Regimen Reference Order

THOR – nivolumab + ipilimumab + PACLitaxel + CARBOplatin

ARIA: LUNG - [nivo + ipi + PACL + CARBO]

Planned Course: **Cycle 1: nivolumab + ipilimumab + PACLitaxel + CARBOplatin, then**
Cycle 2: nivolumab + PACLitaxel + CARBOplatin, then
Cycle 3 and Onwards: nivolumab + ipilimumab alternating with nivolumab until disease progression or unacceptable toxicity up to a maximum of 33 cycles
(1 cycle = 21 days)

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

Drug Alert: Immune Checkpoint Inhibitor (nivolumab and ipilimumab)

CVAD: At Provider's Discretion

Proceed with treatment if:

Cycles 1 and 2

- ***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 30 mL/minute***

Cycle 3 and Onwards

- ***ANC equal to or greater than 1.5 x 10^9/L AND Platelets equal to or greater than 50 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 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 – nivolumab + ipilimumab + PACLitaxel + CARBOplatin

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1 – nivolumab + ipilimumab + PACLitaxel + CARBOplatin		
nivolumab	4.5 mg/kg	IV in normal saline 100 mL over 30 minutes *Use 0.2 or 0.22 micron filter* **Nursing Alert: After completion of nivolumab infusion, wait 30 minutes before administering ipilimumab* **Nursing Alert: Start a new primary infusion line for ipilimumab*
ipilimumab	1 mg/kg	IV in normal saline 50 mL over 30 minutes *Use 0.2 or 0.22 micron filter*
cetirizine	20 mg	Orally 1 hour prior to PACLitaxel
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to PACLitaxel **Nursing Alert: PACLitaxel starts **1 hour after completion** of dexamethasone infusion*
Wait 1 hour after completion of IV pre-medication(s) before starting PACLitaxel		
PACLitaxel	200 mg/m^2	IV in normal saline 500 mL over 3 hours, following the administration rates below: • Administer at 100 mL/hour for 15 minutes, then • Administer remaining volume over 2 hours and 45 minutes *Use non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter* **Nursing Alert: Gently invert bag 8 to 10 times immediately prior to administration of PACLitaxel to evenly distribute the drug*
CARBOplatin	AUC 6 mg/mL.min; maximum dose 900 mg (see table below)	IV in D5W 250 mL over 30 minutes
Cycle 2 – nivolumab + PACLitaxel + CARBOplatin		
nivolumab	4.5 mg/kg	IV in normal saline 100 mL over 30 minutes *Use 0.2 or 0.22 micron filter*
cetirizine	20 mg	Orally 1 hour prior to PACLitaxel
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy

dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to PACLitaxel **Nursing Alert: PACLitaxel starts **1 hour after completion** of dexamethasone infusion*
Wait 1 hour after completion of IV pre-medication(s) before starting PACLitaxel		
PACLitaxel	200 mg/m^2	IV in normal saline 500 mL over 3 hours, following the administration rates below: • Administer at 100 mL/hour for 15 minutes, then • Administer remaining volume over 2 hours and 45 minutes *Use non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter* **Nursing Alert: Gently invert bag 8 to 10 times immediately prior to administration of PACLitaxel to evenly distribute the drug*
CARBOplatin	AUC 6 mg/mL.min; maximum dose 900 mg (see table below)	IV in D5W 250 mL over 30 minutes
Cycles 3 to 35 **(Note: Cycles alternate between nivolumab + ipilimumab [odd Cycles] and nivolumab [even Cycles])**		
Cycles 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33 and 35 – nivolumab + ipilimumab		
nivolumab	4.5 mg/kg	IV in normal saline 100 mL over 30 minutes *Use 0.2 or 0.22 micron filter* **Nursing Alert: After completion of nivolumab infusion, wait 30 minutes before administering ipilimumab* **Nursing Alert: Start a new primary infusion line for ipilimumab*
ipilimumab	1 mg/kg	IV in normal saline 50 mL over 30 minutes *Use 0.2 or 0.22 micron filter*
Cycles 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32 and 34 – nivolumab		
nivolumab	4.5 mg/kg	IV in normal saline 100 mL over 30 minutes *Use 0.2 or 0.22 micron filter*
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
- Cortisol levels should be checked prior to each ipilimumab dose (every second cycle) and at physician's discretion
- 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
- No observation period is required after nivolumab, ipilimumab or PACLitaxel. Patient can be discharged from treatment room if stable whether they had a reaction or not

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
Cycles 1 and 2		
aprepitant	80 mg	Orally once daily on Days 2 and 3
dexamethasone	8 mg	Orally once daily on Days 2 and 3
metoclopramide	10 – 20 mg	Orally every 4 hours as needed for nausea and vomiting
Cycles 3 to 35		
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 and 2

- 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

- Grade 3/4 toxicities are very common with this regimen
- PACLitaxel may cause progressive, irreversible neuropathy
- nivolumab and ipilimumab are Immune Checkpoint Inhibitors. Consult with oncologist for immune-mediated adverse reactions; corticosteroids are often indicated
- Administration site restrictions are in place for ipilimumab. ipilimumab should only be administered at a facility where pharmacy compounding occurs on site

- CARBOplatin dose considerations:
  - CCMB Thoracic DSG uses **actual body weight** to calculate GFR
  - CCMB Thoracic DSG uses a maximum CARBOplatin dose of 900 mg for this regimen
  - If calculated CARBOplatin dose differs **more than 10%** from prescribed CARBOplatin dose, contact the prescriber

CARBOplatin Dosing Calculations per CCMB Thoracic DSG

Calculation of CARBOplatin dose: (maximum 900 mg)

Dose (mg) = target AUC (GFR + 25)

$$GFR = \frac{N \times (140 - \text{age in years}) \times \text{Actual Body Weight (kg)}}{\text{serum creatinine in micromol/L}} = \_\_\_ \text{ mL/min}$$

N = 1.23 in males
N = 1.04 in females

$$\frac{\text{AUC (mg/mL.min)}}{6} \times \frac{\text{GFR + 25 (mL/min)}}{\_\_\_\_ + 25} = \frac{\text{Total Dose (mg)}}{}$$

AUC = Area Under Curve

The estimated creatinine clearance is based on limited evidence. Sound clinical judgment and interpretation of the estimation are required, because the equation above may not be appropriate for some patient populations (for example, acute renal failure).