Regimen Reference Order – GENU – nivolumab + ipilimumab

ARIA: GENU – [nivolumab + ipilimumab (Phase 1)]
GENU – [nivolumab q 14 days (Phase 2)]
GENU – [nivolumab q 28 days (Phase 2)]

Planned Course: **Phase 1: nivolumab and ipilimumab every 21 days for 4 cycles**
Phase 2: nivolumab every 14 days OR every 28 days until disease progression or unacceptable toxicity

Indication for Use: **Renal Cell Cancer, Advanced or Metastatic**

Drug Alert: Immune Checkpoint Inhibitor

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 50 x 10^9/L***
- ***AST/ALT less than 3 times upper limit of normal***
- ***Total bilirubin less than 1.5 times upper limit of normal***
- ***Creatinine clearance greater than 30 mL/min***
  - **Contact Physician if parameters not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen – GENU – nivolumab + ipilimumab

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Phase 1 nivolumab + ipilimumab (Cycles 1 to 4)		
nivolumab	3 mg/kg	IV in normal saline 100 mL over 30 minutes Use 0.2 or 0.22 micron filter Concentration dependent drug: Pharmacy will adjust diluent volume to ensure drug stability **After completion of nivolumab infusion, wait 30 minutes before administering ipilimumab**
ipilimumab	1 mg/kg	IV in normal saline 50 mL over 30 minutes Use 0.2 or 0.22 micron filter Concentration dependent drug: Pharmacy will adjust diluent volume to ensure drug stability

All doses will be automatically rounded that fall within the DSG Approved Dose Bands. See GENU DSG – Dose Banding document for more information

Phase 2 nivolumab monotherapy		
nivolumab 3 mg/kg dose: Phase 2 starts three weeks after Phase 1 (Cycle 4) **OR** **nivolumab 6 mg/kg dose: Phase 2 starts six weeks after Phase 1 (Cycle 4)**		
nivolumab	3 mg/kg (every 14 days) **OR**	IV in normal saline 100 mL over 30 minutes Use 0.2 or 0.22 micron filter Concentration dependent drug: Pharmacy will adjust diluent volume to ensure drug stability
	6 mg/kg (every 28 days)	IV in normal saline 100 mL over 30 minutes Use 0.2 or 0.22 micron filter Concentration dependent drug: Pharmacy will adjust diluent volume to ensure drug stability
<u>Phase 2 ONLY:</u> Maximum nivolumab dose is 240 mg (every 14 days) OR 480 mg (every 28 days) All doses will be automatically rounded that fall within the DSG Approved Dose Bands. See GENU DSG – Dose Banding document for more information		

Flush after each medication:

- 50 mL over 6 minutes (500 mL/hr)

In the event of an infusion-related hypersensitivity reaction, refer to the '**Hypersensitivity Reaction Standing Order'**

REQUIRED MONITORING

All Cycles

- CBC, creatinine, electrolytes, liver enzymes, total bilirubin, TSH, T4 and glucose as per Physician Orders
- Cortisol levels should be checked prior to each cycle of Phase 1 due to the ipilimumab and then at physician's discretion starting with Phase 2
- Lipase level 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
- Patient can be discharged from treatment room if stable whether they had a reaction or not

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
Not Applicable		

DISCHARGE INSTRUCTIONS

- 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

ADDITIONAL INFORMATION

- Phase 1 GENU – nivolumab + ipilimumab doses are different than Phase 1 CUTA - nivolumab + ipilimumab doses
- Grade 3/4 toxicities are very common with this regimen
- 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 nivolumab and ipilimumab. Cycle 1 nivolumab and ipilimumab combination must be administered at CCMB MacCharles in Winnipeg. ipilimumab should only be administered at a facility where pharmacy compounding occurs on site