BC Cancer Protocol for Primary Treatment of Advanced/Recurrent Non-Small Cell Cancer of the Cervix with CARBOplatin and DOCEtaxel in Ambulatory Care Settings

Protocol Code	*GOCXCAD*
Tumour Group	*Gynecology*
Contact Physician	*Dr. Jenny Ko*
Contact Pharmacist	*Winnie Cheng*

ELIGIBILITY:
- non-small cell cancer of the cervix (squamous, adenocarcinoma or mixed)
- recurrent or IIIb, IVa or IVb
- ineligible for GOCXCRT
- Note: The GOCXCAT and GOCXCAD regimens are alternatives. The clinician's selection should be based upon the patient's circumstances. The DOCEtaxel-containing combination produces more neutropenic complications, diarrhea, edema and hypersensitivity; the PACLitaxel-containing combination produces more peripheral neurotoxicity, arthralgia, myalgia, and alopecia.[1] Physician may choose between PACLitaxel (GOCXCAT) and DOCEtaxel (GOCXCAD). A maximum of 6 cycles* of taxane treatment will be reimbursed for each line of therapy. However, a patient who had previously responded to 6 cycles* of say, a PACLitaxel-based regimen may be retreated with another 6 cycles* of a taxane-based regimen.

* may extend to 9 cycles if the patient has not achieved a complete response but is continuing to improve.

EXCLUSIONS:
- any small cell component
- creatinine greater than 150 micromol/L
- neutrophils less than 1 x 10^9/L
- ECOG performance status greater than 2

TESTS:
- Baseline: CBC & diff, platelets, creatinine, tumor marker (CA 125, CA 15-3, CA 19-9), ALT, Alk Phos, bilirubin, GGT, chest X-ray, abdominopelvic imaging, camera nuclear renogram for GFR (if available)
- Day 7 and 14 after first cycle (and in subsequent cycle if dose modification made): CBC & diff; once nadir pattern established, check CBC & diff at that point only
- Before each treatment: CBC & diff, creatinine, any initially elevated tumor marker
    - If clinically indicated: bilirubin, ALT, Alk Phos, LDH, GGT, albumin, protein level

PREMEDICATIONS AND ANTIEMETIC THERAPY:
- dexamethasone 8 mg PO BID for 3 days, starting one day prior to each DOCEtaxel administration; patient must receive minimum of three doses pre-treatment
- ondansetron 8 mg PO 30 minutes pre-CARBOplatin
- dimenhyDRINATE 50 to 100 mg PO prn after treatment
- DOCEtaxel-induced onycholysis and cutaneous toxicity of the hands may be prevented by wearing frozen gloves starting 15 minutes before DOCEtaxel infusion until 15 minutes after end of DOCEtaxel infusion; gloves should be changed after 45 minutes of wearing to ensure they remain cold during the entire DOCEtaxel infusion.

TREATMENT (give DOCEtaxel first):

Drug	Starting Dose	BC Cancer Administration Guideline
DOCEtaxel	75 mg/m^2 *	IV in 250 to 500 mL NS or D5W over 1 hour (see Precaution #2) Use non-DEHP equipment.
CARBOplatin	Dose = AUC** x (GFR +25)	IV in 100 to 250 mL NS over 30 minutes

***** Use 60 mg/m^2 if patient has a history of neutropenic complications following chemotherapy or prior extended field radiotherapy. In patients greater than 75 years of age, begin at 60 mg/m^2, with subsequent escalation to 75 mg/m^2 if tolerated.
** use AUC of 5. If patient has received extensive prior radiation therapy, use AUC of 4

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

$$\text{GFR} = \frac{1.04 \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

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).

Repeat every 21 days* up to a maximum of 6 cycles (may extend to 9 cycles if the patient has not achieved a complete response but is continuing to respond.)
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*If a delay due to hematologic recovery has occurred, extend all future cycles to 28 day intervals.

