

## TOPOTECAN VINCRISTINE DOXORUBICIN

### INDICATION (ICD10) C49

1. Rhabdomyosarcoma. PS 0, 1, 2

### REGIMEN

Day 1 TOPOTECAN 1.5mg/m<sup>2</sup> in 100ml\* sodium chloride 0.9% IV infusion over 30 minutes  
 Day 2 TOPOTECAN 1.5mg/m<sup>2</sup> in 100ml\* sodium chloride 0.9% IV infusion over 30 minutes  
 Day 3 TOPOTECAN 1.5mg/m<sup>2</sup> in 100ml\* sodium chloride 0.9% IV infusion over 30 minutes  
 Day 4 TOPOTECAN 1.5mg/m<sup>2</sup> in 100ml\* sodium chloride 0.9% IV infusion over 30 minutes  
 Day 5 TOPOTECAN 1.5mg/m<sup>2</sup> in 100ml\* sodium chloride 0.9% IV infusion over 30 minutes  
 VINCRISTINE 1mg/m<sup>2</sup>/day (maximum 1mg/day) IV infusion over 48 hours  
 DOXORUBICIN 22.5mg/m<sup>2</sup>/day IV infusion over 48 hours  
 \*doses 0.52mg to 2.4mg in 50ml sodium chloride

### CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 to 28 days for 2 to 6 cycles

### ANTI-EMETICS

Low emetic risk days 1, 2, 3 and 4

Moderate emetic risk days 5, 6 and 7

### CONCURRENT MEDICATION REQUIRED

Doxorubicin	None required
Topotecan	None required
GCSF	GCSF starting at least 72 hours after completing chemotherapy

### EXTRAVASATION AND TYPE OF LINE / FILTERS

Doxorubicin - vesicant

Topotecan - exfoliant

Vincristine - vesicant

Central line

### INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E, Mg<sup>++</sup>, Ca<sup>++</sup> and LFTs every cycle

Neutrophils x 10<sup>9</sup>/L ≥1.0

Platelets x 10<sup>9</sup>/L ≥100

Ideally EDTA GFR should be used

Creatinine clearance (GFR) calculated, at the Consultants discretion

Serum creatinine

Baseline weight and every cycle

## MAIN TOXICITIES AND ADVERSE REACTIONS

Doxorubicin	Cardiotoxicity – Monitor cardiac function to minimise the risk of anthracycline induced cardiac failure. Doxorubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
Topotecan	Interstitial lung disease Haematological toxicity
Vincristine	Neuropathy

## INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS (not exhaustive list check SPC/BNF/Stockleys)

Topotecan	Amiodarone, verapamil, azithromycin, clarithromycin, ciclosporin, azoles, vemurafenib may increase exposure to topotecan
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## DOSE MODIFICATIONS

Doxorubicin maximum lifetime dose

= 400mg/m<sup>2</sup> (in patients with cardiac dysfunction or exposed to mediastinal irradiation)

= 450-550mg/m<sup>2</sup> (with normal cardiac function)

### Haematological

Topotecan

Severe neutropenia (neutrophil count <0.5x10<sup>9</sup>/l) for seven days or more or severe neutropenia associated with fever or infection, or who have had treatment delayed due to neutropenia, or the platelet count falls below 25x10<sup>9</sup>/l.

Reduce dose to 0.60mg/m<sup>2</sup>/day for subsequent courses (or subsequently down to 0.45mg/m<sup>2</sup>/day if necessary).

### Hepatic impairment

Doxorubicin

Bilirubin 20-50micromol/L	give 50% dose
Bilirubin 51-86micromol/L	give 25% dose
Bilirubin >86micromol/L or Child-Pugh C	not recommended

Topotecan

In the absence of Gilbert's syndrome:

Bilirubin <170micromol/L	give 100% dose
Bilirubin >170micromol/L	not recommended

Vincristine

Bilirubin 25-51 or AST 60-180u/L	give 50%
Bilirubin >51micromol/L and normal AST	give 50%
Bilirubin >51micromol/L and AST >180u/L	omit

### Renal impairment

Topotecan

CrCl >40ml/min	give 100% dose
CrCl 20-39ml/min	give 50% dose
CrCl <20ml/min	contraindicated



## REFERENCES

1. Meazza et al. Efficacy of topotecan plus vincristine and doxorubicin in children with recurrent/refractory rhabdomyosarcoma. *Med Oncol.* 2009;26(1):67-72
2. Garaventa A, Luksch R, Biasotti S, Severi G, Pizzitola MR, Viscardi E, et al. A phase II study of topotecan with vincristine and doxorubicin in children with recurrent/refractory neuroblastoma. *Cancer.* 2003 Dec 1;98(11):2488–94.