). At present, the Subcommittee advises the Committee to Evaluate Drugs of the results of its evaluation, and the Committee, in turn, makes a recommendation to the Executive Officer regarding funding.

35 As part of its transparency initiative, the Ministry has posted recommendations from the Committee to Evaluate Drugs since July 2007 on the Ministry's website. The Ministry plans to post information in future about the status of submissions as they progress through Ontario's drug review process.

36 Before reviewing the Ministry's decision-making regarding Avastin, it is useful to consider the drug's role with respect to treating metastatic colorectal cancer.

[6] Two patient members were added as full voting members of the Committee to Evaluate Drugs as a result of the amendments brought in by the *Transparent Drug System for Patients Act, 2006*. The Committee has about 16 members. The majority are physicians, two members are pharmacists and at least one is a health economist.

Metastatic Colorectal Cancer and Avastin

37 In Ontario this year, an estimated 8,100 people will be diagnosed with colorectal cancer, and approximately 3,300 will die as a result of the disease. [7] "Colorectal cancer" refers to cancer of the colon (large bowel) and of the rectum. "Metastatic colorectal cancer" is cancer that has spread to other parts of the body, such as the liver and lung. Typically, treatment of metastatic colorectal cancer involves a combination of intravenous infusion chemotherapy. Two standard combination regimens are FOLFIRI (combining folinic acid, fluorouracil and irinotecan) and FOLFOX (combining folinic acid, fluorouracil and oxaliplatin).

38 Avastin is the brand name for bevacizumab, a drug manufactured by F. Hoffmann-La Roche Ltd. (Roche). Avastin is used to treat metastatic colorectal cancer, usually in combination with FOLFOX or FOLFIRI. It works by inhibiting the growth of blood vessels supplying tumours, blocking the supply of oxygen and nutrients tumours need to thrive. Avastin may also cause blood vessels to change in ways that assist chemotherapy in targeting tumours more effectively. In some patients, Avastin may stop tumour growth, shrink tumours, and generally increase the rate of overall patient survival. Avastin is considered to be palliative treatment. It may stave off the progression of the cancer and therefore prolong life, but it is not considered a cure for the disease. In some cases, however, Avastin has been known to shrink tumours to the point where they can be surgically removed. Avastin costs approximately $1,500 to $2,000 per treatment, depending on the dosage, which varies according to a patient's weight. Avastin treatments are generally administered every two weeks. At some point, patients typically become immune to the therapy, the disease progresses and other treatment modalities have to be considered.

39 In September 2005, Health Canada approved Avastin for the "first-line" treatment of patients with metastatic colorectal cancer to be used in combination with fluoropyrimidine-based chemotherapy (both FOLFOX and FOLFIRI are fluoropyrimidine-based therapies). In arriving at its decision, Health Canada noted that in a Phase III, randomized, double-blind, controlled clinical trial, when Avastin was added to a fluoropyrimidine-based chemotherapy regimen it resulted in a

[7] Canadian Cancer Society Steering Committee, *Canadian Cancer Statistics 2009* (Toronto: Canadian Cancer Society, 2009), online: Canadian Cancer Society <http://www.cancer.ca/Ontario/About%20cancer/Cancer%20statistics/Ontario%20cancer%20statistics.aspx?sc_lang=en > (last accessed 14 August 2009).

statistically significant increase in median overall survival of 4.7 months (20.3 months vs. 15.6 months).

40 Roche had some initial discussions with Cancer Care Ontario concerning Avastin in 2004. After it received Health Canada's approval it made a formal funding request for coverage under Ontario's Public Drug Programs.[8]

Initial Review of Avastin

41 On December 12, 2005, Cancer Care Ontario's Gastrointestinal Disease Site Group, composed of approximately 30 oncologists with expertise in the clinical treatment of colorectal cancer, developed guideline recommendations as part of Cancer Care Ontario's Program in Evidence Based Care. One of the treatment recommendations was that Avastin be added together with fluoropyrimidine-based chemotherapy for the first-line treatment of patients with advanced colorectal cancer, and that it be considered for use as a second-line therapy for patients who had not yet received it as part of their initial treatment. They suggested that in both cases Avastin should be administered until progression of the disease and concluded that the role of continuing Avastin after disease progression was unclear due to the absence of evidence. The Disease Site Group's recommendations were based on clinical evidence and did not address considerations of cost-effectiveness.

42 Two days later, the subcommittee composed of Cancer Care Ontario officials and members of the Drug Quality and Therapeutics Committee (now known as the Committee to Evaluate Drugs) discussed Avastin for the first time. After considering Roche's submission and the draft guidelines from the Disease Site Group, the subcommittee recommended that the Ministry reimburse Avastin for first-line metastatic colorectal cancer patients and for second-line treatment of patients who had not received Avastin previously, until progression of the disease.

43 While Ontario pondered the question of whether to fund Avastin, British Columbia took the lead in January 2006, becoming the first Canadian province to publicly fund the drug. British Columbia's funding was not open-ended. Given the difficulty of predicting the costs associated with funding Avastin until disease progression, the British Columbia Cancer Agency decided to compromise, restricting funding to 12 treatment cycles. Officials in that province advised that this "cutoff" was based on evidence suggesting that the most substantial

[8] Review of Avastin predated the implementation of the Joint Oncology Drug Review.

improvements in patient response rates occurred within the first six months of treatment.

44 On January 11, 2006, Ontario's Drug Quality and Therapeutic Committee considered whether to recommend that Ontario fund Avastin. The committee reviewed the clinical trial results, noting that they showed improved median overall survival when Avastin was used in combination with chemotherapy by up to five months in first-line treatment and 1.8 months when used in second-line therapy. However, the committee was concerned about the cost associated with using Avastin, which it estimated to be approximately $30-35,000 per patient per treatment course when combined with FOLFIRI.

45 The committee suggested that the "incremental cost-effectiveness ratio" applying to Avastin – approximately $150,000 per "Quality Adjusted Life Years" gained – exceeded the accepted range.[9] The committee contrasted this with another cancer drug, Herceptin, which it had recommended for funding. In the case of Herceptin, the incremental cost-effectiveness ratio had only been $22,000 to $44,000 per Quality Adjusted Life Years gained.[10] The committee found the potential budget impact of funding Avastin "striking," noting that the manufacturer's conservative estimate was that it would cost $30 million in three years, and that Cancer Care Ontario had estimated the cost as being upwards of $60 million per year. The committee concluded that while there was good clinical evidence to support the use of Avastin, the drug was far from being cost-effective compared to available treatments. The committee unanimously agreed that funding for the drug should not be considered unless the manufacturer could offer it at a more cost-effective price. Although the committee decided that the drug did not represent good value for money in comparison to other drugs, it expressed an interest in the opinions of policy makers and the public as to their willingness to bear these high costs. The committee suggested that with finite resources available for health care spending, the sustainability of drug programs had to be taken into consideration. Ultimately, the committee voted not to recommend Avastin for funding through the New Drug Funding Program, and the Ministry was content to accept this recommendation.

46 Following the Drug Quality and Therapeutic Committee's review, Ministry officials responded to requests for funding of Avastin using a template letter that observed:

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[9] The Quality Adjusted Life Years (QALY) scale is used throughout the world to determine cost-effectiveness. The scale allows evaluators to quantify the benefit of a drug adjusted for the quality of life and compares healthcare benefit for dollars spent.

[10] Herceptin was approved for funding for breast cancer treatment in March 2001.

> The Committee acknowledged the clinical benefits associated with Avastin, however, the cost-effectiveness analysis revealed that Avastin was significantly out of line with that of other effective anti-cancer agents used to treat other types of cancers. The Committee concluded that the drug did not meet the standards of scientific evidence and cost-effectiveness applied to all other drug therapies that are required to support a funding recommendation. The Committee recommended to the Ministry that funding for AVASTIN should not be provided under the CCO's NDFP.
>
> …In an environment where we have limited funds, we have to make careful decisions on our future drug spending – and being careful means relying on strong evidence.

