Systemic Therapy Education Bulletin

BC Cancer news and updates from across the province for Systemic Therapy teams

Provincial Systemic Therapy Drug Programs Under Consideration

The goal of the Education Bulletin is to support health care staff as they prepare for new treatments and to ensure safe patient care during the administration, distribution and management of new and complex treatments. These new drug treatments may also be delivered to patients prior to formal listing through manufacturer patient support programs or clinical trials. **Full details around the funded indications and eligibility criteria will be available in the Protocol Summaries and summarized in the Systemic Therapy Update newsletter once funding decisions have been finalized.** More details about the drugs, approved indications, and side effects can be found in the BC Cancer drug monographs, accessible from the Cancer Drug Manual Drug Index.

GOTDLRA

Treatment Programs	Indication: Under Review (Refer to protocol for more details)	Associated Adverse Events

Dactinomycin	Therapy for **Low Risk Gestational Trophoblastic** Cancer	Possible adverse events (**of any grade**):
		• Myelosuppression
		  ○ Anemia
		  ○ Thrombocytopenia
		  ○ Neutropenia
		  ○ leukopenia
		• Rash
		• Mucositis
		• Nausea and vomiting
		• Stomatitis
		• Hepatotoxicity

Dosing and Administration Information

Pre-medications:

- **Antiemetic:** moderate emetogenicity (see SCNAUSEA)

Dosing and Schedule:

- **Dactinomycin** 1.25 mg/m^2 (maximum dose of 2 mg) IV push
  - Repeat every 14 days until 2 cycles post fall of quantitative b-hCG to below lower limit of normal

Additional Protocol Information:

- Dactinomycin is considered a vesicant and can cause tissue necrosis if extravasated
  - Please refer to Policy III-20: Prevention and Management of Extravasation of Chemotherapy for more information

GIAAVCT

Treatment Programs	Indication: Under Review (Refer to protocol for more details)	Associated Adverse Events

Paclitaxel plus Carboplatin	Palliative Treatment of **Metastatic Anal Squamous Cell Carcinoma**	Possible adverse events (**of any grade**):
		• Myelosuppression
		  ○ Anemia
		  ○ Thrombocytopenia
		  ○ Neutropenia
		  ○ leukopenia
		• Infusion-related reactions
		• Peripheral sensory neuropathy
		• Mucositis
		• Nausea and vomiting
		• Fatigue
		• Arthralgia and/or myalgia
		• Alopecia
		• Hepatic dysfuction
		• Neurotoxicity
		• Nephrotoxicity

Dosing and Administration Information

Pre-medications:

- **Antiemetic:** moderate emetogenicity (see SCNAUSEA)
- **Prior to paclitaxel:**
  - IV dexamethasone 10 mg
  - IV diphenhydramine 25 mg + IV ranitidine 50 mg (compatible up to 3 hours when mixed in bag)

Dosing and Schedule: Repeat every 28 days

Days of Treatment	Day 1	Day 8	Day 15
Chemotherapy	**IV paclitaxel*** 80 mg/m^2 (Dose modification 70 or 60 mg/m^2) PLUS **IV carboplatin** AUC 5 (Dose modification AUC 4 or 3)	**IV paclitaxel*** 80 mg/m^2	**IV paclitaxel*** 80 mg/m^2

* Use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter

Additional Protocol Information:

- **If no paclitaxel hypersensitivity reactions occur**:
  - No premedications may be needed for subsequent doses and may be omitted at physician's discretion.
  - dexamethasone 8 mg PO may be given on Day 1 of each cycle in place of the IV dexamethasone
- **If paclitaxel hypersensitivity reactions occur**:
  - Premedications for re-challenge include dexamethasone 20 mg PO given 12 hours and 6 hours prior to treatment, **plus** IV premedications given 30 minutes prior to paclitaxel: dexamethasone 10 mg, diphenhydramine 50 mg, and ranitidine 50 mg.
- Paclitaxel causes pain and may cause tissue necrosis if extravasated
  - Please refer to Policy III-20: Prevention and Management of Extravasation of Chemotherapy for more information
- Paclitaxel is a CYP 2C8/9 and CYP 3A4 substrate. Paclitaxel serum concentrations may be increased by inhibitors of these enzymes and decreased by inducers of these enzymes.

GIPAVFFOX

Treatment Programs	Indication: Under Review (Refer to protocol for more details)	Associated Adverse Events
Oxaliplatin plus Leucovorin plus Fluorouracil	Palliative Treatment of **Metastatic Pancreatic Cancer**	Possible adverse events (**of any grade**): • Myelosuppression • Infusion-related reactions • Peripheral sensory neuropathy • Pharyngolaryngeal dysesthesia • Reversible posterior leukoencephalopathy syndrome • Cardiotoxicity • diarrhea • stomatitis • Venous Occlusive Disease • Dihydropyrimidine dehydrogenase (DPD) deficiency

Dosing and Administration Information

Pre-medications:

- **Antiemetic:** high to moderate emetogenicity (see SCNAUSEA)

Dosing and Schedule: Repeat every 14 days

- **Oxaliplatin*** 85 mg/m^2 administer over 2 hours
  Plus
- **Leucovorin*** 400 mg/m^2 administer over 2 hours
  Plus
- **Fluorouracil** 400 mg/m^2 IV push
  Plus
- **Fluorouracil** 2400 mg/m^2 IV over 46 h in D5W to a total volume of 230 mL by continuous infusion at 5 mL/h via Baxter LV5 INFUSOR

* Oxaliplatin and leucovorin may be infused over the same two hour period by using a Y- site connector placed immediately before the injection site.

