SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

DA & GEMTUZUMAB OZOGAMYCIN (MYLOTARG®) ACUTE MYELOID LEUKAEMIA (AML)

PROTOCOL REF: MPHAMDAHA
(Version No. 2.1)

Approved for use in:

Gemtuzumab ozogamicin (Mylotarg®) is indicated in combination with daunorubicin and cytarabine (DA), for the treatment of previously untreated CD33-positive AML (not APML) in patients fit for intensive treatment. If cytogenetics results are awaited, urgent systemic treatment can be started, but if results indicate adverse cytogenetics, discontinue treatment with gemtuzumab ozogamicin.

Note this protocol should only be used to treat patients not in a clinical trial. Refer to relevant trial protocol for enrolled patients.

Blueteq request for gemtuzumab ozogamycin (Mylotarg®) must be completed prior to initiation. The use of Mylotarg® is exempt from NHS England treatment break policy.

Dosage:

Cycle	Drug	Dose	Route	Frequency
First Induction	**Daunorubicin**	**60mg/m^2**	IV	Days 1 to 3
	Cytarabine	**200mg/m^2**	IV	Once daily days 1 to 7
	Gemtuzumab ozogamycin (Mylotarg®)	**3mg/m^2** (Max 5mg)	IV	Days 1, 4 and 7
A bone marrow examination should be performed on day 14. If there was definitive evidence of clinically significant residual leukemia, a second cycle of induction therapy without gemtuzumab ozogamicin may be given. Patients who achieved complete remission after induction therapy will receive two cycles of consolidation treatment				
***Second Induction** (if required)	**Daunorubicin**	**35mg/m^2**	IV	Days 1 to 2
	Cytarabine	**1000mg/m^2**	IV	Every 12 hours on days 1 to 3
****First Consolidation**	**Daunorubicin**	**60mg/m^2**	IV	Days 1
	Cytarabine	**1000mg/m^2**	IV	Every 12 hours on days 1 to 4
	Gemtuzumab ozogamycin (Mylotarg®)	**3mg/m^2** (Max 5mg)	IV	Day 1
Second Consolidation	**Daunorubicin**	**60mg/m^2**	IV	Days 1 and 2
	Cytarabine	**1000mg/m^2**	IV	Every 12 hours on days 1 to 4
	Gemtuzumab ozogamycin (Mylotarg®)	**3mg/m^2** (Max 5mg)	IV	Day 1

***If residual disease on D14 bone marrow biopsy**

****For patients experiencing a complete remission (CR) following induction, defined as fewer than 5% blasts in a normocellular marrow and an absolute neutrophil count (ANC) >1.0 × 10^9 cells/L with a platelet count of ≥100 × 10^9/L in the peripheral blood in the absence of transfusion, up to 2 consolidation courses can be given.

At clinicians discretion consider schedule modification for hyperleukocytosis: If leukocyte count ≥30x10^9/L, cyto-reduction is recommended 48 hours prior to commencing gemtuzumab ozogamycin (Mylotarg®) in order to reduce the peripheral white cell count. See recommended changes to induction schedule below.

Options for cyto-reduction include: leukapheresis, oral hydroxycarbamide, or cytarabine +/- hydroxycarbamide.

If cytarabine is used for leuko-reduction, (with or without hydroxycarbamide); in patients with previously untreated *de novo* hyperleukocytic AML, receiving gemtuzumab ozogamycin (Mylotarg®) in combination therapy, apply the following modified schedule for the first induction cycle:

Treatment course	Drug	Dosage	Route	Frequency
Induction	Hydroxycarbamide*		PO	Day 1
	Cytarabine	200 mg/m^2	IV	Days 1 to 7
	Daunorubicin	60 mg/m^2	IV	Days 3 to 5
	Gemtuzumab ozogamycin (Mylotarg®)	3 mg/m^2 (max 5mg/dose)	IV	Days 3,6 and 9

***Consider hydroxycarbamide at clinician discretion**

Administration (+/- Counselling Points):

- Unless urgent clinical need precludes insertion, should be given via central line
- Patients will need admitting for therapy
- Gemtuzumab ozogamycin (Mylotarg®) has moderate influence on the ability to drive and use machines. Patients should be advised they may experience fatigue, dizziness and headache during treatment with gemtuzumab ozogamycin. Therefore, caution should be exercised when driving or operating machines.
- Contraceptive advise- use at least 2 methods of contraception during treatment with gemtuzumab ozogamycin (Mylotarg®), and for at least 7 months (females) and 4 months (males) after the last dose.
- Hypotension may occur, therefore it is advisable to withhold anti-hypertensive medications 12hours before and 12 hours after treatment with gemtuzumab ozogamycin (Mylotarg®)

- There is an increased risk of veno-occlusive disease/sinusoidal obstruction syndrome with gemtuzumab ozogamycin (Mylotarg®) – use with caution in moderate/severe hepatic impairment
- 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 and cytarabine are contraindicated during breast-feeding.
- 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 or concomitant use of cardiotoxic agents – discuss with consultant.

