

Regimen Reference Order

THOR – pembrolizumab + gemcitabine + CISplatin

ARIA: LUNG – [pembro + gemcitabine + CISplatin]

LUNG – [pembrolizumab q 21 days (maintenance)]

LUNG – [pembrolizumab q 42 days (maintenance)]

Planned Course: pembrolizumab + gemcitabine + CISplatin every 21 days for 4 cycles, followed by pembrolizumab every 21 days up to 31 cycles or until disease progression or unacceptable toxicity (maximum 2 years of therapy)

OR

pembrolizumab + gemcitabine + CISplatin every 21 days for 4 cycles, followed by pembrolizumab every 42 days up to 16 cycles or until disease progression or unacceptable toxicity (maximum 2 years of therapy)

Indication for Use: Lung Cancer Non-Small Cell Squamous Metastatic

Drug Alert: Immune Checkpoint Inhibitor (pembrolizumab)

CVAD: At Provider’s Discretion

Proceed with treatment if:

Day 1 of Cycles 1 to 4

- *ANC equal to or greater than $1.5 \times 10^9/L$ AND Platelets equal to or greater than $100 \times 10^9/L$*
- *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 greater than 45 mL/minute*

Day 8 of Cycles 1 to 4

- *ANC equal to or greater than $1.5 \times 10^9/L$ AND Platelets equal to or greater than $100 \times 10^9/L$*

pembrolizumab Maintenance

- *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 – THOR – pembrolizumab + gemcitabine + CISplatin

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
pembrolizumab + gemcitabine + CISplatin (Cycles 1 to 4)		
Day 1		
pembrolizumab	2 mg/kg	IV in normal saline 50 mL over 30 minutes Use 0.2 or 0.22 micron filter <i>Concentration dependent drug: Pharmacy will adjust diluent volume to ensure drug stability</i>
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
gemcitabine	1000 mg/m ²	IV in normal saline 250 mL over 30 minutes
CISplatin	75 mg/m ²	IV in normal saline 500 mL over 1 hour <i>*Alert: CISplatin infusion must be complete prior to mannitol administration</i>
mannitol	12.5 g	IV in normal saline 1000 mL over 2 hours (Post hydration)
Day 8		
dexamethasone	8 mg	Orally 30 minutes pre-chemotherapy
gemcitabine	1000 mg/m ²	IV in normal saline 250 mL over 30 minutes
pembrolizumab Maintenance (Cycles 1 to 31 OR Cycles 1 to 16)		
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 <i>Concentration dependent drug: Pharmacy will adjust diluent volume to ensure drug stability</i>
	4 mg/kg (every 42 days)	IV in normal saline 50 mL over 30 minutes Use 0.2 or 0.22 micron filter <i>Concentration dependent drug: Pharmacy will adjust diluent volume to ensure drug stability</i>
<p>Maximum pembrolizumab dose is 200 mg (every 21 days) or 400 mg (every 42 days) All doses will be automatically rounded that fall within the DSG Approved Dose Bands. See THOR DSG – Dose Banding document for more information</p>		

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

REQUIRED MONITORING

All Cycles

Day 1

- CBC, serum creatinine, urea, liver enzymes, total bilirubin, albumin, glucose, electrolytes, TSH and T4 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 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

Cycles 1 to 4

Day 1

- Baseline blood pressure prior to magnesium infusion and repeat 15 minutes after start of magnesium infusion

Day 8

- CBC

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
pembrolizumab + gemcitabine + CISplatin (Cycles 1 to 4)		
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 (Cycles 1 to 31 OR Cycles 1 to 16)		
None required		

DISCHARGE INSTRUCTIONS

All Cycles

- 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

Cycles 1 to 4

- 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 oncologist for immune-mediated adverse reactions; corticosteroids are often indicated
- CISplatin is ototoxic and nephrotoxic
- CISplatin can cause hypomagnesemia
- Upon completion of 4 cycles of **LUNG – [pembro + gemcitabine + CISplatin]**, patients should be started on maintenance treatment with **LUNG – [pembrolizumab q 21 days (maintenance)]** or **LUNG – [pembrolizumab q 42 days (maintenance)]**
 - LUNG – [pembrolizumab q 21 days (maintenance)] or LUNG – [pembrolizumab q 42 days (maintenance)] regimen starts three weeks after completing LUNG – [pembro + gemcitabine + CISplatin]