PEGYLATED LIPOSOMAL DOXORUBICIN

INDICATION (ICD10) C46

1. Treatment of AIDS-related Kaposi's sarcoma. It may be used as first-line systemic chemotherapy, or as second line chemotherapy in AIDS-KS patients with disease that has progressed with, or in patients intolerant to, prior combination systemic chemotherapy comprising at least two of the following agents: a vinca alkaloid, bleomycin and standard doxorubicin (or other anthracycline).

REGIMEN

Day 1 PEGYLATED LIPOSOMAL DOXORUBICIN 20mg/m^2 in #ml glucose 5% IV infusion over 30 minutes

diluent volume for dose prescribed as per national standardised product specification

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 14 days (may be given every 21 days).
Continue treatment as required to maintain a therapeutic response.

ANTI-EMETICS

Low emetic risk day 1

CONCURRENT MEDICATION REQUIRED

Liposomal doxorubicin	Benzdyamine mouthwash, saltwater mouthwash

EXTRAVASATION AND TYPE OF LINE / FILTERS

Liposomal doxorubicin - exfoliant

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.5 (also see haematological dose modifications)
Platelets x 10^9/L ≥100 (also see haematological dose modifications)
ECG (possible ECHO) required if patient has preexisting cardiac disease
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Liposomal doxorubicin	Avoid where hypersensitivity to the active substance, peanut or soya. Cardiotoxicity – monitor cardiac function. Liposomal doxorubicin may be stopped in future cycles if signs of cardiotoxicity eg cardiac arrhythmias, pericardial effusion, tachycardia with fatigue. GI disturbances, mucositis, stomatitis. Paraesthesia. Infusion related reactions – allergic or anaphylactic like reactions discontinue infusion, treat, once fully recovered restart at reduced infusion rate. Palmar-plantar erythema - treat with steroids prednisolone 30mg od or dexamethasone 8mg od. Consider pyridoxine.

DOSE MODIFICATIONS

Liposomal doxorubicin maximum lifetime dose
= 400mg/m^2 (in patients with cardiac dysfunction or exposed to mediastinal irradiation)
= 450-550mg/m^2 (with normal cardiac function)

Haematological

Haematological toxicity may require dose reduction or suspension or delay of therapy.
Temporarily suspend doxorubicin pegylated liposomal treatment in patients when the neutrophil count is <1.0x10^9/l and/or the platelet count is <50x10^9/l.
G-CSF may be given as concomitant therapy to support the blood count when the ANC count is <1.0x10^9/l in subsequent cycles.

Non-haematological

Palmar-plantar erythrodysesthesia – week after prior pegylated liposomal doxorubicin dose

Current assessment	Week 4	Week 5	Week 6
Grade 1 (not interfering with daily activities)	Redose unless patient has experienced a previous grade 3 or 4 skin toxicity, in which case wait an additional week	Redose unless patient has experienced a previous grade 3 or 4 skin toxicity, in which case wait an additional week	Give 75% dose return to previous interval
Grade 2 (interfere with, but not preclude normal physical activities. Blisters <2cm diameter	Wait an additional week	Wait an additional week	Give 75% dose return to previous interval
Grade 3 (interfere with walking or normal daily activities. Can't wear regular clothes)	Wait an additional week	Wait an additional week	Withdraw patient
Grade 4 (diffuse or local infections, bedridden or hospitalised)	Wait an additional week	Wait an additional week	Withdraw patient

Stomatitis week after prior pegylated liposomal doxorubicin dose

Current assessment	Week 4	Week 5	Week 6
Grade 1 (painless ulcers, erythema, mild soreness)	Redose unless patient has experienced a previous grade 3 or 4 stomatitis toxicity, in which case wait an additional week	Redose unless patient has experienced a previous grade 3 or 4 stomatitis toxicity, in which case wait an additional week	Give 75% dose return to previous interval or withdraw patient per physician's assessment
Grade 2 (painful erythema, oedema, ulcers, but can eat)	Wait an additional week	Wait an additional week	Give 75% dose return to previous interval or withdraw patient per physician's assessment
Grade 3 (painful erythema, oedema, ulcers, but can't eat)	Wait an additional week	Wait an additional week	Withdraw patient
Grade 4 (requires parenteral or enteral support)	Wait an additional week	Wait an additional week	Withdraw patient

Hepatic impairment

Bilirubin 20-50micromol/L	give 75% dose
Bilirubin >51micromol/L	give 50% dose

Patients with impaired hepatic function should be reduced based as follows:
at initiation of therapy, if the bilirubin 1.2-3.0mg/dl, the first dose is reduced to 75%,
bilirubin >3.0mg/dl, the first dose is reduced to 50%.
If the patient tolerates the first dose without an increase in serum bilirubin or liver enzymes, the dose for cycle 2 can be increased to the next dose level, i.e., if reduced to 75% for the first dose, increase to full dose for cycle 2; if reduced to 50% for the first dose, increase to 75% of full dose for cycle 2.
Dosage can be increased to full dose for subsequent cycles if tolerated.
It can be administered to patients with liver metastases with concurrent elevation of bilirubin and liver enzymes up to 4xULN.
Prior to administration, evaluate hepatic function using conventional clinical laboratory tests such as ALT/AST, alkaline phosphatase, and bilirubin.

REFERENCES

1. SPC January 2024