47 Although Ontario had decided early into 2006 that it would not provide public funding for Avastin, other jurisdictions continued to grapple with the issue of whether to fund the drug, at times taking divergent approaches. In July 2006, Newfoundland and Labrador began paying for Avastin as a first-line treatment for metastatic colorectal cancer. A year later, Nova Scotia went in the opposite direction, rejecting Avastin coverage in July 2007. That same month, the newly appointed Executive Officer [11] and the Chief Executive Officer of Cancer Care Ontario engaged in an email discussion concerning Nova Scotia's decision on Avastin. In the context of this exchange, there was some suggestion that Ontario might be prepared to reconsider its stance if the cost implications shifted favorably. The Chief Executive Officer explained to the Executive Officer that he had just met with representatives from Roche and that there had been some discussion around negotiating a reduced price for Avastin. He remarked:

> They needed some clear indication of what it would take to get into the "sweet zone" for funding…. We need to give some clear picture of a number. If they can't meet it, so be it. If they can stretch towards it we are closer to victory for all.

48 Later in July 2007, Ministry and Cancer Care Ontario representatives continued to engage in discussion about the cost of Avastin, while at the same time, recognizing, in the words of one official, "the importance of keeping the discussion on this going and not closing the door too quickly."

[11] The Executive Officer was appointed in October 2006.

49 By October 2007, Quebec became the third province to fund Avastin. An email exchange between Ministry and Cancer Care Ontario officials concerning Quebec's funding announcement referred to the fact that there had been new data relating to Avastin presented at the American Society of Clinical Oncology in 2007. At that time, one Ministry official questioned whether Avastin would be reviewed again based on the new evidence. During our investigation, the Ministry explained that it "was unable to re-evaluate its decision" not to fund Avastin in the fall of 2007, since, although it was aware of the new data concerning Avastin, it had not received a submission from the manufacturer or the Disease Site Group at Cancer Care Ontario containing this evidence. Over the course of the next few months, other jurisdictions were gradually joining the ranks of those funding the drug.

50 In January 2008, Saskatchewan agreed to provide public funding for Avastin. In February 2008, British Columbia revisited its practice, and decided to extend funding for Avastin from 12 to 16 treatment cycles through British Columbia's Compassionate Access Program, and allow oncologists to apply through that Program on a case-by-case basis for extension of Avastin funding beyond 16 treatment cycles. British Columbia health officials explained that they chose "16 cycles" as a general cutoff because the clinical trials had shown that the median number of cycles used by patients having an excellent response was approximately 16. They also advised that the policy shift was influenced by the growing consensus that Avastin had become the standard of care across the United States and Europe, and by the criticism of local oncologists, who expressed concern that the funding cap was out of line with the clinical trials that had treated patients until their disease progressed.

51 In the spring of 2008, the push for public funding of Avastin began to gain further momentum in Ontario.

Getting Into the 'Sweet Zone' – A Second Look at Avastin

52 The Colorectal Cancer Association of Canada issued a press release on April 15, 2008, calling on Ontario to fund Avastin. The association also began encouraging stakeholders to join a "write-in campaign" to lobby for funding of the drug. Cancer Care Ontario minutes from April 2008 record that the Chief Executive Officer had encountered considerable concern about the lack of public funding for the drug during a recent tour of Ontario. That same month, the Ministry requested that Cancer Care Ontario make a submission concerning the treatment of metastatic

colorectal cancer sufferers.

53 In an April 23, 2008 presentation to the Ministry, Cancer Care Ontario officials observed that the current funding for metastatic colorectal cancer had resulted in high costs through the Ontario Health Insurance Plan's out-of-country program and "sub-optimal" treatment. It suggested that expenditures could be reallocated in an evidence-based way to "dramatically improve" patient care and treatment outcomes. Cancer Care Ontario made a number of recommendations. It urged the province to implement KRAS genetic testing to identify patients most likely to benefit from treatment. It also recommended that instead of funding patients through the Ontario Health Insurance Plan's out-of-country program to travel to the United States for treatment with Erbitux, Ontario should fund an alternative therapy in Ontario using the new drug Vectibix. Finally, Cancer Care Ontario encouraged the Ministry to fund Avastin to improve patient outcomes. According to Cancer Care Ontario's estimates the additional yearly cost of funding Avastin, which it projected to be $34 million for 1,151 patients in the first year, $40.9 million for 1,376 patients in the second year and $41.9 million for 1,410 patients in the third year, would be significantly offset by the savings achieved by eliminating out-of-country treatment with Erbitux and implementing KRAS screening.

54 Cancer Care Ontario observed that Ontario was facing increasing pressure to fund Avastin and that there was "strong evidence" that Avastin offered survival advantage in first-line treatment. It also referred to the funding practice in four other provinces, British Columbia, which funded the drug to a maximum of 16 cycles for first-line treatment, and Saskatchewan, Quebec and Newfoundland and Labrador, which funded the drug until disease progression for first- and second-line treatment.

55 By the beginning of May 2008, the Ministry had begun a formal assessment of the costs associated with public funding of Avastin. It retained three consultants to assist it with this undertaking. In a May 5, 2008 email, a medical consultant briefed Ministry officials concerning the results of a number of studies involving Avastin that had been reported after the Ministry's initial review in 2006 of Roche's funding submission. One of the studies conducted in 2007, which had used both FOLFIRI and Avastin, had shown a median progression-free survival rate of 11.1 months after 22-23 treatment cycles. Another study, reported in 2008, had used the same therapeutic combination, and found median progression-free survival of 11.2 months with similar dosages. It was noted that all of the clinical studies were based on treatment until progression of the disease.

56 In response to inquiries regarding the typical number of Avastin treatment cycles used by patients, a Cancer Care Ontario official advised the Ministry that usually 75% of patients receive 12 doses of Avastin, 60% make it to dose 16, and 45-50% to dose 22. Ministry files contain multiple versions of Budget Impact Analysis documents prepared based on different funding scenarios. A number of the later cost projections were based on a manufacturer's price discount that was under review.

57 On May 28, 2008, Ministry documents note that the predicted cost of continuing funding of first-line treatment with FOLFOX and FOLFIRI would be $30.6 million in 2008, $33.8 million in 2009, and $37.8 million in 2010. It was estimated that this cost would increase by $10 million a year, if Avastin was added to these chemotherapy regimes for only 12 treatment cycles, $16.7 million a year, if Avastin was capped at 16 cycles, and $25.4 million per year if Avastin was funded to 22-23 cycles (essentially treatment until progression of the disease.) The same day, Cancer Care Ontario's Gastrointestinal Disease Site Group issued revised Evidence Based Care guidelines, which continued to recommend first-line treatment of metastatic colorectal cancer patients with a combination of Avastin and chemotherapy until disease progression.

58 While the clinical studies conducted using Avastin had not restricted the number of treatment cycles available to participants, and had provided the drug to participants until their disease progressed, Ministry records indicate that early on officials were focused on limiting the number of treatment cycles that would be considered for funding. In the words of one official in a May 30, 2008 email, "our main decision point is whether to fund or not and if so, is it 12 or 16?"

59 Ministry officials explained to us that British Columbia's utilization data had indicated that the average dosage of Avastin used by patients was 10 cycles, and at the time, they reasoned that 16 cycles would be sufficient to meet the needs of the majority of patients in Ontario. However, unlike British Columbia, the Ministry was not interested in creating a compassionate access program to address individual cases in which 16 treatment cycles proved insufficient.

60 In the meantime, conscious of the need to contain costs, the Ministry had entered into negotiations with Roche concerning Avastin and another cancer drug, in an attempt to obtain some financial concessions. Ministry documents indicate that while, at the urging of Cancer Care Ontario, there had been some discussion of funding Avastin for second-line treatment in patients who had never used it before, this was apparently taken "off the table" during discussions with Roche. In

addition, while Cancer Care Ontario officials were calling for funding of Avastin with FOLFOX, the Ministry decided that since the Committee to Evaluate Drugs had not reviewed this combination it would not be considered as a funding option.

61 Negotiations with Roche proceeded quickly. A June 4, 2008 email from the Executive Officer to Cancer Care Ontario signaled that the Ministry was able to arrive at a satisfactory discount for Avastin, and noted that funding would be capped at 12 cycles with the option of receiving 16 "on an exceptional basis." The Executive Officer explained that the cost of the drug would be in the range of $10 million per year for 12 cycles and an additional $5 million for patients receiving up to a limit of 16 cycles. She commented:

> While we are satisfied with the discount, we acknowledge that it still **does not** make AVASTIN cost-effective – and this will be noted in the transparency bulletin once published. HOWEVER, we are funding Avastin within the context of improving treatment for CRC patients, and in consideration of the approximately $25 million that the Ministry is spending sending patients out-of-country for Erbitux. Therefore, we have negotiated the Avastin agreement within the context of a larger package that will be communicated to physicians and eventually the public. [12]

62 On July 2, 2008 the Ministry sent a memorandum to hospitals and cancer centres throughout Ontario announcing that the Ministry had agreed to fund Avastin effective July 2, 2008 for first-line treatment in combination with FOLFIRI. It was noted that Avastin would be available for 12 treatment cycles plus an additional four cycles for patients where an assessment demonstrated either that they were responding to the drug or that their condition had stabilized.

