

Regimen Reference Order

BRST – BrightNess AC (Dose Dense) followed by PACLitaxel + CARBOplatin

ARIA: BRST - [BrightNess - dose dense AC]

BRST - [BrightNess - PACL + CARBO]

Planned Course: AC every 14 days for 4 cycles,
followed by PACLitaxel (weekly) + CARBOplatin every 21 days for 4 cycles

Indication for Use: Breast Cancer Neo-Adjuvant; “Triple negative”

CVAD: Preferred (VESICANT INVOLVED)

Proceed with treatment if:

Cycles 1 to 4 (AC [Dose Dense])

- ANC equal to or greater than $1 \times 10^9/L$ AND Platelets equal to or greater than $100 \times 10^9/L$
- Creatinine clearance greater than 10 mL/minute
- Bilirubin less than upper limit of normal
- AST/ALT less than 2 times upper limit of normal

Cycles 5 to 8 (PACLitaxel + CARBOplatin)

- ANC equal to or greater than $1 \times 10^9/L$ AND Platelets equal to or greater than $100 \times 10^9/L$
- Bilirubin less than 1.25 times upper limit of normal
- AST/ALT less than 10 times upper limit of normal
- ❖ Contact Physician if parameters not met

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Cycles 1 to 4 – AC (Dose Dense)		
Instruct patient to start vigorous oral pre-hydration (600-900 mL) the morning of cyclophosphamide treatment (Self-administered at home)		

Treatment Regimen

BRST – BrightNess AC (Dose Dense) followed by PACLitaxel + CARBOplatin

Establish primary solution 500 mL of: normal saline		
Drug	Dose	CCMB Administration Guideline
Cycles 1 to 4 – AC (Dose Dense) every 14 days		
Day 1		
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy

OLANzapine	2.5 mg	Orally 30 minutes pre-chemotherapy
DOXOrubicin	60 mg/m ²	IV Push over 10 to 15 minutes
cyclophosphamide	600 mg/m ²	IV in normal saline 250 mL over 1 hour
Cycle 5 starts two weeks after Cycle 4, Day 1 (AC [Dose Dense])		
Cycles 5 to 8 – PACLitaxel + CARBOplatin every 21 days		
Day 1		
cetirizine	20 mg	Orally 1 hour prior to PACLitaxel
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to PACLitaxel <i>*Nursing Alert: PACLitaxel starts 1 hour after completion of dexamethasone infusion</i>
Wait 1 hour after completion of IV pre-medication(s) before starting PACLitaxel		
PACLitaxel	80 mg/m ²	IV in normal saline 250 mL over 1 hour, following the administration rates below: <ul style="list-style-type: none"> • Administer at 100 mL/hour for 15 minutes, then • Administer remaining volume over 45 minutes <i>Use non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter</i> <i>*Nursing Alert: Gently invert bag 8 to 10 times immediately prior to administration of PACLitaxel to evenly distribute the drug</i>
CARBOplatin	AUC 6 mg/mL.min; maximum dose 900 mg (see table below)	IV in D5W 250 mL over 30 minutes
Days 8 and 15		
cetirizine	20 mg	Orally 1 hour prior to PACLitaxel
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to PACLitaxel <i>*Nursing Alert: PACLitaxel starts 1 hour after completion of dexamethasone infusion</i>
Wait 1 hour after completion of IV pre-medication(s) before starting PACLitaxel		
PACLitaxel	80 mg/m ²	IV in normal saline 250 mL over 1 hour, following the administration rates below: <ul style="list-style-type: none"> • Administer at 100 mL/hour for 15 minutes, then • Administer remaining volume over 45 minutes <i>Use non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter</i> <i>*Nursing Alert: Gently invert bag 8 to 10 times immediately prior to administration of PACLitaxel to evenly distribute the drug</i>

All doses will be automatically rounded that fall within CCMB Approved Dose Bands. See Dose Banding document for more information

In the event of an infusion-related hypersensitivity reaction, refer to the ‘Hypersensitivity Reaction Standing Order’

REQUIRED MONITORING

Cycles 1 to 4 (AC [Dose Dense])

- CBC, biochemistry and liver enzymes as per Physician Orders
- Cardiac monitoring:
 - Left Ventricular Ejection Fraction (LVEF) monitoring is recommended at baseline; only repeated as clinically indicated

Cycles 5 to 8 (PACLitaxel + CARBOplatin)

Day 1

- CBC, biochemistry and liver enzymes as per Physician Orders
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O₂ saturation) at baseline and as clinically indicated
- No observation period required after PACLitaxel administration. Patient can be discharged from treatment room if stable whether they had a reaction or not

