# BC Cancer Protocol Summary for Palliative Therapy for Metastatic Triple Negative Breast Cancer using Sacituzumab Govitecan

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| ***Protocol Code:*** | *BRAVSG* |
| ***Tumour Group:*** | *Breast* |
| ***Contact Physician:*** | *Dr. Nathalie LeVasseur* |

**ELIGIBILITY:**
Patients must have:
- Locally advanced unresectable or metastatic breast cancer,
- Triple negative (ER, PR and HER2 negative),
- Previously received two or more lines of therapy for breast cancer, with at least one of them in the metastatic setting, and
- Asymptomatic/stable brain metastases (if applicable).

Patients should have:
- Good performance status, and
- Adequate hematological, renal and hepatic function

**CAUTIONS:**
- Patients with Gilbert's syndrome or who are homozygous for UGT1A1*28 allele

**TESTS:**
- Baseline: CBC and differential, platelets, total bilirubin, ALT, alkaline phosphatase, LDH, glucose, creatinine, albumin, sodium, potassium, calcium, magnesium, phosphorus, and ECG
- Before each treatment (for Days 1 and 8): CBC and differential, platelets
- If clinically indicated: glucose, creatinine, BUN, total bilirubin, ALT, alkaline phosphatase, albumin, total protein, sodium, potassium, calcium, magnesium, phosphorus, LDH, direct bilirubin, CA 15-3, ECG

**PREMEDICATIONS:**
- 30 minutes prior to sacituzumab govitecan give:
  - diphenhydrAMINE 50 mg IV in NS 50 mL over 15 minutes and famotidine 20 mg IV in NS 100 mL over 15 minutes (Y-site compatible)
  - acetaminophen 325 to 975 mg PO
- If prior reaction to sacituzumab govitecan, premedications for subsequent cycles include dexamethasone 20 mg PO given 12 hours and 6 hours prior to treatment. Patients will receive dexamethasone 8 mg or 12 mg PO 30 to 60 minutes prior to treatment as part of antiemetic protocol.
- Atropine may be required for treatment or prophylaxis of diarrhea (see precautions)
- Use antiemetic protocol for highly emetogenic chemotherapy protocols (see protocol SCNAUSEA)

**TREATMENT:**

| Drug | Dose | BC Cancer Administration Guideline |
|---|---|---|
| sacituzumab govitecan | 10 mg/kg on<br>Days 1 and 8 | IV in 100 to 1000 mL NS<br>▪ Infuse over 3 hours for the first dose<br>▪ Over 1 hour for all subsequent doses if no adverse reactions<br>Observe for 30 minutes post-infusion |

- Repeat every 21 days until disease progression or unacceptable toxicity.

All patients should be advised to obtain an adequate supply of loperamide (IMODIUM®) with directions for the management of diarrhea.

**DOSE MODIFICATIONS:**

**1. Hematologic**

**Day 1**

| ANC (x $10^9$/L) | | Platelets (x $10^9$/L) | Dose of sacituzumab govitecan |
|---|---|---|---|
| 1.5 | and | 75 | 100% |
| Less than 1.5 | and/or | Less than 75 | Delay by one week until recovery to ANC 1.5 and platelets 75* |

*If recovery of counts takes more than 3 weeks, discontinue treatment. Dose reduction may be necessary. See Hematological Dose Reduction Table, below

**Day 8**

| ANC (x $10^9$/L) | | Platelets (x $10^9$/L) | Dose of sacituzumab govitecan |
|---|---|---|---|
| 1.0 | and | 75 | 100% |
| Less than 1.0 | and/or | Less than 75 | Delay by one week until recovery to ANC 1.0 and platelets 75* |

*If recovery of counts takes more than 3 weeks, discontinue treatment. Dose reduction may be necessary. See Hematological Dose Reduction Table, below

**Hematological Dose Reduction Table**

| Hematological Toxicities | Dose Reduction** | | |
|---|---|---|---|
| | 1st Occurrence | 2nd Occurrence | 3rd Occurrence |
| ▪ ANC less than 0.5 for 7 or more days, or<br>▪ ANC less than 1.0 with fever greater than or equal to 38.5°C, or<br>▪ ANC 0.99 or less for 2 to 3 weeks | 75% and give filgrastim (G-CSF) | 50% | Discontinue |
| ▪ ANC 0.99 or less that lasts more than 3 weeks | Discontinue | - | - |
| ▪ Platelets 49 or less for 2 to 3 weeks | 75% | 50% | Discontinue |

** Dose reductions should be maintained for subsequent doses and not re-escalated.

† Consider filgrastim if clinically indicated and filgrastim is available. Filgrastim is not covered as a benefit drug by BC Cancer.

**2. Gastrointestinal Toxicity: Diarrhea, Nausea and Vomiting**

- Delay for Grade 2, 3 or 4 symptoms, until resolved to Grade 1 (see Grading table, below).
- Manage diarrhea per Precautions section, below. Escalate antiemetic therapy as required.
- Dose reduction required for symptoms that occur despite treatment. See Gastrointestinal Toxicity dose reduction table, below.

