A clinical consensus guideline on nursing and patient management for metastatic colorectal cancer patients receiving bevacizumab with systemic therapy

REPORT FROM AN ADVISORY BOARD MEETING OF GASTROINTESTINAL ONCOLOGY NURSES HELD IN DECEMBER 2010

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ABSTRACT
Bevacizumab was approved for use in patients with metastatic colorectal cancer (mCRC) in Canada in 2005. Public reimbursement in each province was granted at different times between 2005 and 2009. As a result, nurses offer a wide range of clinical experience in the management of patients on bevacizumab. The need to share best practices among nurses from across the country and to create consistent evidence-based approaches was identified. A practical guidelines discussion regarding infusion reaction, infusion time, proteinuria, hypertension and wound healing was conducted among gastrointestinal (GI) oncology nurses, based on their clinical experience in mCRC and as informed by the salient research. This meeting was held in December 2010 as part of an advisory board that included management discussions about patients receiving bevacizumab.

KEY WORDS
Bevacizumab, colorectal cancer, consensus, guideline, hypertension, infusion, management, nursing, oncology, proteinuria, wound-healing

TERMS OF REFERENCE
Purpose
The purpose of the meeting reported here was to create a consistent nursing approach, by way of a clinical consensus guideline, to define best nursing management practices for patients with metastatic colorectal cancer (mCRC) who receive bevacizumab with their palliative chemotherapy.

Participants
Participants included oncology nurses from academic, community and tertiary centres in Nova Scotia, Québec, Ontario, Alberta and British Columbia, as well as a medical oncologist from Alberta.

Target Audience
• The primary target audience of this report is the nursing health professionals involved in the care of patients with mCRC.
• While not specifically targeted to patients and their families, this report may provide information that these individuals may find useful.

Basis of Recommendation
All of the recommendations presented are based on the available evidence and discussions of that evidence, along with a review of the individual provinces’...
bevacizumab clinical guidelines and the bevacizumab product monograph in mCRC. Each statement comes with a statement of the level of evidence available for the recommendation.\textsuperscript{1} Where applicable, these references are cited. Overall, the nurses supported the full adoption of the Alberta guideline for all aspects of bevacizumab management; in this consensus, two areas (hypertension and proteinuria) have been highlighted. For the full Alberta guideline, the link is provided in the references.\textsuperscript{2}

## OPENING STATEMENTS

### APPLICATION OF RECOMMENDATIONS
- Consensus statements apply to a broad group of patients with mCRC and may not apply to the unique circumstances of each patient. These statements represent the minimum recommendations for nursing practice. Individual decisions for care should always be made within an oncology team-patient relationship.
- These consensus statements focused on four main areas of inconsistent bevacizumab management. A full understanding of all bevacizumab and chemotherapy-related side effects should be available, and nursing management should not be limited to the areas of focus in this report.

## CONSENSUS STATEMENTS

### DRUG INFUSION

**What is the optimal infusion time for both initial and subsequent doses of bevacizumab for patients with metastatic colorectal cancer?**

Initial and all subsequent infusions can be administered at 0.5 mg/kg/minute (10 minutes for a dose of 5 mg/kg or 15 minutes for 7.5 mg/kg).\textsuperscript{2,4} If a patient has an infusion reaction, a physician should be consulted and, as a general guideline, the infusion should be stopped and diphenhydramine with or without corticosteroid administered to treat acute symptoms. Subsequent infusions should be administered at half the rate at which the reaction occurred, unless otherwise specified by the treating physician or institution guidelines. (Level B)

**What is the optimal infusion time for both initial and subsequent doses of bevacizumab for patients with metastatic colorectal cancer?**

**What are the key patient teaching points pertaining to bevacizumab-related infusion reactions?**

1. Educate patients that all drugs have side effects. People can be sensitive to ANY type of medication (e.g. chemotherapy, biologics, antiemetics, steroids).
2. Explain that although both chemotherapy and biologic therapy are meant to treat the cancer cells in the body, there is a difference between the actions of bevacizumab (a biologic agent) and the actions of chemotherapy. Both issues should be emphasized in patient teaching.
3. Explain that bevacizumab is a humanized antibody and, therefore, the incidence of infusion reactions is very low.
4. Describe symptoms that constitute a hypersensitivity reaction. (Level C)

**During ongoing assessment of chemotherapy infusion, what signs and symptoms should alert a nurse to consider an infusion reaction?**

