Regimen Reference Order

ESOPH – pembrolizumab + CISplatin + fluorouracil

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

Planned Course: **pembrolizumab + CISplatin + 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/Gastroesophageal Junction Tumor/Gastric Cancer; 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 greater than 45 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 + CISplatin + fluorouracil

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycles 1 to 6 – pembrolizumab + CISplatin + fluorouracil		
pembrolizumab	2 mg/kg	IV in normal saline 50 mL over 30 minutes *Use 0.2 or 0.22 micron filter*
magnesium sulfate	2 g	IV in normal saline 1000 mL over 2 hours (Pre hydration)
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
CISplatin	80 mg/m^2	IV in normal saline 500 mL over 1 hour **Alert: CISplatin infusion must be complete prior to mannitol administration*
mannitol	12.5 g	IV in normal saline 1000 mL over 2 hours (Post hydration)
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 and glucose as per Physician Orders
- TSH every 6 weeks 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
- Cycles 1 to 6 only (cycles with CISplatin): Baseline blood pressure prior to magnesium infusion and repeat 15 minutes after start of magnesium infusion
- 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 + CISplatin + 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, 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
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
- CISplatin is ototoxic and nephrotoxic
- CISplatin can cause hypomagnesemia
- **ARIA ordering:**
  Note: Upon completion of 6 cycles of **ESOPH - [pembro + CISplatin + 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 21 days after Cycle 6, Day 1 of **ESOPH - [pembro + CISplatin + 5FU]**