

Regimen Reference Order – ESOPH – pembrolizumab + FOLFOX-6

ARIA: ESOPH - [pembrolizumab + FOLFOX-6]

ESOPH - [pembro q21d (maintenance)]

ESOPH - [pembro q42d (maintenance)]

Planned Course: FOLFOX-6 every 14 days for 9 cycles with pembrolizumab every 42 days, 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)

See Appendix (page 5) for regimen Dosing Schema

Indication for Use: Esophageal/Gastroesophageal Junction Tumor/Gastric Cancer Metastatic

Drug Alert: Immune Checkpoint Inhibitor (pembrolizumab)

CVAD: Required (Ambulatory Pump)

Proceed with treatment if:

FOLFOX-6

- *ANC equal to or greater than $1.5 \times 10^9/L$ AND Platelets equal to or greater than $100 \times 10^9/L$*
 - *ANC equal to or greater than $1.5 \times 10^9/L$ AND Platelets equal to or greater than $50 \times 10^9/L$*
 - *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 – ESOPH – pembrolizumab + FOLFOX-6

Establish primary solution 500 mL of: D5W

Drug	Dose	CCMB Administration Guideline
Cycles 1, 4 and 7 – pembrolizumab + FOLFOX-6		
pembrolizumab	4 mg/kg	IV in normal saline 100 mL over 30 minutes Use 0.2 or 0.22 micron filter

ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
oxaliplatin	85 mg/m ²	IV in D5W 500 mL over 2 hours
fluorouracil	2400 mg/m ²	IV in D5W continuously over 46 hours by ambulatory infusion device
Cycles 2, 3, 5, 6, 8 and 9 – FOLFOX-6		
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
oxaliplatin	85 mg/m ²	IV in D5W 500 mL over 2 hours
fluorouracil	2400 mg/m ²	IV in D5W continuously over 46 hours by ambulatory infusion device
pembrolizumab Maintenance starts two weeks after Cycle 9, 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 <i>Use 0.2 or 0.22 micron filter</i>
	4 mg/kg (every 42 days)	IV in normal saline 100 mL over 30 minutes <i>Use 0.2 or 0.22 micron filter</i>
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 dose of pembrolizumab
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O₂ 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 + FOLFOX-6 (Cycles 1 to 9)		
dexamethasone	8 mg	Orally once daily on Days 2 and 3
prochlorperazine	10 mg	Orally every 6 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 9

- 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
- Numerous dosing variations exist for FOLFOX and depend on the primary cancer diagnosis
- oxaliplatin causes cold intolerance and laryngopharyngeal dysesthesia
 - no ice chips or cold drinks
- oxaliplatin may cause progressive, irreversible neuropathy
 - dose modification may be required
- **ARIA ordering:**

Note: Upon completion of 9 cycles of **ESOPH - [pembrolizumab + FOLFOX-6]**, 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 14 days after Cycle 9, Day 1 of **ESOPH - [pembrolizumab + FOLFOX-6]**

Appendix Dosing Schema

ESOPH - [pembrolizumab + FOLFOX-6] – Cycles 1 to 9 (14-day cycle)

		Cycle 1			Cycle 2			Cycle 3			Cycle 4			Cycle 5			Cycle 6			
		Day	1	8	Day	1	8	Day	1	8	Day	1	8	Day	1	8	Day	1	8	
	pembrolizumab		█									█								
	FOLFOX-6		█		█			█			█			█			█			█

		Cycle 7			Cycle 8			Cycle 9		
		Day	1	8	Day	1	8	Day	1	8
	pembrolizumab		█							
	FOLFOX-6		█		█			█		

Starting 14 days after Cycle 9, Day 1 of ESOPH - [pembrolizumab + FOLFOX-6]:

ESOPH - [pembro q21d (maintenance)]

		Cycles 1 to 29 (21-day cycle)			
		Day	1	8	15
	pembrolizumab		█		

OR

ESOPH - [pembro q42d (maintenance)]

		Cycles 1 to 15 (42-day cycle)						
		Day	1	8	15	22	29	36
	pembrolizumab		█					

Key:



Indicates that *pembrolizumab* will be administered on this day



Indicates that *chemotherapy* will be administered on this day