Regimen Reference Order

ESOPH – pembrolizumab + CARBOplatin + fluorouracil

ARIA: ESOPH - [pembro + CARBOplatin + 5FU]
ESOPH - [pembro q21d (maintenance)]
ESOPH - [pembro q42d (maintenance)]

Planned Course: **pembrolizumab + CARBOplatin + fluorouracil every 21 days for 6 cycles, followed by maintenance pembrolizumab:**

pembrolizumab every 21 days up to 29 cycles or until disease progression or unacceptable toxicity (maximum 2 years of therapy total)

OR

pembrolizumab every 42 days up to 15 cycles or until disease progression or unacceptable toxicity (maximum 2 years of therapy total)

Indication for Use: **Esophageal Cancer/Gastroesophageal Junction Tumor; Metastatic**

Drug Alert: Immune Checkpoint Inhibitor (pembrolizumab)

CVAD: Required (Ambulatory Pump)

Proceed with treatment if:

Cycles 1 to 6

- ***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***

pembrolizumab Maintenance

- ***ANC equal to or greater than 1.5 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 are not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen – ESOPH – pembrolizumab + CARBOplatin + fluorouracil

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycles 1 to 6 – pembrolizumab + CARBOplatin + fluorouracil		
pembrolizumab	2 mg/kg	IV in normal saline 50 mL over 30 minutes *Use 0.2 or 0.22 micron filter*
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
CARBOplatin	AUC 5 mg/mL.min; maximum dose 750 mg (see table below)	IV in D5W 250 mL over 30 minutes
fluorouracil	4000 mg/m^2	IV in D5W continuously over 96 hours by ambulatory infusion device
pembrolizumab Maintenance starts three weeks after Cycle 6, Day 1		
pembrolizumab Maintenance (Cycles 1 to 29 OR Cycles 1 to 15)		
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*

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

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 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
pembrolizumab + CARBOplatin + fluorouracil (Cycles 1 to 6)		
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
pembrolizumab Maintenance		
None required		

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 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
- Ensure patient has received a home chemotherapy spill kit and instructions for use
- 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 oncologist for immune-mediated adverse reactions; corticosteroids are often indicated
- **Note:** Upon completion of 6 cycles of **ESOPH - [pembro + CARBOplatin + 5FU]**, patients should be started on maintenance treatment with **ESOPH - [pembro q21d (maintenance)]** or **ESOPH - [pembro q42d (maintenance)]**
    - **ESOPH - [pembro q21d (maintenance)]** or **ESOPH - [pembro q42d (maintenance)]** regimen starts three weeks after Cycle 6, Day 1 of **ESOPH - [pembro + CARBOplatin + 5FU]**
- CARBOplatin dose considerations:
    - CCMB Gastrointestinal DSG and Thoracic DSG use **actual body weight** to calculate GFR
    - CCMB Gastrointestinal DSG and Thoracic DSG use a maximum CARBOplatin dose of 750 mg for this regimen
    - If calculated CARBOplatin dose differs **more than 10%** from prescribed CARBOplatin dose, contact the prescriber

CARBOplatin Dosing Calculations
per CCMB Gastrointestinal DSG & Thoracic DSG

Calculation of CARBOplatin dose: (maximum 750 mg)

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 = 1.23 in males

N = 1.04 in females

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

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