BC Cancer Protocol Summary for Neoadjuvant Treatment of Muscle-Invasive Bladder Cancer using Durvalumab, Platinum and Gemcitabine

Protocol Code	*GUBNADURPG*
Tumour Group	*Genitourinary*
Contact Physician	*GU Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Muscle-invasive bladder cancer (MIBC),
- Clinical stage T2N0-1M0 to T4aN0-1M0,
- No prior systemic treatment for MIBC,
- Planned radical cystectomy or bladder-sparing trimodal therapy

Patients should have:

- Good performance status,
- Adequate hepatic and renal function,
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of durvalumab

Notes:

- Patients who started neoadjuvant gemcitabine/platinum prior to 1 Sep 2026 may switch to GUBNADURPG if progression-free and all other eligibility criteria are met

EXCLUSIONS:

Patients must not have:

- Any small-cell histologic features
- Pure non-urothelial carcinoma

CAUTIONS:

- Inadequate renal function (creatinine clearance less than 45 mL/min by GFR measurement or Cockcroft formula) unless treated with CARBOplatin
- Active or previous autoimmune disease
- Patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)

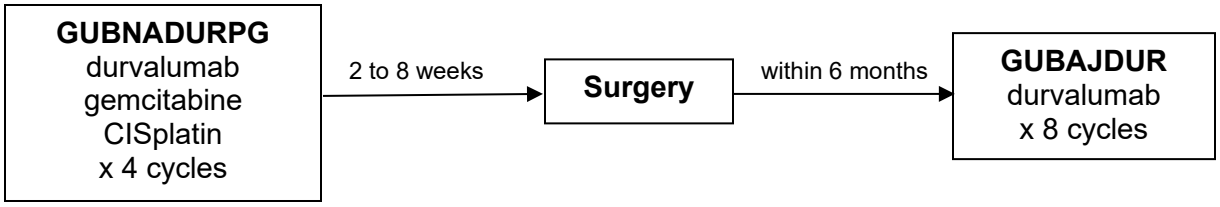
TESTS:

- Baseline: CBC & Diff, creatinine, sodium, potassium, ALT, alkaline phosphatase, total bilirubin, LDH, TSH, morning serum cortisol, chest x-ray or CT chest
- Prior to each treatment:
  - Day 1: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH
  - Day 8: CBC & Diff
  - Day 8, if using split-dose CISplatin: creatinine
- If clinically indicated: chest x-ray, morning serum cortisol, lipase, serum or urine HCG (required for woman of childbearing potential if pregnancy suspected), free T3 and free T4, serum ACTH levels, testosterone, estradiol, FSH, LH, random glucose, ECG, C-reactive protein (CRP), creatine kinase (CK), troponin
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (optional).

PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy (see SCNAUSEA)
- If prior infusion reactions to durvalumab: diphenhydrAMINE 50 mg PO, acetaminophen 325 to 975 mg PO, and hydrocortisone 25 mg IV 30 minutes prior to treatment

TREATMENT SCHEMA:



TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
durvalumab	20 mg/kg* on Day 1 (maximum 1500 mg)	IV in 100 mL NS over 60 minutes Using a 0.2 micron in-line filter
gemcitabine	1000 mg/m^2 on Days 1 and 8	IV in 250 mL NS over 30 minutes
CISplatin	70 mg/m^2 on Day 1	Prehydrate with 1000 mL NS over 1 hour, then CISplatin IV in 500mL NS with 20 mEq potassium chloride, 1 g magnesium sulfate, 30 g mannitol over 1 hour

* Select dose per Dose Banding Table (appendix)

- Repeat every 3 weeks for 4 cycles, then proceed to surgery.
- If patients are intolerant of the chemotherapy after at least one cycle, durvalumab can be continued as single agent.

DOSE MODIFICATIONS:

- No specific dose modifications for durvalumab. Toxicity managed by treatment delay and other measures (see SCIMMUNE for management of immune-mediated adverse reactions to checkpoint inhibitor immunotherapy).

