Clofarabine and Cytarabine

Indication
Third line treatment of relapsed/refractory acute myeloid leukaemia (AML).

ICD-10 codes
Codes with a prefix C92

Regimen details

Day	Drug	Dose	Route
1-5	Clofarabine	25mg/m^2	IV infusion
1-5	Cytarabine	2000mg/m^2	IV infusion
0-5*	GCSF	As per local policy	SC

* i.e. to start the day before chemotherapy

Cycle frequency
4-6 weeks

Number of cycles
2 cycles (second cycle to be administered following response assessment and count recovery)

Administration
Prior to clofarabine, patients should receive 500mL sodium chloride 0.9% pre hydration. Clofarabine is then administered in 100 mL sodium chloride 0.9% over 60 minutes via a 22 micron filter.

Cytarabine is administered in 1000mL sodium chloride 0.9% over 4 hours.

GCSF is administered via SC injection daily for 6 days starting the day before chemotherapy.

Pre-medication
Nil required

Emetogenicity
This regimen has high emetic potential

Additional supportive medication
Allopurinol 300mg OD (100mg OD if CrCl < 20mL/min) for the first 2 weeks.
Antifungal prophylaxis as per local policy.
Antiviral prophylaxis as per local policy.
Prednisolone 0.5% eye drops QDS (to avoid chemical conjunctivitis associated with cytarabine)
Mouthwashes as per local policy.
GCSF as per local policy until neutrophils ≥ 1.0 x 10^9/L.

Extravasation
Clofarabine and cytarabine are neutral (Group 1)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC (with film)	72 hours
U+E (including creatinine)	72 hours
LFTs	72 hours

Bone marrow aspirate and trephine biopsy

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	Daily during chemotherapy
U+E (including creatinine)	Daily during chemotherapy
LFTs	Daily during chemotherapy

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	> 1.0 x 10^9/L
Platelets	> 100 x 10^9/L
Creatinine clearance (CrCl)	≥ 60 mL/min
Bilirubin	≤ 1.5 ULN
AST/ALT	≤ ULN

Dose modifications

- ### Haematological toxicity

If neutrophils ≤ 1.0 x 10^9/L and/or platelets ≤ 100 x 10^9/L delay until recovery.

- ### Renal impairment

Clofarabine

Serum creatinine should be measured each day.

CrCl (mL/min)	**Clofarabine dose**
> 60	100%
≤ 60	Consultant decision

If serum creatinine is increasing each day discuss with consultant (even if within normal range).
Clofarabine should be used with caution in mild-moderate renal impairment and is contraindicated in severe renal impairment.

Cytarabine

CrCl (mL/min)	**Cytarabine dose**
> 60	100%
46-60	60%
31-45	50%
< 30	Consultant decision

- ### Hepatic impairment

There is no information on the use of clofarabine in hepatic impairment. Use with caution in mild-moderate hepatic impairment. Contraindicated in severe renal impairment.

Cytarabine dose should be reduced to 50% if bilirubin > 1.5 x ULN. Doses may be escalated in the absence of toxicity. Discuss with consultant.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Severe myelosuppression
Tumour lysis syndrome
Cerebellar toxicity

- **Frequently occurring side effects**

Fatigue
Nausea and vomiting
Myelosuppression
Peripheral neuropathy
Conjunctivitis (cytarabine)
Headache
Photophobia and blurred vision
Dizziness

- **Other side effects**

Bone pain
Dermatitis

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Nephrotoxic drugs should be avoided as far as possible.

Cytarabine:
Digoxin: cytarabine may affect plasma digoxin levels – consider monitoring.

Additional comments

Patients must receive irradiated blood products due to risk of transfusion-associated graft versus host disease.

References

- Summary of Product Characteristics Clofarabine (Sanofi) accessed 28 Jan 2015 via www.medicines.org.uk
- Summary of Product Characteristics Cytarabine (Pfizer) accessed 28 Jan 2015 via www.medicines.org.uk
- Becker, P.S. et al; Clofarabine in combination with high dose cytarabine and granulocyte colony-stimulating factor priming for relapsed and refractory acute myeloid leukaemia. BJH 2011; 155(2): 182-189
- Farder, S. et al; Results of a phase 1-2 study of clofarabine in combination with cytarabine in relapsed and refractory acute leukaemias. Blood 2005; 105 (3): 940-947

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