63 The same day, the Ministry issued a press release concerning three new cancer drugs that would be available in Ontario, including Avastin. It noted:

> Ontario is investing $50 million to give cancer patients better treatment options with three new drugs – including Avastin for the treatment of colorectal cancer.

[12] By July 2008, genetic screening for the KRAS gene for patients with colorectal cancer was being carried out in Ontario, assisting in identifying patients most likely to benefit from chemotherapy treatment. By November 17, 2008, Vectibix was added to the list of cancer fighting drugs funded under Ontario's drug programs thereby reducing reliance on and costs associated with out-of-country treatment using Erbitux.

> $30 million over the next three years will fund Avastin, a groundbreaking drug that works by cutting off the blood supply specifically to cancerous tumours rather than affecting all the cells in the body. Clinical trials have shown that Avastin is most effective when used as the initial treatment for advanced colorectal cancer.
>
> The average length of survival for patients who receive Avastin in combination with other chemotherapy treatments is close to 2 years, compared to 15 months for patients who do not receive Avastin as part of their therapy.

64 The press release quoted the Executive Officer of the Ontario Drug Programs as stating:

> Many patients in Ontario will benefit from the availability of Avastin as first-line therapy through our publicly funded drug programs. We continue to be transparent in or decision-making and ensure that all of our decisions have clear, clinical outcomes to support them.[13]

65 Nowhere in the Ministry's press release did it refer to the fact that provincial funding was restricted to 16 treatment cycles. However, the backgrounder accompanying the release indicated that Avastin would only be funded in combination with FOLFIRI and that it would only be available for 12 cycles (treatment for six months) initially, and four additional cycles (treatment for 2 months), if the patient's disease had not worsened. In a document prepared by the Ministry to provide set answers to potential questions from the media, it was noted that the conditions applying to the funding were very similar to those used by the British Columbia Cancer Agency.

66 Despite the new legislative emphasis on transparency, the Ministry did not disclose any details publicly about the reasoning behind restricting funding of Avastin to a 16-cycle maximum. This left many to guess at the rationale behind the decision, particularly in light of the fact that Cancer Care Ontario's Gastrointestinal Disease

[13] Ontario Ministry of Health and Long-Term Care, News Release/Communiqué, "Three New Cancer Drugs Now Available In Ontario: McGuinty Government Investing $50 million To Improve Treatment Options" (2 July 2008), online: Ministry of Health and Long-Term Care <http://www.health.gov.on.ca/en/news/release/2008/jul/nr_20080702.aspx>.

Site Group had been recommending treatment with Avastin up to disease progression since December 2005.

As Transparent as Mud

67 A number of oncologists we interviewed expressed disappointment with the secrecy surrounding the Ministry's decision-making process concerning the funding of Avastin as well as the lack of opportunity for input into the decision. Unlike the earlier review in 2006, the Ministry did not seek the advice of the joint Committee to Evaluate Drugs and Cancer Care Ontario subcommittee. While not knowing the precise reasoning behind the funding restriction, most oncologists divined that it was likely linked to cost containment. They told us that it was "not a medical issue" as much as it was a "money issue," and suggested "the Ministry operates in mysterious ways." Many clinicians also expressed frustration at having to try to explain the cutoff to their patients when they didn't understand the basis for it themselves.

68 Ironically, even some Ministry officials had difficulty explaining to us why the 16-cycle cap was chosen. Around the time of the funding announcement, Ministry officials were quoted in the media as saying "that they found there wasn't enough evidence to support funding it beyond that 16-week cycle in terms of benefit to the patient" and "we made the decision to fund this drug for first-line treatment, based on scientific review of evidence where it's used in other jurisdictions as well as scientific data." However, a number of Ministry officials we interviewed acknowledged that there is actually no clinical support for the "16-cycle" cap and confirmed that the decision to limit funding of Avastin was a purely financial one. Despite this reality, the Ministry has continued to try to justify the funding restriction by suggesting it is supported by medical evidence. For instance, a Ministry template letter prepared to respond to requests for Avastin funding beyond 16 cycles contains the following statements:

> We continue to be transparent in our decision-making and ensure that all of our decisions have clear, clinical outcomes to support them. While funding decisions are often difficult, these decisions are always grounded in clinical evidence.

69 Ministry records reveal that a number of cancer sufferers received a version of this

template letter when they wrote to inquire about extending funding for their treatment. One patient wrote the Ministry on February 22, 2009, explaining that in July 2007, at the age of 39, she had been diagnosed with metastatic colorectal cancer, and had been told she had a median life expectancy of two years. At the time she wrote, she was taking Avastin with no signs of progression and was rapidly approaching the limit of her publicly funded treatments. Her oncologist had advised her that it would be detrimental to her health to stop Avastin, and had even suggested that clinical studies had shown that premature cessation of the treatment might actually have a rebound effect accelerating her disease. She pleaded to be covered by the drug for as long as it continued to work, emphasizing that "I NEED this drug to continue my fight." The Executive Officer sent her a standard template response.

70 Similarly, in a May 29, 2009 email from a Ministry official to a Member of Provincial Parliament responding to an inquiry concerning funding for Avastin, the official explained:

> Last July we started funding AVASTIN to improve treatment options for colon cancer. …. The decision to fund it for 16 cycles was based on clinical evidence. As an aside, this is consistent with funding in other jurisdictions.

71 Not only is the suggestion that the limit was based on clinical evidence misleading, Ontario's practice with respect to funding of Avastin is also significantly different than that applying in other Canadian jurisdictions where the drug is publicly funded. Even British Columbia's program, which a number of Ministry officials suggested was the basis for Ontario's practice, allowed for extension of the number of cycles on compassionate grounds.

72 The Ministry appears to have hit closer to the mark when it responded to our complainant, Robert Anderson. Mr. Anderson wrote an urgent appeal to the Ministry on April 8, 2009, noting that the decision to cut off funding access to Avastin amounted to "a death sentence" for him, as he was unable to fund the drug on his own. The Executive Officer replied on May 22, 2009, noting in part that:

> The ministry is committed to open lines of communication with manufacturers, and if in the future the manufacturer of Avastin provides a submission, supported by new cost-effectiveness evidence, requesting the Ministry to re-evaluate the current reimbursement criteria, the ministry would ask the CED to review this new information.

73 Based on our review of Ministry records, it is readily apparent that cost-effectiveness was the cardinal factor in the Ministry's decision to provide qualified funding approval for Avastin. Yet, the Ministry has repeatedly downplayed the influence of monetary considerations when responding to inquiries about its decision.

74 During our investigation, a number of Ministry officials tried to explain the "16 cycle" limit by referring to the fact that the Ministry has "capped" funding in the case of two other drug therapies. However, this tack was not particularly persuasive. In the case of one drug, Xeloda, which is used to treat stage III colorectal cancer, the drug is used as an adjuvant therapy for six months. However, specialists advised us that Xeloda is quite different than Avastin. It is used following surgical removal to prevent or delay the recurrence of cancer. It is considered curative and, based on clinical studies, it is always given for a limited number of cycles. In the case of another drug, Alimta, which is used for non-small cell lung cancer, it is funded for six cycles as a second-line therapy. According to oncologists we spoke to, clinical studies found four cycles to be the mean number of cycles used by patients, and it is uncommon for patients to require this medication beyond six cycles. While the Committee to Evaluate Drugs initially rejected Alimta for public funding, the Ministry was apparently able to reach a satisfactory negotiated price.

75 What makes the limit on Avastin funding all the more challenging for medical practitioners in this province is that since December 2005, the guidelines published by Cancer Care Ontario's Gastrointestinal Disease Site Group have recommended that Avastin be used in combination with chemotherapy as a first-line treatment for metastatic colorectal cancer up to disease progression. When the Disease Site Group first met on July 11, 2008, to debrief about the Ministry funding decision, it was suggested that clinicians should continue to advocate for funding of Avastin until disease progression, and that they consider referring patient's with unique clinical situations to Roche's Patient Assistance Program as a funding alternative. For those who have private insurance coverage, Roche will pay the balance not covered by the insurer through this Program. Those patients without insurance must undergo a financial means test to determine the maximum amount of financial assistance available through the Program. The Site Group's recommended treatment protocol has remained consistent through revisions of the guidelines in November 2007 and May 2008. It is also in line with the standard of practice in other jurisdictions.

