Regimen Reference Order

GYNE – pembrolizumab + PACLitaxel + CARBOplatin (cervix)

ARIA: GYNE - [pembro + PACL + CARBO]

Planned Course: **pembrolizumab + PACLitaxel + CARBOplatin every 21 days for 6 cycles, followed by pembrolizumab every 21 days until disease progression or unacceptable toxicity to a maximum of 2 years total (35 cycles)**

Indication for Use: **Cervical Cancer Recurrent/Metastatic**

Drug Alert: Immune Checkpoint Inhibitor (pembrolizumab)

CVAD: At Provider's Discretion

Proceed with treatment if:

Cycle 1

- ***ANC equal to or greater than 1.5 x 10^9/L AND Platelets equal to or greater than 100 x 10^9/L***
- ***AST/ALT equal to or less than 3 times the upper limit of normal***
- ***Total bilirubin equal to or less than 1.5 times the upper limit of normal***
- ***Creatinine clearance is equal to or greater than 30 mL/minute***

Cycles 2 to 6

- ***ANC equal to or greater than 1.2 x 10^9/L AND Platelets equal to or greater than 75 x 10^9/L***
- ***AST/ALT equal to or less than 3 times the upper limit of normal***
- ***Total bilirubin equal to or less than 1.5 times the upper limit of normal***
- ***Creatinine clearance is equal to or greater than 30 mL/minute***

Cycles 7 to 35

- ***ANC equal to or greater than 1.2 x 10^9/L AND Platelets equal to or greater than 50 x 10^9/L***
- ***AST/ALT equal to or less than 3 times the upper limit of normal***
- ***Total bilirubin equal to or less than 1.5 times the upper limit of normal***
- ***Creatinine clearance is equal to or greater than 30 mL/minute***

❖ **Contact Physician if parameters not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen – GYNE – pembrolizumab + PACLitaxel + CARBOplatin (cervix)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycles 1 to 6 (pembrolizumab + PACLitaxel + CARBOplatin)		
pembrolizumab	2 mg/kg	IV in normal saline 50 mL over 30 minutes *Use 0.2 or 0.22 micron filter*
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 **Nursing Alert: PACLitaxel starts **1 hour after completion** of dexamethasone infusion*
Wait 1 hour after completion of IV pre-medication(s) before starting PACLitaxel		
PACLitaxel	175 mg/m^2	IV in normal saline 500 mL over 3 hours, following the administration rates below: • Administer at 100 mL/hour for 15 minutes, then • Administer remaining volume over 2 hours and 45 minutes *Use non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter* **Nursing Alert: Gently invert bag 8 to 10 times immediately prior to administration of PACLitaxel to evenly distribute the drug*
CARBOplatin	AUC 5 mg/mL.min; maximum dose 900 mg (see table below)	IV in D5W 250 mL over 30 minutes
Cycles 7 to 35 (pembrolizumab)		
pembrolizumab	2 mg/kg	IV in normal saline 50 mL over 30 minutes *Use 0.2 or 0.22 micron filter*

Maximum pembrolizumab dose is 200 mg

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

All Cycles

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin, glucose and TSH as per Physician Orders
- Medical oncologist or designate (i.e. family practitioner in oncology) must assess patient for immune-mediated adverse reactions prior to each cycle
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline and as clinically indicated
- No observation period is required after pembrolizumab or 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 6 ONLY		
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

All Cycles

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Confirm that patient has received the CCMB Immune Checkpoint Inhibitor Medical Alert wallet card
- Reinforce to patient the immune-mediated adverse reactions and the importance of reporting immediately
    - For severe symptoms, the patient should be instructed to go to the nearest emergency room. Oncologist on call should be contacted

Cycles 1 to 6

- Instruct patient to continue taking anti-emetic(s) at home
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

ADDITIONAL INFORMATION

- pembrolizumab is an Immune Checkpoint Inhibitor. Consult with Medical oncologist for immune-mediated adverse reactions; corticosteroids are often indicated
- PACLitaxel may cause progressive, irreversible neuropathy
- CARBOplatin dose considerations:
    - CCMB uses **actual body weight** to calculate GFR
    - CCMB Gynecological DSG uses a maximum CARBOplatin dose of 900 mg for this regimen. **Note that maximum dose is different than standard used in other regimens**
    - If calculated CARBOplatin dose differs **more than 10%** from prescribed CARBOplatin dose, contact the prescriber

CARBOplatin Dosing Calculations per CCMB Gynecological DSG

Calculation of CARBOplatin dose: (maximum 900 mg*)

****maximum dose is different than standard***

Dose (mg) = target AUC (GFR + 25)

$$\text{GFR} = \frac{\text{N} \times (140 - \text{age in years}) \times \text{Actual Body Weight (kg)}}{\text{serum creatinine in micromol/L}} = \_\_\_ \text{ mL/min}$$

N = 1.04 in females

$$\frac{\text{AUC (mg/mL.min)}}{5} \times \frac{\text{GFR + 25 (mL/min)}}{\_\_\_\_ + 25} = \frac{\text{Total Dose (mg)}}{}$$

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 may not be appropriate for some patient populations (for example, acute renal failure).