Regimen Reference Order

H&N – pembrolizumab + CISplatin + fluorouracil

ARIA: H&N – [pembro + CISplatin + fluorouracil]
H&N – [pembrolizumab q 21 d (maintenance)]
H&N – [pembrolizumab q 42 d (maintenance)]

Planned Course: **pembrolizumab + CISplatin + fluorouracil every 21 days for 6 cycles, followed by pembrolizumab every 21 days up to 29 cycles or until disease progression or unacceptable toxicity (maximum 2 years of therapy)**

OR

pembrolizumab + CISplatin + fluorouracil every 21 days for 6 cycles, followed by pembrolizumab every 42 days up to 15 cycles or until disease progression or unacceptable toxicity (maximum 2 years of therapy)

Indication for Use: **Squamous Cell Cancer of Head and Neck, Advanced/Recurrent**

Drug Alert: Immune Checkpoint Inhibitor (pembrolizumab)

CVAD: Required (Ambulatory Pump)

Proceed with treatment if:

Cycles 1 to 6

- ***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 greater than 45 mL/minute***

pembrolizumab Maintenance

- ***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 are not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen – H&N – pembrolizumab + CISplatin + fluorouracil

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
pembrolizumab + CISplatin + fluorouracil (Cycles 1 to 6)		
pembrolizumab	2 mg/kg	IV in normal saline 50 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	12 mg	Orally 30 minutes pre-chemotherapy
OLANZapine	2.5 mg	Orally 30 minutes pre-chemotherapy
CISplatin	100 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)
fluorouracil	4000 mg/m^2	IV in D5W continuously over 96 hours by ambulatory infusion device
pembrolizumab Maintenance (Cycles 1 to 29 OR Cycles 1 to 15)		
pembrolizumab	2 mg/kg (every 21 days) **OR**	IV in normal saline 50 mL over 30 minutes *Use 0.2 or 0.22 micron filter*
	4 mg/kg (every 42 days)	IV in normal saline 50 mL over 30 minutes *Use 0.2 or 0.22 micron filter*

Maximum pembrolizumab dose is 200 mg (every 21 days) or 400 mg (every 42 days)
All doses will be automatically rounded that fall within the DSG Approved Dose Bands. See H&N 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 O_2 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

Cycles 1 to 6 Only

- 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 + CISplatin + fluorouracil (Cycles 1 to 6)		
aprepitant	80 mg	Orally once daily on Days 2 and 3
dexamethasone	8 mg	Orally once daily on Days 2, 3 and 4
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 Maintenance (Cycles 1 to 29 OR Cycles 1 to 15)		
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 to 6

- Instruct patient to continue taking anti-emetic(s) at home
- Ensure patient has received a home chemotherapy spill kit and instructions for use
- 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
- Upon completion of 6 cycles of **H&N – [pembro + CISplatin + fluorouracil]**, patients should be started on maintenance treatment with **H&N – [pembrolizumab q 21 d (maintenance)]** or **H&N – [pembrolizumab q 42 d (maintenance)]**
    - H&N – [pembrolizumab q 21 d (maintenance)] or H&N – [pembrolizumab q 42 d (maintenance)] regimen starts three weeks after completing H&N – [pembro + CISplatin + fluorouracil]