Topotecan – oral (lung)

Indication
Treatment of relapsed small cell lung cancer when retreatment with first line chemotherapy is inappropriate **and** treatment with CAV (cyclophosphamide, doxorubicin and vincristine) combination therapy is contraindicated.
WHO Performance Status 0-2

(NICE TA184)

ICD-10 codes
Codes with a prefix C34

Regimen details

Day	Drug	Dose	Route
1-5	Topotecan	2.3mg/m^2	PO

* day 1 may be administered in the hospital setting as per local policy.

Cycle frequency
21 days

Number of cycles
6 cycles

Administration
Topotecan is available as 0.25mg and 1mg capsules.
Capsules must be swallowed whole and not chewed or crushed.
May be taken with or without food.
Capsules must be stored in a refrigerator (2-8^{o}C)

Pre-medication
Nil

Emetogenicity
This regimen has moderate emetic potential.

Additional supportive medication
GCSF may be required as secondary prophylaxis if a patient experiences neutropenic sepsis in a previous cycle.

Extravasation
N/A

Investigations – pre first cycle

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

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local practice)
FBC	96 hours
U+E (including creatinine)	7 days
LTFs	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	≥1.0 x 10^9/L
WCC	≥3.0 x 10^9/L
Platelets	≥100 x 10^9/L
Haemoglobin	≥10 g/dL
Creatinine Clearance (CrCl)	>60mL/min
Bilirubin	≤ULN

Dose modifications

- **Haematological toxicity**

Investigation	**Limit**	**Dose adjustment**
Neutrophils	<1.0 x 10^9/L	Delay 1 week and recheck FBC prior to treatment. Consider dose reduction of 0.4mg/m^2 for future cycles
WCC	<3.0 x 10^9/L	
Platelets	<100 x 10^9/L	
Haemoglobin	<10 g/dL	Consider blood transfusion

If febrile neutropenia (neutrophils <0.5 x 10^9/L plus fever requiring IV antibiotics +/- hospitalisation) – reduce dose of next cycle by 0.4mg/m^2.

If thrombocytopenia (platelet nadir of <25 x 10^9/L) - reduce dose of next cycle by 0.4mg/m^2.

- **Renal impairment**

Creatinine Clearance (mL/min)	**Dose adjustment**
≥ 60	100%
20-59	Limited evidence - consultant decision
< 20	Contraindicated

- **Hepatic impairment**

There are no dosage recommendations available for patients with liver impairment-consultant decision.
Topotecan is not recommended in patients with bilirubin > 1.5 x ULN.

- **Other toxicities**

For Grade 2-4 diarrhoea or any Grade 3/4 non-haematological toxicities (apart from alopecia), consider dose reductions similar to those for haematological toxicities i.e. dose reductions of 0.4mg/m^2 to a minimum dose of 1.5mg/m^2/day.

Toxicity	Definition	Dose adjustment
Diarrhoea	≥ Grade 2	Delay until resolved. Consider dose reductions of 0.4mg/m^2 to a minimum dose of 1.5mg/m^2/day. Treatment-emergent diarrhoea should be managed aggressively. Patients should be advised how to manage chemotherapy-induced diarrhoea, including, recognition of early warning signs, use of antidiarrhoeals and antibiotics, changes in fluid intake and diet, and the need for hospitalisation.
Anaemia	≥ Grade 2	Delay until haemoglobin ≥ 9 g/dL (after transfusion if necessary)

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

- **Serious side effects**

Myelosuppression
Neutropenic colitis*
Interstitial lung disease
Teratogenicity/fertility effects

* Topotecan-induced neutropenia can cause neutropenic colitis (potentially fatal). In patients presenting with fever, neutropenia, and abdominal pain, the possibility of neutropenic colitis should be considered.

- **Frequently occurring side effects**

Nausea and vomiting
Myelosuppression
Fatigue
Alopecia
Anorexia
Diarrhoea

- **Other side effects**

Constipation
Stomatitis
Pruritis
Rash

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

Clozapine : increased risk of agranulocytosis, avoid concomitant use
Digoxin tablets : reduced absorption (resolved by giving the digoxin in liquid form)
P-glycoprotein inhibitors (cyclosporin, ketoconazole, ritonavir, saquinavir): increased exposure of topotecan
Phenytoin : may possibly increase topotecan clearance

Additional comments

References

- NICE Guidance TA184 – Topotecan for the treatment of relapsed small cell lung cancer. Accessed 11 November 2014 via www.nice.org.uk
- Summary of Product Characteristics Topotecan (GSK) 0.25mg and 1mg hard capsules. Accessed 11 November 2014 via http://www.medicines.org.uk
- Baxter K, editor. Stockley's Drug Interactions. Pharmaceutical Press; 2009. Accessed via www.medicinescomplete.com/mc/
- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.

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Date: 13 November 2014