IRINOTECAN TEMOZOLOMIDE VINCRISTINE - local funding required

INDICATION (ICD10) C40, C41, C49

1. Relapsed alveolar rhabdomyosarcoma. PS 0, 1, 2

REGIMEN

Day 1 VINCRISTINE 1.5mg/m^2 (maximum 2mg) in 50ml sodium chloride 0.9% IV infusion
Days 1 to 5 TEMOZOLOMIDE 100-125mg/m^2 orally once daily 1 hour before irinotecan
Days 1 to 5 Premedication: Atropine 250mcg subcutaneously 30 minutes prior to treatment
Days 1 to 5 IRINOTECAN 50mg/m^2 in 250ml sodium chloride 0.9% (or licensed dose volume) IV infusion over 30 minutes
Day 8 VINCRISTINE 1.5mg/m^2 (maximum 2mg) in 50ml sodium chloride 0.9% IV infusion

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for 6 cycles

ADMINISTRATION

Available as various strength capsules
Take on an empty stomach

ANTI-EMETICS

Moderate emetic risk days 1 to 5
Low emetic risk day 8

CONCURRENT MEDICATION REQUIRED

Irinotecan	Ensure premedication atropine given 30 minutes prior to treatment
Temozolomide	Cotrimoxazole 480mg bd M/W/F for duration of chemotherapy.
Vincristine	Laxatives should be prescribed

EXTRAVASATION AND TYPE OF LINE / FILTERS

Irinotecan - irritant
Vincristine - vesicant

Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Ideally DTPA GFR should be used
Creatinine clearance (GFR) calculated, at the Consultants discretion
Serum creatinine
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Irinotecan	Acute cholinergic syndrome (including diarrhea and delayed diarrhoea, abdominal pain, hypotension, dizziness, malaise, increased salivation). Drink large volumes of fluid containing electrolytes and an appropriate antidiarrhoeal therapy - loperamide 4mg initially then 2mg every 2 hours, continuing for 12 hours after the last liquid stool (maximum of 48 hours in total). Consider antibiotic if indicated (cefixime 400mg daily days 1 to 8).
Temozolomide	Myelosuppression Hepatic toxicity – may still occur several weeks after end of treatment. High risk of PJP.
Vincristine	Neuropathy

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

Irinotecan	Aprepitant and fosaprepitant increases exposure to irinotecan. Carbamazepine decreases exposure to irinotecan, avoid. Enzalutamide, mitotane, phenobarbitone, phenytoin, primidone and rifampicin decreases exposure to irinotecan, avoid.

DOSE MODIFICATIONS

Haematological

If neutrophils <1.0x10^9/L or platelets <75x10^9/L delay 1 week, only treat when neutrophils and platelets are above these limits.
Delay >14 days give 80% temozolomide dose for next cycle.
In the event of febrile neutropenia give 80% for all subsequent cycles.

Non-haematological

Irinotecan
If patients suffer from severe diarrhoea, which required IV rehydration or neutropenic fever, consider reduction in subsequent cycles, discuss with SpR or Consultant.

Hepatic impairment

Irinotecan

Bilirubin 24-50micromol/L	give 50% dose
Bilirubin >51micromol/L	Clinical decision

Temozolomide
Stop temozolomide if there is a progressive rise in transaminases or rise in bilirubin.

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

REFERENCES

1. Mixon BA et al, J Paediatric Haematol Oncol Volume 35, number 4 May 2013
2. Raciborska A et al, Paediatric Blood Cancer 2013;60;