76 Published provincial treatment guidelines in Quebec, British Columbia and the Eastern/Western Canadian Colorectal Cancer Consensus, state that as long as toxicity is not an issue for the patient, treatment with Avastin should be continued until the drug stops working and the cancer progresses. Similarly, in the United States, the National Comprehensive Cancer Network guidelines state that treatment with Avastin should continue as long as the patient does not show evidence of tumour progression.

77 The drug's manufacturer also supports funding the drug to disease progression. It suggested that Avastin should be "funded according to the Health Canada-approved label, the body of supporting clinical evidence and as recommended in treatment guidelines around the world."

78 Currently, there is a clear disconnect between the Ministry's concerns about limiting costs through restricting funding for Avastin to 16 cycles and the medical community's goal of providing patient care based on best practices. The gap has become increasingly problematic as more individuals have come up against the 16-cycle limit.

Getting Past 'No'

79 The Ministry's decision to fund Avastin for up to 16 treatment cycles was a start. However, as the first patients to use Avastin at government expense began to approach their final treatment, clinicians again raised concerns. In a February 12, 2009 email from a member of the Gastrointestinal Disease Site Group to other oncologists, he notes:

> In patients that are responding and tolerating treatment, I feel it is appropriate to continue treatment beyond the 16 cycles. We are encouraging patients with private insurance to transfer funding to their plans, but unfortunately many patients do not have supplemental insurance.

80 Unlike British Columbia where funding requests are considered on compassionate grounds, under the Ministry's current policy, there is no room for consideration of individual response to Avastin beyond 16 cycles. One Cancer Care Ontario official noted when responding to an inquiry from an oncologist about the possibility of

extending treatment that there are "No exceptions. We at CCO recognize the challenge this presents to you, but we have zero flexibility with this drug."

81 During our investigation, specialists informed us that the median duration of treatment in clinical trials using Avastin was approximately 17 cycles; meaning half of the patients in the trial needed less than 17 cycles and half needed more. The trials were all based on treating patients until progression of the disease. Various oncologists we interviewed expressed the view that the 16-cycle limit on public funding of Avastin is both artificial and arbitrary. The Head of Cancer Care Ontario's Gastrointestinal Disease Site Group explained to us that the clinical trials have shown the addition of Avastin has led to improvement in median survival to 20 months, and the newer data suggests an even longer-term improvement. He remarked that typically cancer begins to progress at the point patients are receiving 20-22 cycles, and that in his view the choice of a 16-cycle cap was unsupported. Oncologists uniformly expressed concern about stopping treatment of Avastin without reference to patient response. They suggested that this was unacceptable, detrimental to patient health, and presented an ethical dilemma since there is no medical reason to stop treating patients with Avastin while they continue to respond positively.

82 On May 12, 2009, the Colorectal Cancer Association of Canada wrote to the Ministry calling for changes in the practices around the treatment of colorectal cancer including removing the 16-cycle cap on Avastin.

83 In late June 2009, a group of interested oncologists met with a senior Ministry official to discuss Avastin. However, they did not hold out much hope for change. According to one of the physicians who attended:

> … they didn't give us any decision, they said they were aware of the issues and they're looking into it. But … they did not give us any indication about what they're going to do about it.

84 While the Executive Officer suggested that the Ministry would review Avastin funding further if it received an additional submission from Roche or the Disease Site Group, she was quite emphatic that the Ministry stands by its original decision and that no extensions of Avastin funding beyond 16 treatment cycles would be considered. It was clear in discussions with the Executive Officer that fiscal considerations were at the root of the problem, and she expressed that she often had to make difficult decisions with a finite amount of money.

Standing Out in the Crowd

85 Ontario's dogged adherence to the 16-cycle limit is unique amongst the jurisdictions that fund Avastin. It is the only province of the six that now provide funding for Avastin that restricts the number of publicly funded treatment cycles available to patients.[14]

86 British Columbia began funding the drug in January 2006, and has twice modified its funding practice. As of October 2008, Avastin is funded in that province for up to 24 treatment cycles through British Columbia's Compassionate Access Program. In addition patients can apply for funding past 24 cycles if their condition remains stable. Last year, British Columbia spent $6.3 million to treat 390 patients with Avastin, and an estimated 30% of those individuals received funding beyond 12 cycles. From January 2006 to June 2009, 108 patients had requested funding beyond 16 cycles, and 96 had requested funding beyond 24 cycles. We were advised that funding extension requests are routinely granted. British Columbia has recently published data on patient outcomes in 2006, the year that Avastin was introduced, which show a median increase in overall survival of five months in patients, while public funding was capped at 12 treatment cycles. This analysis applies to the median benefit, rather than individual patient response at the clinical level.

87 Newfoundland and Labrador began funding Avastin in July 2006. While that province's clinical practice guidelines state that Avastin should be used, "until progression up to 12 cycles," officials advised that there is considerable flexibility, and in practice patients may receive funding for treatments beyond 12 cycles.

88 In Québec, Avastin has been funded through individual hospital budgets since October 1, 2007. There is no cap on funding. From October 2007 to March 2008, 823 patients were treated with Avastin in that province at a cost of $8.6 million.

89 Saskatchewan began funding Avastin in January 2008. The duration of publicly funded therapy is dependent on patient response. The province tracks usage statistics every quarter. Its research indicates that from January 2008 to March 2009, it spent $2.643 million on Avastin. The highest number of treatment cycles a patient had received is 23, and the average number of cycles per patient was 8.8.

[14] Manitoba officials also indicated that Avastin is available to patients on a case-by-case basis, but we were unable to obtain further details at the time of writing this report.

90 In August 2008, Nova Scotia reversed its earlier decision and commenced funding of Avastin retroactive to April 2008 for those patients who had paid for the drug from other sources. Patients can continue receiving Avastin as long as they continue to respond to treatments. The projected per annum cost of funding for Avastin is $3.6 million.

91 On April 1, 2009, Alberta became the latest province to introduce public funding for Avastin. There is no restriction on the number of cycles that are funded, however, a limited number of physicians are entitled to prescribe the drug.

92 Clearly, the cost of Avastin weighed against its benefits has been an important consideration for policy makers in deciding whether to fund the treatment publicly. Officials from two provinces that chose not to fund the drug; New Brunswick and Prince Edward Island, confirmed that it was an overriding factor. Similarly, the United Kingdom recently decided not to fund Avastin on the basis that it "would not represent value for money," while Australia began funding Avastin on July 1, 2009 to progression of the disease after initially rejecting funding for reasons of cost-effectiveness.

93 Some private health insurance plans also cover Avastin. A recent analysis of the Roche Patient Assistance Program database for the period July 2006 to August 2008 showed that of 877 patients contacting the program, 647 had private coverage, 310 of these individuals were approved coverage for Avastin and 204 actually received the therapy.

94 While officials in other provinces appear to closely track the costs associated with funding Avastin, we found that despite Ontario's original preoccupation with cost projections and concerns with cost containment, the Ministry has not devoted any particular time or attention to figuring out what it has actually spent on Avastin since July 2008 and whether its predictions regarding usage have been borne out.

Following the Money

95 Ministry officials were unable to confirm how many patients in Ontario had or were currently receiving Avastin. The Ministry relies on Cancer Care Ontario to gather this information, and has not bothered to monitor it centrally. Cancer Care Ontario does issue reports to the Ministry on all New Drug Funding Program drugs,

however, the figures are presented in an aggregate form, and accordingly it is not apparent how much relates to Avastin. The next update was expected in September. A Ministry official suggested that if Roche were interested in presenting information about actual usage and costs, it could always bring this information to the Ministry's attention, although it was acknowledged that Roche would first have to purchase the relevant data from Cancer Care Ontario.

96 During our investigation, Cancer Care Ontario officials advised that 283 patients had started using Avastin in July and August 2008, of these 41 individuals were still using the drug at the 16th treatment mark, most of these patients stopped taking the drug at 12 cycles, and the mean dosage was 9.6 cycles. The data available to date shows that the disease progressed in 84% of the patients before they reached the 16-cycle cap, and only 14% of those taking the drug made it to 16 cycles. This does not take into account those patients who may be accessing the drug on their own beyond the 16 cycles.

