CISPLATIN and GEMCITABINE for biliary tract cancers

DRUG ADMINISTRATION SCHEDULE

NHS Northern Cancer Alliance

Day	Drug	Dose	Route	Diluent	Rate
1	Sodium Chloride 0.9%	1000 ml	IV	Pre-hydration	2 hours
	Ondansetron	8 mg	Oral /Slow bolus/15 min infusion		
	Dexamethasone	8 mg	IV		Slow Bolus
	Furosemide	20 mg	ORAL	If no contra-indication	
	Cisplatin	**25 mg/m^2**	**IV**	**500 ml NaCl 0.9%**	**1 hours**
	Gemcitabine*	**1000 mg/m^2**	**IV**	**250 ml NaCl 0.9%**	**30 minutes**
	Magnesium Sulphate	10mmol	IV	1000ml NaCl 0.9% + KCl 0.15%	2 hours
8	Sodium Chloride 0.9%	1000 ml	IV	Pre-hydration	2 hours
	Ondansetron	8 mg	Oral /Slow bolus/15 min infusion		
	Dexamethasone	8 mg	IV		Slow Bolus
	Furosemide	20 mg	ORAL	If no contra-indication	
	Cisplatin	**25 mg/m^2**	**IV**	**500 ml NaCl 0.9%**	**1 hours**
	Gemcitabine*	**1000 mg/m^2**	**IV**	**250 ml NaCl 0.9%**	**30 minutes**
	Magnesium Sulphate	10mmol	IV	1000ml NaCl 0.9% + KCl 0.15%	2 hours

*Ondansetron IV must be infused over 15 minutes in patients over 65 years of age.

Hydration schedules may be modified according to local agreement.

CYCLE LENGTH AND NUMBER OF DAYS
Administered on a 21-day cycle for up to 6 cycles

APPROVED INDICATIONS
Palliative treatment for biliary tract cancers

ELIGIBILITY CRITERIA
Adequate cardiac and renal function (GFR over 45 ml/min)

EXCLUSION CRITERIA
Patients not fitting the above criteria

PREMEDICATION
Furosemide

Adequate hydration and urinary flow is essential when administering cisplatin. Ideally patients should be weighed (with bladder empty) prior to commencing treatment and to use 20 mg of oral or IV Furosemide as a diuretic given routinely if there is no contraindication. Alternatively, urine output should be measured with a target output of > 100ml/hour. Patient should be re-weighed at the end of cisplatin (with empty bladder) and consideration given to administering a further dose of Furosemide if weight gain is more than 1.5 Kg.

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RECOMMENDED TAKE HOME MEDICATION

Ondansetron 8mg twice daily for 2 to 3 days
Dexamethasone 4mg twice daily for 1 to 3 days
Metoclopramide 10 mg three times daily as required
Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle:
FBC, U&Es (Calculated CrCl, or measured GFR), LFTs, Mg & Ca,

Prior to each cycle: U&Es, LFTs, Mg, FBC, CrCl.
Check renal function before commencing platinum. Use EDTA or Wright to calculate GFR. GFR should usually be above 60 ml/min for cisplatin-based treatment. If GFR < 60 ml/min discuss with an Oncology Specialist.

ASSESSMENT OF RESPONSE

Metastatic: Tumour size and patient symptomatic response

REVIEW BY CLINICIAN

To be reviewed by either a Nurse, Pharmacist or Clinician before every cycle.

NURSE / PHARMACIST LED REVIEW

On cycles where not seen by clinician.

ADMINISTRATION NOTES

- Maintain oral intake of 1-2 liters of fluids for 6 hours after IV fluids are discontinued. Magnesium Sulphate and Potassium Chloride are required due to the renal toxicity of Cisplatin resulting in excess loss.
- Gemcitabine is a radio-sensitiser – use with caution if receiving concomitant radiotherapy.

EXTRAVASATION *See NCA/Local Policy*

TOXICITIES

- Nausea & Vomiting
- Neurotoxicity (ototoxicity)
- Nephrotoxic
- Electrolyte disturbance
- Myelosuppression
- Dizziness during infusion
- Oedema/peripheral oedema
- Flu like symptoms
- Rarely pulmonary effects e.g. ARDS
- Lethargy
- Alopecia, Myalgia, Tinnitus, Metallic taste

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

- Delay treatment on days 1 & 8 if ANC < 1.0 x 10^9 cells/l or PLT < 100 x 10^9 cells/l.
- If ANC or Platelets still below required levels for treatment at week 2, delay treatment again and patient will need assessed and chemotherapy dose reduction by Oncologist
- If Hb < 10 & patient symptomatic will need blood transfusion, but may proceed with chemotherapy as planned if performance status (PS) stable.

Non-Haematological Toxicity

- If PS deteriorates to 3 or 4 and on assessment patient is more symptomatic withhold treatment and discuss with Oncologist

Neurotoxicity

Grade	Cisplatin Dose
1	100%
2	50%
3 or 4	Omit

Renal Function:

Cisplatin is renally excreted, an EDTA GFR should be performed if CrCl < 60 ml/min and dose modification of cisplatin should be considered if GFR < 60ml/min.

- Patients with pre-existing renal impairment should be monitored closely for haemolytic uremic syndrome

Hepatic Function:

- Gemcitabine toxicity increases when Bilirubin is > 28µmol/l – consideration of a 25% dose reduction may be appropriate.
- IF ALT > 3ULN or Bilirubin is > 1.5ULN, DO NOT GIVE and consult with prescriber before proceeding

TREATMENT LOCATION

Can be given at Cancer Centre or Cancer Unit

REFERENCES:

1. J. W. Valle et al ABC-01 Trial Gemcitabine with or without cisplatin in patients (pts) with advanced or metastatic biliary tract cancer (ABC): Results of a multicenter, randomized phase III trial (the UK ABC-02 trial). J Clin Oncol 27:15s, 2009 (suppl; abstr 4503)

Document Control

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Reviewer:	Chris Beck – Chemo Pharmacist NCA	**Date Approved:**	13.03.2018
Approved by:	Steve Williamson Consultant Pharmacist Northern Cancer Alliance	**Due for Review:**	13.03.2021
Summary of Changes	1.2	Added cycle length 21 days	
	1.3	Protocol reviewed. Typing errors corrected.	
	1.4	Protocol reviewed and reissued, Antiemetic advice updated	
	1.5	Protocol updated against Chemocare protocol	