PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Subcutaneous Low Dose Cytarabine (Ara-C) ACUTE MYELOID LEUKAEMIA (AML)

PROTOCOL REF: MPHALDCHA
(Version No. 2.0)

Approved for use in:

Non curative / palliative therapy in the following disorders:

- Acute Myeloid Leukaemia (AML), for patients not fit for intensive therapy.
- MDS patients with intermediate, high-risk disease and some patients with very high risk disease by the International Prognostic Score System (IPSS-R).
- CMML-2 (blasts / promonocyte: 5-19% in peripheral blood and/or 10%-19% in bone marrow or Auer rods, irrespective of blast / promonocyte percentage.)
- Myelofibrosis with increased blasts (10%-19%) in elderly patients.

Blueteq registration not required

Dosage:

Drug	Dose	Route	Frequency
Cytarabine	**20 mg**	SC	Twice a day on days 1 to 10 (inclusive)

Cycle length every 28 to 42 days (can be extended at clinician discretion). Minimum 4 cycles (if tolerated) to be continued as long as clinical benefit or until disease progression.

Administration (+/- Counselling Points):

- Patients should be trained to self-administer cytarabine when they start treatment. Clinical Nurse Specialists are responsible for providing this training.

- Syringes should be kept at room temperature. An appropriate sharps bin should be given to the patient for disposal of used syringes. The bin should be returned to the day case treatment unit once full and a new one supplied
- Pregnancy: The use of cytarabine in women who are or who may become pregnant should be undertaken only after due consideration of the potential benefits and hazards. Because of the potential for abnormalities with cytotoxic therapy, particularly during the first trimester, a patient who is or who may become pregnant while on cytarabine should be apprised of the potential risk to the foetus and the advisability of pregnancy continuation. There is a definite, but considerably reduced risk if therapy is initiated during the second or third trimester.
- Breast-feeding: It is not known whether this drug is excreted in human milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
- Cytarabine has no effect on intellectual function or psychomotor performance. Nevertheless, patients receiving chemotherapy may have an impaired ability to drive or operate machinery and should be warned of the possibility and advised to avoid such tasks if so affected.

Emetogenic risk:

Mild emetogenic.

Supportive treatments:

- Allopurinol 300mg once daily oral (cycle 1 only)
- Aciclovir 400mg twice daily oral
- Consider antifungal prophylaxis if persistent neutropenia (posaconazole tablets 300mg twice daily for 2 doses then once daily thereafter)

Dosing in renal and hepatic impairment:

Renal and Hepatic Impairment
No dose modifications are necessary

Drug Interactions:

Cumulative effect of increasing myelosuppression with a number of other medicines, liaise with pharmacist for further advice.

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

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1 to 10	**Cytarabine**	20mg twice daily (every 12 hours)	SC	Inject into the upper arm, thigh or abdomen. Injection sites should be rotated. New injections should be given at least 2.5cm from the previous site and never into tender, bruised or hardened areas.

Main toxicities:

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

Cytarabine

- Bone marrow suppression (anaemia, thrombocytopenia, neutropenia)
- Nausea
- Diarrhoea
- Oral ulceration
- Hepatic dysfunction
- Fatigue
- Injection-site reactions
- Less common – maculopapular rash, conjunctivitis and malaise

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Investigations and treatment plan:

	Pre	Cycle 1 Day 1	Cycle 2+ D1	Ongoing
Informed Consent	x			
Clinical Assessment	x	x	x	Every cycle
SACT Assessment (to include PS and toxicities)	x	x	x	Every cycle
Subcutaneous administration training		x		To be delivered by Clinical Nurse Specialist
FBC, U&E & LFTs & Magnesium	x	x	x	Every cycle
Hepatitis B core antibody and surface antigens & Hep C & HIV 1+2	X			
CrCl (Cockcroft and Gault)	x	x	x	Every cycle
CT scan**	x			At the end of treatment and if clinically indicated
ECG				If clinically indicated
Bone Marrow	x			Repeat if clinically indicated
Blood pressure measurement	x			Repeat if clinically indicated
Respiratory Rate				If clinically indicated
Height/Weight recorded	x	x	x	Every cycle
Blood glucose	x			Repeat if clinically indicated
Pregnancy test	X			If applicable

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed with **Cycle 1** irrespective of neutrophil and platelet counts.

Proceed with **subsequent cycles** if:

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

Cytopenias are often due to disease and treatment may continue despite cytopenias at clinician discretion. Consideration should be given to continuing therapy if recovery from previous cycles is slow and myelosuppression is a symptom of disease burden – discuss these cases with the treating consultant.

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. https://www.medicines.org.uk/emc Cytarabine 20mg/ml - accessed July 2023.
2. Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)
3. Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3 - updated January 2009)
4. BNF available via: https://bnf.nice.org.uk/

5. Burnett, A. K., Milligan, D., Prentice, A.G., Goldstone, A. H., McMullin, M.F., Hills, R. K., and Wheatley, K. (2007). A comparison of low-dose cytarabine and hydroxyurea with or without all-trans retinoid acid for acute myeloid leukemia and high-risk myelodysplastic syndrome in patients not considered fit for intensive treatment. Cancer 109, 1114-1124.

6. Thames Valley Strategic Clinical Network, Myeloid Group, Low Dose Ara-C, November 2021, Version 1.2

7. AML LI-1 Protocol, A Programme of Development for Older Patients with Acute Myeloid Leukaemia and High Risk Myelodysplastic Syndrome, Trial Reference ISRCTN40571019, Version 11.1, October 2019

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
June 2020	V1.0	**Niamh McLaughlin, Advanced pharmacist**	New protocol
Sept 2023	V2.0	**Sophie Hughes, Advanced pharmacist**	Three yearly review. Transferred to new template.