

BCCA Protocol Summary for Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for Patients with Peritoneal Mesothelioma Using DOXOrubicin, CISplatin and PACLitaxel

Protocol Code

GIPMHIPEC

Tumour Group

Gastrointestinal

Contact Physician

GI Systemic Therapy

The cytoreductive surgery and hyperthermic intraperitoneal chemotherapy are to be carried out only at the Vancouver General Hospital with the participation of Medical Oncology, BCCA.

ELIGIBILITY:

- All cases considered for cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) must be reviewed in a multidisciplinary tumour conference, including subspecialty pathology review.
- Peritoneal mesothelioma
- Adequate marrow reserve (ANC greater than or equal to $1.5 \times 10^9/L$, platelets greater than $100 \times 10^9/L$)
- Adequate renal (Creatinine Clearance greater than or equal to 60 mL/min) and liver function

ABSOLUTE CONTRAINDICATIONS:

- ECOG > 2
- Unresectable disease on preoperative imaging
- Extra-abdominal metastases
- Multifocal malignant small bowel obstruction
- Co-morbidities precluding extensive surgery (renal failure, cardiac disease, COPD, irreversible hematological disorders, and other)

RELATIVE CONTRAINDICATIONS:

- Age > 70 years
- Extensive disease not amenable for R0/1 resection
- Synchronous liver metastases
- Disease progression while on chemotherapy
- Sarcomatoid variant of mesothelioma
- Bilateral hydronephrosis

TESTS:

Before treatment:

- Baseline: CBC and differential, Creatinine, LFTs (Bilirubin, AST, Alkaline Phosphatase) and appropriate tumour markers.
- CT chest/abdomen/pelvis to evaluate extent of disease

PREMEDICATIONS:

- For most patients this regimen has low/moderate emetogenicity. Some patients may require pre-treatment antiemetics.
- See SCNAUSEA protocol.

TREATMENT:

Drug	Dosage	BCCA Administration Guidelines
CISplatin	50 mg/m ²	INTRAPERITONEAL mixed together in 3L of 1.5% dextrose peritoneal dialysis solution with calcium 2.5 mEq/L (DIANEAL®) and perfused for 90 minutes at intraperitoneal temperature 40 - 42°C using open “coliseum” technique and Belmont hyperthermia pump, flow rate 1000mL/minute
DOXOrubicin	15 mg/m ²	
PACLitaxel	20 mg/m ² daily for 5 days, starting on post-operative day 1	By intraperitoneal catheter in 1.5 L of 1.5% dextrose peritoneal dialysis solution with calcium 2.5 mEq/L (DIANEAL®): 23-hour dwell time, 1 hour drainage time), daily for up to 5 days* (POD 1-5)

*The course of postoperative paclitaxel may be shortened, at the discretion of the supervising surgical oncologist, if the patient experiences side effects, postoperative complications, or some other adverse reaction.

DOSES FOR CISplatin, DOXOrubicin, AND PACLitaxel TO BE BASED ON IDEAL BODY WEIGHT (IBW):

$$BSA (m^2) = \sqrt{\frac{Height (cm) \times Weight (kg)}{3600}}$$

Ideal Body Weight (IBW):

Males:

- IBW (kg) = 51.65 + 0.73 (height in cm – 152.4)

Females:

- IBW (kg) = 48.67 + 0.65 (height in cm – 152.4)

DOSE MODIFICATIONS:

Clinical Criteria for Dose Modification	Dose
Age greater than 60 y	75%

DOSE MODIFICATION IN RENAL DYSFUNCTION

Creatinine Clearance (mL/min)	CISplatin Dose
Greater than 60	100%
45 to 60	75%
Less than 45	Consider omitting

Cockcroft/Gault formula:

$$\text{CrCl (mL/min)} = \frac{N (140-\text{age}) \times \text{weight (kg)}}{\text{serum creatinine (micromol/L)}}$$

Where $N = 1.04$ for females, and 1.23 for males

NON-HEMATOLOGICAL TOXICITY REQUIRING DOSE MODIFICATIONS:

1. **Hepatic dysfunction:** Dose reduction may be required for PACLitaxel (See BCCA Cancer Drug Manual).
2. **Neuropathy:** Dose modification or discontinuation may be required (See BCCA Cancer Drug Manual).

PRECAUTIONS:

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BCCA Febrile Neutropenia Guidelines.
2. **Hypersensitivity reactions:** Reactions are common with PACLitaxel. See BCCA Hypersensitivity Guidelines.
3. **Arthralgia and/or myalgia** may develop with PACLitaxel. See BCCA Cancer Drug Manual.
4. **Cardiac toxicity:** DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction. Refer to BCCA Cancer Drug Manual
5. **Nephrotoxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics.

Call Dr. Yarrow McConnell at 604-875-4111 or Dr. Barb Melosky (or GI tumour group delegate) at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: 1 Jan 2014

Date revised: 1 Dec 2015 (Requirement for CAP approval deleted, protocol code updated)

References:

1. Yan TD, Deraco M, Baratti D, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for malignant peritoneal mesothelioma: multi-institutional experience. *J Clin Oncol* 2009;27(36):6237–42.
2. Simon GR, Verschraegen CF, Jänne PA, et al. Pemetrexed plus gemcitabine as first-line chemotherapy for patients with peritoneal mesothelioma: final report of a phase II trial. *J Clin Oncol* 2008 20;26(21):3567-72.