Carboplatin and Etoposide (gynae)

Indication
First line chemotherapy for patient with small cell cancer of gynaecological origin.

ICD-10 codes
Codes pre-fixed with C54, 55, 56, 57, 58.

Regimen details

Day	Drug	Dose	Route
1	Carboplatin	AUC5*	IV infusion
1	Etoposide	100mg/m²**	IV infusion
2 and 3	Etoposide	100mg/m²**	IV infusion
OR 2 and 3	Etoposide	200mg/m^{2**}	PO

* Carboplatin dose calculated using the Calvert equation: **Carboplatin dose (mg) = AUC (CrCl +25)**
The creatinine clearance (CrCl) is calculated using the Cockcroft and Gault equation, however for patients where the creatinine level may not truly reflect renal function (e.g. in extremes of BSA or debilitated patients) an EDTA should be performed.
CrCl should be capped at 125mL/min

** For patients with poor performance status (WHO PS ≥ 2) consider switching etoposide to 50mg/day PO for 4 days.

Cycle frequency
21 days

Number of cycles
4 - 6 cycles (usually 4)

Administration
Day 1
Carboplatin is administered in 500mL 5% glucose over 30 minutes.
Etoposide is administered in 1000mL sodium chloride 0.9% and infused over a minimum of 1 hour.

Days 2 and 3
Etoposide IV is administered in 1000mL sodium chloride 0.9% and infused over a minimum of 1 hour.

Oral etoposide is available as 50mg and 100mg capsules. The dose should be rounded to nearest 50mg and swallowed whole on an empty stomach or an hour before food. In the event that the patient cannot swallow capsules, etoposide injection can be taken orally (diluted with orange juice immediately prior to administration) at a dose of 70% of the usual oral capsule dose on Day 2 and Day 3. (This is an unlicensed use based on medical information from Bristol- Myers Squibb).
Note: oral absorption of etoposide is variable.

Pre-medication
Antiemetics as per local guidelines.

Emetogenicity

This regimen has moderate emetic potential.

Additional supportive medication

Consider prophylactic ciprofloxacin 250mg BD and fluconazole 50mg OD for 7 days, starting on day 7, for patients with poor performance status or age >70 years.

Extravasation

Carboplatin and Etoposide – irritant (Group 3)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days

Standard limits for administration to go ahead

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

Investigation	**Limit**
Neutrophils	≥1.5 x 10^9/L
Platelets	≥100 x 10^9/L
Bilirubin	≤1.5 x ULN
ALT/AST	≤1.5 x ULN
Alkaline phosphatase	≤2.5 x ULN

Dose modifications

- ### Haematological toxicity

Defer therapy for 1 week if neutrophils < 1.5 x 10^9/L or platelets < 100 x 10^9/L. Repeat FBC and if within range continue with treatment.

If significant myelosuppression consider reducing oral etoposide dose to 100mg/m^2 on days 2 and 3. Consider prophylactic GCSF support.

- ### Renal impairment

CrCl (mL/min)	**Etoposide dose**
>50	100%
15-50	75%
<15	50% (consultant decision)

Carboplatin is contraindicated if CrCl <20mL/min

- **Hepatic impairment**

Bilirubin (micromol/L)		AST/ALT	Carboplatin dose	Etoposide dose
<26	and	< 5 x ULN	100%	100%
26-50	or	< 5 x ULN	100%	50%
<50	and	≥ 5 x ULN	100%	25% or omit (consultant decision)
51-68	and	< 5 x ULN	100%	25% or omit (consultant decision)
>68			Omit/delay	Omit/delay

- **Other toxicities**

Any Grade 3-4 toxicity (except mucositis and alopecia) – delay until ≤ Grade 1 toxicity and reduce doses of carboplatin and etoposide to 75%.

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

- **Rare or serious side effects**

Myelosuppression

- **Frequently occurring side effects**

Alopecia
Nausea and vomiting
Electrolyte disturbances

- **Other side effects**

Nil

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

Phenylbutazone, sodium salicylate and salicylic acid: can affect protein binding of etoposide.

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.

Carboplatin only:
Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity
Clozapine: increased risk of agranulocytosis, avoid concomitant use
Diuretics: increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs: increased nephrotoxicity ; not recommended
Phenytoin: carboplatin reduces absorption and efficacy of phenytoin

Additional comments

Nil

References

- Summary of Product Characteristics Carboplatin (Hospira) accessed 25 Sept 2014 via www.medicines.org.uk
- Summary of Product Characteristics Etoposide (Bristol Myers Squibb) accessed 25 Sept 2014 via www.medicines.org.uk
- The North London Cancer Network. Dose adjustments in renal impairment. January 2009.

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