The recommended assessment parameters for infusion reaction list\textsuperscript{8} include “anything different from when they came in,” pruritus/itching, urticaria (hives, welts, wheals), rash/desquamation, angioedema, bronchospasm, dyspnea, cough, hypotension, back pain, fatigue (asthenia, lethargy, malaise), arthralgia, myalgia, rigor/chills, dizziness, sweating, nausea/emesis, tachycardia, drug fever. (Level B)

**Should premedications be routinely used to prevent infusion reactions prior to bevacizumab administration?**

There is no evidence to suggest that premedications should be routinely administered specifically for bevacizumab.\textsuperscript{2,6} Patients may already receive premedications for the chemotherapy component of their treatment. In the rare case that an infusion reaction occurs and is deemed to be related to bevacizumab, premedications may be warranted for all future infusions. (Level B)

### HYPERTENSION

**How frequently should blood pressure be monitored on a cycle-by-cycle basis?**

A patient receiving bevacizumab should have blood pressure monitored every cycle.\textsuperscript{7} Communication among healthcare practitioners is vital, especially with regards to discrepant blood pressure readings (e.g. medical daycare and outpatient clinic). (Level A)

**Should blood pressure be monitored throughout the infusion?**

Blood pressure should be established at baseline and monitored once prior to the administration of each dose of bevacizumab.\textsuperscript{2}

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Monitoring during and after the infusion is not required as bevacizumab-related hypertension is thought to result from the decreased production of nitric oxide (a vasodilator) and reduced excretion of sodium by the kidneys, and not a result of the drug infusion. Review of the blood pressure trend should be a consistent component of each bevacizumab administration. (Level A)

At what blood pressure grade should nursing alert the medical team for intervention?
Upon group discussion of available provincial clinical guidelines, the group consensus was to adopt the recommendations outlined in the Alberta Health Services Bevacizumab (Avastin®) Administration Guidelines (Table 1). (Level B)

What are the key patient teaching points regarding bevacizumab-related hypertension?
1. Educate patients that high blood pressure is a potential adverse effect of bevacizumab and that intervention may be necessary (e.g., antihypertensive drugs).
2. Educate patients that hypertension may be asymptomatic and, therefore, blood pressure should be monitored throughout the course of treatment with bevacizumab.
3. Explain that, if initiated, blood pressure management may need to persist for a period of time even after bevacizumab therapy has been discontinued. (Level A)

What is the preferred testing method for proteinuria (dipstick vs urinalysis)?
Ideally, urinalysis should be completed by the laboratory prior to the administration of bevacizumab (along with the rest of the relevant bloodwork). A 24-hour urine collection for protein should be requested if the urinalysis reveals 2+ or 3+ protein. A urinalysis performed in the laboratory exploits the established quality assurance programs for accurate testing. Therefore, optimal monitoring for proteinuria is achieved when the urine is tested by laboratory services (urinalysis) rather than by nursing (dipstick). (Level C)

What is the optimal testing frequency for proteinuria?
This is best managed as per individual institution’s protocol. (Level C)

### TABLE 1. Reproduced Alberta Health Services guideline for bevacizumab-related hypertension

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3 (occurs in 15%)</th>
<th>Grade 4 (occurs in 1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Describes an asymptomatic or transient (&lt;24h) rise in the diastolic blood pressure by &gt;20 mm Hg or in the blood pressure to over 150/100 if previously within normal limits.</td>
<td>Describes a persistent (≥24h) or symptomatic rise in the diastolic blood pressure by &gt;20 mm Hg or in the blood pressure to over 150/100 if previously within normal limits.</td>
<td>Describes the need to introduce more intensive therapy (e.g.: addition of another antihypertensive agent).</td>
<td>Describes a rise in the blood pressure with life-threatening consequences (“hypertensive crisis”). This is characterized by end-organ toxicity (e.g.: angina, headaches, reduced level of consciousness, etc.).</td>
</tr>
<tr>
<td>Action</td>
<td>Action</td>
<td>Action</td>
<td>Action</td>
</tr>
<tr>
<td>Continue with the bevacizumab infusion.</td>
<td>Initiate an antihypertensive medication and resume the bevacizumab only if the blood pressure remains controlled under 160/100.</td>
<td>Add another antihypertensive agent and withhold the bevacizumab until adequate control of the blood pressure is achieved.</td>
<td>Obtain urgent intervention (e.g.: ICU/CCU for labetalol, hydralazine, nitroprusside, cardiac monitoring, etc.). Permanently discontinue the bevacizumab.</td>
</tr>
</tbody>
</table>

