

Regimen Reference Order

THOR – pembrolizumab + PEMEtrexed + CISplatin

ARIA: LUNG – [pembro + PEMEtrexed + CIS]

LUNG – [pembro + PEMEtrexed (maint)]

LUNG – PEMEtrexed + pembro support

Planned Course: pembrolizumab + PEMEtrexed + CISplatin every 21 days for 4 cycles, followed by pembrolizumab and PEMEtrexed every 21 days for up to 31 cycles or until disease progression or unacceptable toxicity (maximum 35 doses total = 2 years of therapy)

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

Drug Alert: Immune Checkpoint Inhibitor (pembrolizumab)

CVAD: At Provider's Discretion

Proceed with treatment if:

- *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*
- ❖ Contact Physician if parameters not met

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
folic acid	1 mg	Orally daily beginning 7 – 14 days prior to first dose of PEMEtrexed and continuing daily until 21 days after the last dose of PEMEtrexed (Self-administered at home)
vitamin B12	1000 mcg	Intramuscularly 7 – 14 days prior to first dose of PEMEtrexed (Note: vitamin B12 continues every 9 weeks until 6 weeks after last dose of PEMEtrexed)
dexamethasone	8 mg	Orally once daily the day before, day of and the day after each dose of PEMEtrexed (Higher or additional doses are permitted) (Self-administered at home)

Treatment Regimen – THOR – pembrolizumab + PEMEtrexed + CISplatin

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
pembrolizumab + PEMEtrexed + CISplatin (Cycles 1 to 4)		
pembrolizumab	2 mg/kg	IV in normal saline 50 mL over 30 minutes <i>Use 0.2 or 0.22 micron filter</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	4 mg	Orally 30 minutes pre-chemotherapy *Nursing Alert: this dose is in addition to the 8 mg self-administered dose taken at home morning of Day 1
OLANzapine	2.5 mg	Orally 30 minutes pre-chemotherapy
PEMEtrexed	500 mg/m ²	IV in normal saline 100 mL over 10 minutes *Nursing Alert: CISplatin starts at least 30 minutes after completion of PEMEtrexed infusion
CISplatin	75 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)
vitamin B12	1000 mcg	Intramuscularly once Cycle 4
pembrolizumab + PEMEtrexed Maintenance (Cycles 1 to 31)		
pembrolizumab	2 mg/kg	IV in normal saline 50 mL over 30 minutes <i>Use 0.2 or 0.22 micron filter</i>
PEMEtrexed	500 mg/m ²	IV in normal saline 100 mL over 10 minutes
vitamin B12	1000 mcg	Intramuscularly once every 9 weeks throughout treatment and for one additional dose upon discontinuation of PEMEtrexed *Nursing Alert: vitamin B12 will be given on Day 1 of maintenance Cycles 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, and six weeks after Cycle 31, Day 1

Maximum pembrolizumab dose is 200 mg

All doses will be automatically rounded that fall within the DSG Approved Dose Bands. See THOR DSG – 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 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

pembrolizumab + PEMEtrexed + CISplatin (Cycles 1 to 4)

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

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
pembrolizumab + PEMEtrexed + CISplatin (Cycles 1 to 4)		
aprepitant	80 mg	Orally once daily on Days 2 and 3
dexamethasone	8 mg	Orally once daily on Days 3 and 4 Note additional Pre-treatment Requirements for PEMEtrexed
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 + PEMEtrexed Maintenance (Cycles 1 to 31)		
metoclopramide	10 – 20 mg	Orally every 4 hours as needed for nausea and vomiting

DISCHARGE INSTRUCTIONS

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Instruct patient to continue taking folic acid, dexamethasone and anti-emetic(s) at home. Patients should be instructed not to use olanzapine and metoclopramide concurrently due to drug interactions
- vitamin B12 is part of this treatment regimen. Patient should notify clinic if they are receiving vitamin B12 for other indications
- 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
- 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
- folic acid, vitamin B12 and dexamethasone are prescribed to decrease PEMEtrexed toxicity
- During pembrolizumab + PEMEtrexed + CISplatin cycles, dexamethasone is also prescribed post treatment for delayed nausea
- Non-Steroidal Anti-Inflammatory drugs (NSAIDs) may increase the toxicity of PEMEtrexed. Hold NSAIDs for 2 days before, the day of and for 2 days after PEMEtrexed
- Support protocol under **PEM + pembro Support** in the “Lung Cancer” folder is to be used to order folic acid and the first and last dose of vitamin B12
- **Note:** Upon completion of 4 cycles of **LUNG – [pembro + PEMEtrexed + CIS]**, patients should be started on maintenance treatment with **LUNG – [pembro + PEMEtrexed (maint)]**
 - **LUNG – [pembro + PEMEtrexed (maint)]** should begin 21 days after Cycle 4, Day 1 of **LUNG – [pembro + PEMEtrexed + CIS]**