

FLA(G)-IDA

Fludarabine, high dose cytarabine (HD-Ara-C), idarubicin +/- G-CSF

INDICATION

- Induction in acute myeloid leukaemia (AML)
- Relapsed / refractory AML or ALL

For patients under 60 years of age but it can be applied to older patients according to clinician's assessment.

TREATMENT INTENT

Curative

PRE-ASSESSMENT

1. Ensure diagnosis is confirmed with appropriate tests and is documented in notes.
2. Blood tests - FBC, DCT, U&Es, LDH, ESR, urate, calcium, magnesium, creatinine, LFTs, glucose, Igs, β 2 microglobulin, hepatitis B core antibody and hepatitis B surface antigen, hepatitis C antibody, EBV, CMV, VZV, HIV 1+2, group and save.
3. Pregnancy test - for all women with childbearing potential before each new course.
4. Tissue typing of patient and any siblings to be carried out. Donor search to be initiated if no matched sibling donor available.
5. ECG +/- Echo.
6. Record performance status (WHO/ECOG).
7. Record height and weight.
8. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent prior to treatment.
9. Fertility - it is very important the patient understands the potential risk of infertility. All patients should be offered fertility advice (see fertility guidelines).
10. Send a "group and save" sample to transfusion and inform patient and transfusion laboratory that they will require **irradiated blood products** for all future transfusions. Ensure irradiation card is attached to the patient's notes. See 'Guidelines for the use of blood components in adult haematology'.
11. Document previous cumulative anthracycline use, which may dictate amount of idarubicin that can be given as part of this regimen. For patients under 25 years of age, consider use of Cardioxane® (dexrazoxane) for cardioprotection as per [paediatric haematology-oncology guideline](#) (OUH guideline).
12. Hydration and tumour lysis prevention, according to tumour lysis protocol.
13. Consider dental assessment / Advise dental check is carried out by patient's own dental practitioner before treatment starts in practical.
14. Treatment should be agreed in the relevant MDT.
15. **Central venous access should be used, e.g. Hickman line or PICC. In urgent cases it may be necessary to start chemotherapy via a peripheral cannula.**

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DRUG REGIMEN

- Days 1 to 7** **FILGRASTIM** 30 MU (or 48 MU if > 80kg) subcutaneously daily, treatment may continue up to 28 days.
GCSF may be omitted by the treating clinician in patients with AML with a high white count, or in ALL patients.
- Days 2 to 6** **FLUDARABINE** 30 mg/m² daily in 100 mL sodium chloride 0.9% intravenous infusion over 30 minutes.
- Days 2 to 6** **Commence 4 hours after start of fludarabine infusion:**
CYTARABINE* 2 g/m² daily in 250 mL sodium chloride 0.9% intravenous infusion over 4 hours.
Patients over 60 years old should receive 1000 mg/m² per dose as a modification.
- Days 4, 5 and 6** **IDARUBICIN** 8 mg/m² intravenous bolus daily.

Idarubicin use and dosage must be carefully considered in Course 2 due to total lifetime anthracycline dose and high risk of delayed regeneration.

CYCLE FREQUENCY

Maximum two courses. Course 2 can be considered upon count recovery - neutrophils >1 x 10⁹/L and platelets >100 x 10⁹/L.

DOSE MODIFICATIONS

There are no haematological modifications required.

Renal impairment

| Drug | Recommendations |
|----------------------|---|
| Fludarabine | GFR > 70 mL/min: 100% dose GFR 30 - 70 mL/min: 80% dose GFR < 30 mL/min: Contra-indicated |
| Cytarabine high dose | GFR < 31 - 59 mL/min: 50% dose GFR < 30 mL/min: Omit Haemodialysis (HD): Give 50% dose, start HD 4-5 hours after administration |
| Idarubicin | GFR ≥ 30 mL/min: 100% dose GFR < 30 ml/min: 67% dose |

Hepatic impairment

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| Fludarabine | No dose changes recommended |
| Cytarabine high dose | Mild/moderate impairment: No dose adjustment necessary Severe impairment: 25 - 50% dose and increase as tolerated |
| Idarubicin | Bilirubin 2 - 4 x ULN: 50% dose Bilirubin > 4 x ULN: Not recommended |

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Other toxicities

Anthracycline cumulative dosing

Assess for previous anthracycline use and calculate existing exposure and intended exposure.

Recommended maximum cumulative dose of **intravenous** idarubicin:

- 150 mg/m² (in normal cardiac function)*
- Carefully risk assess extent of exposure in patients with pre-existing cardiac dysfunction or prior mediastinal irradiation.

*Cardiomyopathy has been reported in 5% of patients who received cumulative IV doses of 150-290 mg/m². Many institutions adhere to the lower cumulative threshold as a measure of caution.

Consider use of cardioprotective Cardioxane® (dexrazoxane) for patients under 25 years of age in accordance with NHSE commissioning criteria.

INVESTIGATIONS

- FBC, U&E, LFT, coagulation screen.
- Recent bone marrow aspirate - this should be evaluated cytologically before proceeding with Course 2.

