SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

VYXEOS®
(LIPOSOMAL DAUNORUBICIN AND CYTARABINE)
ACUTE MYELOID LEUKAEMIA (AML)

PROTOCOL REF: MPHAVYXHA
(Version No. 2.0)

Approved for use in:

Vyxeos® is recommended for previously untreated acute myeloid leukaemia (AML) with one of the following subtypes:

- Therapy related AML (t-AML) with a documented history of prior cytotoxic therapy or ionising radiotherapy for an unrelated disease
- Chronic Myelomonocytic Leukaemia (CMMoL AML) with a documented history of CMMoL prior to transformation to AML
- Myelodysplasia AML (MDS AML) with a documented history of MDS prior to transformation
- De novo AML with karyotypic changes typical of MDS

Blueteq request MUST be completed prior to initiation

Note:

Vyxeso® (liposomal daunorubicin + cytarabine 144mg/m^2) = Daunorubicin 44mg/m^2 and CYTARABINE 100mg/m^2 encapsulated in liposomes.

Review and confirm any previous anthracycline administration prior to initiation of Vyxeos®.

Dosage:

Drug	Dose	Route	Frequency
Induction cycle 1			
Vyxeos® (Daunorubicin 44mg /Cytarabine 100mg)	***144mg/m²**	IV	Days 1,3 and 5 (once daily)
Following recovery from first induction cycle, bone marrow should be evaluated to determine if a second induction cycle is required. A 2nd induction course may be given to patients who do not show disease progression or unacceptable toxicity.			
Induction Cycle 2 (if clinically indicated)			
Vyxeos® (Daunorubicin 44mg /Cytarabine 100mg)	***144mg/m²**	IV	Days 1 and 3 (once daily)
Consolidation Cycles (1 or 2 cycles)			
Vyxeos® (Daunorubicin 44mg /Cytarabine 100mg)	***94mg/m²**	IV	Days 1 and 3 (once daily)

*note each vial of Vyxeos® contains 44mg Daunorubicin and 100mg Cytarabine, expressed as total quantity of 144mg and 29mg/65mg dose which is expressed at 94mg

Cycle length dependent upon count recovery. Maximum of two induction and two consolidation cycles.

Administration (+/- Counselling Points):

- Unless urgent clinical need precludes insertion, should be given via central line
- **Vyxeos® has a short expiry (4 hours)** once reconstituted and requires 90 minutes to infuse. It must be ready to administer on arrival at the ward. Ensure effective communication with aseptics manufacturing unit, nursing and pharmacy team to avoid wastage.
- Ideally, cycle 1 should start on a Monday. If this leads to a clinically unacceptable delay, then the day 3 or 5 dose may be delayed 24 hours.
- Vyxeos® must not be substituted or interchanged with other daunorubicin and/or cytarabine containing products
- An in-line membrane filter may be used for the intravenous infusion of Vyxeos®, provided the minimum pore diameter of the filter is greater than or equal to 15 µm.

- Possible hypersensitivity reactions may occur – see further information in 'Non-Haematology Dose Modifications' section.
- Blood transfusion requirements – give alert card.
- Contraceptive advice – males and females of childbearing potential must use effective contraceptive measures during and for up to 6 months following treatment.
- Men should receive counselling on sperm conservation before start of daunorubicin treatment because of the possibility of irreversible infertility.
- For women who want to become pregnant after completing daunorubicin treatment, genetic counselling is also recommended.
- Caution in wilsons disease or copper-related disorders

Emetogenic risk:

Moderately emetogenic

Supportive treatments:

- Allopurinol oral 300mg once daily (first cycle only). Consider rasburicase and IV hydration in patients at high risk of tumour lysis syndrome
- Aciclovir 400mg twice daily oral
- Ciprofloxacin 500mg twice daily oral (until neutrophils >1.0x10^9/L for 2 consecutive days)
- Chlorhexidine 0.2% mouthwash 10mL four times daily
- Ondansetron 8mg twice daily oral for 5 days and then when required.
- Metoclopramide 10mg three times daily when required
- Norethisterone 5-10mg three times daily (women of childbearing potential) until platelets >50x10^9/L
- Nystatin oral suspension 1mL four times daily
- Posaconazole 300mg twice daily for 2 doses and then once daily thereafter (until neutrophils >1.0x10^9/L for 2 consecutive days)

Consider if patient is on existing or has a history of immunosuppression;

- Co-trimoxazole 480mg daily (until neutrophils >1.0x10^9/L for 2 consecutive days)

Extravasation risk:

Vyxeos®**:** Vesicant

Refer to the CCC policy for the 'Prevention and Management of Extravasation Injuries'

Dosing in renal impairment:

Renal Dose Modifications
No dose adjustment required for renal impairment. No data in end stage renal impairment. Use with caution at clinitian discretion.

Dosing in hepatic impairment:

Hepatic Dose Modification		
Bilirubin	≥50µmol/L	Only use if benefit outweighs risk
Note that significantly impaired hepatic function might be a sign of disease progression and require cessation or change of treatment. Always discuss deteriorating organ function with consultant		

Interactions:

Please refer to the SPC for full list of interactions and further information

- No interaction studies have been performed with Vyxeos®. The delivery of daunorubicin and cytarabine in the Vyxeos® liposomal formulation is anticipated to reduce the possibility of interactions, because systemic free-drug concentrations of daunorubicin and cytarabine are much lower than [when] administered as the non-liposomal formulation.
- Concurrent use of cardiotoxic medications should be avoided where possible.
- Concurrent use of hepatotoxic agents may affect the metabolism of Vyxeos®.

