Durvalumab in combination with gemcitabine plus cisplatin

NHS Lancashire and South Cumbria Cancer Alliance

Indication

Histologically confirmed unresectable, locally advanced, or metastatic adenocarcinoma of the biliary tract, including intrahepatic or extrahepatic cholangiocarcinoma and gallbladder carcinoma based on TOPAZ-1 trial

Regimen details`

Durvalumab (1500mg) on day 1 of each cycle, in combination with gemcitabine (1000mg/m^2) and cisplatin (25mg/m^2), which were administered on days 1 and 8 of each cycle. After completion of gemcitabine and cisplatin, 1500mg of durvalumab monotherapy was administered once every 4 weeks until clinical or imaging disease progression or until unacceptable toxicity, withdrawal of consent

Table 1 – Treatment regimen details

DRUG	DOSE	DILUENT	ROUTE	FREQUENCY/DURATION
Durvalumab	1500mg (if body weight < 30 kg, dose at 20 mg/kg IV)	100mL Sodium Chloride 0.9% Administer the drug solution over 60 minutes using a volumetric pump through an in-line 0.2µm or 1.2µm polyethersulfone or 0.2µm positively charged nylon filter	intravenous infusion over 1 hour	Day 1
		1 litre 0.9% sodium chloride + 20mmol potassium chloride + 10mmol magnesium sulphate	intravenous infusion over 1 hour	Day 1, 8
Cisplatin	25mg/m^2	500ml 0.9% sodium chloride	intravenous infusion over 1 hour	Day 1, 8
Gemcitabine	1000mg/m^2	250ml 0.9% sodium chloride	intravenous infusion over 1 hour	Day 1, 8
After 8 cycles of the above				
Durvalumab	1500mg (if body weight < 30 kg, dose at 20 mg/kg IV)	100mL Sodium Chloride 0.9% Administer the drug solution over 60 minutes using a volumetric pump through an in-line 0.2µm or 1.2µm polyethersulfone or 0.2µm positively charged nylon filter	intravenous infusion over 1 hour	Every 4 weeks

Cycle frequency

Cycles 1-8 in combination with chemotherapy.

Treatment on day 1 and day 8 of each 21 day cycle.

Cycle 9+ as a single agent Durvalumab

Each cycle is 28 days.

Number of cycles

8 cycles of Durvalumab + combination chemotherapy, to be followed by 4 weekly Durvalumab until disease progression or unacceptable toxicity.

Administration

Intravenous infusion as stated above.

Durvalumab: Administer the drug solution over 60 minutes using a volumetric pump through an in-line 0.2µm or 1.2µm polyethersulfone or 0.2µm positively charged nylon filte

Pre-medication

As per anti-emetic guideline

Emetogenicity – consult anti-emetic policy for full details

High Risk (Category A)

Additional supportive medication

None Specific

Investigations – pre first cycle

Table 2 - Standard Investigations prior to first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
TFTs	14 days
Cortisol	Baseline
LH/FSH	Baseline
Testosterone	Baseline

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST), TFTs

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Table 3 – Standard test result limits for each administration to go ahead and Dose modifications.

Day 1:
Neutrophils ≥ 1
Platelets ≥ 100
Creatinine clearance ≥ 50
Bilirubin ≤ 1.5x ULN
ALT < 3x ULN

Day 8:

Neutrophils		Platelets	Gemcitabine dose	Cisplatin dose
≥ 1	And	>100	100%	100%
0.5-1	Or	50-100	75%	100%
< 0.5	Or	<50	Omit	omit

If treatment with gemcitabine and/or cisplatin are discontinued before completion of cycle 8 due to treatment related toxicity, then treatment with durvalumab may continue. In this case, durvalumab should be administered 4-weekly.

For Durvalumab: No dose reductions are recommended.

Pneumonitis: Grade 2 Withhold therapy, resume when complete or partial resolution occurs (Grade <1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone < or equal 10 mg/day.

Colitis: Grade 2 or 3: Withhold therapy; resume when complete or partial resolution occurs (Grade<1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone < or equal 10 mg/day. Grade 4: Permanently discontinue.

Hepatitis with no tumour involvement of the liver: AST or ALT increases to >3 and <8x ULN or total bilirubin increases to >1.5 and <3x ULN: Withhold therapy; resume when complete or partial resolution occurs (Grade<1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone < or equal 10 mg/day. AST or ALT increases to >8x ULN or total bilirubin increases to >3x ULN: Permanently discontinue.

Hepatitis with tumour involvement of the liver: Refer to consultant.

Myocarditis: Grade2, 3, 4: Permanently discontinue durvalumab

Renal Impairment:
Mild to moderate (CrCl >30 mL/min): No dosage adjustment of durvalumab necessary
Severe (CrCl <30 mL/min): Pharmacokinetics unknown.

Infusion-Related Reactions:
Grade1 or 2: Interrupt or slow infusion rate
Grade 3 or 4: Permanently discontinue.

Adverse Effects

Anaemia
Nausea
Constipation
Neutropenia
Immune mediated adverse events

References

1. Durvalumab with gemcitabine and cisplatin for treating unresectable or advanced biliary tract cancer [ID4031] - https://www.nice.org.uk/guidance/indevelopment/gid-ta10920 (accessed 11/12/23)
2. Durvalumab plus Gemcitabine and Cisplatin in Advanced Biliary Tract Cancer. Published June 1, 2022 NEJM Evid 2022;1(8)