Emetogenic risk:

Moderately emetogenic

Supportive treatments:

Gemtuzumab ozogamycin (Mylotarg®) pre-infusion medicines:

- Paracetamol PO 1g
- Chlorphenamine IV bolus 10mg
- Hydrocortisone sodium succinate IV bolus 100mg

Supportive medicines:

- Allopurinol PO 300mg daily (depending on renal function) for first cycle. Consider rasburicase if high risk of tumour lysis syndrome.
- Aciclovir 400mg PO twice daily
- Ciprofloxacin 500mg twice daily (until neutrophils >1.0x10^9/L on 2 consecutive days)
- Metoclopramide 10mg three times daily when required
- Nystatin 1mL four times daily
- Ondansetron PO 8mg twice daily
- Posaconazole 300mg twice daily for 2 doses and then once daily thereafter (start 5 days after gemtuzumab ozogamycin treatment has finished as per AML19 recommendation due to risk of hepatotoxicity). Consider caspofungin as an alternative if required sooner.
- Prednisolone 0.5% eye drops 1 drop into both eyes QDS for 10 days from day 1 (after second induction and consolidation cycles only)

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: Neutral

Gemtuzumab ozogamycin (Mylotarg®): Irritant

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 dose reductions for cycle 1 as low dose (<1g/m^2)	
	31 – 59	50%
	≤30	Not recommended
	Haemodialysis	50% dose Start HD 4-5hrs after cytarabine

Gemtuzumab ozogamycin (Mylotarg®)	No dose adjustment required in patients with mild to moderate renal impairment. Mylotarg® has not been studied in patients with severe renal impairment. Dosing in renal impairment would be a clinical decision.

Hepatic Dose Modifications		
	Bilirubin (micromol/L)	**Dose Modification**
Daunorubicin	20 - 50	75% dose
	>50	50% dose
Cytarabine	>34	50% dose and titrate as tolerated
Gemtuzumab ozogamycin (Mylotarg®)	Use with caution due to increased risk of veno-occlusive disease. Always discuss deteriorating organ function with a consultant	
	Bilirubin >2xULN and AST/ALT >2.5xULN	Defer Mylotarg until recovery of bilirubin to ≤ 2 × ULN and AST/ALT ≤ 2.5 × ULN prior to each dose. Consider omitting scheduled dose if delayed more than 2 days between sequential infusions

Interactions:

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

Gemtuzumab ozogamycin (Mylotarg®):

- The concomitant use of hepatotoxic drugs should be risk assessed on a patient by patient basis (e.g. azole antifungals)

Daunorubicin:

Concomitant use with cardiotoxic agents is not recommended

Cytarabine

- Cytarabine may reduce digoxin levels. Digoxin level monitoring is recommended.
- Methotrexate: Intravenous cytarabine given concomitantly with intrathecal methotrexate may increase the risk of severe neurological adverse reactions such as headache, paralysis, coma and stroke like episodes
- An *in-vitro* interaction study between gentamicin and cytarabine showed a cytarabine related antagonism for the susceptibility of *K. pneumoniae* strains. In patients on cytarabine being treated with gentamicin for a *K.pneumoniae* infection, a lack of a

prompt therapeutic response may indicate the need for re-evaluation of antibacterial therapy.

Treatment schedule:

First Induction Cycle (Cycle 1)

Do not give other drugs through the same infusion line as gemtuzumab ozogamycin (Mylotarg®)

