Regimen Reference Order

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

ARIA: LUNG - [nivo + PEME + CIS (neoadj)]
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 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 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	360 mg	IV in normal saline 100 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	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 completed prior to mannitol administration*
mannitol	12.5 g	IV in normal saline 1000 mL over 2 hours (Post hydration)
vitamin B12	1000 mcg	Cycle 3 only: Intramuscular once **Alert: This is the last dose of vitamin B12 that will be given as part of this regimen*

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 O_2 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. 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
- 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