Regimen Reference Order

GYNE – pembrolizumab + PACLitaxel + CISplatin (cervix)

ARIA: GYNE - [pembro + PACL + CISplatin]

Planned Course: **pembrolizumab + PACLitaxel + CISplatin 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 greater than 45 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 greater than 45 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 + CISplatin (cervix)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycles 1 to 6 (pembrolizumab + PACLitaxel + CISplatin)		
Day 1		
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
OLANZapine	2.5 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*
magnesium sulfate	1 g	IV in normal saline 500 mL over 1 hour (Pre hydration) **Nursing Alert: PACLitaxel starts **immediately after completion** of magnesium sulfate 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*
CISplatin	50 mg/m^2	IV in normal saline 500 mL over 1 hour **Nursing Alert: CISplatin and mannitol may be infused over the same 1-hour period using a Y-site connector (this regimen ONLY)*
mannitol	12.5 g	IV in normal saline 500 mL over 1 hour (Post hydration) **Alert: diluent volume and duration of infusion are different than standards used in other regimens*
Day 2		
magnesium sulfate	2 g	IV in normal saline 1000 mL over 2 hours
Cycles 7 to 35 (pembrolizumab)		
pembrolizumab	200 mg	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
- Baseline blood pressure prior to magnesium infusion and repeat 15 minutes after start of magnesium infusion
- No observation period is required after pembrolizumab and 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, 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

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
- CISplatin is ototoxic and nephrotoxic
- CISplatin can cause hypomagnesemia
- Due to the duration of treatment, administration site restrictions may be in place