TRABECTEDIN (Yondelis)

INDICATION (ICD10) C49

1. Advanced soft tissue sarcoma if: treatment with anthracyclines and ifosfamide has failed or they are intolerant of or have contraindications for treatment with anthracyclines and ifosfamide. PS 0, 1, 2. (TA185)

REGIMEN

Days 1 Premedication 30 minutes prior to infusion:
Dexamethasone 20mg IV
TRABECTEDIN 1.5mg/m^2 IV infusion device over 24 hours

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days (use free of charge stock from cycle 6 onwards)

ANTI-EMETICS

Moderate emetic risk

CONCURRENT MEDICATION REQUIRED

Trabectedin	Ensure premedication given before trabectedin
GCSF	GCSF may be required for hematologic toxicity

EXTRAVASATION AND TYPE OF LINE / FILTERS

Trabectedin – vesicant

Central line
If central venous access is not available trabectedin can be given peripherally in at least 1000ml of sodium chloride 0.9% IV infusion.

INVESTIGATIONS

Blood results required before SACT administration (see dose modifications for between cycle blood results)
FBC, U&E and LFTs weekly during the first two cycles of therapy, and at least once mid cycle between treatments in subsequent cycles.
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Hb g/dl ≥9
Creatine kinase - CK >2.5xULN must be decreased prior to treatment. Weekly during the first two cycles of therapy, and at least once mid cycle between treatments in subsequent cycles and if patient presents/admitted with neutropenia or other symptoms.
CrCl ≥30ml/min every cycle
ALT ≤2.5xULN every cycle
Albumin ≥25g/l every cycle
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Trabectedin	Cardiac dysfunction LFT abnormalities Rhabdomyolysis

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

Trabectedin	Antiepileptics – avoid, may decrease exposure to trabectedin Antivirals - - avoid or adjust dose may increase exposure to trabectedin Azoles - avoid or adjust dose may increase exposure to trabectedin Clarithromycin – avoid or adjust dose, may increase exposure to trabectedin

DOSE MODIFICATIONS
Starting dose 1.5mg/m^2
First reduction 1.2mg/m^2
Second reduction 1.0mg/m^2
If further dose reductions are necessary, treatment discontinuation should be considered.
Once a dose has been reduced due to toxicity, dose escalation in the subsequent cycles is not recommended. If any of these toxicities reappear in subsequent cycles in a patient exhibiting clinical benefit, the dose may be further reduced.

Haematological
Prior to retreatment, patients must fulfill the baseline criteria.
If any of the following events occur at any time between cycles, the dose must be reduced one level, for subsequent cycles
- Neutropenia <0.5x10^9/L lasting for more than 5 days or associated with fever or infection
- Thrombocytopenia <25x10^9/L

Non-haematological
Prior to retreatment, patients must fulfill the baseline criteria.
If any of the following events occur at any time between cycles, the dose must be reduced one level, for subsequent cycles.
- Any other grade 3 or 4 adverse reactions (such as nausea, vomiting, fatigue)
- Normal creatine kinase level, check every week in cycle 1 and 2 and prior to each administration

Hepatic impairment
Special caution is advised and dose adjustments may be necessary in patients with hepatic impairment since systemic exposure to trabectedin is increased and the risk of hepatotoxicity might be increased. Patients with elevated serum bilirubin levels at baseline must not be treated with trabectedin.
Liver function tests should be monitored during treatment with trabectedin as dose adjustments may be indicated.
Prior to retreatment, patients must fulfill the baseline criteria. If any of the following events occur at any time between cycles, the dose must be reduced one level, according to reductions, for subsequent cycles:
- Increase of bilirubin >ULN and/or alkaline phosphatase >2.5xULN
- Increase of aminotransferases (AST or ALT) >2.5xULN which has not recovered by day 21.

Renal impairment
CrCl >30ml/min no adjustments required
CrCl <30ml/min trabectedin must not be used

REFERENCES

1. R. Garcia-Carbonero, J.G. Supko, R.G. Maki, J. Manola, D.P. Ryan, D. Harmon, T.A. Puchalski, G. Goss, M.V. Seiden, A. Waxman, M.T. Quigley, T. Lopez, M.A. Sancho, J. Jimeno, C. Guzman, and G.D. Demetri Ecteinascidin-743 (ET-743) for Chemotherapy-Naive Patients With Advanced Soft Tissue Sarcomas: Multicenter Phase II and Pharmacokinetic Study JCO VOLUME 23 NUMBER 24 AUGUST 20 2005