

Regimen Reference Order

THOR – nivolumab + PEMEtrexed + CISplatin (Neo-Adjuvant)

ARIA: LUNG - [nivo + PEME + CIS (neoadj)]

ARIA Support: LUNG - PEMEtrexed Support (NSCLC)

Planned Course: Every 21 days for 3 cycles

Indication for Use: Lung Cancer Non-Small Cell Non-Squamous, Resectable; Neo-Adjuvant

Drug Alert: Immune Checkpoint Inhibitor (nivolumab)

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 equal to or greater than 45 mL/minute
- ❖ DO NOT DELAY OR CANCEL THERAPY WITHOUT CONSULTING MEDICAL ONCOLOGIST

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
folic acid	1 mg	Orally daily beginning 7 to 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	Intramuscular 7 to 14 days prior to first dose of PEMEtrexed (Note: a second dose of vitamin B12 to be administered on Cycle 3, Day 1)
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 – nivolumab + PEMEtrexed + CISplatin (Neo-Adjuvant)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
nivolumab	4.5 mg/kg	IV in normal saline 100 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 <i>*Nursing Alert: This dose is in addition to the 8 mg self-administered dose taken at home morning of Day 1</i>
OLANzapine	2.5 mg	Orally 30 minutes pre-chemotherapy
PEMEtrexed	500 mg/m ²	IV in normal saline 100 mL over 10 minutes <i>*Nursing Alert: CISplatin starts at least 30 minutes after completion of PEMEtrexed infusion</i>
CISplatin	75 mg/m ²	IV in normal saline 500 mL over 1 hour <i>*Alert: CISplatin infusion must be completed prior to mannitol administration</i>
mannitol	12.5 g	IV in normal saline 1000 mL over 2 hours (Post hydration)
vitamin B12	1000 mcg	Cycle 3 only: Intramuscular once <i>*Alert: This is the last dose of vitamin B12 that will be given as part of this regimen</i>
Maximum nivolumab dose is 360 mg 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 O₂ saturation) at baseline and as clinically indicated
- Baseline blood pressure immediately prior to magnesium infusion and repeat 15 minutes after start of magnesium infusion
- No observation period is required after nivolumab 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
aprepitant	80 mg	Orally once daily on Days 2 and 3
dexamethasone	8 mg	Orally once daily on Day 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

DISCHARGE INSTRUCTIONS

- 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
- Instruct patient to continue taking folic acid, dexamethasone and anti-emetic(s) at home
- vitamin B12 is part of this treatment regimen. Patient should notify clinic if they are receiving vitamin B12 for other indications
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

ADDITIONAL INFORMATION

- nivolumab is an Immune Checkpoint Inhibitor. Consult with oncologist for immune-mediated adverse reactions; corticosteroids are often indicated
- Thoracic Surgeon will order and assess morning cortisol and TSH pre-operative to assess for preoperative immune-related endocrinopathies
- CISplatin is ototoxic and nephrotoxic
- CISplatin can cause hypomagnesemia
- folic acid, vitamin B12 and dexamethasone are prescribed to decrease PEMEtrexed toxicity
- 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 **PEME Support (NSCLC)** in the “Lung Cancer” folder is to be used to order folic acid and the first dose of vitamin B12