BC Cancer Protocol Summary for First-line Palliative Chemotherapy for Advanced Gallbladder, Pancreatic Carcinoma, and Cholangiocarcinoma using Gemcitabine and Platinum

Protocol Code	*GIAVPG*
Tumour Group	*Gastrointestinal*
Contact Physician	*GI Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Metastatic or unresectable gallbladder or pancreatic carcinoma or ampullary cancer or cholangiocarcinoma

Patients should have:

- ECOG performance status 0 to 2
- Adequate marrow reserve and renal function

CAUTIONS:

- Inadequate renal function (creatinine clearance less than 45 mL/min by GFR measurement or Cockcroft formula) unless treated with CARBOplatin

TESTS:

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

PREMEDICATIONS:

- For CISplatin: antiemetic protocol for moderately emetogenic chemotherapy protocols
- For CARBOplatin: antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)

Activated: 1 Aug 2009 Revised: 1 May 2024 (Eligibility, cautions, tests updated, treatment duration clarified)

TREATMENT:

A Cycle equals -

Drug	Dose	BC Cancer Administration Guideline
gemcitabine	1000 mg/m^2 on Days 1 and 8	IV in 250 mL NS over 30 min
CISplatin	25 mg/m^2 on Days 1 and 8	IV in 100 to 250 mL NS over 30 min

Repeat every 21 days until disease progression or unacceptable toxicity

DOSE MODIFICATIONS:

1. Hematology:

ANC ($\times 10^9$/L)		Platelets ($\times 10^9$/L)	Day 1		Day 8	
			Gemcitabine	CISplatin	Gemcitabine	CISplatin
Greater than or equal to 1.0	and	Greater than or equal to 100	100%	100%	100%	100%
0.5 to less than 1.0	or	75 to less than 100	75%	100%	75%	100%
Less than 0.5	or	Less than 75	Delay	Delay	Omit	Omit

2. Renal Dysfunction:

Creatinine Clearance (mL/min)	Day 1		Day 8	
	Gemcitabine	CISplatin	Gemcitabine	CISplatin
Greater than or equal to 60	100%	100%	100%	100%
45 to 59	100%	50%	100%	50%
Less than 45	Delay	Delay	100%	Omit

Alternatively, CARBOplatin may be used instead of CISplatin:

Drug	Dose	BC Cancer Administration Guidelines
CARBOplatin	AUC 5 DAY 1 only Dose = AUC x (GFR* +25)	IV in 100 to 250 mL NS over 30 min

* *Measured GFR* (e.g., nuclear renogram) is preferred whenever feasible, *particularly* in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, etc.). The lab reported GFR (MDRD formula) may be used as an alternative to the Cockcroft-Gault estimate of GFR; the estimated GFR reported by the lab or calculated using the Cockcroft-Gault equation should be capped at

125 mL/min when it is used to calculate the initial carboplatin dose. When a nuclear renogram is available, this clearance would take precedence.

Cockcroft-Gault Formula

$$\text{GFR} = \frac{\text{N* x (140 - age in years) x wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

*For males N = 1.23; for females N = 1.04

Note: The ***same*** method of estimation should be used throughout the treatment course (i.e., if lab reported GFR was used initially, this should be used for dosing in all subsequent cycles and not the Cockcroft-Gault estimate).

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal dysfunction.
3. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.
4. **Drug Interaction:** Possible interaction between gemcitabine and warfarin has been reported and may occur at any time. Close monitoring is recommended (monitor INR weekly during gemcitabine therapy and for 1 to 2 month after discontinuing gemcitabine treatment).

Call the GI Systemic Therapy physician at your regional cancer centre or the GI Systemic Therapy Chair Dr. Theresa Chan at (604) 930-2098 with any problems or questions regarding this treatment program.

References:

1. Heinemann V; Quietzsch D; Gieseler F et al. Randomized phase III trial of gemcitabine plus cisplatin compared with gemcitabine alone in advanced pancreatic cancer. J Clin Oncol 2006;24(24):3946-52.
2. Valle JW, Wasan H, et al. Gemcitabine alone or in combination with cisplatin in patients with advanced or metastatic cholangiocarcinomas or other biliary tract tumours: a multicentre randomised phase II study – The UK ABC-01 Study. Br J Cancer 2009;101:621-7.
3. Valle JW, Wasan H et al. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. N Engl J Med 2010;362(14):1273-81.