BC Cancer Protocol Summary for Alternative Adjuvant Therapy for Breast Cancer using PACLitaxel NAB (ABRAXANE)

Protocol Code:	*BRAJPN*
Tumour Group:	*Breast*
Contact Physician:	*Dr. Nathalie LeVasseur*

ELIGIBILITY:

Patients must have:

- Previous severe hypersensitivity reaction or anaphylaxis to PACLitaxel or DOCEtaxel that is not manageable despite use of premedications,
  or
- Previous moderate PACLitaxel or DOCEtaxel 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 one of the following curative intent (neoadjuvant or adjuvant) protocols: BRAJACT, BRAJACTG, BRAJACTW, BRAJFECD, BRLAACD.

EXCLUSIONS:

Patients must not have:

- Severe hepatic dysfunction contraindicating PACLitaxel NAB

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, bilirubin, ALT, creatinine
- If clinically indicated: GGT, alkaline phosphatase, urea

PREMEDICATIONS:

- Additional anti-emetics not usually required.

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

Repeat every 21 days to complete total number of cycles in original PACLitaxel or DOCEtaxel protocol.

DOSE MODIFICATIONS:

1. **Hematological**

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**

	1st Occurrence	**2nd Occurrence**
Febrile Neutropenia	Delay until recovery (ANC greater than or equal to 1.5 x 10^9/L and plts 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 plts 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

2. Hepatic Dysfunction

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

3. Sensory Neuropathy

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.

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 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**: PACLitaxel NAB causes pain and may, rarely, cause 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. **Renal Dysfunction:** No adjustment required for mild to moderate renal impairment. PACLitaxel NAB has not been studied in patients with creatinine clearance less than 30 mL/min.
5. 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. 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. Sanchez-Munoz A, Jimenez B, Garcia-Tapiador A et al. Cross-sensitivity between taxanes in patients with breast cancer. *Clin Transl Oncol*. 2011; 13:904-906.
2. Gianni L, Mansutti M, Anton A, Calvo L 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; 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.* 2020 Oct 24; doi: 10.1002/onco.13574. Epub ahead of print.
5. Brufsky, A. *nab*-Paclitaxel for the treatment of breast cancer: an update across treatment settings. *Exp Hematol Oncol.* 2017; 6, 7.