Day	Time	Drug	Dose	Route	Diluent and rate
1	08:00	**Paracetamol**	**1g**	**PO**	1 hour prior to gemtuzumab ozogamycin
		Chlorphenamine	**10mg**	**IV**	
		Hydrocortisone	**100mg**	**IV**	
		Ondansetron	**8mg**	**PO**	Prior to chemotherapy
	Monitor vital signs during and for 4 hours after gemtuzumab ozogomycin				
	09:00	**Gemtuzumab ozogamycin (Mylotarg®)**	**3mg/m²** (Max 5mg)	**IV**	In 50mL 0.9% sodium chloride over 2 hours, via low-protein binding 0.2 micron filter.
	11:00	**Daunorubicin**	**60mg/m²**	**IV**	In 100mL Sodium Chloride 0.9% over 30 mins
	11:30	**Cytarabine**	**200mg/m²**	**IV**	In 1000mL Sodium Chloride 0.9% over 22 hours
2	08:00	**Ondansetron**	**8mg**	**PO**	Prior to chemotherapy
	09:00	**Daunorubicin**	**60mg/m²**	IV	In 100ml 0.9% sodium chloride given over 30mins
	09:30	**Cytarabine**	**200mg/m²**	**IV**	In 1000mL Sodium Chloride 0.9% over 22 hours
3	08:00	**Ondansetron**	**8mg**	**PO**	Prior to chemotherapy
	09:00	**Daunorubicin**	**60mg/m²**	IV	In 100ml 0.9% sodium chloride given over 30mins
	09:30	**Cytarabine**	**200mg/m²**	**IV**	In 1000mL Sodium Chloride 0.9% over 22 hours
4	08:00	**Paracetamol**	**1g**	PO	1 hour prior to gemtuzumab ozogamycin
		Chlorphenamine	**10mg**	IV	
		Hydrocortisone	**100mg**	IV	
		Ondansetron	**8mg**	**PO**	Prior to chemotherapy
	Monitor vital signs during and for 4 hours after gemtuzumab ozogomycin				

	09:00	**Gemtuzumab ozogamycin (Mylotarg®)**	**3mg/m²** (Max 5mg)	IV	In 50mL 0.9% sodium chloride over 2 hours, via low-protein binding 0.2 micron filter.
	11:00	**Cytarabine**	**200mg/m²**	**IV**	In 1000mL Sodium Chloride 0.9% over 22 hours
5	08:00	**Ondansetron**	**8mg**	**PO**	Prior to chemotherapy
	09:00	**Cytarabine**	**200mg/m²**	**IV**	In 1000mL Sodium Chloride 0.9% over 22 hours
6	09:00	**Cytarabine**	**200mg/m²**	**IV**	In 1000mL Sodium Chloride 0.9% over 22 hours
7	08:00	**Paracetamol**	**1g**	PO	1 hour prior to gemtuzumab ozogamycin
		Chlorphenamine	**10mg**	IV	
		Hydrocortisone	**100mg**	IV	
	Monitor vital signs during and for 4 hours after gemtuzumab ozogomycin				
	09:00	**Gemtuzumab ozogamycin (Mylotarg®)**	**3mg/m²** (Max 5mg)	IV	In 50mL 0.9% sodium chloride over 2 hours, via low-protein binding 0.2 micron filter.
	11:00	**Cytarabine**	**200mg/m²**	**IV**	In 1000mL Sodium Chloride 0.9% over 22 hours

Second Induction Cycle

(Only if there was definitive evidence of clinically significant residual leukemia on bone marrow biopsy post cycle 1)

Day	Time	Drug	Dose	Route	Diluent and rate
1	08:00	**Ondansetron**	**8mg**	**PO**	Prior to chemotherapy
	09:00	**Daunorubicin**	**35mg/m²**	**IV**	In 100mL Sodium Chloride 0.9% over 30 mins
	10:00	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
	22:00	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
2	08:00	**Ondansetron**	**8mg**	**PO**	Prior to chemotherapy
	09:00	**Daunorubicin**	**35mg/m²**	**IV**	In 100mL Sodium Chloride 0.9% over 30 mins
	10:00	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
	22:00	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours

3	10:00	**Cytarabine**	**1000mg/m^2**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
	22:00	**Cytarabine**	**1000mg/m^2**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours

First Consolidation Cycle

Do not give other drugs through the same infusion line as gemtuzumab ozogamycin (Mylotarg®)

