

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

Protocol Code

BRLAPNACG

Tumour Group

Breast

Contact Physician

Dr. Angela 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 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
- Before each treatment: CBC & diff, platelets
- If clinically indicated: bilirubin, ALT, GGT, alkaline phosphatase, urea, creatinine, MUGA scan or echocardiogram

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/m ²	IV push
cyclophosphamide	600 mg/m ²	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

	1 st Occurrence	2 nd 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/m²**	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/m²**

**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 – 1 st Occurrence	Dose – 2 nd 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. **Arthralgia and/or myalgia:** 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 daysIf arthralgia and/or myalgia persist, reduce subsequent PACLitaxel NAB doses to 220 mg/m².

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 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/m² (see BC Cancer Drug Manual).
7. **Theoretical risk of viral disease transmission**, due to human albumin component, is extremely remote.

Call Dr. Angela Chan or tumour group delegate at 604-877-6000 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.