SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

DA (DAUNORUBIN & CYTARABINE) ACUTE MYELOID LEUKAEMIA (AML)

PROTOCOL REF: MPHAFLAGHA
(Version No. 1.2)

Approved for use in:

Induction chemotherapy for AML in patients who are < 60 years of age. Can be used in older patients at the clinician's discretion.

Blueteq not required

Dosage:

Induction cycle 1 (DA 3+10):

Drug	Dose	Route	Frequency
Daunorubicin	**60mg/m^2**	IV	Day 1, 3 and 5 (once daily)
Cytarabine	**100mg/m^2**	IV	Days 1 to 10 (twice daily)

Induction cycle 2 (DA 3+8):

Drug	Dose	Route	Frequency
Daunorubicin	**50mg/m^2**	IV	Day 1, 3 and 5 (once daily)
Cytarabine	**100mg/m^2**	IV	Days 1 to 8 (twice daily)

Maximum of 2 cycles

Administration (+/- Counselling Points):

Unless urgent clinical need precludes insertion, should be given via central line

Patients will need admitting for therapy

- Possible infusional reactions – Anaphylaxis and anaphylactoid reactions may occur.
- 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.
- Daunorubicin hydrochloride causes episodes of nausea and vomiting, which sometimes can lead to impairment of the ability to drive or use machines.
- Special caution should be exercised in patients with preceding, concurrent or planned radiotherapy. These patients have an increased risk of local reactions in the radiation area (recall phenomena) during treatment with daunorubicin hydrochloride. Discuss with consultant.
- Anthracyclines should be avoided in patients with arrhythmias, recent myocardial infarction or myocardial insufficiency – discuss with consultant.

Emetogenic risk:

Moderately emetogenic

Supportive treatments:

- Allopurinol for 28 days (first cycle only). Consider rasburicase and IV hydration in patients at high risk of tumour lysis syndrome
- Aciclovir 400mg twice daily
- Ciprofloxacin 500mg twice daily (until neutrophils >1.0x10^9/L for 2 consecutive days)
- Chlorhexidine 0.2% mouthwash 10mL four times daily
- Metoclopramide 10mg three times daily prn
- Norethisterone 5-10mg TDS (women of childbearing potential)
- Nystatin 1mL four times daily

- Ondansetron 8mg twice daily PO for 5 days and then when required.
- 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:

Daunorubicin – vesicant

Cytarabine – non-vesicant

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

Dosing in renal and hepatic impairment:

Renal Dose Modifications		
	CrCl (ml/min)	**Dose Modification**
Daunorubicin	30 - 50	75% dose
	<30 or haemodialysis	50% dose
Cytarabine	No adjustment required	

Hepatic Dose Modifications		
Daunorubicin	**Bilirubin (micromol/L)**	**Dose Modification**
	20 - 50	75% dose
	>50	50% dose
Cytarabine	>34	50% dose*

*Doses can be escalated in further cycles in the absence of toxicity

Interactions:

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

Daunorubicin

- Ciclosporin - Increased concentration of daunorubicin and risk of toxicity
- Increased risk of cardiac toxicity when given with other cardiotoxic drugs such as trastuzumab

Cytarabine

- Digoxin: Possible reduction of digoxin levels – monitor levels closely.
- Intrathecal methotrexate: Possible increased risk of severe neurological adverse reactions such as headache, paralysis, coma and stroke like episodes when given concomitantly with IV cytarabine.

Treatment schedule:

Day	Time	Drug	Dose	Route	Diluent and rate
1	08:30	**Ondansetron**	**8mg**	**PO**	
	09:00	**Daunorubicin**	**60mg/m^2** (50mg/m^2 if cycle 2)	**IV**	100mls sodium chloride 0.9% over 60 mins
	10:00	**Cytarabine**	**100mg/m^2**	**IV**	100mls sodium chloride 0.9% over 30mins
	20:00	**Ondansetron**	**8mg**	**PO**	
	22:00	**Cytarabine**	**100mg/m^2**	**IV**	100mls sodium chloride 0.9% over 30 mins
2	08:30	**Ondansetron**	**8mg**	**PO**	
	10:00	**Cytarabine**	**100mg/m^2**	**IV**	100mls sodium chloride 0.9% over 30mins
	20:00	**Ondansetron**	**8mg**	**PO**	
	22:00	**Cytarabine**	**100mg/m^2**	**IV**	100mls sodium chloride 0.9% over 30 mins
3	08:30	**Ondansetron**	**8mg**	**PO**	
	09:00	**Daunorubicin**	**60mg/m^2** (50mg/m^2 if cycle 2)	**IV**	100mls sodium chloride 0.9% over 60 mins
	10:00	**Cytarabine**	**100mg/m^2**	**IV**	100mls sodium chloride 0.9% over 30mins
	20:00	**Ondansetron**	**8mg**	**PO**	
	22:00	**Cytarabine**	**100mg/m^2**	**IV**	100mls sodium chloride 0.9% over 30 mins
4	08:30	**Ondansetron**	**8mg**	**PO**	
	10:00	**Cytarabine**	**100mg/m^2**	**IV**	100mls sodium chloride 0.9% over 30mins
	20:00	**Ondansetron**	**8mg**	**PO**	
	22:00	**Cytarabine**	**100mg/m^2**	**IV**	100mls sodium chloride 0.9% over 30 mins