### TABLE 2. Reproduced Alberta Health Services guideline for bevacizumab-related proteinuria

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1+ protein on urinalysis (or 0.15 to 1.0 g of protein in a 24-hour urine collection)</td>
<td>2+/3+ protein on urinalysis (or 1.0 to 3.5 g of protein in a 24-hour urine collection)</td>
<td>4+ protein on urinalysis (or over 3.5 g of protein in a 24-hour urine collection)</td>
<td>Nephrotic syndrome (over 3.5 g of protein in a 24-hour urine collection plus edema and hypertension).</td>
</tr>
<tr>
<td>Action</td>
<td>Action</td>
<td>Action</td>
<td>Action</td>
</tr>
<tr>
<td>Continue with bevacizumab but obtain a 24-hour urine collection for protein before the patient’s next treatment.</td>
<td>Continue with bevacizumab and monitor the urine protein levels by urinalysis.</td>
<td>Withhold bevacizumab and obtain a 24-hour urine collection for protein before the patient’s next treatment.</td>
<td>Permanently discontinue the bevacizumab.</td>
</tr>
</tbody>
</table>

GR 2/3: If the 24-hour urine collection for protein retrieves <1 g, proceed with bevacizumab and resume monitoring with urinalysis. If the 24-hour urine collection for protein retrieves ≥2 g, monitor with 24-hour collection and resume bevacizumab only if <2 g.
At what proteinuria grade should nursing staff alert the medical team for intervention?
Upon group discussion of available provincial clinical guidelines, the group consensus was to adopt the recommendations outlined in the Alberta Health Services Bevacizumab (Avastin®) Administration Guidelines (Table 2). (Level B)

**What are the key patient teaching points for bevacizumab-related proteinuria?**
1. Patients should be aware that proteinuria can occur and can only be identified through urine tests.
2. Educate patients that, like hypertension, proteinuria does not typically cause symptoms.
3. Educate patients that if 2+ or 3+ protein is found on urinalysis, they will need to complete a 24-hour urine collection and bevacizumab may need to be held or discontinued; chemotherapy may still be continued.
4. Patients should be aware that if the 24-hour urine collection shows <1.0 g, then it is appropriate to revert back to urinalysis monitoring. (Level B)

These consensus statements for hypertension and proteinuria take into account Alberta, British Columbia, Nova Scotia and Ontario bevacizumab clinical guidelines; and Wu et al 2010.9

**References**

**Additional references**

**WOUND HEALING**

**Before a planned surgery, when should preoperative bevacizumab therapy be stopped?**
Bevacizumab therapy should be held for 4 to 6 weeks prior to a planned major surgery. Collaboration between nurses, medical oncologists and surgeons is essential to optimal patient care. (Level B)

**For minor surgical procedures (e.g. central venous access device [CVAD] insertion/ removal), what is the optimal bevacizumab management?**
Peripheral intravenous central catheter (PICC)/Port-A-Cath®/Central Venous Device: Bevacizumab can be initiated immediately.

  For dental procedures: It is recommended that planned invasive procedures be completed prior to the initiation of chemotherapy/bevacizumab, if possible. If emergency dental work is required, the patient should notify their dental health care provider that they are receiving bevacizumab, and their cancer centre that they will undergo a dental surgical procedure. (Level B)

**What parameters should be included in a nursing assessment of surgical wound healing prior to initiation of bevacizumab?**
For large invasive postoperative wounds, routine nursing wound assessment is necessary.

**What are the key patient teaching points for bevacizumab-related wound healing issues and surgical considerations?**
1. Advise patients that wound healing may be impaired due to bevacizumab.
2. Educate patients on what they can expect for the normal wound healing process and timelines, what to self-assess for their wound healing while at home, and when to contact their medical team for assessment and intervention.
3. Inform patients that surgical procedures may be delayed if they receive bevacizumab.
4. Advise patients that the initiation of bevacizumab may be delayed due to wound healing issues.
5. Alert patients to the importance of informing ALL healthcare professionals of bevacizumab use in case of emergency surgical intervention (wallet cards may be a useful tool). (Level C)

These consensus statements for wound healing have taken account of Alberta, British Columbia, Nova Scotia and Ontario bevacizumab clinical guidelines, and the Bevacizumab (Avastin®) Product Monograph.7

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