IRINOTECAN TEMOZOLOMIDE

INDICATION (ICD10) C40, C41, C49

1. Relapsed Ewings sarcoma. PS 0, 1, 2

REGIMEN

Days 1 to 5 TEMOZOLOMIDE 100mg/m^2 orally once daily 1 hour before irinotecan

Premedication: Atropine 250mcg subcutaneously 30 minutes prior to treatment

IRINOTECAN 50mg/m^2 in 250ml sodium chloride 0.9% (or licensed dose volume) IV infusion over 30 minutes

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

CONCURRENT MEDICATION REQUIRED

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

EXTRAVASATION AND TYPE OF LINE / FILTERS

Irinotecan - irritant

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 EDTA 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.

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.

REFERENCES
1. Pediatric Blood Cancer 2009;53:1029-1034
2. Clinical Cancer Research Vol 10, 840-848, Feb 1, 2004