Day	Time	Drug	Dose	Route	Diluent and rate
1	08:00	**Paracetamol**	**1g**	**PO**	1 hour prior to gemtuzumab ozogamycin
		Chlorphenamine	**10mg**	**IV**	
		Hydrocortisone	**100mg**	**IV**	
		Ondansetron	**8mg**	**PO**	Prior to chemotherapy
	Monitor vital signs during and for 4 hours after gemtuzumab ozogomycin				
	09:00	**Gemtuzumab ozogamycin (Mylotarg®)**	**3mg/m^2** (Max 5mg)	**IV**	In 50mL 0.9% sodium chloride over 2 hours, via low-protein binding 0.2 micron filter.
	11:00	**Daunorubicin**	**60mg/m^2**	**IV**	In 100mL Sodium Chloride 0.9% over 30 mins
	11:30	**Cytarabine**	**1000mg/m^2**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
	23:30	**Cytarabine**	**1000mg/m^2**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
2	09:00	**Cytarabine**	**1000mg/m^2**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
	21:00	**Cytarabine**	**1000mg/m^2**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
3	09:00	**Cytarabine**	**1000mg/m^2**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
	21:00	**Cytarabine**	**1000mg/m^2**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
4	09:00	**Cytarabine**	**1000mg/m^2**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
	21:00	**Cytarabine**	**1000mg/m^2**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours

Second Consolidation Cycle

Do not give other drugs through the same infusion line as gemtuzumab ozogamycin (Mylotarg®)

Day	Time	Drug	Dose	Route	Diluent and rate
1	08:00	**Paracetamol**	**1g**	**PO**	1 hour prior to gemtuzumab ozogamycin
		Chlorphenamine	**10mg**	**IV**	
		Hydrocortisone	**100mg**	**IV**	
		Ondansetron	**8mg**	**PO**	Prior to chemotherapy
	Monitor vital signs during and for 4 hours after gemtuzumab ozogomycin				
	09:00	**Gemtuzumab ozogamycin (Mylotarg®)**	**3mg/m²** (Max 5mg)	**IV**	In 50mL 0.9% sodium chloride over 2 hours, via low-protein binding 0.2 micron filter.
	11:00	**Daunorubicin**	**60mg/m²**	**IV**	In 100mL Sodium Chloride 0.9% over 30 mins
	11:30	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
	23:30	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
2	08:00	**Ondansetron**	**8mg**	**PO**	Prior to chemotherapy
	09:00	**Daunorubicin**	**60mg/m²**	**IV**	In 100mL Sodium Chloride 0.9% over 30 mins
	09:30	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
	21:30	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
3	09:00	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
	21:30	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
4	09:00	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours
	21:30	**Cytarabine**	**1000mg/m²**	**IV**	In 500mL Sodium Chloride 0.9% over 3 hours

Main toxicities:

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

General toxicity
Commonly reported (>10%): Febrile neutropenia, thrombocytopenia, anaemia, leucopenia, infections, hyperglycaemia, diarrhoea, nausea, vomiting, headache, stomatitis, electrolyte imbalance, deranged liver function tests.
Daunorubicin
Bone marrow suppression (anaemia, thrombocytopenia, neutropenia), Posterior Reversible Encephalopathy Syndrome (PRES), alopecia, mucositis, chronic and acute cardiac failure and dysrrhythmias,. There is a recommended maximum cumulative lifetime dose of daunorubicin of 600 mg/m^2.
Cytarabine
Diarrhoea, abdominal pain, oral ulceration, hepatic dysfunction. CNS, GI and pulmonary toxicity, reversible corneal toxicity, somnolence, convulsion, pulmonary oedema. A cytarabine syndrome is also recognised in which patients suffer from fever, myalgia, bone pain, occasional chest pains, maculopapular rash, conjunctivitis and malaise. It usually occurs 6 to 12 hours following administration.
Gemtuzumab ozogamycin (Mylotarg®)
Veno-occlusive disease (VOD)/sinusoidal obstruction syndrome (SOS), tumour lysis syndrome, infusion related reaction, chills, haemorrhage, pyrexia, fatigue, abdominal pain. Due to the risk of VOD, liver function tests, hepatomegaly (which may be painful), rapid weight gain, and ascites should be closely monitored before each dose. All haematopoietic stem cell transplant patients with previous gemtuzumab ozogamicin exposure should receive ursodeoxycholic acid prophylaxis from the start of conditioning chemotherapy

PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Investigations and treatment plan:

	Pre	Ind C1, D1	Ind C1 D4	Ind C1 D7	Ind C1 D14	Ind C2	Cons C1	Cons C2	Ongoing
Clinical Assessment	X	X				X	X	X	Every cycle
SACT Assessment, including toxicities and performance status		X				X	X	X	Every cycle
FBC	X	X				X	X	X	Every cycle
U&E, LFT, bone profile, CrCl	X	X				X	X	X	Every cycle
Glucose (and HbA1c if indicated)	X	X				X	X	X	Every cycle
Uric Acid	X								Repeat as clinically indicated
LDH	X								Repeat as clinically indicated
Hepatitis B sAg and core Antibody and hepatitis C antibody, HIV 1+2	X								
ECG/ECHO	X								ECG/ECHO for all patients should be documented before starting anthracycline, unless stated by medical team that it is not required
Informed Consent	X								
Weight recorded	X	X				X	X	X	Every cycle
Height	X								
Pregnancy test	X					X	X	X	If applicable each cycle
Temperature, respiratory rate, pulse		X	X	X			X	X	Continuous monitoring required if on mylotarg and for four hours after
Bone marrow biopsy	X				X		X	X	