CONCURRENT MEDICATION

| Indication | Dose / duration / frequency |
|---|---|
| TLS prophylaxis | Allopurinol 300 mg daily with hydration for 7 days of initial course of treatment. Rasburicase may be required in high-risk patients, refer to TLS protocol . |
| Viral prophylaxis | Aciclovir 200 mg three times a day for duration of treatment and for 3 months after completion. |
| Fungal prophylaxis | High risk. Prophylaxis with posaconazole or voriconazole as per antifungal guidelines is recommended until neutrophil recovery. |
| Gastroprotection | Proton pump inhibitor (PPI, e.g. omeprazole) or H ₂ receptor antagonist (H ₂ RA, e.g. famotidine) in line with local formulary. Continue throughout treatment cycle and for periods of persistent thrombocytopenia, or longer if other clinical reason to continue. |
| Pneumocystis jiroveci pneumonia (PJP) prophylaxis | Non-mandatory - at discretion of the treating clinician, consider: Co-trimoxazole 960 mg once daily on Mondays, Wednesdays, Fridays each week (refer to local PJP guidance e.g. OUH Quris for alternate treatments in allergy / intolerance / neutropenia) |
| Ocular toxicity prophylaxis e.g. reversible keratitis, conjunctivitis | <ul style="list-style-type: none"> • Prednisolone 0.5 – 1% eye drops 1 drop BE QDS OR • Dexamethasone 0.1% eye drops 1 drop BE QDS Initiate day 1 of cytarabine treatment and continue for 5 days following final cytarabine dose. In the event of conjunctivitis / other ocular symptoms, increase the dose frequency to every 2 hours until resolution of symptoms. Liaison with local ophthalmologists may be necessary in this situation. |

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| Menstrual suppression | <p>Consider in all patients who have experienced menstruation in the past 6 months.</p> <p>Norethisterone 5 – 10 mg PO TDS. Increase dose to 10 mg if evidence of breakthrough bleeding.</p> <p>OR</p> <p>Medroxyprogesterone 10 mg PO TDS (if norethisterone unavailable)</p> |
|------------------------------|---|

EMETIC RISK

Day 1: Minimal
Day 2 - 6: High

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

- Fludarabine** Nausea, vomiting, alopecia, cough, fever, fatigue, weakness, diarrhoea. Central nervous system (CNS) side-effects have been rarely described (agitation, confusion, visual disturbance).
- Cytarabine** Nausea, diarrhoea, abdominal pain, oral ulceration, hepatic dysfunction, CNS, gastrointestinal (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 - 12 hours following administration. Neurotoxicity also reported, e.g. cerebellar damage.
- Idarubicin** Cardiotoxicity may occur - cumulative dose associated with cardiotoxicity is not known but it is thought that a total dose of 60-80 mg/m² is not problematic. Red discoloration of urine for 2 to 3 days after administration. Alopecia. Nausea and vomiting. Elevation of liver enzymes may occur.
- Filgrastim** Muscle or bony pain. Allergic reactions are rare and usually occur with the first dose.

Others: myelosuppression, infections, mucositis.

EXTRAVASATION RISK

Cytarabine: Neutral
Fludarabine: Neutral
Idarubicin: Vesicant

INTERACTIONS

Fludarabine: Fludarabine has minimal known interactions.

- Dipyridamole and other inhibitors of adenosine uptake: May reduce the therapeutic efficacy. Avoid combination where possible.

Cytarabine: Interaction potential is generally limited.

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- Cytidine deaminase (CDA) inhibitors (e.g. cedazuridine) - Potential increased effect/toxicity of cytarabine due to reduced clearance. There are no NHS-approved treatments of this type in the UK currently

Idarubicin:

- **Cardiotoxic drugs (eg. calcium channel blockers, propranolol):** Avoid combination or monitor closely for cardiotoxicity

TREATMENT RELATED MORTALITY

AML induction therapy is associated with a relatively high mortality risk generally between 5-10%. This should be discussed with the patient at the time of consent. This risk is not only due to chemotherapy but also consequent to the fact that patients treated with AML induction are unwell because of having uncontrolled / untreated AML

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REVIEW

| Name | Revision | Date | Version | Review |
|---|---|------------|---------|----------|
| Dr Lynn Quek | New protocol | April 2017 | 1.0 | |
| Cheuk-kie Jackie Cheung, Haematology Pharmacist. NSSG Myeloid Group | Annual protocol meeting. Cytarabine diluent changed. | Oct 2019 | 1.1 | Oct 2021 |
| Yen Lim, Haematology Pharmacist Andy Peniket, Consultant Haematologist NSSG Myeloid Group | Annual protocol meeting. Updated renal/hepatic dosing. | Nov 2021 | 1.2 | Nov 2023 |
| Connor Sweeney, Consultant Haematologist | Annual protocol meeting. Added guidance on tissue typing, cumulative anthracycline doses and tumour lysis prevention. | Sep 2023 | 1.3 | Sep 2025 |

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| Donna Constantine, Advanced Cancer Pharmacist | Publication of 2023 changes. New formatting. Minor changes to supportive care table. Filgrastim generally used as common GCSF in network and incorporated into regimen - dose banding added. Bilirubin converted to ULN range to account for variance in individual lab assays between institutions. Protocol merged with ML9 (FLA-IDA) | Dec 2025 | 2.0 | Dec 2026 |
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