5	08:30	**Ondansetron**	**8mg**	**PO**	
	09:00	**Daunorubicin**	**60mg/m²** (50mg/m² if cycle 2)	**IV**	100mls sodium chloride 0.9% over 60 mins
	10:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30mins
	20:00	**Ondansetron**	**8mg**	**PO**	
	22:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30 mins
6	10:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30mins
	22:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30 mins
7	10:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30mins
	22:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30 mins
8	10:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30mins
	22:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30 mins
ONLY CONTINUE BELOW IF CYCLE 1 INDUCTION (DA 3+10)					
9	10:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30mins
	22:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30 mins
10	10:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30mins
	22:00	**Cytarabine**	**100mg/m²**	**IV**	100mls sodium chloride 0.9% over 30 mins

Main toxicities:

Cytarabine
Bone marrow suppression, nausea, diarrhoea, abdominal pain, oral ulceration, hepatic dysfunction, CNS, GI and pulmonary toxicity, reversible corneal toxicity, somnolence, convulsion, pulmonary oedema. A cytarabine syndrome is also recognized in which patients suffer from fever, myalgia, bone pain, occasional chest pains, maculopapular rash, conjunctivitis and malaise. It usually occurs 6 - 12 hours following administration. Neurotoxicity also reported, e.g. cerebellar damage.
Daunorubicin

Cardiotoxicity may occur - cumulative dose associated with cardiotoxicity is not known but it is thought that a total dose of 60-80 mg/m^2 is not problematic. Discoloration of urine for 2 to 3 days after administration. Alopecia. Nausea and vomiting. Elevation of liver enzymes may occur

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

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Investigations and treatment plan:

	Before Treatment	Cycle 1	Cycle 2 onwards	Ongoing
Informed Consent	X			
Clinical Assessment and PS recorded	X	X	X	Before treatment and prior to every cycle
SACT Assessment	X	X	X	
Observations (Blood pressure/ Pulse/ Temperature/ Respiratory rate)	X	X	X	Daily during treatment
FBC	X	X	X	
U&E and LFTs, bone profile, CrCl	X	X	X	
ECHO/MUGA	X			ECHO for all patients should be documented before starting anthracycline, unless stated by medical team that it is not required
ECG	X			ECG for all patients should be documented before starting anthracycline, unless stated by medical team that it is not required
Bone Marrow	X		X	Before treatment and at count recovery or at day 28, depending on which is earliest. Further to be confirmed by consultant
Immunoglobulins	X			Before treatment
Virology (Hepatitis B/C serology, HIV)	X			Before treatment
Pregnancy test	X			As appropriate
Height	X			
Weight	X	X	X	
Tissue Typing	X			
Imaging as per NICE/network guidance and clinical indication	X			Before treatment and to restage as indicated

Dose Modifications and Toxicity Management:

Haematological toxicity:

First cycle to start regardless of neutrophil and platelet count.

Subsequent cycles to proceed when-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

Note therapy can proceed if values are below these levels if cytopenias known to be secondary to disease.

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'

References:

1. Summary of Product Characteristics, Daunorubicin 20mg Powder for Injection, Zentiva Ltd. August 2018. Monograph available from: http://www.medicines.org.uk [accessed April 2023].
2. Summary of Product Characteristics, Cytarabine Injection solution 100mg/ml, Hospira UK Ltd. February 2018. Monograph available from: http://www.medicines.org.uk [accessed April2023].

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
		Aileen McCaughey	New protocol
May 2023	1.1	**Jennifer Gibson**	**Three yearly review. Transferred to new template. Added main toxicities information. Treatment schedule updated. Updated daunorubicin hepatic dose modifications.**
Sept 2023	1.2	**Sophie Hughes – Advanced Pharmacist**	**Update re ECHO/ECG pre anthracycline**