Dose Modifications and Toxicity Management:

Haematological Toxicity

Induction cycle(s) to be completed regardless of neutrophil and platelet counts.

Proceed with consolidation cycle(s) if all apply:-

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

If these parameters are not met- see below:

Haematological Toxicity	Dose Modification
Persistent thrombocytopenia Platelets <100 x 10^9/L	• Postpone start of consolidation course. • If platelet count recovers to ≥ 100 x 10^9/L within 14 days following the planned start date of the consolidation course: initiate consolidation therapy • If platelet count recovers to between 50-100 x 10^9/L within 14 days following the planned start date of the consolidation course: gemtuzumab ozogamycin (Mylotarg®) should not be re-introduced and consolidation therapy should consist of DA only. • If platelet count recovery remains < 50 x 10^9/L for greater than 14 days, takes longer than 14 days, or if platelet count does not recover to ≥ 50 x 10^9/L consolidation therapy should be re-evaluated and a bone marrow should be performed to re-assess the patients' status.
Persistent neutropenia ANC ≤ 1.0 x 10^9/L	If neutrophil count does not recover to greater than 5 x 10^9/L within 14 days following the planned start date of the consolidation cycle (14 days after haematologic recovery following previous cycle), discontinue gemtuzumab ozogamycin (Mylotarg®) (do not administer Mylotarg® in the consolidation cycles).

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'

Toxicity	Recommendation
Veno-occlusive disease (VOD) / Sinusoidal Obstruction Syndrome (SOS)	Note Mylotarg® frequently causes a transient elevation of liver function around 8-10 days following infusion. This usually settles within 2-3 days and is not usually indicative of VOD. Signs and symptoms include: Hyperbilirubinaema, ascites, weight gain (fluid retention) and hepatomegaly. Send for urgent doppler ultrasound of liver to assess hepatic blood flow IV Defibrotide should be considered for a minimum of 7 days (6.25mg/kg every 6 hours- i.e. total 25mg/kg/day) If Defibrotide is required, contact your pharmacist immediately for further advice, requires blueteq.
Infusion-related reactions	Signs and symptoms of infusion related reactions may include fever and chills, and less frequently hypotension, tachycardia, and respiratory symptoms that may occur during the first 24 hours after administration. Infusion of Mylotarg® should be performed under close clinical monitoring, including pulse, blood pressure, and temperature. Premedication with a corticosteroid, antihistamine and acetaminophen (or paracetamol) is recommended 1 hour prior to Mylotarg® dosing. Infusion should be interrupted immediately for patients who develop evidence of severe reactions, especially dyspnoea, bronchospasm, or clinically significant hypotension. Patients should be monitored until signs and symptoms completely resolve. Discontinuation of treatment should be strongly considered for patients who develop signs or symptoms of anaphylaxis, including severe respiratory symptoms or clinically significant hypotension
Other reported adverse reactions	Fever, chills, nausea, vomiting, headache, dyspnoea, hypotension, hypertension, hyperglycaemia, infection, bleeding, mucositis, rash, cutaneous herpes simplex, early mortality, abdominal pain, asthenia, back pain, pain, sepsis, tachycardia, anorexia, constipation, diarrhoea, abnormal LFTs, stomatitis, hypokalemia, raised LDH, peripheral oedema, anxiety, depression, dizziness, insomnia, cough, epistaxis, pharyngitis, pneumonia, local reaction.

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Circulation/Dissemination

Date added into Q-Pulse	31st January 2024
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
		Niamh McLaughlin	Version 1.1
May 2023	2.0	**Jennifer Gibson Principal Pharmacist**	Transferred to new template. Formatting adjustments. Cycle 1 cytarabine changed to BD dosing. High dose cytarabine duration changed to 3 hours.
October 2023	2.1	**Sophie Hughes Advance Pharmacist**	Update re ECHO/ECG pre anthracycline. Daunorubicin consolidaion1 should be day 1 only (corrected error from previous version)