DOSE MODIFICATIONS:
1. **Hematology**:

a) on treatment day if patient *has never had* neutropenic sepsis on DOCEtaxel:

ANC (x 10^9/L)		Platelets (x 10^9/L)	Doses (both drugs)
greater than or equal to 1.5	and	greater than or equal to 100	treat as per nadir
1.0 to less than 1.5	and	greater than or equal to 100	DOCEtaxel 60 mg/m^2; CARBOplatin per nadir counts
less than 1.0	or	less than 100	delay until recovery

b) on treatment day if patient *has had* neutropenic sepsis on DOCEtaxel:

ANC (x 10^9/L)		Platelets (x 10^9/L)	Doses
greater than or equal to 1.5	and	greater than or equal to 100	DOCEtaxel 60 mg/m^2; CARBOplatin per nadir counts
1.0 to less than 1.5	and	greater than or equal to 100	DOCEtaxel 60 mg/m^2; CARBOplatin per nadir counts
less than 1.0	or	less than 100	delay until recovery

c) at nadir:

ANC (x 10^9/L)		Platelets (x 10^9/L)	DOCEtaxel	CARBOplatin
greater than or equal to 0.5	and	greater than or equal to 75	100%	100%
less than 0.5	and	less than or equal to 75	80%	80%
less than 0.5	and	greater than or equal to 75	80%	100%
greater than or equal to 0.5	and	less than or equal to 75	100%	80%
febrile neutropenia at any time			75%	80%

As noted above, if a delay due to hematologic recovery has occurred, extend all future cycles to 28 day intervals.

2. **Renal dysfunction**: If significant increase (greater than 20%) in creatinine, repeat nuclear renogram (if available) and recalculate CARBOplatin dose using new GFR.

3. **Hepatic dysfunction**:

Alkaline Phosphatase		AST +/or ALT	DOCEtaxel Dose
less than 2.5 x ULN	and	less than or equal to 1.5 x ULN	100%
2.5 to 5 x ULN	and	1.6 to 6 x ULN	60 mg/m^2
greater than 5 x ULN	or	greater than 5 ULN	discuss with contact physician

ULN= Upper limit of normal range

PRECAUTIONS:

1. **Fluid Retention**: dexamethasone premedication must be given to reduce incidence and severity of fluid retention.
2. **Hypersensitivity** reactions to DOCEtaxel are common but it is not necessary to routinely initiate the infusion slowly. If slow initiation of infusion is needed, start infusion at 30 mL/h x 5 minutes, then 60 mL/h x 5 minutes, then 120 mL/h x 5 minutes, then complete infusion at 250 mL/h (for 500 mL bag, continue 250 mL/h for 5 minutes and then complete infusion at 500 mL/h). Refer to BC Cancer Hypersensitivity Guidelines.
3. **Extravasation**: DOCEtaxel causes pain and may cause tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
4. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
5. **Hepatic Dysfunction**: DOCEtaxel undergoes hepatic metabolism. Hepatic dysfunction (particularly elevated AST) may lead to increased toxicity and usually requires a dose reduction. Baseline liver enzymes are recommended before Cycle 1 and then if clinically indicated (e.g. – repeat lever enzymes prior to each treatment if liver enzymes are elevated, liver metastases are present or there is severe toxicity such as neutropenia). If liver enzymes are normal and there is no evidence of lever metastases or severe toxicity, check liver enzymes after three cycles (i.e. – at Cycle 4). Note: this information is intended to provide guidance, but physicians must use their clinical judgement when making decisions regarding monitoring and dose adjustments.

Call Dr. Jenny Ko or tumour group delegate at (604) 851-4710 or 1-877-547-3777 with any problems or questions regarding this treatment program.

References:

1. Vasey PA. Role of docetaxel in the treatment of newly diagnosed advanced ovarian cancer. J Clin Oncol 2003;21(90100):136s-44s.