Days 8 and 15

- CBC
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O₂ saturation) at baseline and as clinically indicated
- No observation period required after PACLitaxel administration. Patient can be discharged from treatment room if stable whether they had a reaction or not

Recommended Support Medications		
Drug	Dose	CCMB Administration Guideline
Cycles 1 to 4 – AC (Dose Dense)		
pegfilgrastim (brand name specific) (See Filgrastim Clinical Guide)	6 mg	Subcutaneous once on Day 2 <i>*Alert: pegfilgrastim to be given as a single dose once per chemotherapy cycle no sooner than 24 hours after chemotherapy</i>
aprepitant	80 mg	Orally once daily on Days 2 and 3
dexamethasone	8 mg	Orally once daily on Days 2, 3 and 4
OLANzapine	2.5 mg	Orally the evening of Day 1 then twice daily on Days 2, 3 and 4. Also use OLANzapine 2.5 to 5 mg AS NEEDED for breakthrough nausea and vomiting (including Days 1 to 4) up to a maximum of 10 mg per day. Contact clinic if nausea/vomiting is not adequately controlled
Cycles 5 to 8 – PACLitaxel + CARBOplatin		
aprepitant	80 mg	Orally once daily on Days 2 and 3
dexamethasone	8 mg	Orally once daily on Days 2 and 3
metoclopramide	10 – 20 mg	Orally every 4 hours as needed for nausea and vomiting

DISCHARGE INSTRUCTIONS

Cycles 1 to 4 (AC [Dose Dense])

- Ensure patient receives pegfilgrastim supply if patient is self-administering at home
- Instruct patient to:
 - Continue taking anti-emetic(s) at home
 - Maintain oral intake of 2000 mL (8 glasses) of fluid daily at home
 - Empty bladder every 2 hours while awake and at bedtime for 24 hours after each dose of cyclophosphamide
 - Obtain immediate assistance as per your clinic's contact instructions if:
 - Symptoms of hemorrhagic cystitis (e.g. dysuria, hematuria)
 - Unable to drink recommended amount of fluid
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

Cycles 5 to 8 (PACLitaxel + CARBOplatin)

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Instruct patient to continue taking anti-emetic(s) at home. Patients should be instructed not to use OLANzapine and metoclopramide concurrently due to drug interactions
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

ADDITIONAL INFORMATION

- PACLitaxel may cause progressive, irreversible neuropathy
- Cumulative DOXOrubicin dose should be calculated and should not exceed 360 mg/m². If exceeding 360 mg/m², consideration to adding dexrazoxane should be given if patient is benefiting from DOXOrubicin therapy
- **Note:** Upon completion of 4 cycles of **BRST - [BrighTNess - dose dense AC]**, patients should be started on **BRST - [BrighTNess - PACL + CARBO]** to complete 8 cycles
 - **BRST - [BrighTNess - PACL + CARBO]** should begin 14 days after Cycle 4, Day 1 of **BRST - [BrighTNess - dose dense AC]**
- **Note:** At Cycle 4 of each regimen, an entry called “*Physician Reminder – BRIGHTNESS protocol timing 1 Units Insert Miscellaneous once*” will appear in the electronic drug order. No action is required. **This prompt is to remind the prescriber to order the next regimen as part of the BrighTNess protocol**
- CARBOplatin dose considerations:
 - CCMB Breast DSG uses **actual body weight** to calculate GFR
 - CCMB Breast DSG uses a maximum CARBOplatin dose of 900 mg for this regimen
 - If calculated CARBOplatin dose differs **more than 10%** from prescribed CARBOplatin dose, contact the prescriber

CARBOplatin Dosing Calculations per CCMB Breast DSG		
Calculation of CARBOplatin dose: (maximum 900 mg)		
Dose (mg) = target AUC (GFR + 25)		
$\text{GFR} = \frac{N \times (140 - \text{age in years}) \times \text{Actual Body Weight (kg)}}{\text{serum creatinine in micromol/L}} = \text{___ mL/min}$		
N = 1.23 in males N = 1.04 in females		
<div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;"> AUC (mg/mL.min) <hr style="width: 80%; margin: 0 auto;"/> 6 </div>	X	<div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;"> GFR + 25 (mL/min) <hr style="width: 80%; margin: 0 auto;"/> ___ + 25 </div>
		=
<div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;"> Total Dose (mg) <hr style="width: 80%; margin: 0 auto;"/> </div>		

AUC= Area Under Curve

The estimated creatinine clearance is based on limited evidence. Sound clinical judgment and interpretation of the estimation are required, because the equation above may not be appropriate for some patient populations (for example, acute renal failure).