TOPOTECAN & CISPLATIN

Recurrent or Stage IVB cervical cancer

NICE approved 2009 for patients who have not previously received cisplatin
Funding approved 2013 for patients who have already received cisplatin

Drugs/Dosage:	Topotecan	0.75mg/m^2/day	IV	Day 1, Day 2 and Day 3
	Cisplatin	50mg/m^2	IV	Day 1

Administration: Topotecan in 100ml (50ml for dose < 1mg) of 0.9 % sodium chloride over 30 minutes, given before cisplatin on Day 1

Cisplatin: 1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hours
Mannitol 20% 100ml IV over 15 minutes
Cisplatin in 1 litre 0.9% sodium chloride IV over 2 hours
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hours
500ml sodium chloride 0.9% IV **or** 500ml water orally over 1 hour

Frequency: 3 weekly cycle until disease progression or unacceptable toxicity, for a maximum of 6 cycles

Main Toxicities: myelosuppression; stomatitis; alopecia; diarrhoea; nephrotoxicity; neuropathy / ototoxicity; ovarian failure/infertility

Anti – emetics:
Cisplatin: highly emetogenic
Topotecan: mildly emetogenic

Extravasation: non-vesicants

Regular investigations:	FBC	Day 1
	U&Es & LFTs	Day 1
	Mg^{2+} and Ca^{2+}	Day 1
	EDTA	Prior to Cycle 1

Comments: For patients on Cycle 1 whose EDTA is not yet available, Cockcroft & Gault may be used to predict GFR. Topotecan and cisplatin doses should be adjusted if necessary once EDTA available. EDTA should only be repeated if the result is borderline at the start of treatment or if there is a 30% change in serum creatinine.

Ensure that patient is reviewed for side effects indicative of neurotoxicity or ototoxicity.

Check electrolytes – additional supplementation of magnesium, calcium or potassium may be required.

Weight should be recorded prior to and at the end of cisplatin treatment, and a strict fluid balance chart should be maintained. An average urine output of at least 100ml/hr must be maintained throughout treatment, and cisplatin infusion should not be commenced unless this urine output is achieved. If the urine output is inadequate, the patient should be assessed and urine output increased by administering 500ml sodium chloride +/- furosemide 20 - 40mg. Furosemide 20 – 40mg po may also be given if there is a positive fluid balance of 1.5 litres, a weight gain of 1.5kg or symptoms of fluid overload. The patient

should be asked to drink 2 litres of fluid in the 24hrs following treatment, and to contact the hospital if this is impossible because of problems e.g. nausea and vomiting.

Dose Modifications

Haematological Toxicity:	Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l	Delay treatment for 1 week. Repeat FBC after one week and, if within normal parameters, resume treatment at full dose.

If patient experiences any episode of febrile neutropenia (temperature ≥ 38ºC and neutrophils < 1.0 x 10^9/l), the topotecan dose should be reduced to 0.6mg/m^2/day for remaining cycles (or subsequently down to 0.45mg/m^2/day, if necessary)

If platelets < 10 x 10^9/l at any point, topotecan dose should be reduced to 0.6mg/m^2/day

Renal Impairment: NB. Cisplatin is both eliminated primarily (> 90%) in the urine and is itself nephrotoxic.

GFR (ml/min)	Cisplatin Dose
≥ 60	Give 100%
45 – 59	Give 75%
20 - 44	Cisplatin contra-indicated Carboplatin AUC 4*, administered in 250ml 5% Glucose over 30 minutes on Day 1, may be substituted. It may be given according to this protocol, with however no requirement for pre- or post-hydration, nor fluid balance/urine monitoring
< 20	Carboplatin contra-indicated

*Dose as agreed with Dr Essapen – no published data or written information available in the literature regarding the combination of topotecan and carboplatin.
Carboplatin dose calculated using the Calvert Formula: Dose = Target AUC x (25 + GFR).

GFR (ml/min)	Topotecan Dose
> 40	Give 100% dose
20 - 39	Give 50% dose (in combination with carboplatin)
< 20	Nil – contra indicated

Neuropathy: If patient develops Grade 2 neuropathy or ototoxicity, discuss with Consultant.

References:
Long, HJ et al; JCO 2005; 23 (21): 4626 – 4633
Monk, BJ et al; JCO 2005; 23 (21): 4617 - 4625

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