

# BC Cancer Protocol Summary for Alternative NEOAdjuvant Therapy for Locally Advanced Breast Cancer using PACLitaxel NAB followed by DOXOrubicin and Cyclophosphamide

**Protocol Code:**

*BRLAPNAC*

**Tumour Group:**

*Breast*

**Contact Physician:**

*BR Systemic Therapy*

## **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 BRLATWAC

Patients should have:

- Adequate hematological, renal and hepatic function

Note:

- Primary prophylaxis with G-CSF is not mandatory, but may be considered if patient has one or more of the following risk factors:
  - Prior chemotherapy or radiation therapy
  - Persistent neutropenia
  - Recent surgery and/or open wounds
  - Liver dysfunction
  - Renal dysfunction
  - Older than 65 years of age and receiving full chemotherapy dose intensity

## **EXCLUSIONS:**

Patients must not have:

- Severe cardiovascular disease with LVEF less than 45%
- Severe hepatic dysfunction contraindicating PACLitaxel NAB or DOXOrubicin

## **CAUTION:**

- Greater than or equal to [Grade 2](#) sensory or motor neuropathy

**TESTS:**

- Baseline: CBC & Diff, total bilirubin, ALT, GGT, alkaline phosphatase, creatinine
- Baseline, if clinically indicated: LDH, urea, MUGA scan or echocardiogram
- For Cycles of PACLitaxel NAB prior to treatment: CBC & Diff, total bilirubin, ALT, creatinine
- For Cycle of DOXOrubicin and cyclophosphamide prior to treatment: CBC & Diff
- If clinically indicated: GGT, alkaline phosphatase, urea, MUGA scan or echocardiogram
- If clinically indicated, for cycles of DOXOrubicin and cyclophosphamide: total bilirubin, ALT, 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	260 mg/m <sup>2</sup> *	IV over 30 minutes**

\* Select dose per Dose Banding Table (appendix).

\*\*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 BRLATWAC 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 <sup>2</sup>	IV push
cyclophosphamide	600 mg/m <sup>2</sup>	IV in 100 to 250 mL NS over 20 to 60 minutes

- Repeat every 21 days for 4 cycles

## DOSE MODIFICATIONS:

### 1. Hematological

For the cycles of PACLitaxel NAB only:

ANC (x 10 <sup>9</sup> /L)		Platelets (x 10 <sup>9</sup> /L)	Dose
Greater than or equal to 1.5	and	Greater than or equal to 100	100% (260 mg/m <sup>2</sup> )
1.0 to less than 1.5	and	Greater than or equal to 100	220 mg/m <sup>2</sup>
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 <sup>2</sup>

For cycles of DOXOrubicin and cyclophosphamide only:

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /L)	Dose (both drugs)
Greater than or equal to 1.5	and	Greater than or equal to 90	100%
1.0 to less than 1.5	or	70 to less than 90	75%
Less than 1.0	or	Less than 70	Delay

### 2. Febrile Neutropenia: PACLitaxel NAB

	1 <sup>st</sup> Occurrence	2 <sup>nd</sup> Occurrence
Febrile Neutropenia	Delay until recovery (ANC greater than or equal to 1.5 x 10 <sup>9</sup> /L and platelets greater than or equal to 100 x 10 <sup>9</sup> /L), then dose reduce to <b>220 mg/m<sup>2</sup>**</b>	Delay until recovery (ANC greater than or equal to 1.5 x 10 <sup>9</sup> /L and platelets greater than or equal to 100 x 10 <sup>9</sup> /L), then dose reduce to <b>180 mg/m<sup>2</sup>**</b>

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

### 3. Hepatic Dysfunction:

#### PACLitaxel NAB

ALT or AST		Total 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

ULN = upper limit of normal

#### DOXOrubicin:

ALT or AST		Total 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

ULN = upper limit of normal

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 <sup>st</sup> Occurrence	Dose – 2 <sup>nd</sup> 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 <sup>2</sup> ** Consider holding treatment until resolved to grade 2	Reduce dose to 180 mg/m <sup>2</sup> ** Consider holding treatment until resolved to grade 2
4	Disabling	Hold treatment until resolved to grade 2, then reduce dose to 220 mg/m <sup>2</sup> ** or discontinue further treatment at the discretion of physician	Hold treatment until resolved to grade 2, then reduce dose to 180 mg/m <sup>2</sup> ** or discontinue further treatment at the discretion of physician

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

6. **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 for 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 for 7 to 10 days

If arthralgia and/or myalgia persist, reduce subsequent PACLitaxel NAB doses to 220 mg/m<sup>2</sup>.

### 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. **Febrile Neutropenia:** Risk of febrile neutropenia is 10 to 20%. If a patient has additional risk factors outlined in Eligibility Note above, risk of febrile neutropenia may be considered to be greater than 20%; consider prophylactic filgrastim per discretion of the treating physician. Febrile neutropenia can result in serious patient harm, treatment delays, and hospitalization. Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **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<sup>2</sup> (see BC Cancer Drug Manual).
7. **Theoretical risk of viral disease transmission,** due to human albumin component, is extremely remote.

**Contact the BR Systemic Therapy physician at your regional cancer centre or the BR Systemic Therapy Chair 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.

## Appendix. Dose Bands

### PACLitaxel NAB DOSE BANDING TABLE

Ordered Dose (mg)		Rounded dose (mg)
From:	To:	
Less than 96		Pharmacy prepares specific dose
96	104.49	100
104.5	108.49	105
108.5	115.49	110
115.5	125.49	120
125.5	135.49	130
135.5	145.49	140
145.5	155.49	150
155.5	165.49	160
165.5	177.49	170
177.5	190.49	185
190.5	210.49	200
210.5	230.49	220
230.5	250.49	240
250.5	270.49	260
270.5	286.49	275
286.5	314.49	300
314.5	329.49	315
329.5	344.49	330
344.5	362.49	345
362.5	388.49	370
388.5	419.49	400
419.5	439.49	420
439.5	459.49	440
459.5	479.49	460
479.5	499.49	480
499.5	524.49	500
524.5	566.49	540
566.5	596.49	580
596.5	630.49	600
630.5	683.49	650
More than 683.49		Pharmacy prepares specific dose