Treatment schedule:

Induction Cycle(s):

***Note that administration must be completed before the product expires – note 4 hours expiry from dilution**

Day	Drug	Dose	Route	Diluent and rate
1	**Ondansetron**	8mg	PO	30 minutes prior to Vyxeos
	Vyxeos®	144mg/m^2	IV	500mls sodium chloride 0.9% over 90 mins
3	**Ondansetron**	8mg	PO	30 minutes prior to Vyxeos
	Vyxeos®	144mg/m^2	IV	500mls sodium chloride 0.9% over 90 mins*
5	**Ondansetron**	8mg	PO	30 minutes prior to Vyxeos
	Vyxeos®	144mg/m^2	IV	500mls sodium chloride 0.9% over 90 mins*

Consolidation Cycle(s):

***Note that administration must be completed before the product expires – note 4 hours expiry from dilution**

Day	Drug	Dose	Route	Diluent and rate
1	**Ondansetron**	8mg	PO	30 minutes prior to Vyxeos
	Vyxeos®	94mg/m^2	IV	500mls sodium chloride 0.9% over 90 mins*
3	**Ondansetron**	8mg	PO	30 minutes prior to Vyxeos
	Vyxeos®	194mg/m^2	IV	500mls sodium chloride 0.9% over 90 mins*

Main toxicities:

Please refer to the SPC for full list of toxicities and further information

Vyxeos®
Neutropenia, anaemia, thrombocytopenia, hypersensitivity, infection, tumour lysis syndrome, sleep disorders, anxiety, headaches, dizziness, visual imparinement, cardiotoxicity, arrhythmia, chest pain, hypo/hypertension, haemorrhage, shortness of breath, pleural effusion, nausea, vomiting, diarrhea, constipation, mucositis, abdominal pain, reduced appetite, fatigue, night sweats, alopecia, pyrexia, chills, infertility

Investigations and treatment plan:

	Pre	Induction	Second Induction	1st and 2nd Consolidation	Ongoing
Informed Consent	X				
Clinical Assessment, PS recorded, SACT assessment	X	X	X	X	Every cycle
Observations (Blood pressure/Pulse/Temperature/Respiratory Rate)	X	X	X	X	Every cycle
FBC, U&E & LFT & Mg	X	X	X	X	Every cycle
Creatinine clearance (C-G)	X	X	X	X	Every cycle
TFTs	X				Before Treatment
Tissue Typing	X				Before Treatment
Virology (Hepatitis B/C serology, HIV)	X				Before Treatment
Imaging as per NICE/network guidance and clinical indication	X				End of treatment or as clinically indicated
ECG and ECHO/MUGA	X				ECG /ECHO for all patients should be documented before starting anthracycline, unless stated by the medical team that this is not required
Immunoglobulins	X				Repeat if clinically indicated
Bone marrow	X	X	X	X	Following each cycle of induction and as clinically indicated
Height and Weight recorded	X	X	X	X	Every cycle
Pregnancy	X				If clinically appropriate

Dose Modifications and Toxicity Management:

Haematological toxicity:

Induction Cycle(s)

Induction cycle(s) can go ahead despite cytopenias, if thought to be due to disease.

Consolidation Cycle(s)

Cycles can proceed if-

ANC ≥ 0.5 x 10^9/L	Platelets ≥ 50 x 10^9/L

Delay 1 week on day 1 of consolidation cycles if these parameters are not met and then review.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non- Haematological toxicity:

See section entitled 'Dosing in Renal and Hepatic Impairment'

Hypersensitivity reaction management:

Vyxeos®- Hypersensitivity reaction management	
Mild hypersensitivity symptoms (e.g. mild flushing, rash, pruritus),	Treatment should be stopped, and the patient should be supervised, including monitoring of vital signs. The treatment should be restarted slowly once the symptoms have resolved, by halving the rate of infusion and intravenous chlorphenamine 10mg and intravenous dexamethasone (10 mg) should be given.
Moderate hypersensitivity symptoms (e.g., moderate rash, flushing, mild dyspnoea, chest discomfort)	Treatment should be stopped. Intravenous chlorphenamine 10mg and intravenous dexamethasone (10 mg) should be given. The infusion should not be restarted. When the patient is retreated, Vyxeos should

	be given at the same dose and rate and with pre-medication.
Severe/life-threatening hypersensitivity symptoms (e.g., hypotension requiring vasopressor therapy, angioedema, respiratory distress requiring bronchodilation therapy, generalised urticaria)	Treatment should be stopped. Intravenous chlorphenamine 10mg and dexamethasone (10 mg) should be given, and an epinephrine (adrenaline) or bronchodilators should be added if indicated. Do not reinitiate infusion, and do not retreat. Treatment with Vyxeos should be permanently discontinued. Patients should be monitored until symptoms resolve

References:

- Vyxeos 44 mg/100 mg powder for concentrate for solution for infusion. Summary of Product Characteristics Jazz Pharmaceuticals UK. Available from. Last updated December 2022 www.medicines.org.uk/emc
- NICETA522. Liposomal cytarabine-daunorubicin for untreated acute myeloid leukaemia. The National Institute for Health and Care Excellence (2018).

Circulation/Dissemination

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

Version History

Date	Version	Author name and designation	Summary of main changes
May 2020	1.1	**David Breen – Principal pharmacist HO**	
July 2023	2.0	**Sophie Hughes – Advanced Pharmacist**	3 yearly review. Transferred to new template, updated supportive medication. Standard ECHO/ECG comment added