CARBOPLATIN

01. Assay details

Assay not available

02. Therapeutic range

The target AUC (area under the concentration-time curve) is 80-120 mg/L.h when used as a single agent.

The target AUC is 50-80 mg/L.h when used in combination with cyclophosphamide.

How well established:
Ranges are well established for ovarian cancer and testicular cancer (AUC >80 mg/L.h required), moderately to poorly established for lung cancer, and not established for head and neck cancer or paediatric cancers. The AUC correlates well with grade 3 thrombocytopenia when used as single therapy [AUC >150 mg/L.h is associated with a 50% risk]. When used with cyclophosphamide, the AUC correlates better with neutropenia.

03. Pharmacokinetics

F: <0.1	**Vd** (L/kg): 0.28-0.43	**Cl** (L/h/kg): 0.09-0.13	**t½:** 4-8 hours
Fe: 0.75	**Elimination route:** Renal and spontaneous degradation		
CYP:		**Protein binding:** 0.2	

F = Bioavailability, Vd = volume of distribution, Cl = clearance, t½ = terminal half-life of elimination, Fe = fraction excreted unchanged in the urine, CYP = cytochrome P450 enzyme/s
Other PK data: Nil

04. Indications

Cancers of the ovary, testicle, small cell lung, head and neck, and paediatric cancers.

05. Loading dose

Not used

06. Maintenance Dose

Dose 300 to 900 mg, Dosing Frequency: every 28 days
The first predicted maintenance dose is determined by the method of Calvert:

Dose (mg) = AUC (mg/ml.min) x (GFR+25)
(where GFR is the clearance of 99mTc-DTPA in ml/min)
(80 mg/L.h = 5 mg/ml.min)

07. Notes on administration

The drug is given in 500 ml 5% dextrose over 1 hour intravenously. Additional hydration can be used if necessary. Premedication includes ondansetron, dexamethasone and metoclopramide for prevention of emesis. Avoid infusion sets and needles containing aluminium as these may cause an inactivating precipitation of carboplatin.

08. When to monitor

Two concentrations should be measured after the dose in order to calculate AUC
First concentration: 30 minutes post infusion
Second concentration: between 2 and 6 hours post infusion

09. Dose individualisation

Subsequent doses may be predicted using calculated AUC's either done manually or using a computer programme at the Drug Information Service (ph 80900).

10. Adverse effects

>10%

GI: nausea/vomiting
HAEM: myelosuppression - a dose limiting effect. The risk of myelosuppression increases with (1) poor performance status (2) renal impairment (3) increasing age (4) prior cisplatin or radiotherapy (5) other myelosuppressing agents. Neutropenia - more common when used with cyclophosphamide and occurs in 55% patients treated for ovarian cancer. Thrombocytopenia - occurs in 30% patients with a nadir platelet count at 21 days.

1-10%

DERM: alopecia
LIVER: mild reversible elevation of LFT's

<1%

CNS: neuropathy, reversible loss of vision
ENT: ototoxicity
LIVER: hepatotoxicity (only at very large doses >600-800 mg/m2)
RENAL: nephrotoxicity
MISC: anaphylaxis (rare reports): dose independent

11. Drug interactions

Cisplatin appears to reduce the clearance of carboplatin. Aminoglycosides may increase nephrotoxicity and ototoxicity. Pharmacodynamic potentiation of cytopenia may occur when co-administered with other myelosuppressants. Avoid live vaccines in immunosuppressed patients.

12. Factors that may give a false assay result

Nil known.

13. Overdose

There are no reported intentional overdoses. Management of cytopenias is supportive with neutropenic cares and transfusions.

14. Dialysability

Haemodialysis alters the pharmacokinetics of carboplatin but the extent of this is unknown.

15. Comments

The intraperitoneal route has been tried for stage 3/4 ovarian carcinoma. This has the advantage of lower plasma concentrations and systemic adverse effects such as myelosuppression, with greater drug concentrations in the peritoneal cavity, but necessitates a peritoneal catheter with risks of infection.

16. Key References

Nil.

17. Date

Oct 1997