# BC Cancer Protocol Summary for Alternative Treatment of Gynecological Malignancies using CARBOplatin and PACLitaxel NAB (ABRAXANE)

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| ***Protocol Code*** | *GOCABR* |
| ***Tumour Group*** | *Gynecologic Oncology* |
| ***Contact Physician*** | *Dr. Theresa Chan* |

**ELIGIBILITY:**

Patients must have:
- Previous severe hypersensitivity reaction or anaphylaxis to PACLitaxel that is not manageable despite use of premedications, or
- Previous moderate PACLitaxel hypersensitivity reaction that cannot be managed by premedications due to a strong contraindication to high dose steroids, such as poorly controlled diabetes, and
- Been treated with and eligible for the following protocols:
  - GOOVCATM, GOOVCATR, GOOVCATX, GOOVDDCAT
  - GOCXCAT, UGOCXCATP
  - GOENDCAT

**EXCLUSIONS:**

Patients must not have:
- Platinum resistant/refractory disease
- Disease progression on prior taxane therapy
- Severe hepatic dysfunction contraindicating PACLitaxel NAB

**CAUTION:**
- Greater than or equal to grade 2 sensory or motor neuropathy

**TESTS:**
- **Baseline:** CBC & diff, platelets, creatinine, bilirubin, ALT, tumour marker (CA 125, CA 15-3, CA 19-9, CEA), camera nuclear renogram for GFR (optional)
- Day 14 (and Day 21 if using a 4 week cycle interval) of first cycle (optional, if not done with prior regimen) and subsequent cycles if a dose modification has been made: CBC & diff, platelets. No need for interim count check once safe nadir pattern has been established.
- **Before each treatment:** CBC & diff, creatinine, any initially elevated tumour marker
- **If clinically indicated:** bilirubin, Alk Phos, GGT, ALT, LDH, albumin, total protein

**PREMEDICATIONS:**

- Antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)

**TREATMENT:**

| Drug | Dose | BC Cancer Administration Guideline |
|---|---|---|
| PACLitaxel NAB (ABRAXANE) | 260 mg/m² | IV over 30 minutes* |
| CARBOplatin | Dose = AUC** x (GFR +25) | IV in 100 to 250 mL NS over 30 minutes |

*in empty sterile bags and tubing with 15 micron filter; no specific material required for bag or tubing

**use AUC of 6; if extensive prior radiation therapy, use AUC of 5

Repeat every 21 to 28 days to complete total number of cycles in original CARBOplatin and PACLitaxel protocol.

*Measured GFR* (e.g. nuclear renogram) is preferred in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, age greater than 70, 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

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

Recalculate GFR if creatinine increases by greater than 20% or rises above the upper limit of normal.

## DOSE MODIFICATIONS:

1. **Hematological**

a) on treatment day:

| 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 (if applicable); otherwise, proceed at same doses |
| less than 1.5 | or | less than 100 | Delay until recovery. If using 21-day interval, switch to 28-day interval. If 2nd delay, use filgrastim (G-CSF) or dose reduction. |

b) at nadir (until nadir pattern established):

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

* % of previous cycle's dose, at physician's discretion. If dose is changed, subsequent nadir counts must be checked.
Note: If dose has been reduced, dose increase/re-escalation for good nadir counts is not recommended.

2. **Sensory Neuropathy:** PACLitaxel NAB

| Grade | Toxicity | Dose – 1st Occurrence | Dose – 2nd Occurrence |
|---|---|---|---|
| **1** | Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function | Maintain dose | Maintain dose |
| **2** | Sensory alteration or paresthesia (including tingling) but not interfering with function, but not interfering with ADL | Maintain dose | Maintain dose |
| **3** | Sensory alteration or paresthesia interfering with ADL | Hold treatment until resolved to grade 2, then reduce dose to 85%** | Hold treatment until resolved to grade 2, then reduce dose to 70%** |
| **4** | Disabling | Hold treatment until resolved to grade 2, then reduce dose to 85%** | Hold treatment until resolved to grade 2, then reduce dose to 70%** or discontinue further therapy |

** Dose reductions should be maintained for subsequent cycles and not re-escalated.

3. **Hepatic dysfunction**: PACLitaxel NAB

| ALT or AST | | Bilirubin | PACLitaxel NAB |
|---|---|---|---|
| Less than or equal to 10 x ULN | and | Greater than 1 to less than or equal to 1.5 x ULN | 100% |
| Less than or equal to 10 x ULN | and/or | Greater than 1.5 to less than or equal to 5 x ULN | 80%* |
| Greater than 10 x ULN | or | Greater than 5 x ULN | Hold |

*may re-escalate dose if hepatic function normalizes and reduced dose is tolerated for at least 2 cycles

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 NAB
   - gabapentin 300 mg PO on day before chemotherapy, 300 mg bid on treatment day, then 300 mg tid x 5-15 days (based on duration of arthromyalgia)

   If arthralgia and/or myalgia persist, reduce subsequent PACLitaxel NAB doses to 85%

5. **Renal dysfunction:** If significant increase (greater than 20% or rises above the upper limit of normal) in creatinine, recheck/recalculate GFR and recalculate CARBOplatin dose using new GFR. No modification is required for PACLitaxel NAB in mild to moderate renal impairment. PACLitaxel NAB has not been studied in patients with creatinine clearance less than 30 mL/min.

**PRECAUTIONS:**

1. An albumin form of PACLitaxel may substantially affect a drug's functional properties relative to those of drug in solution. **Do not** substitute with or for other PACLitaxel formulations.
2. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
3. **Extravasation**: PACLitaxel NAB causes pain and may, rarely, cause tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
4. **Hypersensitivity:** Reactions to CARBOplatin may occur. Refer to BC Cancer Hypersensitivity Guidelines.
5. **Drug interactions:** PACLitaxel NAB is metabolized by CYP2C8 and CYP3A4; caution should be exercised when administering with drugs which are CYP2C8 or CYP3A4 inducers or inhibitors.
6. **Cardiac toxicity** has been reported rarely while patients receive PACLitaxel NAB. Severe cardiovascular events (3%), including chest pain, cardiac arrest, supraventricular tachycardia, edema, thrombosis, pulmonary thromboembolism, pulmonary emboli, and hypertension.
7. **Theoretical risk of viral disease transmission**, due to human albumin component, is extremely remote.

**Call Dr. Theresa Chan or tumour group delegate at (604) 930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.**

**References**:

1. Alberts DS, Blessing JA, Landrum LM, et al. Phase II trial of nab-paclitaxel in the treatment of recurrent or persistent advanced cervix cancer: a gynecologic oncology group study. Gynecol Oncol. 2012 Dec;127(3): 451-5.
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3. Parisi A, Palluzzi E, Cortellini A, et al. First-line carboplatin/nab-paclitaxel in advanced ovarian cancer patients, after hypersensitivity reaction to solvent-based taxanes: a single-institution experience. Clin Transl Oncol. 2020;22:158-62.
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5. Pellegrino B, Boggiani D, Tommasi C, et al. Nab-paclitaxel after docetaxel hypersensitivity reaction: case report and literature review. Acta Biomed. 2017;88(3):329-33.
6. Dizon DS, Schwartz J, Rojan A, et al. Cross-sensitivity between paclitaxel and docetaxel in a women's cancers program. Gyencol Oncol. 2006;100:149-51.
7. Sanchez-Munoz A, Jimenez B, Garcia-Tapiador A. Cross-sensitivity between taxanes in patients with breast cancer. Clin Transl Oncol. 2011;13:904-6.
8. Celgene Inc. ABRAXANE® product monograph. Mississauga, Ontario; 31 August 2018