Regimen Reference Order – GYNE – pembrolizumab + lenvatinib

ARIA: GYNE - [pembro q21days + lenvatinib]
ARIA: GYNE - [pembro q42days + lenvatinib]
ARIA: GYNE - [pembro + lenvatinib Maint]

Planned Course: **pembrolizumab every 21 days up to a maximum of 2 years (35 cycles) AND lenvatinib once daily until disease progression or unacceptable toxicity**

OR

pembrolizumab every 42 days up to a maximum of 2 years (18 cycles) AND lenvatinib once daily until disease progression or unacceptable toxicity

Indication for Use: **Advanced Endometrial Carcinoma**

Drug Alert: **Immune Checkpoint Inhibitor (pembrolizumab)**

CVAD: **At Provider's Discretion**

Proceed with treatment if:

pembrolizumab + lenvatinib

- ***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 equal to or greater than 30 mL/minute***

lenvatinib Maintenance

- ***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 5 times the upper limit of normal***
- ***Total bilirubin equal to or less than 3 times the upper limit of normal***
- ***Creatinine clearance 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 + lenvatinib

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
pembrolizumab + lenvatinib (Cycles 1 to 35 OR Cycles 1 to 18)		
lenvatinib	14 mg	Orally once daily with or without food Swallow whole **(Self-administered at home)** lenvatinib dose may be increased to 20 mg once daily **at Gyne Oncologist's discretion**
Day 1 ONLY		
pembrolizumab	2 mg/kg (every 21 days) **OR**	IV in normal saline 50 mL over 30 minutes *Use 0.2 or 0.22 micron filter*
	4 mg/kg (every 42 days)	IV in normal saline 100 mL over 30 minutes *Use 0.2 or 0.22 micron filter*
lenvatinib Maintenance (maintenance starts after 2 years of pembrolizumab)		
lenvatinib	14 mg	Orally once daily with or without food Swallow whole **(Self-administered at home)** lenvatinib dose may be increased to 20 mg once daily **at Gyne Oncologist's discretion**

Maximum pembrolizumab dose is 200 mg (every 21 days) or 400 mg (every 42 days)
All doses will be automatically rounded that fall within CCMB Approved Dose Bands. See Dose Banding document for more information

lenvatinib (LENVIMA®) available dosage strengths: 4 mg and 10 mg capsules
Classification: Cytotoxic, Hazardous

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

REQUIRED MONITORING

Cardiac Monitoring (lenvatinib)

- Blood pressure
  - At baseline
  - Weekly during Cycle 1, then
  - Prior to each cycle thereafter
- EKG
  - At baseline
  - Prior to Cycle 2, then as clinically indicated as per Physician Orders
- Monitor for signs of cardiac decompensation
  - Each cycle

Urine protein (lenvatinib)

- Urinalysis for protein: Where urinalysis is not possible, use dipstick. If lab urinalysis for protein is greater than or equal to 1 g/L or dipstick proteinuria shows 2+ or 3+, notify prescriber
    - Prior to each cycle and as clinically indicated

All Cycles
Day 1

- CBC, serum creatinine, urea, electrolytes including calcium, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders
- TSH at baseline, then every 6 weeks thereafter as per Physician Orders

Cycle 1 only
Day 8

- Liver enzymes and total bilirubin as per Physician Orders

pembrolizumab monitoring

- 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 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
metoclopramide	10 – 20 mg	Orally every 4 hours as needed for nausea and vomiting **Alert: If three or more doses of metoclopramide are required in a 24-hour period, please contact Gynecologic cancer Clinic for further instructions*

DISCHARGE INSTRUCTIONS

All Cycles (lenvatinib)

- Ensure patient has been provided with patient information sheet
- Patient should monitor blood pressure at home and record measurements on blood pressure log. This should be done daily for at least the first 2 cycles
- Contact your cancer care team if systolic blood pressure is greater than or equal to 160 mmHg or diastolic blood pressure is greater than or equal to 100 mmHg on two consecutive readings
- Advise patient to report unusual bleeding
- lenvatinib has potential for significant drug-drug interactions. Patients should notify clinic prior to starting any new medication
- Avoid grapefruit and grapefruit juice, Seville oranges (i.e. orange marmalade), and starfruit
- Reinforce applicable safe handling precautions of medications, blood and body fluids while on lenvatinib

Cycles 1 to 35 only OR Cycles 1 to 18 (pembrolizumab)

- Patient 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 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

ADDITIONAL INFORMATION

- pembrolizumab is an Immune Checkpoint Inhibitor. Consult with oncologist for immune-mediated adverse reactions; corticosteroids are often indicated
- lenvatinib can cause hypertension, diarrhea, wound healing complications and thromboembolic events
- lenvatinib can prolong QT interval
- Rare but serious adverse effects such as gastrointestinal perforation and fistulas, posterior reversible encephalopathy syndrome (PRES), arterial thromboembolism, hemorrhage and hepatic, renal and cardiac failure have been reported with lenvatinib
- lenvatinib will be dispensed by CCMB Pharmacy