SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Paclitaxel

Kaposi's Sarcoma

PROTOCOL REF: MPHAPAKS
(Version No. 1.1)

Approved for use in:

Second line chemotherapy for progressive Kaposi's sarcoma. Prior chemotherapy may have been given at another centre.

Dosage:

Drug	Dose	Route	Frequency
Paclitaxel	**100mg/m^2**	IV Infusion	Every 14 days

Maximum of 10 cycles

Administration / Counselling Points:

Paclitaxel must be administered via a non-PVC giving set with a 0.22 micron filter.

Avoid excessive agitation of paclitaxel as may cause precipitation.

Paclitaxel in solution may show haziness due to the formulation and this is not removed by filtration. This does not affect the potency.

Emetogenic risk:

Low emetogenic risk

Supportive treatments:

Premedication: Dexamethasone and Chlorphenamine to reduce hypersensitivity risk

TTO: Metoclopramide 10mg three times a day when required.

Extravasation risk:

Paclitaxel - Vesicant

Dosing in renal and hepatic impairment:

Renal	No dose adjustment needed.

Hepatic

Transaminase < 10 x ULN, dose at 100%
Transaminase ≥ 10 x ULN – contraindicated

Bilirubin (µmol/ L)		**Paclitaxel dose (mg/m^2)**
≤ 26	≤1.25 x ULN	100
27 to 42	1.26 to 2 x ULN	75
43 to 105	2.01-5 x ULN	50
>106	>5 x ULN	Contraindicated

Interactions:

Inhibitors of CYP2C8 or CYP3A4 (e.g. imidazole antifungals, erythromycin, fluoxetine, gemfibrozil, clopidogrel, ritonavir, saquinavir) may increase exposure to paclitaxel therefore increasing risk of toxicity.

Inducers of CYP2C8 or CYP3A4 (e.g. rifampicin, carbamazepine, phenytoin, efavirenz) may lower paclitaxel exposure therefore reducing efficacy.

For more detailed interactions, please refer to summary of product characteristics.

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
	Dexamethasone	**6.6mg**	**IV**	30 mins before paclitaxel
	Chlorphenamine	**10mg**	**IV**	30 mins before chemotherapy
	Paclitaxel	**100 mg/m^2**	**IV**	Sodium Chloride 0.9% 250ml over 180 minutes

Main toxicities:

Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, hepatobiliary disorders

Haematological	Myelosuppression, neutropenia, anaemia, thrombocytopenia, leucopenia, bleeding
Cardiac and Vascular disorders	Bradycardia and hypotension
Gastrointestinal	Nausea, vomiting, diarrhoea, constipation
Musculoskeletal	Arthralgia, myalgia
Nervous system	Peripheral neuropathy
Hepatobiliary	Elevation of liver transaminases, alkaline phosphatase and bilirubin.
Skin and subcutaneous tissue disorders	Alopecia, mucositis Minor hypersensitivity reactions: flushing, rash
General disorders and administration site conditions	Malaise, fever, chills, urticaria, flu-like syndrome, rash, pruritus Injection site reactions (including localised oedema, pain, erythema, induration, on occasion extravasation can result in cellulitis, skin discolouration, skin fibrosis and skin necrosis

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Informed Consent	x					
Clinical Assessment	x				X	As clinically indicated or at the end of treatment
SACT Assessment (to include PS and toxicities)	x	x	x	x	x	Every cycle
On treatment review						
FBC	x	x	x	x	x	Every cycle
U&E & LFTs & Magnesium	x	x	x	x	X	Every Cycle
CrCl (Cockcroft and Gault)	x					If clinically indicated
CT scan**	x					If clinically indicated
ECG						If clinically indicated
Blood pressure measurement	x					Repeat if clinically indicated
Respiratory Rate						If clinically indicated
Weight recorded	x	x	x	x	X	Every cycle
Height recorded	X					
Blood glucose	x					Repeat if clinically indicated

Dose Modifications and Non-haematological Toxicity Management:

Following assessment, toxicity should be graded according to the CTCAE v5.0 criteria. Withhold treatment for any toxicity until resolved to grade 0 or 1. For dose modification, follow the general guidance below and discuss with treating clinician.

	Grade 2	Grade 3	Grade 4
1st appearance	Omit treatment until resolved to grade 0 or 1. Then continue at 100% of original dose with prophylaxis where possible	Omit treatment until resolved to grade 0 or 1. Then continue at 75% of original dose	Discontinue treatment
2nd appearance	Omit treatment until resolved to grade 0 or 1. Then continue at 75% of original dose	Omit treatment until resolved to grade 0 or 1. Then continue at 50% of original dose	
3rd appearance	Omit treatment until resolved to grade 0 or 1. Then continue at 50% of original dose	Discontinue treatment	
4th appearance	Discontinue treatment		

Paclitaxel	
Severe neutropenia (< 0.5 x 10^9/L for a minimum of 7 days)	Withhold paclitaxel until neutrophils ≥ 1 x 10^9/L. Consider reducing subsequent doses by 25%
Peripheral neuropathy	CTCAE grade 2: Withhold paclitaxel until recovered to grade 1 neuropathy and consider reducing dose by 25% CTCAE ≥ 3: Omit further paclitaxel
Severe mucositis (rare)	CTCAE grade 2: Withhold paclitaxel until recovered to grade 1 mucositis and consider reducing dose by 25% CTCAE ≥ 3: Omit further paclitaxel

Haematological toxicity:

This guide assumes that the patient is well with good performance status, other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Proceed if:

ANC ≥ 1 x 10^9/L	Plt ≥ 75 x 10^9/L

Omit if:

ANC ≤ 0.9 x 10^9/L	Plt ≤ 74 x 10^9/L

Non- Haematological toxicity:

References:

1. https://www.medicines.org.uk/emc
2. Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)
3. BNF available via: https://bnf.nice.org.uk/
4. https://www.clatterbridgecc.nhs.uk/application/files/7216/2514/8673/Paclitaxel_Weekly_Advanced_Breast_Cancer_Protocol_V1.1.pdf vsb
5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3112249/

Circulation/Dissemination

Date added into Q-Pulse	For completion by DCM
Date document posted on the Intranet	For completion by DCM

Version History

		Author name and designation	Summary of main changes
22/03/23	1.0	**Blessing Opawole (Pharmacist)**	**New protocol**
27/06/23	1.1	**Rob Challoner Pharmacist**	**Following discussion with Dr Ali. Hepatic impairment table updated with actual figures for bilirubin. % dose reductions round to nearest 5%. Dose reduction recommendation changed to "consider" 25% dose reduction**