

Regimen Reference Order

THOR – nivolumab + gemcitabine + CARBOplatin (Neo-Adjuvant)

ARIA: LUNG - [nivo + gem + CARBO (neoadj)]

Planned Course: Every 21 days for 3 cycles
Indication for Use: Non-Small Cell Lung Cancer Squamous Cell, Resectable; Neo-Adjuvant
Drug Alert: Immune Checkpoint Inhibitor (nivolumab)
CVAD: At Provider’s Discretion

<u>Proceed with treatment if:</u>
Day 1
<ul style="list-style-type: none"> • 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 30 mL/minute
Day 8
<ul style="list-style-type: none"> • ANC equal to or greater than $1.5 \times 10^9/L$ AND Platelets equal to or greater than $100 \times 10^9/L$ <p style="text-align: center;">❖ DO NOT DELAY OR CANCEL THERAPY WITHOUT CONSULTING MEDICAL ONCOLOGIST</p>

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements		
Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen		
THOR – nivolumab + gemcitabine + CARBOplatin (Neo-Adjuvant)		
Establish primary solution 500 mL of: normal saline		
Drug	Dose	CCMB Administration Guideline
Day 1		
nivolumab	4.5 mg/kg	IV in normal saline 100 mL over 30 minutes <i>Use 0.2 or 0.22 micron filter</i>
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
gemcitabine	1000 mg/m^2	IV in normal saline 250 mL over 30 minutes

CARBOplatin	AUC 6 mg/mL.min; maximum dose 900 mg (see table below)	IV in D5W 250 mL over 30 minutes
Day 8		
dexamethasone	8 mg	Orally 30 minutes pre-chemotherapy
gemcitabine	1000 mg/m ²	IV in normal saline 250 mL over 30 minutes
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

Day 1

- 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 nivolumab administration. Patient can be discharged from treatment room if stable whether they had a reaction or not

Day 8

- CBC

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 Days 2 and 3
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
- 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 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

- 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
- CARBOplatin dosing 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										
<i>Calculation of CARBOplatin dose: (maximum 900 mg)</i>										
Dose (mg) = target AUC (GFR + 25)										
$\text{GFR} = \frac{N \times (140 - \text{age in years}) \times \text{Actual Body Weight (kg)}}{\text{serum creatinine in micromol/L}} = \text{___ mL/min}$										
N = 1.23 in males N = 1.04 in females										
<table border="1" style="margin: auto; border-collapse: collapse;"> <tr> <td style="padding: 5px;">AUC (mg/mL.min)</td> </tr> <tr> <td style="border-top: 1px solid black; padding: 5px;">6</td> </tr> </table>	AUC (mg/mL.min)	6	X	<table border="1" style="margin: auto; border-collapse: collapse;"> <tr> <td style="padding: 5px;">GFR + 25 (mL/min)</td> </tr> <tr> <td style="border-top: 1px solid black; padding: 5px;">___ + 25</td> </tr> </table>	GFR + 25 (mL/min)	___ + 25	=	<table border="1" style="margin: auto; border-collapse: collapse;"> <tr> <td style="padding: 5px;">Total Dose (mg)</td> </tr> <tr> <td style="border-top: 1px solid black; padding: 5px;"> </td> </tr> </table>	Total Dose (mg)	
AUC (mg/mL.min)										
6										
GFR + 25 (mL/min)										
___ + 25										
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).