Additional Protocol Information:

- Patients with PICC lines should have a weekly assessment of the PICC site for evidence of infection or thrombosis
- **Oxaliplatin administration:**
  - Counsel patients to avoid cold drinks and exposure to cold air, especially for 3-5 days following oxaliplatin administration.
  - Cryotherapy (ice chips) should NOT be used as it may exacerbate oxaliplatin-induced pharyngo-laryngeal dysesthesias.
  - Oxaliplatin causes irritation if extravasated.
    - Please refer to Policy III-20: Prevention and Management of Extravasation of Chemotherapy for more information
- **Fluorouracil drug Interactions:**
  - Fluorouracil is known to increase serum concentrations of warfarin, and may occur at any time. Regular monitoring of anticoagulation parameters (e.g. PTT, INR) is recommended for duration of therapy with fluorouracil.
  - Possible drug interaction with fluorouracil and phenytoin and fosphenytoin has been reported and may occur at any time. Close monitoring of plasma levels and clinical response when starting or stopping fluorouracil is recommended.

GIPAVFFIRI

Treatment Programs	Indication: Under Review (Refer to protocol for more details)	Associated Adverse Events

Irinotecan
plus
Leucovorin
plus
Fluorouracil
	Treatment of **Metastatic Pancreatic Cancer**	Possible adverse events (**of any grade**):
		• Myelosuppression
		• Diarrhea (early & late onset)
		• Other cholinergic symptoms
		  ○ Rhinorrhea
		  ○ Increased salivation
		  ○ Lacrimation
		  ○ Diaphoresis
		  ○ Flushing
		• Gilbert's syndrome
		• Hepatic dysfunction
		• Pulmonary toxicity
		• stomatitis
		• Myocardial ischemia
		• Dihydropyrimidine dehydrogenase (DPD) deficiency

Dosing and Administration Information

Pre-medications:

- **Antiemetic:** high to moderate emetogenicity (see SCNAUSEA)

Dosing and Schedule: Repeat every 14 days

- **Irinotecan*** 180 mg/m^2 administer over 1 hour 30 min
  Plus
- **Leucovorin*** 400 mg/m^2 administer over 1 hour 30 min
  Plus
- **Fluorouracil** 400 mg/m^2 IV push
  Plus
- **Fluorouracil** 2400 mg/m^2 IV over 46 h in D5W to a total volume of 230 mL by continuous infusion at 5 mL/h via Baxter LV5 INFUSOR

* Irinotecan and leucovorin may be infused over the same two hour period by using a Y- site connector placed immediately before the injection site.

Additional Protocol Information:

- Patients with PICC lines should have a weekly assessment of the PICC site for evidence of infection or thrombosis
- **Irinotecan administration:**
  - **Early diarrhea** or abdominal cramps occurring within the first 24 hours is treated with atropine 0.3 to 1.2 mg IV or SC. Prophylactic atropine may be required for subsequent treatments.
  - **Late diarrhea** has an onset of 5 to 11 days post-treatment, a duration of 3 to 7 days and must be treated promptly with loperamide.
- **Irinotecan drug Interactions:**
  - Anticonvulsants and other drugs which induce Cytochrome P450 3A4 isoenzyme activity e.g. carbamazepine, phenytoin and St John's Wort may decrease the therapeutic and toxic effects of irinotecan.
  - Prochlorperazine should be avoided on the same day as irinotecan treatment due to the increased incidence of akathisia
- **Fluorouracil drug Interactions:**
  - Fluorouracil is known to increase serum concentrations of warfarin, and may occur at any time. Regular monitoring of anticoagulation parameters (e.g. PTT, INR) is recommended for duration of therapy with fluorouracil.
  - Possible drug interaction with fluorouracil and phenytoin and fosphenytoin has been reported and may occur at any time. Close monitoring of plasma levels and clinical response when starting or stopping fluorouracil is recommended.

Website Resources and Contact Information

CONTACT INFORMATION	EMAIL
To subscribe or update contact information, please contact:	
Provincial Systemic Therapy Program	ProvincialSystemicOffice@bccancer.bc.ca
Systemic Therapy Education Bulletin: http://www.bccancer.bc.ca/health-professionals/clinical-resources/systemic-therapy/education-bulletin	
EDUCATIONAL OPPORTUNITIES	
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