97 Cancer Care Ontario also advised that the cost to Ontario of all publicly funded drugs in 2007-2008 was $3.4 billion, and that cancer drugs represented $94 million of this figure. From July 2008 to April 2009, the program had spent $12,804,393 on Avastin. Monthly costs vary from $405,428 in the first month to over $1.6 million in March 2009. Initially, in the first three months, there were 100-155 new patients each month receiving Avastin, this volume decreased over time and by October 2008, approximately 58-86 new patients were receiving Avastin each month.

98 Unfortunately, funding has run out for some colorectal cancer patients already, and others are quickly approaching the cutoff point.

Real Patients Running on Empty

99 While Ministry officials appear to consider funding to 16 cycles a reasonable compromise when compared to the expense of the drug, the Ministry's position leaves many individuals, who would otherwise make it beyond 16 cycles because of their positive response to treatment, without the option of continuing to use Avastin, unless they can obtain an alternate source of funding. While lucky enough to beat the odds and be disease-progression-free after eight months of treatment, these patients have the misfortune of falling outside of the Ministry's spending limit. It is one thing to consider statistical probabilities, and numbers to be charted and factored into a cost benefit analysis. It is another to face a terrified individual

already saddled with the diagnosis of metastatic cancer, and tell them that they can no longer count on the government to fund the treatment that is helping to keep them alive.

100 Robert Anderson is 79 years old. He is a retired, long-time employee of Bombardier, who lives with his wife in a modest bungalow in Burlington, surrounded by pictures of his four children, 11 grandchildren and 10 great-grandchildren. In 2007, Mr. Anderson not only learned that he had colorectal cancer, but that it had spread to other organs and was at the metastatic stage. He was terminally ill. However, in September 2008, he began chemotherapy with Avastin and FOLFIRI, and in his case, the results were impressive. After months of treatment, a CT scan revealed that one of his tumours had disappeared, another was shrinking and the largest one showed no signs of new growth. The results sustained Mr. Anderson and renewed his hope, until he received some shocking news. He was told that, despite the success he had experienced with Avastin, his publicly funded treatments were approaching their 16-cycle end point. On May 19, 2009, he received his last dose of the drug. Mr. Anderson's oncologist urged him to continue the life-prolonging treatment, but with a combined household income of $29,000 a year, there was no practical way that Mr. Anderson could afford to pay for the drug on his own.

101 After waging war against a malignant disease for the better part of two years, Mr. Anderson resolved to fight a different sort of campaign, against another threat – the arbitrary funding limit set by the Ministry. He wrote to the Ministry pleading his case and hoping to persuade officials that his individual circumstances called for compassion. He spoke to the local media and consulted his Member of Provincial Parliament, who eventually lodged a complaint with our Office. The Ministry's response was predictable, he was told that "the maximum of 16 cycles is sufficient to cover the majority of patients" and that Avastin " is not considered cost-effective compared to available treatments." Presumably, Mr. Anderson had to be content with the knowledge that for most people, although not for him, 16 cycles was sufficient, and to take solace in the fact that the price of sustaining his life further was no longer economical. To date, Mr. Anderson's private insurer has denied coverage for Avastin and he has been unable to fund further treatment.

102 Charlene Tye is a 48-year-old resident of Lindhurst. She was diagnosed with colon cancer in December 2007. She learned after surgery that the cancer had spread to her lungs and liver. In September 2008, she began chemotherapy treatment with Avastin. After eight months, her cancer was still stable. However, she received the same disheartening news that Mr. Anderson had, there would be no more treatments

at public expense. Ms. Tye called her MPP and contacted our Office. She has no alternative source of funding and simply cannot afford to pay for treatments on her own. She is left bewildered, not understanding why a treatment that was working, is no longer available to her. Since her 16th treatment in May 2009, Ms. Tye has continued treatment with FOLFIRI but without Avastin which she could not afford. Unfortunately, for Ms. Tye, since stopping treatment with Avastin the news has not been good. A CT scan in early August found two tumours in her liver had begun to grow.

103 We heard from one cancer sufferer who was only able to continue treatment with Avastin as a result of local fundraising. Patricia Eldon Holmes, a 69-year-old retired farmer from Winchester, was devastated when she learned that the treatment that had held off the progression of her cancer, would be cut off in a matter of weeks. Thanks to her community and a fellow cancer survivor, $3,800 was collected towards one more Avastin treatment. But beyond that, Ms. Holmes continues to be at the mercy of a government policy that she cannot understand.

104 Some individuals have obtained financial assistance through private insurers to help defray the costs of Avastin. Jim Ross, 60, of Burlington, was diagnosed with cancer in February 2008. After surgery, he received the news that his cancer had spread. He was successfully treated with Avastin and FOLFIRI until he reached the 16th cycle, when he learned that he was at the limit for government funding. His wife has been his advocate, contacting his MPP and approaching the media. Mr. Ross initially incurred $6,000 in bills for Avastin, however, this expense was eventually covered by a cost-sharing arrangement between his company's insurance plan and the Roche Patient Assistance Program. Regrettably, this arrangement was short-lived. A new company insurance plan no longer covers Avastin, and Mr. Ross has now missed three Avastin treatments as a result.

105 Ann Sabin, 64, ended up paying for two $1,750 treatments out of her own pocket, until (with the help of Roche, who made inquiries on her behalf) she was able to obtain funding for additional Avastin treatments through private insurance. She received 22 cycles of FOLFIRI and Avastin before her oncologist changed her treatment. She feels lucky to have received the six extra treatments. Robert Robinson, 59, is one of the more fortunate ones. His insurance company has agreed to pick up 90% of the costs of his continued treatment with Avastin. Even then, it is difficult for him to raise his share of the money, as he struggles together with his wife to care for their adult autistic daughter. In Brian Mowbray's case, the 60-year-old initially thought he would have to give up treatment with Avastin, although his tumours shrank while on the drug, and he had been doing well. However, he later

enlisted Roche's assistance and now the costs of his further treatment with Avastin will be covered through a cost-sharing arrangement between Roche and his private insurer.

106 Debra McCombs is a 55-year-old resident of Oakville and mother of three, who has lived under the pale of cancer for many years. She was initially diagnosed with cancer in her 40s. After six cancer-free years, she was found to have a new cancerous tumour in December 2006 and further testing showed the cancer had spread. Ms. McCombs initially appeared to respond to treatment, but in August 2008 it was discovered that the cancer had metastasized. In October 2008, she began FOLFIRI and Avastin. Ms. McCombs did well on this regimen and her disease stabilized. But when we interviewed her as the investigation was underway, she was almost at her last publicly funded treatment and was desperately seeking other sources of funding. We recently learned that she has found insurance coverage for an additional 6 cycles, which will hopefully begin after she completes surgery in mid-September.

107 We learned of another cancer sufferer, who, at the age of 26, should have been enjoying her new infant child instead of battling cancer. Instead, she started chemotherapy when her baby turned three months old, and was only able to continue Avastin beyond the 16-cycle cap because of private insurance.

108 And then there are those patients who are currently receiving Avastin, with the cutoff looming in their futures. They try not to give up hope, while living with the knowledge that they too will soon come up against the funding wall.

109 Arlene Douglas, 50, is a mother of two. She has responded extremely well to Avastin treatments – so much so that the tumours have shrunk to the point that surgery is now being considered a viable future option if she continues to react positively. When we spoke to the Douglas family, Ms. Douglas was almost halfway through her government-funded treatments and the family remained optimistic and committed to do whatever it takes to continue her treatment.

110 Susanna Prinzo, 49, began taking FOLFIRI and Avastin in March of this year to combat her metastatic colorectal cancer. So far, results indicate that her tumour is shrinking, but when we last spoke to her she was on her 12th cycle of Avastin, and was terrified that she only had 4 cycles left. She feels that her lifeline is about to be taken away.

111 Many who contacted our Office found it bitterly ironic that the Ministry was so

quick to justify cutting off life-sustaining access to funding for Avastin, while at the same time its intemperate spending in connection with e-Health had been exposed and come under fire.

112 If considerations of cost were removed, based on the current standards of practice, it would be difficult to justify restricting funding for Avastin. The question remains to what extent is it reasonable for the province to continue to rely on considerations of cost to set an artificial end date for the life-sustaining treatment.

