# BC Cancer Protocol Summary for Alternative NEOAdjuvant Therapy for Breast Cancer using Dose Dense Therapy: PACLitaxel NAB (ABRAXANE) followed by DOXOrubicin and Cyclophosphamide

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|---|---|
| ***Protocol Code*** | *BRLAPNACG* |
| ***Tumour Group*** | *Breast* |
| ***Contact Physician*** | *Dr. Nathalie LeVasseur* |

## 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 curative intent breast cancer protocol BRLATACG

Note: Filgrastim (G-CSF) is not covered as a benefit at BC Cancer

## EXCLUSIONS:

Patients must not have:

- Congestive heart failure (LVEF less than 45%) or other significant heart disease
- Severe hepatic dysfunction contraindicating PACLitaxel NAB (ABRAXANE) or DOXOrubicin
- Known hypersensitivity to E. coli derived products

## CAUTIONS:

- Greater than or equal to grade 2 sensory or motor neuropathy

## TESTS:

- Baseline: CBC & Diff, platelets, bilirubin, ALT, GGT, LDH, alkaline phosphatase, creatinine
- For the cycles of PACLitaxel NAB, before each treatment: CBC & Diff, platelets, bilirubin, ALT, creatinine
- For the cycles of DOXOrubicin and cyclophosphamide, before each treatment: CBC & Diff, platelets
- If clinically indicated: GGT, alkaline phosphatase, urea, MUGA scan or echocardiogram
- For the cycles of DOXOrubicin and cyclophosphamide, if clinically indicated: ALT, bilirubin, creatinine

**PREMEDICATIONS**:

- For the cycles of PACLitaxel NAB: Additional anti-emetics not usually required
- For the cycles of DOXOrubicin and cyclophosphamide: Antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)

**TREATMENT**:

| Drug | Dose | BC Cancer Administration Guideline |
|---|---|---|
| PACLitaxel NAB (ABRAXANE) | 260 mg/m$^2$ | IV over 30 minutes* |

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

- PACLitaxel NAB to be given every 21 days to complete total number of cycles in original BRLATACG protocol, followed by
- Four consecutive cycles of DOXOrubicin and cyclophosphamide to start 21 days after final cycle of PACLitaxel NAB

| Drug | Dose | BC Cancer Administration Guideline |
|---|---|---|
| DOXOrubicin | 60 mg/m² | IV push |
| cyclophosphamide | 600 mg/m² | IV in NS 100 to 250 mL over 20 minutes to 1 hour |
| filgrastim (G-CSF) | 5 mcg/kg/day Days 3 to 10 (or adjust as needed**) | subcutaneous |

** reduce filgrastim treatment duration if ANC greater than 10 or intolerable bone pain. Filgrastim should not be stopped before the time of the predicted nadir from chemotherapy.

- Repeat every 14 days x 4 cycles.

## DOSE MODIFICATIONS:

1. **Hematological**

**For the cycles of PACLitaxel NAB only:**

| ANC (x $10^9$/L) | | Platelets (x $10^9$/L) | Dose |
|---|---|---|---|
| greater than or equal to 1.5 | and | greater than or equal to 100 | 100% (260 mg/$m^2$) |
| 1.0 to less than 1.5 | and | greater than or equal to 100 | 220 mg/$m^2$ |
| less than 1.0 | or | less than 100 | Delay until ANC greater than or equal to 1.5 and platelets greater than or equal to 100 then consider giving 220 mg/$m^2$ |

**For cycles of DOXOrubicin and cyclophosphamide only (for Day 1 counts):**

| ANC (x $10^9$/L) | | Platelets (x $10^9$/L) | Dose (all drugs) |
|---|---|---|---|
| Greater than or equal to 1.0 | and | Greater than or equal to 100 | 100% |
| Less than 1.0 | and | Greater than or equal to 100 | delay for 1 week (or longer if needed), then give 100% dose if ANC greater than 1 and platelets greater than or equal to 100. Give filgrastim days 3 to 13 for remaining cycles. |
| Greater than or equal to 1.0 | and | Less than 100 | delay for 1 week (or longer if needed), then give 75% if ANC greater than 1 and platelets greater than or equal to 100 |
| Less than or equal to 1.0 | and | Less than 100 | delay for 1 week (or longer if needed), then give 75% if ANC greater than 1 and platelets greater than or equal to 100 |

