BC Cancer Protocol Summary for Second Line Treatment of Advanced Esophageal and Gastroesophageal Junction Squamous Cell Carcinoma using Weekly PACLitaxel

***Protocol Code**:*	*GIGAVTW*
***Tumour Group**:*	*Gastrointestinal*
***Contact Physician**:*	*GI Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Locally advanced unresectable or metastatic esophagus or gastroesophageal junction squamous cell carcinoma not amenable to curative intent therapy, and
- Progression following first line treatment or not a candidate for first line fluoropyrimidine plus platinum-based chemotherapy, per provider discretion

TESTS:

- Baseline: CBC & Diff, total bilirubin, ALT, alkaline phosphatase, albumin, sodium, potassium
- Baseline if clinically indicated: CEA, CA19-9, GGT, ECG
- Prior to Day 1 of each cycle: CBC & Diff, creatinine, total bilirubin, ALT
- Prior to Days 8 and 15 of each cycle: CBC & Diff
- If clinically indicated: CEA, CA 19-9, alkaline phosphatase, albumin, GGT, sodium, potassium, ECG
- For patients on warfarin, weekly INR during treatment until stable warfarin dose established, then INR monthly

PREMEDICATIONS:

- **PACLitaxel must not be started unless the following drugs have been given**:
  - 45 minutes prior to PACLitaxel: dexamethasone 10 mg IV in 50 mL NS over 15 minutes
  - 30 minutes prior to PACLitaxel: diphenhydrAMINE 25 mg IV in 50 mL NS over 15 minutes and famotidine 20 mg IV in 100 mL NS over 15 minutes (Y-site compatible)
- If no PACLitaxel infusion reactions occur, no premedications may be needed for subsequent PACLitaxel doses and may be omitted at physician's discretion.
- If infusion 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 20 mg, diphenhydrAMINE 50 mg, and H_2-antagonist (e.g., famotidine 20 mg). If no infusion reactions occur, standard premedications (see above) will be used for subsequent PACLitaxel doses.
- Additional antiemetics not usually required.

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TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	80 mg/m^2 on Days 1, 8 and 15	IV in 100 to 500 mL NS over 60 minutes (use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter)

- Repeat every 28 days until disease progression or intolerable toxicity.

DOSE MODIFICATIONS:

1. Hematological Toxicity:

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose	Dose after Neutropenic Sepsis on PACLitaxel
Greater than or equal to 1.5	and	Greater than or equal to 100	80 mg/m^2	65 mg/m^2
1.0 to less than 1.5	or	75 to less than 100	65 mg/m^2	50 mg/m^2
Less than 1.0	or	Less than 75	Day 1: Delay and reduce next dose to 65 mg/m^2 Days 8 and 15: Omit and reduce next dose to 65 mg/m^2	Day 1: Delay and reduce next dose to 50 mg/m^2 Days 8 or 15: Omit and reduce next dose to 50 mg/m^2

Note: patients who cannot tolerate treatment after a dose reduction or require a treatment delay of greater than 2 weeks, should discontinue treatment.

2. Hepatic Dysfunction:

Total Bilirubin		AST and/or ALT	Paclitaxel Dose
Less than or equal to 1.25 x ULN	and	Less than 10 x ULN	80 mg/m^2
1.26 to 2 x ULN	and	Less than 10 x ULN	60 mg/m^2
2.01 to 5 x ULN	and	Less than 10 x ULN	40 mg/m^2
Greater than 5 x ULN	and/ or	Greater than or equal to 10 x ULN	Not recommended

ULN = upper limit of normal

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3. Other Non-Hematological Toxicity:

Grade	Dose
Grade 2 motor or sensory neuropathy	Decrease dose by 10 mg/m^2
All other Grade 2 non-hematological toxicity	Hold treatment until toxicity resolved to less than or equal to Grade 1 Decrease subsequent doses by 10 mg/m^2
Greater than or equal to Grade 3	Discontinue treatment

Note: patients who cannot tolerate treatment after 2 dose reductions or require a treatment delay of greater than 2 weeks, should discontinue treatment

4. Arthralgia and/or myalgia: If arthralgia and/or myalgia of Grade 2 (moderate) or higher is not relieved by adequate doses of NSAIDs or acetaminophen with codeine (e.g., TYLENOL #3), a limited number of studies report a possible therapeutic benefit using:
- predniSONE 10 mg PO BID x 5 days starting 24 hours post-PACLitaxel
- gabapentin 300 mg PO on day before chemotherapy, 300 mg BID on treatment day, then 300 mg TID x 7 to10 days

If arthralgia and/or myalgia persist, reduce subsequent PACLitaxel doses to 65 mg/m^2.

5. Neuropathy: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).

PRECAUTIONS:

1. Infusion-related reactions: Reactions to paclitaxel are common. See BC Cancer SCDRUGRX.

Mild symptoms (e.g. mild flushing, rash, pruritus)	▪ complete PACLitaxel infusion. Supervise at bedside ▪ no treatment required
moderate symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension	▪ stop PACLitaxel infusion ▪ give IV diphenhydrAMINE 50 mg and hydrocortisone IV 100 mg ▪ after recovery of symptoms resume PACLitaxel infusion at 20 mL/h for 5 minutes, 30 mL/h for 5 minutes, 40 mL/h for 5 minutes, then 60 mL/h for 5 minutes. If no reaction, increase to full rate. ▪ if reaction recurs, discontinue PACLitaxel therapy
severe symptoms (i.e. *one* or more of respiratory distress requiring treatment, generalised urticaria, angioedema, hypotension requiring therapy)	▪ stop PACLitaxel infusion ▪ give IV antihistamine and steroid as above. Add epinephrine or bronchodilators if indicated ▪ discontinue PACLitaxel therapy

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2. **Extravasation**: PACLitaxel causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.

Contact the GI Systemic Therapy physician at your regional cancer centre or the GI Systemic Therapy Chair with any problems or questions regarding this treatment program.

REFERENCES:

1. Noronha V, Patil VM, Menon N et al. Phase III Randomized Trial Comparing Palliative Systemic Therapy to Best Supportive Care in Advanced Esophageal/GEJ Cancer. Int. J. Cancer. 2024;155(12):2232–2245.
2. Shirakawa T, Kato K, Nagashima K et al. A Retrospective Study of Docetaxel or Paclitaxel in Patients With Advanced or Recurrent Esophageal Squamous Cell Carcinoma Who Previously Received Fluoropyrimidine- and Platinum-Based Chemotherapy. Cancer Chemother Pharmacol. 2014 Dec;74(6):1207-15.
3. Abraham P, Gricar J, Zhang Y, Shankaran V. Real-World Treatment Patterns and Outcomes in Patients Receiving Second-Line Therapy for Advanced/Metastatic Esophageal Squamous Cell Carcinoma. Adv Ther 2020; 37:3392–3403.

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