Reasonable Limits

113 The decision whether to publicly fund an expensive cancer-fighting drug involves difficult choices, ultimately impacting on the quality and duration of individual lives. Funding decisions cannot be made in a vacuum, but must take into account a variety of sometimes countervailing factors. The costs associated with a new drug must be weighed against its medical benefits. In Ontario, the *Ontario Drug Benefit Act* requires that funding decisions be based on the best clinical and economic evidence. The Act also specifically identifies "value-for-money" as one of the fundamental principles underlying the public drug system. Accordingly, government policy makers have the right to decide that a drug is simply too expensive to fund when compared to its prospective benefits.

114 While the Ministry has considerable discretion in arriving at funding decisions, it is not unrestrained. The basic tenets of good governance must still be observed. For instance, funding decisions, and any restrictions placed on funding, must be well informed and reasonable. From an ethical perspective, once a decision is made to fund a drug, any limit on the duration of funding should be firmly supported by medical evidence. Otherwise, government funding practices may interfere with medical protocols, and the general positive effects of funding a new drug, may be offset in individual cases by an arbitrary cutoff.

115 In the case of funding for Avastin, the Ministry could have chosen to continue to reject public funding based on financial considerations. This is the path some other jurisdictions have chosen to follow. But instead, the Ministry looked for a middle ground. It sought to assist colorectal cancer patients, while at the same time trying to satisfy the need to keep expenses down. Fortunately, the Executive Officer was able to use her statutory authority to mitigate the costs associated with funding Avastin through negotiating a price reduction. Unfortunately, while Ministry

officials thought that they had reached an acceptable balance, they failed to adequately factor in the human element and the moral obligations of the medical community.

116 My investigation has disclosed that there was no compelling medical support for the 16-cycle treatment cutoff. The limit was essentially an artificial cost containment measure, in diametric opposition to the generally accepted standard of patient care in Ontario. The casualties of this fiscal-medical conflict are those patients who experienced better treatment results than the statistical norm. These individuals, who have benefited the most from Avastin, are now being forced to either forfeit potential positive future results or fund further Avastin treatments on their own. In some cases, despite the urging of their medical specialists to continue treatment for the sake of their health, these individuals have no recourse but to give up in premature defeat because of their financial circumstances. Regrettably, this situation verges on cruelty for those already afflicted by this unrelenting illness.

117 There may well be cases when a funding limit might be justified based on an assessment of relevant factors. However, it is apparent that the 16-cycle cap applying to Avastin in Ontario is a factitious barrier unsupported by clinical evidence or medical practice. While a treatment cap may be an expedient way to control costs, it should not exist at the expense of compassion and consideration of individual circumstances. In the case of Avastin, it is impossible to justify the human price exacted by the current administration's inflexible and dispassionate application of the funding limit.

118 The battles waged by cancer sufferers are catastrophic enough without government bureaucrats making their struggles harder through slavery to artificial funding rules. I believe that those cancer patients that are medically assessed as progression-free after 16 treatment cycles with Avastin deserve the opportunity, in accordance with medical advice, to continue with the treatment until they have reached the maximum benefit and their disease progresses. There should be recognition by the Ministry that the duration of funding will inevitably vary depending on individual results, and the Ministry's funding structure should take this into account. In addition, it is only fair that those individuals who remained stable after their last publicly funded treatment with Avastin, and were placed in the unconscionable position of incurring extraordinary expenses in an attempt to sustain their lives by privately paying for further treatments, be reimbursed.

119 The Ministry's reluctance to publicize the reasoning behind the 16-cycle treatment cap is understandable given the paucity of medical evidence to support it. Perhaps

if the Ministry's decision had been built on a stronger foundation, it would have had more confidence in opening its decision up for public view. In the end, the Ministry deliberately failed to disclose the true basis for the limit, and persistently attempted to deflect attention away from the fact that it was essentially cost-based. At times the Ministry went so far as to suggest that the restriction was justified by clinical evidence and in line with the practices of other jurisdictions. The Ministry's obfuscation around Avastin is in sharp contrast to the transparency requirements entrenched by the statutory amendments in 2006, and falls well below any acceptable standard for government communications.

120 Finally, although the Ministry has emphasized the cost considerations underlying its funding decision, it has failed to actively monitor the province's actual funding experience when it comes to Avastin. A surprising fact, given the Ministry's overriding concern for the financial bottom line. The Ministry should be keeping better track of the data, in order to properly evaluate the consequences of its funding decisions, and assist in future assessments and decision-making.

Opinion

121 It is my opinion that the Ministry's decision to limit public funding of Avastin to 16 treatment cycles, and its failure to publicize the rationale for the funding cap and to monitor statistical information relating to Avastin funding, were unreasonable and wrong in accordance with s. 21(1)(b) and (d) of the *Ombudsman Act*.

Recommendations

122 To address the concerns that I have identified in my investigation, I am making the following recommendations:

Recommendation 1

The Ministry of Health and Long-Term Care should extend on an expedited basis patient eligibility for funding for first-line treatment using Avastin beyond the current 16-cycle treatment limit in individual cases, until disease progression is evident based on medical assessment.

Subsection 21(3)(g) *Ombudsman Act*

Recommendation 2

The Ministry of Health and Long-Term Care should reimburse metastatic colorectal cancer patients who continued at their own expense and on medical advice to use Avastin beyond the Ministry's 16-cycle funding cutoff.

Subsection 21(3)(g) *Ombudsman Act*

Recommendation 3

The Ministry of Health and Long-Term Care should ensure that decisions of the Executive Officer concerning funding of new drugs, including a summary of financial and medical considerations relied on in reaching those decisions, are publicly posted.

Subsection 21(3)(g) *Ombudsman Act*

Recommendation 4

The Ministry of Health and Long-Term Care should centrally monitor the number of patients receiving drugs under the New Drug Funding Program, the duration of treatment, and the expenses associated with funding.

Subsection 21(3)(g) *Ombudsman Act*

Recommendation 5

The Ministry of Health and Long-Term Care should report back to my Office at quarterly intervals on its progress towards implementing my recommendations until such time as I am satisfied that adequate steps have been taken to address them.

Subsection 21(3)(g) *Ombudsman Act*

Ministry's Response

123 The Ministry was provided with a copy of my Preliminary Report on August 19, 2009 and provided its comments on August 26, 2009. The response is appended to this report.

124 In response to my first and second recommendations, the Ministry was not willing to reconsider its funding cap on Avastin at this time. However, it did indicate that it will work with Cancer Care Ontario to finalize a compassionate review policy for oncology products. It stated that in the meantime, physicians may submit requests for their patients according to the Ministry's current compassionate review policy (which does not generally apply to products funded under the New Drug Funding Program), and that the Ministry would consider funding "if the patient's clinical circumstances meet the criteria for funding as detailed in the compassionate review policy." Given the nature of the Ministry's existing compassionate review policy and the specific criteria that must be met to qualify for funding under that policy, it was not clear to us how patients requesting continuation of Avastin beyond 16 cycles for the treatment of metastatic colorectal cancer would ever be found eligible. Accordingly, we posed a hypothetical scenario to the Ministry, based on a typical patient profile we had encountered during our investigation, and asked a series of questions.

125 We wanted to know how a patient with metastatic colorectal cancer, who was receiving first-line treatment with FOLFIRI combined with Avastin, would be treated under the policy if they requested extension of public funding for Avastin beyond 16 cycles and could demonstrate that their condition was stable and that there had been no progression of the disease. Under British Columbia's Compassionate Access Program such patients are routinely granted funding for

additional Avastin treatments.

126 The Ministry gave the following answers to our questions:

1. Would the patient be approved for continued treatments under the policy?

Due to the availability of alternate chemotherapy regimens funded by the New Drug Funding Program (NDFP), they would all have to be ruled out as appropriate for the patient to meet the compassionate review policy criteria. It is anticipated that there would be a limited number of circumstances however it is possible that pre-existing conditions would preclude patients from other funded options. As outlined in the Avastin scenario provided, options include:

Alternative first-line treatments for metastatic colorectal cancer:

- *FOLFIRI regimen (NDFP)*
- *FOLFOX regiment (NDFP)*
- *CAPOX regimen (NDFP/ODB Limited Use)*
- *Tomudex (NDFP)*
- *Irinotecan monotherapy (NDFP)*

Alternative second-line treatments for metastatic colorectal cancer:

- *FOLFOX regimen (NDFP)*
- *Tomudex (NDFP)*

For a patient specific example, a patient may not be suitable for treatment with oxaliplatin (due to pre-existing sensory neuropathy, hypersensitivity to the drug or other platinum agents, or pre-existing severe renal impairment), which is a funded treatment option in both the first- and second-line settings.