**Gastrointestinal Toxicity Dose Reduction Table:**

| Grade | Sacituzumab Govitecan Dose* | | |
|---|---|---|---|
| | 1st Occurrence | 2nd Occurrence | 3rd Occurrence |
| 1 | 100% | 100% | 100% |
| 2 | 100% | 75% | 50% |
| 3 | 75% | 50% | Discontinue |
| 4 | 75% | 50% | Discontinue |

* Dose reductions should be maintained for subsequent doses and not re-escalated.

**Grading for Severity of Gastrointestinal Toxicities**

| Grade | Toxicity | |
|---|---|---|
| | **Diarrhea** | **Nausea and Vomiting** |
| **1** | Increase of less than 4 stools per day over baseline; mild increase in ostomy output compared to baseline | Loss of appetite without alteration in eating habits, or 1 to 2 episodes of vomiting (separated by 5 minutes) in 24 hours |
| **2** | Increase of 4 to 6 stools per day over baseline; moderate increase in ostomy output compared to baseline | Oral intake decreased without significant weight loss, dehydration or malnutrition, or 3 to 5 episodes of vomiting (separated by 5 minutes) in 24 hours |
| **3** | Increase of 7 or more stools per day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care ADL | Inadequate oral caloric or fluid intake, or 6 or more episodes of vomiting (separated by 5 minutes) in 24 hours; tube feeding, TPN or hospitalization indicated |
| **4** | Life-threatening consequences; urgent intervention indicated | |

**PRECAUTIONS:**

1. **Neutropenia:** Grade 3 and 4 neutropenia, febrile neutropenia and fatal neutropenia are reported during treatment with sacituzumab govitecan. Interrupt treatment for neutropenic fever or ANC less than 1.5 x $10^9$/L on Day 1, or 1.0 x $10^9$/L on Day 8. Dose modifications may be required; see Dose Modifications, above.
   Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Diarrhea:** may be life threatening and requires prompt, aggressive treatment.

- Evaluate for infectious causes.
- Advise patients to have loperamide on hand before treatment initiation.
- At the onset of diarrhea, promptly initiate loperamide:
  - 4 mg stat, followed by
  - 2 mg with every episode of diarrhea to a maximum of 16 mg daily
- Discontinue loperamide 12 hours after diarrhea resolves.
- Fluid and electrolyte replacement can be given as supportive measures

3. **Cholinergic symptoms:** may occur during or shortly after infusion of sacituzumab govitecan including abdominal cramping, diarrhea, rhinorrhea, increased salivation, lacrimation, diaphoresis and flushing. These should be treated with atropine 0.3 mg to 0.6 mg IV or subcutaneously. This dose may be repeated at the physician's discretion. Blood pressure and heart rate should be monitored.

- Prophylactic atropine 0.3 mg subcutaneously prior to sacituzumab govitecan may be required for subsequent treatments for cholinergic response. Dose modification for diarrhea may be required; See Dose Modifications, above.

4. **Infusion-related reactions:** are reported in up to 37% of patients and may include **hypersensitivity** reactions. Symptoms usually occur within 24 hours of completion of infusion. Premedicate prior to infusion and monitor patient during infusion and for 30 minutes after each dose. First dose to be given over 3 hours, with subsequent doses given over 1 hour if no reaction to first dose.
   Monitor patient for signs including anaphylaxis, chest discomfort, hypotension, bronchospasm, dyspnea, wheezing, angioedema, swelling of face, lips, tongue or throat, skin reactions, flushing, fever, chills or rigor.
   For management of infusion-related reactions, see BC Cancer Protocol SCDRUGRX Management of Infusion-Related Reactions to Systemic Therapy Agents.
   Instruct patient to seek immediate medical attention for new onset of serious symptoms that occur after they leave clinic. Discontinue treatment if allergic or hypersensitivity reaction occur despite premedication (e.g., hives, wheezing, hypoxia, dyspnea).
5. Patients with **Gilbert's syndrome** or who are **homozygous for UGT1A1*28 allele** are at increased risk of febrile neutropenia, neutropenia, and anemia, and possibly other adverse reactions. Optimal dosing in these patients is unknown. Monitor closely for adverse reactions in patients with known reduced UGT1A1 activity. Consider screening for Gilbert's Syndrome using direct/indirect serum bilirubin in patients who experience acute early-onset or unusually severe adverse reactions.

**Call Dr. Nathalie LeVasseur or tumour group delegate at (604) 930-2098 or 1-800-663-3333 with any problems or questions regarding this treatment program.**

**References:**


1. Bardia A, Hurvitz SA, Tolaney SM, et al; ASCENT Clinical Trial Investigators. Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. N Engl J Med. 2021 Apr 22;384(16):1529-1541.
2. Bardia A, Mayer IA, Vahdat LT, et al. Sacituzumab Govitecan-hziy in Refractory Metastatic Triple-Negative Breast Cancer. N Engl J Med. 2019 Feb 21;380(8):741-751.
3. CADTH: Sacituzumab Govitecan (Trodelvy) CADTH Reimbursement Recommendation. Canadian Journal of Health Technologies 2022; 2(2): 1-16.