## 2. Febrile Neutropenia:

**PACLitaxel NAB**

| | 1st Occurrence | 2nd Occurrence |
|---|---|---|
| Febrile Neutropenia | Delay until recovery (ANC greater than or equal to 1.5 x $10^9$/L and platelets greater than or equal to 100 x $10^9$/L), then dose reduce to **220 mg/m$^{2**}$** | Delay until recovery (ANC greater than or equal to 1.5 x $10^9$/L and platelets greater than or equal to 100 x $10^9$/L), then dose reduce to **180 mg/m$^{2**}$** |

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

**DOXOrubicin and cyclophosphamide:** Consider 75% of dose for current and subsequent cycles**.**

## 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

**DOXOrubicin**:

| ALT or AST | | Bilirubin (micromol/L) | Dose |
|---|---|---|---|
| 2 to 3 x ULN | | - | 75% |
| greater than 3 x ULN | or | 20 to 51 | 50% |
| - | | 51 to 85 | 25% |
| - | | greater than 85 | Do not administer |

4. **Renal dysfunction**: 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.
   Dose modification may be required for cyclophosphamide. Refer to BC Cancer Drug Manual.

5. **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 | Reduce dose to 220 mg/m$^{2**}$ Consider holding treatment until resolved to grade 2 | Reduce dose to 180 mg/m$^{2**}$ Consider holding treatment until resolved to grade 2 |
| **4** | Disabling | Hold treatment until resolved to grade 2, then reduce dose to 220 mg/m$^{2**}$ or discontinue further treatment at the discretion of physician | Hold treatment until resolved to grade 2, then reduce dose to 180 mg/m$^{2**}$ or discontinue further treatment at the discretion of physician |

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

3. **<u>Arthralgia and/or myalgia</u>:** If arthralgia and/or myalgia from PACLitaxel NAB 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 7 to 10 days

   If arthralgia and/or myalgia persist, reduce subsequent PACLitaxel NAB doses to 220 mg/m$^2$.

**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. **Extravasation**: DOXOrubicin and PACLitaxel NAB cause pain and tissue necrosis (rarely for PACLitaxel NAB) if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **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.
5. **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.
6. **Cardiac Toxicity**: DOXOrubicin is cardiotoxic and must be used with caution in patients with cardiac dysfunction. Cardiac assessment recommended once cumulative dose reaches 300 mg/m$^2$ (see BC Cancer Drug Manual).
7. **Theoretical risk of viral disease transmission**, due to human albumin component, is extremely remote.

**Call Dr. Nathalie LeVasseur or tumour group delegate at (604)-930-2098 or 1-800-663-3333 with any problems or questions regarding this treatment program.**

**References**:


1. Sánchez-Muñoz A, Jiménez B, García-Tapiador A, et al. Cross-sensitivity between taxanes in patients with breast cancer. Clin Transl Oncol. 2011 Dec;13(12):904-6.
2. Gianni L, Mansutti M, Anton A, et al. Comparing Neoadjuvant Nab-paclitaxel vs Paclitaxel Both Followed by Anthracycline Regimens in Women With ERBB2/HER2-Negative Breast Cancer-The Evaluating Treatment With Neoadjuvant Abraxane (ETNA) Trial: A Randomized Phase 3 Clinical Trial. JAMA Oncol. 2018 Mar 1;4(3):302-308.
3. Untch M, Jackisch C, Schneeweiss A, et al. German Breast Group (GBG); Arbeitsgemeinschaft Gynäkologische Onkologie—Breast (AGO-B) Investigators. Nab-paclitaxel versus solvent-based paclitaxel in neoadjuvant chemotherapy for early breast cancer (GeparSepto-GBG 69): a randomised, phase 3 trial. Lancet Oncol. 2016 Mar;17(3):345-356.
4. Yuan Y, Lee JS, Yost SE, et al. Phase II Trial of Neoadjuvant Carboplatin and Nab-Paclitaxel in Patients with Triple-Negative Breast Cancer. Oncologist. 2021 Mar;26(3):e382-e393.
5. Brufsky A. *nab*-Paclitaxel for the treatment of breast cancer: an update across treatment settings. Exp Hematol Oncol. 2017 Mar 22;6:7.