2. If the patient was over 65 would he be approved under the policy?

From an eligibility perspective, the patient's age is not a factor for the NDFP. NDFP is one of several distinct programs managed by OPDP. The Ontario Drug Benefit (ODB) program is the largest, and is available to Ontarians 65 years of age and over. Although we would be using the criteria under the EAP compassionate review policy, funding for intravenous chemotherapy (i.e., Avastin) would be through the NDFP.

From a clinical perspective, as indicated in the Avastin scenario, the patient's age would have to be considered due to the increased risk of adverse reactions, but age >65 is not a contraindication. The patient's age would also have to be considered as a factor when considering other therapies.

3. Will the decision be made within the two week interval between the 16th and possible 17th treatment?

Provided physicians provide all the necessary information, the ministry [sic] do best effort to review within 10 working days; therefore the physician would need to apply immediately after the 15th cycle. We often receive incomplete requests from physicians and if this is the case and the ministry is required to follow up with the physician, it is possible the approval timeline may exceed 2 weeks. It would be necessary for the requesting physician to provide all the appropriate clinical information and reasons why alternate regimens cannot be considered upfront, with the initial request. Details of contraindications or previous intolerance to other chemotherapy must be provided. For continuation of Avastin, the requesting physician must provide evidence that the patient's disease has not progressed compared to baseline (i.e., prior to initiation of treatment with Avastin) ; no new metastases, no progression of metastatic disease based on chest X-ray or CT scan of thorax for lung lesions and ultrasound or CT scan of abdomen for intraabdominal lesions (as per current NDFP criteria for additional 4 cycles of Avastin). Insufficient information to assess the patient's current clinical status and to rule out other treatment options will delay the review process.

127 Our first impression of the Ministry's response to our questions about the compassionate review policy was that it offered faint hope to those seeking to extend their Avastin treatments past the 16th cycle. The policy as well as the Ministry's response appear to stress that a patient must establish that other treatment alternatives have been tried and failed or are otherwise unsuitable based on clinical evidence before extension of publicly funded treatment with Avastin would be considered. Since Avastin combined with FOLFIRI is the standard treatment recommended by oncologists specializing in colorectal cancer in this province and elsewhere, it is quite common for patients not to have tried other alternatives, let alone ruled out all of them before turning to Avastin. Based on the Ministry's response, it looked like the compassionate review policy would continue to be a dead end for most metastatic colorectal patients attempting to obtain Avastin

beyond the funding cap.

128 Our views were supported by the advice of a prominent gastrointestinal oncologist whom we consulted regarding the implications of the compassionate review policy. He noted that the other treatment alternatives listed by the Ministry are generally only used after treatment with FOLFIRI and Avastin has failed, and it is not sound clinical practice to abandon treatment that is working. He also noted that one of the alternatives suggested by the Ministry, Tomudex, has not even been used as a matter of standard practice for six or seven years.

129 With respect to my third recommendation regarding posting of the Executive Officer's decisions concerning the funding of new drugs, the Ministry reviewed the steps it had taken to communicate with hospitals and clinicians through Cancer Care Ontario. However, it recognized that a detailed rationale for funding Avastin had not been posted, and undertook to remedy this as soon as possible.

130 The Ministry also indicated that with respect to my fourth recommendation, concerning closer monitoring of drug expenditures under the New Drug Funding Program, it does monitor expenses as part of its normal budget forecasting and tracking process and communicates regularly with Cancer Care Ontario to obtain budget information and details on utilization as required. However, it committed to discuss with Cancer Care Ontario its monitoring of drug expenditures under the New Drug Funding Program and noted that it has requested Roche Canada to conduct an analysis.

131 In addition, in response to my fifth recommendation, the Ministry committed to reporting back to my Office on its progress towards implementing my recommendations at six-month intervals over the next two years.

132 In the concluding paragraph of its response, the Ministry suggested that my report contained "statements that mischaracterize information and/or comments provided by ministry staff" and that "some information and/or comments provided by CED members and other experts require additional context in order to be fully understood." The Ministry offered to provide examples of these. Accordingly, we asked the Ministry to provide our Office with this additional information, which was taken into consideration in preparing this final report.

133 In its additional comments, the Ministry took issue with how we had interpreted its conduct relating to its public disclosures concerning Avastin funding. It noted that it had taken steps to provide information to the Disease Site Group at Cancer Care

Ontario, to hospitals and generally through its backgrounder and New Drug Funding Program forms. While this information would have come to the attention of particular groups, primarily of health professionals, my concern rested with the lack of transparency with respect to the information provided to the general public concerning the funding of Avastin as well as the Ministry's failure to accurately and effectively explain the rationale for the funding cap.

134 The Ministry also suggested that patients in Ontario were not faced with an unconscionable choice of having to give up treatment against medical advice when they reached the funding cap or to fund treatment out of their own pockets. It emphasized that there were a host of alternative first- and second-line treatments available. However, as noted throughout this report, Avastin with FOLFIRI is a standard recommended treatment for those with metastatic colorectal cancer. The alternatives that the Ministry lists are generally used only if this treatment fails or is otherwise contraindicated. The standard of clinical practice continues to be treatment with Avastin in conjunction with chemotherapy until disease progression.

135 In addition, the Ministry stated that during its extensive consultations – which included staff oncologists at Cancer Care Ontario, at least one member of the Disease Site Group of practicing gastrointestinal oncologists, and more than 20 Committee to Evaluate Drugs and Cancer Care Ontario joint committee members – no one ever raised a concern about the funding cap, or characterized the decision as "unacceptable, detrimental to patient health" or suggested that it "presented an ethical dilemma." It advised:

> To the contrary, we were uniformly told by oncologists that this would be a step forward to improving patient health, recognizing the lack of cost-effectiveness of the treatment. We were assured at that time by the DSG Head that they would be fine with communicating the criteria to oncologists and that they could work with the recommendation for funding.

136 Since December 2005, Ontario's gastrointestinal oncologists have continued to call for use of Avastin until disease progression, in accordance with the established treatment guidelines. While they may have viewed funding for 16 cycles of Avastin as a start, as early as July 11, 2008, those who attended a technical debriefing at Cancer Care Ontario were suggesting that oncologists continue their advocacy for funding of Avastin until disease progression. The specialists we spoke to during this investigation, who are leaders in their field, were consistent in their criticism of the artificial funding cap.

137 While the Ministry is prepared to take some steps to address my concerns regarding the funding for Avastin, it has not responded to my critical finding that its use of financial considerations to limit the duration of funding without medical support is fallacious. It is possible that the development of a new compassionate review policy specifically addressing oncology products might provide some relief at some as of yet undetermined point in the future. However, in the interim, it does not appear that there is any realistic prospect of assistance for most patients who have come up against the Avastin funding cutoff. If the Ministry is not prepared to remove the cap entirely, individuals who are currently reaching the 16-cycle cap should at least have quick and ready access to a meaningful compassionate review process with a real likelihood that they may obtain extended funding. I will be closely monitoring the Ministry's application of its compassionate review policy to requests for continuation of Avastin beyond 16 cycles, but presently, I am not satisfied that the measures that the Ministry has agreed to introduce are an adequate response to the concerns I have identified. I do not believe that Ontarians, for the sake of cost containment, should be left to pay for treatment with Avastin out of their own pockets or abandon a treatment that is working and that specialists consistently agree should be continued until disease progression. This is a matter of urgency for metastatic colorectal cancer sufferers. What the Ministry is proposing does not provide a concrete or immediate solution. It does not provide a remedy for those featured in this report nor is it clear to what extent it will benefit metastatic colorectal cancer sufferers in future. Instead of a workable solution, supported by sound medical practice, the Ministry's retention of the Avastin treatment cap continues to perpetuate a vast injustice.

André Marin
Ombudsman of Ontario

Appendix

Response Letter from
Ministry of Health and Long-Term Care

Ministry of Health and Long-Term Care

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Ontario

August 26, 2009

Mr. André Marin
Ombudsman of Ontario
Ombudsman Ontario
483 Bay Street
10th Floor South Tower
Toronto ON M5G 2C9

Dear Mr. Marin:

Thank you for the opportunity to respond to your review of the funding of Avastin (bevacizumab) as outlined in the preliminary report "Investigation into the Ministry of Health and Long-Term Care's decision-making around the funding of Avastin for colorectal cancer patients", dated August 2009.