1. Hematology:

For gemcitabine Day 1 of each Cycle

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
Greater than or equal to 1.0	and	Greater than or equal 100	100%
0.5 to less than 1.0	or	75 to less than100	75%
Less than 0.5	or	Less than 75	Delay*
*CISplatin also delayed			

For gemcitabine Day 8 of each Cycle

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose**
Greater than or equal to 1.0	and	Greater than or equal 100	100%
0.5 to less than 1.0	or	75 to less than100	75%
Less than 0.5	or	Less than 75	Omit
**Dose adjustment only for the day of treatment the CBC is drawn			

2. Renal Dysfunction:

Creatinine Clearance (mL/min)	CISplatin	Gemcitabine
Greater than or equal to 60	70 mg/m^2 Day 1	100%
45 to less than 60	35 mg/m^2 on Day 1 and Day 8 (same prehydration as 70 mg/m^2 dose)	100%
Less than 45	Delay	See below *
*Delay if Day 1; if Day 8, omit if serum creatinine greater than 3 x ULN where ULN = local upper limit of normal range.		

Alternatively, CARBOplatin may be used instead of CISplatin:

Drug	Dose	BC Cancer Administration Guidelines
CARBOplatin	AUC 5 Day 1 only Dose = AUC x (GFR* +25)	IV in 250 mL NS over 30 minutes
gemcitabine	1000 mg/m^2 on Days 1 and 8 (total dose per cycle = 2000 mg/m^2)	IV in 250 mL NS over 30 minutes

* *Measured GFR* (e.g. nuclear renogram) is preferred whenever feasible, *particularly* in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, etc.). The lab reported GFR (MDRD formula) may be used as an alternative to the Cockcroft-Gault estimate of GFR; the estimated GFR reported by the lab or calculated using the Cockcroft-Gault equation should be capped at 125 mL/min when it is used to calculate the initial carboplatin dose. When a nuclear renogram is available, this clearance would take precedence.

Cockcroft-Gault Formula

$$\text{GFR} = \frac{\text{N* x (140 - age in years) x wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

Note: The *same* method of estimation should be used throughout the treatment course (i.e. if lab reported GFR was used initially, this should be used for dosing in all subsequent cycles and not the Cockcroft-Gault estimate).

*For males N = 1.23; for females N = 1.04

PRECAUTIONS:

1. **Serious immune-mediated reactions to durvalumab**: can be severe to fatal and usually occur during the treatment course, but may develop months after discontinuation of therapy. They may include enterocolitis, intestinal perforation or hemorrhage, hepatitis, dermatitis, neuropathy, endocrinopathy, pneumonitis, as well as toxicities in other organ systems. Early diagnosis and appropriate management are essential to minimize life-threatening complications (see SCIMMUNE for management of immune-mediated adverse reactions to checkpoint inhibitor immunotherapy).
2. **Infusion-related reactions:** isolated cases of severe infusion reactions have been reported. For mild or moderate infusion reactions, decrease the infusion rate to 50% or temporarily interrupt infusion until the reaction has resolved. Consider premedication for subsequent infusions. Permanently discontinue durvalumab for severe reactions.
3. **Infections:** severe infections such as sepsis, necrotizing fasciitis, and osteomyelitis have been reported. Treat suspected or confirmed infections as indicated. Withhold durvalumab for severe infections.
4. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
5. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal dysfunction.
6. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.
7. **Ototoxicity**: CISplatin is ototoxic and its use must be cautioned in individuals with existing hearing loss.

Call the GU Systemic Therapy physician at your regional cancer centre or the GU Systemic Therapy Chair with any problems or questions regarding this treatment program

REFERENCES:

1. Powles T, Catto JWF, Galsky MD, et al. Perioperative durvalumab with neoadjuvant chemotherapy in operable bladder cancer. N Engl J Med 2024;391:1773-86
2. Durvalumab (Imfinzi) CADTH Reimbursement Recommendation. Canadian Journal of Health Technologies Jan 2026; 6(1): 1-13.

Appendix. Dose Bands

DURVALUMAB DOSE BANDING TABLE (20 mg/kg capped at 1500 mg)

Ordered Dose (mg)		Rounded dose (mg)
From:	To:	
Less than 369		**Pharmacy prepares specific dose**
369	440.49	**400**
440.5	475.49	**450**
475.5	555.49	**500**
555.5	666.49	**600**
666.5	777.49	**700**
777.5	888.49	**800**
888.5	999.49	**900**
999.5	1099.49	**1000**
1099.5	1199.49	**1100**
1199.5	1299.49	**1200**
1299.5	1399.49	**1300**
1399.5	1499.49	**1400**
1499.5	1500	**1500**