BC Cancer Protocol Summary for Treatment of Advanced Biliary Tract Cancer using Durvalumab

Protocol Code	*GIAVDUR4*
Tumour Group	*Gastrointestinal*
Contact Physician	*GI Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Metastatic or unresectable biliary tract (cholangiocarcinoma or gallbladder) cancer, and
- Eligibility for and no disease progression after treatment with durvalumab-chemotherapy per protocol GIAVDURPG

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

Note:

- durvalumab monotherapy (GIAVDUR4) to start 21 days after final cycle of durvalumab-chemotherapy (GIAVDURPG)

CAUTIONS:

- 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, platelets, creatinine, sodium, potassium, total bilirubin, ALT, TSH
- Prior to each treatment: CBC & Diff, platelets, creatinine, sodium, potassium, total bilirubin, ALT, TSH
- If clinically indicated: alkaline phosphatase, albumin, morning serum cortisol, lipase, random glucose, serum or urine HCG (required for women of childbearing potential if pregnancy suspected), free T3 and free T4, creatine kinase, troponin, serum ACTH levels, testosterone, estradiol, FSH, LH, GGT, CEA, CA 19-9, ECG, chest x-ray
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (Optional)

PREMEDICATIONS:

- Antiemetics are not usually required
- 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:

Drug	Dose	BC Cancer Administration Guideline
durvalumab	20 mg/kg (maximum 1500 mg)	IV in 100 mL NS over 60 minutes Using a 0.2 micron in-line filter

- Repeat every 4 weeks until disease progression or unacceptable toxicity

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: http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCIMMUNE_Protocol.pdf).

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: http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCIMMUNE_Protocol.pdf).
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.

Call the GI Systemic Therapy physician at your regional cancer centre or the GI Systemic Therapy Chair Dr. Theresa Chan at (604) 930-2098 with any problems or questions regarding this treatment program

References:

1. Oh DY, Ruth He A, Qin S, et al. Durvalumab plus Gemcitabine and Cisplatin in Advanced Biliary Tract Cancer. NEJM Evid. 2022 Aug;1(8):EVIDoa2200015.
2. Durvalumab (Imfinzi) CADTH Reimbursement Recommendation. Canadian Journal of Health Technologies Feb 2023; 3(2): 1-18.