DURVALUMAB (Imfinzi) GEMCITABINE CISPLATIN

INDICATION (ICD10) C23

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (DUR2)

1. Durvalumab in combination with gemcitabine and cisplatin for the 1st line treatment of patients with locally advanced or unresectable or recurrent or metastatic biliary tract adenocarcinoma cancer (intrahepatic cholangiocarcinoma or extrahepatic cholangiocarcinoma or gall bladder carcinoma. intrahepatic cholangiocarcinoma or extrahepatic cholangiocarcinoma or gall bladder carcinoma but a patient with a primary pancreatic or small bowel carcinoma which is sited at the ampulla is not eligible for access to durvalumab plus gemcitabine and cisplatin). (Patients who have received prior adjuvant or neoadjuvant chemotherapy are eligible for durvalumab plus gemcitabine and cisplatin provided that the adjuvant or neoadjuvant chemotherapy did not contain the combination of gemcitabine and cisplatin). No symptomatic brain or leptomeningeal metastases. PS 0 or 1.

REGIMEN

Cycles 1 to 8

Day 1 DURVALUMAB 1500mg in 250ml sodium chloride 0.9% IV infusion over 60 minutes
Prehydration
CISPLATIN 25mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 60 minutes
GEMCITABINE 1000mg/m^2 in 250ml sodium chloride 0.9% (or licensed dose volume) IV infusion over 30 minutes
Posthydration

Day 8 Prehydration
CISPLATIN 25mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 60 minutes
GEMCITABINE 1000mg/m^2 in 250ml sodium chloride 0.9% (or licensed dose volume) IV infusion over 30 minutes
Posthydration

Cycles 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52
Day 1 DURVALUMAB 1500mg in 250ml sodium chloride 0.9% IV infusion over 60 minutes

Cycles 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53
Day 8 DURVALUMAB 1500mg in 250ml sodium chloride 0.9% IV infusion over 60 minutes

Cycles 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50
Day 15 DURVALUMAB 1500mg in 250ml sodium chloride 0.9% IV infusion over 60 minutes

CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination every 21 days for 8 cycles.
Formal medical review as to whether treatment with durvalumab in combination with gemcitabine and cisplatin should continue will occur at least by the end of the 2nd cycle of treatment.
Durvalumab monotherapy every 28 days until disease progression (on Aria if treatment to continue beyond cycle 53 discontinue regimen and restart at cycle 10)

ANTI-EMETICS

Moderate risk days 1 and 8
Minimal risk durvalumab monotherapy

CONCURRENT MEDICATION REQUIRED

Cisplatin	Ensure adequate pre and post hydration. If urine output is <100ml/hour or if patient gains >2kg in weight during IV administration post cisplatin give 20-40mg furosemide PO/IV.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cisplatin - exfoliant
Gemcitabine – neutral

Durvalumab administer with low-protein binding 0.2 or 0.22 micron in-line filter.
Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC every dose, U&E, LFTs and creatinine every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
GFR assessed using EDTA result or calculated creatinine clearance at the Consultant's discretion.
Random blood glucose every cycle
Thyroid function baseline and every 1 to 2 cycles
Random cortisol baseline and every 1 to 2 cycles
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Cisplatin	Nephrotoxicity – ensure adequate pre and post hydration is prescribed. Ototoxicity – assess patient for tinnitus or hearing abnormalities.
Durvalumab	Immune mediated pneumonitis Immune mediated hepatitis Immune mediated colitis Immune mediated endocrinopathies
Gemcitabine	Diarrhoea – see dose modifications, treat with, loperamide or codeine Mucositis – see dose modifications, use routine mouthcare

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Cisplatin	Aminoglycosides increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests as required. Cisplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.

DOSE MODIFICATIONS

Haematological

Neutrophils >1.5x10^9/L and platelets >100x10^9/L	give 100% dose
Neutrophils 1.0-1.5x10^9/L or platelets <100x10^9/L	Discuss with consultant
Neutrophils <1.0x10^9/L or platelets <100x10^9/L	Day 1 delay treatment Day 8 platelets <100x10^9/L omit gemcitabine treatment, and consider giving 75% gemcitabine dose subsequent cycles

Non-haematological
If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

Durvalumab
Immune-related adverse reactions - refer to TV immune-oncology agent immune related adverse event clinical guideline.

Hepatic impairment
Durvalumab
No dose adjustment is needed for patients with hepatic impairment.

Gemcitabine

Bilirubin >27µmol/L	initiate treatment with 80% dose

Renal impairment
Cisplatin

CrCl >60ml/min	give 100% dose
CrCl 45-60ml/min	give 75% dose
CrCl <45ml/min	not recommended

Durvalumab
No dose adjustment is required in mild or moderate renal impairment. There is insufficient data from patients with severe renal impairment (CrCl <30ml/min) for dosing recommendations.

REFERENCES
1. NHSE policy