

BC Cancer Protocol Summary for Alternative Treatment of Gynecological Malignancies using CARBOplatin and PACLitaxel NAB

Protocol Code

GOCABR

Tumour Group

Gynecologic Oncology

Contact Physician

GO 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 and eligible for the following protocols:
 - GOOVCATM, GOOVCATR, GOOVCATX, GOOVDDCAT
 - GOCXCAT, UGOCXCATP
 - GOENDAJCAT, GOENDAVCAT

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, creatinine, total bilirubin, ALT, alkaline phosphatase
- Baseline, if clinically indicated: sodium, potassium, magnesium, calcium, CA 125, CA 15-3, CA 19-9, CEA, SCC
- If clinically indicated, for nadir monitoring, Day 14 (and Day 21 if using 28-day interval) of first cycle (optional, if not done with prior regimen) and subsequent cycles if a dose modification has been made: CBC & Diff
- Before each treatment: CBC & Diff, creatinine, total bilirubin, ALT, alkaline phosphatase
- If clinically indicated: sodium, potassium, magnesium, calcium, CA 125, CA 15-3, CA 19-9, CEA, SCC

PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy (see protocol [SCNAUSEA](#))

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel NAB	260 mg/m ² *	IV over 30 minutes**
CARBOplatin	Dose = AUC*** x (GFR +25)	IV in 100 to 250 mL NS 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

*** 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	Proceed with same dose unless nadir labs completed. If nadir labs completed, treat according to nadir values.
Less than 1.5	or	Less than 100	Delay until recovery. If using 21-day interval, switch to 28-day interval. If 2 nd delay, use filgrastim (G-CSF) or dose reduction.

b) at nadir:

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 – 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	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		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

- 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 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 5 to 15 days (based on duration of arthromyalgia)
 If arthralgia and/or myalgia persist, reduce subsequent PACLitaxel NAB doses to 85%
- 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:

- 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.
- Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
- Extravasation:** PACLitaxel NAB causes pain and may, rarely, cause tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
- Hypersensitivity:** Reactions to CARBOplatin may occur. Refer to BC Cancer SCDRUGRX protocol.
- 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.
- 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.
- Theoretical risk of viral disease transmission**, due to human albumin component, is extremely remote.

Contact the GO Systemic Therapy physician at your regional cancer centre or [the GO Systemic Therapy Chair](#) 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.
2. Srinivasan KN, Rauthan A, Gopal R. Combination therapy of albumin-bound paclitaxel and carboplatin as first line therapy in a patient with ovarian cancer. *Case Rep Oncol Med* [Internet]. 2014 [cited 23 Jul 2020]. Available from: <https://doi.org/10.1155/2014/940591>
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.
4. Maurer K, Michener C, Mahdi H, Rose PG. Universal tolerance of nab-paclitaxel for gynecologic malignancies in patients with prior taxane hypersensitivity reactions. *J Gynecol Oncol.* 2017 Jul;28(4):e38
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. *Gynecol 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

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