We respectfully submit that one of the Government's key principles as outlined in the *Transparent Drug System for Patients Act* (TDSPA), 2006 which amended the *Ontario Drug Benefit Act* (ODBA) was to enshrine in legislation that drug funding decisions are based in evidence. The Government, through the Transparent Drug System for Patients Act, devolved the authority to make funding decisions under the Ontario Public Drug Programs (OPDP) to the newly created Executive Officer role. The Executive Officer has the mandate to make decisions based on evidence, cost-effectiveness and overall budget impact.

The ministry's Committee to Evaluate Drugs has an important role in this process. As background, the Committee to Evaluate Drugs (CED), formerly the Drug Quality and Therapeutics Committee, was established in 1968 to provide independent, specialized advice to the Ministry of Health and Long-Term Care on drug-related matters. The Committee provides essential advice to the Executive Officer and the Minister of Health and Long-Term Care through its rigorous, evidence-based review of drug products, and subsequent recommendations concerning which drug products to fund. The Committee's role is focused on reviewing clinical and cost-effectiveness evidence, and not on the pricing and listing negotiations with pharmaceutical companies. It is the express role of the Executive Officer and her staff to determine the need for and engage in negotiations with pharmaceutical companies with respect to pricing and listing agreements. This approach is routinely implemented by OPDP.

For oncology products, the Executive Officer relies on the advice of up to 20 individual clinical experts, from the Committee to Evaluate Drugs (CED) and its joint CED/Cancer Care Ontario (CCO) subcommittee. The Executive Officer also considers the advice of external clinical experts and highly qualified staff within the Ontario Public Drug Programs Division and Cancer Care Ontario to interpret evidence on the clinical benefit and cost-effectiveness of each drug submitted for funding.

The funding decision for Avastin considered the clinical evidence, cost-effectiveness evidence, the Program in Evidence Based Care disease site guidelines, clinical opinions from the CED, CED-CCO, and medical experts, as well as the overall budget impact. The ministry also considered the manufacturer's own submissions, as well as the status of funding and rationale for funding in other provinces.

The CED recommended not to fund Avastin for the treatment of colorectal cancer. The main concern was that Avastin was not cost-effective in combination with an irinotecan-based chemotherapy regimen; in addition, the Committee was concerned about the lack of cost-effectiveness data with respect to Avastin in combination with oxaliplatin. Clinical and cost-effectiveness advice was provided by committee members, members of the oncology Disease Site Group (DSG), and CCO. The clinical experts engaged in these discussions were

individuals who have extensive experience in treating colorectal cancer and are well informed of the evidence regarding the use of Avastin.

There were four key randomized controlled studies that were used to support the evidence based guidelines published by the Disease Site Group. These guidelines form the base of evidence that was discussed at the CED/CCO Subcommittee and the CED. Recognizing that the studies used various doses of Avastin and compared it to various chemotherapy regimens in different groups of patients, the CED relied on the advice of oncology experts to explain how the product would be used in clinical practice, particularly since the standard of care (FOLFIRI – combination chemotherapy containing infusional 5-fluorouracil, folinic acid and irinotecan) was not a direct comparator within any of the studies. This is particularly concerning to the CED since it is difficult to extrapolate the results of the studies to patients in Ontario since the treatment regimens are different. Each study reviewed by the Committees had differing lengths of times to progression free survival and outcome status for patients.

The pharmacoeconomic analysis indicated that the incremental cost-effectiveness ratio for Avastin was $151,000 per quality-adjusted life year (QALY) when compared to the standard of care containing irinotecan based combination chemotherapy. QALY calculations are used to compare increase in cost with increased health benefit (in same natural units, e.g., years of survival). QALY is a standard indicator used globally when assessing the funding of drug therapy. The Committee typically considers a range of $40 - $60,000 QALY as an acceptable range. The concept of QALY has been written about extensively and this range is consistent with many other jurisdictions. Therefore, Avastin was 3 times the traditionally acceptable cost-effectiveness range. Based on discussions with CCO, clinicians and pharmacoeconomic experts, it was estimated that the incremental expenditures for Avastin would be in the range of $45 to $50 million annually.

Recommendations 1 and 2

The final funding decision took into consideration clinical, cost-effective and budget impact information noted above, as well as experience from British Columbia which was funding the product at that time. As noted in your report British Columbia funded Avastin based on a cap of 16 cycles and it is our understanding that at that time the majority of patients receiving Avastin were under the cap. Therefore, due to the high cost of this product and poor cost-effectiveness, the Ministry decided to set a cap for funding at 16 weeks.

Recognizing that clinical and cost-effectiveness evidence changes over time and that funding decisions are based on the best available clinical and cost-effectiveness evidence at the point of that decision, manufacturers and representatives of the DSG are aware that new information can be submitted to the ministry for review by the CED and its subcommittee. The ministry has always been and will continue to be willing to review new evidence. In our ongoing discussions with Roche Canada, we have requested that they submit any new evidence related to the criteria for funding Avastin in first-line therapy. There is reference in the preliminary report that the Head of the DSG refers to availability of newer outcome data. Neither the manufacturer nor the DSG has submitted new information for consideration by the ministry.

On May 21st, 2009, the ministry met with Roche Canada to discuss, among other things, the funding of Avastin. The ministry followed up with a subsequent meeting on June 15, 2009 to discuss the Avastin cycle cap issue. The spirit of the ministry's willingness to review the funding of Avastin is characterized in the first paragraph of the letter from Roche Canada, "It is encouraging to see the Ministry's willingness to look at how this issue might be resolved so that patients can receive appropriate care for their metastatic colorectal cancer."

As follow-up to both the May 21st, 2009 and June 15th, 2009 meetings, the ministry requested additional data from Roche Canada. More specifically, Roche provided statistics with respect to duration of treatment of Avastin in B.C., Quebec, and Ontario. The average duration of treatment in Ontario was 9.1 cycles, and the median duration of treatment was 8 cycles.

Until such time as we receive and review any new evidence, the ministry intends to continue funding to a cap of 16 cycles – this is based on cost-effectiveness and overall affordability within a limited drug budget. Avastin's cost-effectiveness ratio of $151,000 –almost triple the 'acceptable' range – is simply not cost-effective. As you will appreciate, the cap on funding allows more people to receive Avastin: admittedly this is a difficult decision to make but we think it is better that more people have some access to this expensive drug than for none to have access at all.

We have developed a compassionate review policy that is posted on the ministry's website for products funded under the Ontario Public Drug Programs. The ministry will work with CCO to finalize a similar policy that has been under development for oncology products. In the meantime, and until the policy has been finalized, physicians may submit requests for their patients according to the compassionate review policy; the ministry will consider funding if the patient's clinical circumstances meet the criteria for funding as detailed in the compassionate review policy.

Recommendation 3

While the ministry has publicly communicated the funding criteria for Avastin and communicated the rationale for same to the oncologist community through Cancer Care Ontario, we recognize that the detailed rationale for funding Avastin has not been posted. We commit to posting this as soon as possible.

The ministry communicated to hospitals and clinicians through CCO that funding was available and that communication included information on the criteria and conditions for funding. Consistent with the CCO mandate, staff from CCO also met with the Disease Site Group (DSG) to explain the criteria for funding. The communications from the ministry and CCO were proactive to explain the decision. It our understanding that there were no objections to this approach at that time. For the reasons described above, the ministry did not disclose the full details of the agreement with the clinicians due to confidentiality restrictions within the agreement but the details on the clinical criteria for funding and 16 cycles limit were fully disclosed.

The ministry does monitor expenditures under the New Drug Funding Program as part of its normal budget forecasting and tracking process. Furthermore, we communicate regularly with CCO to obtain budget information and details on utilization as required. As an operational service agency of Government, it is part of CCO's mandate to monitor and manage the expenditures under the Program, including expenditures of Avastin. We will discuss with CCO their monitoring of drug expenditures under the New Drug Funding Program. Additionally, the ministry requested Roche Canada to do an analysis.

Recommendation 4

As for the suggestion to report quarterly, the ministry is prepared to report back to the Ombudsman on a biannual basis over a two-year period regarding our progress.

In closing, we believe that the report contains statements that mischaracterize information and/or comments provided by ministry staff to Ombudsman staff; we also believe that some information and/or comments provided by CED members and other experts require additional context in order to be fully understood. We would be pleased to identify specific instances should that be helpful in your investigation.

Sincerely,

Original signed by John McKinley, A/Deputy Minister

Ron Sapsford
Deputy Minister

Ombudsman
ONTARIO

ONTARIO'S WATCHDOG

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