Cisplatin & gemcitabine

Indication

Recurrent or metastatic nasopharyngeal carcinoma
Neoadjuvant or adjuvant treatment of nasopharyngeal carcinoma

Regimen details

Table 1 – Treatment regimen details

DRUG	DOSE	DILUENT	ROUTE	FREQUENCY
Gemcitabine	1000mg/m^2	250mL Sodium chloride 0.9%	Intravenous infusion over 30 min	Day 1 and 8
	20mmol potassium chloride and 10mmol magnesium sulphate in 1litre sodium chloride 0.9%		Intravenous infusion over 2 hours	Day 1
Cisplatin	80mg/m^2	1000mL Sodium Chloride 0.9%	Intravenous infusion over 2 hours	Day 1
	20mmol potassium chloride and 10mmol magnesium sulphate in 1litre sodium chloride 0.9%		Intravenous infusion over 2 hours	Day 1

Cycle frequency

Every 3 weeks

Number of cycles

-Neoadjuvant or Adjuvant 3 cycles
-Recurrent or metastatic nasopharyngeal cancer up to 6 cycles

Administration

Gemcitabine is administered first over 30 minutes; volume will vary depending on product used. Longer infusion times may lead to increased toxicity

Cisplatin is administered over 2 hours

Pre-medication

None given routinely

Emetogenicity – consult anti-emetic policy for full details

Day 1 - High Risk (Category A)
Day 8 - Low Risk (Category C)

Additional supportive medication

None given routinely

Extravasation

Table 2 – Extravasation Risk Category for each intravenous drug in the regimen

Cisplatin	Exfoliants: Group 4
Gemcitabine	Neutral: Group 1

Investigations – pre first cycle

Table 3 - Standard Investigations prior to first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Calcium	14 days
Magnesium	14 days

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST), calcium, magnesium

Standard limits for administration to go ahead

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

Table 4 – Standard test result limits for each administration to go ahead

Investigation	Limit
Neutrophil count	≥ 1.5 x 10^9/L (but see "Dose modifications" below)
Platelet count	≥ 100 x 10^9/L (but see "Dose modifications" below)
Creatinine clearance	≥ 50 mL/min (≥ 60ml/min prior to cycle 1)
Bilirubin	≤ 1.5 x ULN
AST	< 1.5 x ULN

Dose modifications

Table 5 – Dose modification for haematological toxicity

Dose modification for haematological toxicity	
• Neutrophils > 1.5 AND Platelets >100	Proceed with full dose
• Neutrophils 1.0-1.5	Discuss with consultant
• Neutrophils < 1.0 OR Platelets < 100	Defer 1 week

Table 6 – Dose modification for neurological toxicity

Dose modification for neurological toxicity	
• CTCAE grade 0-1	Proceed with full dose
• CTCAE grade 2	Defer until recovery, then replace Cisplatin with Carboplatin AUC5
• CTCAE grade 3+	Change to less neurotoxic regime if appropriate

Hepatic impairment

Use gemcitabine in caution in hepatic impairment.
Raised transaminases do not seem to cause dose limiting toxicity
If bilirubin > 1.5 x ULN, initiate gemcitabine at dose of 800 mg/m^2

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Infertility
Interstitial pneumonitis, ARDS
Cardiotoxicity
Hepatotoxicity
Haemolytic uraemic syndrome
Ocular toxicity
Ototoxicity
Nephrotoxicity
Peripheral neuropathy

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Mucositis, stomatitis
Diarrhoea, constipation
Oedema
Haematuria

- **Other side effects**

Raised transaminases
Alopecia
Fatigue

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Cisplatin only:
Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity when given within 2 weeks of cisplatin.
Diuretics: increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs: increased nephrotoxicity ; not recommended
Ototoxic drugs: increased risk of ototoxicity
Phenytoin: cisplatin reduces absorption and efficacy of phenytoin, monitor levels and adjust dose as necessary.
Anti-gout agents: cisplatin may increase plasma concentration of uric acid therefore dose adjustments may be required to control hyperuricaemia and gout.

Additional comments

Nil

References

1. SWCN protocol - https://www.swagcanceralliance.nhs.uk/wp-content/uploads/2020/09/Cisplatin-Gemcitabine-NSCLC.pdf
2. Clatterbridge Cancer Centre Systemic Anti0Cancer Treatment Protocol Procedure Ref MPHACISGEM v1.2 https://www.clatterbridgecc.nhs.uk/application/files/3816/1659/7417/Cisplatin__Gemcitabine_Head_and_Neck_Cancer_Protocol_V1.2.pdf
3. https://www.nejm.org/doi/10.1056/NEJMoa1905287?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed