

Chemotherapy Protocol

ACUTE MYELOID LEUKAEMIA

DA (3+10)–Cytarabine-Daunorubicin

In-Patient Regimen

Regimen

- Acute Myeloid Leukaemia – InP-DA (3+10)–Cytarabine-Daunorubicin

Indication

- Acute myeloid leukaemia in patients who are less than 60 years of age or older patients deemed fit for intensive therapy at clinician discretion.

Toxicity

Drug	Adverse Effect
Cytarabine	Nausea, vomiting, diarrhoea, fever, rash, anorexia, oral and anal inflammation or ulceration, and hepatic dysfunction
Daunorubicin	Nausea, alopecia, chronic and acute cardiac failure and dysrhythmias

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, and U&Es, LFTs and coagulation screen on day 1 (the FBC may not be necessary for induction treatment)
- Blood pressure, fluid balance and weight throughout
- Recent bone marrow aspirate
- A baseline MUGA scan or echocardiogram should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, elderly, previous exposure to anthracyclines, previous thoracic radiotherapy. MUGA scan or ECHO should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative anthracycline dose approaches the maximum cumulative dose.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing. The approach may be different depending on the clinical circumstances.

Haematological

Consider blood transfusion or erythropoietin if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL (80g/L).

All dose reductions and delays should be discussed with the relevant consultant. In general if these levels are not met then treatment should be delayed for three days at a time. Treatment should re-start as soon as these haematological parameters are met. Dose delays rather than dose reductions are recommended.

Hepatic Impairment

Drug	Bilirubin μmol/L		AST/ALT units/L	Dose (% of original dose)
Cytarabine	greater than 34		N/A	50% Escalate doses in subsequent cycles in the absence of toxicity
Daunorubicin	25 - 50			75%
	51 - 85			50%
	greater than 85			omit

Renal Impairment

Drug	Creatinine (μmol/L)	Dose (% of original dose)
Cytarabine		Dose reduction not necessary normally as doses not considered high dose
Daunorubicin	less than 105	100%
	105-265	75%
	more than 265	50%

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose of the causative agent(s) may then be reduced or discontinued at the discretion of the consultant.

[Regimen](#)

1 cycle will be set in ARIA

Drug	Dose	Days	Administration
Cytarabine	100mg/m ² twice a day	1, 2, 3, 4, 5, 6, 7, 8, 9, 10	Intravenous bolus
Daunorubicin	60mg/m ²	1, 3, 5	Intravenous infusion in 100ml sodium chloride 0.9% over 60 minutes or a slow intravenous bolus over 20 minutes (Infusion set as default in ARIA)

[Dose Information](#)

- Cytarabine will be dose banded according to the national dose bands (20mg/ml)
- Daunorubicin will be dose banded according to the national dose bands (5mg/ml)
- There is a recommended maximum cumulative lifetime dose of daunorubicin of 500-600mg/m² or 400mg/m² in patients with cardiac dysfunction or exposed to mediastinal irradiation

[Administration Information](#)

[Extravasation](#)

- Daunorubicin – vesicant
- Cytarabine – neutral

[Other](#)

- The final concentration of daunorubicin **must not** exceed 1mg/mL

[Additional Therapy](#)

This is an inpatient regimen please ensure all supportive and take home medication not on ARIA are prescribed on the inpatient chart or general electronic prescribing system.

- Antiemetics

Starting 15-30 minutes prior to chemotherapy

- metoclopramide 10mg three times a day when required oral
- ondansetron 8mg twice a day on days 1, 2, 3, 4, 5, 6, 7 oral
- Allopurinol 300mg oral once a day for first 7 days of initial induction chemotherapy (if a remission is attained, the subsequent use of allopurinol is not required) or intravenous rasburicase in high risk cases
- Aciclovir 400mg twice a day oral

- Discuss the need and choice of antifungal with a consultant
- Mouthwashes according to local or national policy on the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Coding

- Procurement – X71.1
- Delivery – Not applicable

References

1. National Cancer Research Institute (2016). *AML 18 - A Trial For Older Patients With Acute Myeloid Leukaemia And High Risk Myelodysplastic Syndrome trial protocol - Version 5.0, 03/2016*. Cardiff University: Research and Commercial Division.
2. Zentiva Limited (2016). *Daunorubicin 20mg Powder for Injection-Summary of Product Characteristics. Electronic Medicines Compendium*. Online at <http://www.medicines.org.uk/emc/medicine/26175>, accessed 26 June 2017

REGIMEN SUMMARY

InP – DA (3+10)–Cytarabine-Daunorubicin

This is an in-patient regimen. Other than those listed below, supportive medication for this regimen will not appear in Aria as prescribed agents. The administration instructions for each warning describes the agents which must be prescribed on the in-patient chart or general electronic prescribing system

Day 1

1. Warning – Check supportive medicines prescribed

Administration Instructions

- metoclopramide 10mg three times a day when required oral or intravenous
- ondansetron 8mg twice a day on days 1, 2, 3, 4, 5, 6, 7 oral or intravenous
- aciclovir 400mg twice a day oral
- discuss the need and choice of antifungal with a consultant
- allopurinol 300mg once a day for 7 days oral or rasburicase intravenous infusion
- gastric protection according to local policy

2. Daunorubicin 60mg/m² intravenous infusion in 100mL sodium chloride 0.9% over 60 minutes

Administration Instructions

Alternatively, daunorubicin can be administered as a slow intravenous bolus over 20 minutes, according to local practice. Whatever the mode of administration, the final concentration of daunorubicin **must not** exceed 1mg/mL.

3. Warning – Cytarabine is TWICE a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

4. Cytarabine 100mg/m² intravenous bolus twice a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

Day 2

5. Warning – Check supportive medicines prescribed

Administration Instructions

- metoclopramide 10mg three times a day when required oral or intravenous
- ondansetron 8mg twice a day on days 1, 2, 3, 4, 5, 6, 7 oral or intravenous
- aciclovir 400mg twice a day oral
- discuss the need and choice of antifungal with a consultant
- allopurinol 300mg once a day for 7 days oral or rasburicase intravenous infusion
- gastric protection according to local policy

6. Warning – Cytarabine is TWICE a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

7. Cytarabine 100mg/m² intravenous bolus twice a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

Day 3

8. Warning – Check supportive medicines prescribed

Administration Instructions

- metoclopramide 10mg three times a day when required oral or intravenous
- ondansetron 8mg twice a day on days 1, 2, 3, 4, 5, 6, 7 oral or intravenous
- aciclovir 400mg twice a day oral
- discuss the need and choice of antifungal with a consultant
- allopurinol 300mg once a day for 7 days oral or rasburicase intravenous infusion
- gastric protection according to local policy

9. Daunorubicin 60mg/m² intravenous infusion in 100ml sodium chloride 0.9% over 60 minutes

Administration Instructions

Alternatively, daunorubicin can be administered as a slow intravenous bolus over 20 minutes, according to local practice. Whatever the mode of administration, the final concentration of daunorubicin **must not** exceed 1mg/mL.

10. Warning – Cytarabine is TWICE a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

11. Cytarabine 100mg/m² intravenous bolus twice a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

Day 4

12. Warning – Check supportive medicines prescribed

Administration Instructions

- metoclopramide 10mg three times a day when required oral or intravenous
- ondansetron 8mg twice a day on days 1, 2, 3, 4, 5, 6, 7 oral or intravenous
- aciclovir 400mg twice a day oral
- discuss the need and choice of antifungal with a consultant
- allopurinol 300mg once a day for 7 days oral or rasburicase intravenous infusion
- gastric protection according to local policy

13. Warning – Cytarabine is TWICE a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

14. Cytarabine 100mg/m² intravenous bolus twice a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

Day 5

15. Warning – Check supportive medicines prescribed

Administration Instructions

- metoclopramide 10mg three times a day when required oral or intravenous
- ondansetron 8mg twice a day on days 1, 2, 3, 4, 5, 6, 7 oral or intravenous
- aciclovir 400mg twice a day oral
- discuss the need and choice of antifungal with a consultant
- allopurinol 300mg once a day for 7 days oral or intravenous infusion
- gastric protection according to local policy

16. Daunorubicin 60mg/m² intravenous infusion in 100ml sodium chloride 0.9% over 60 minutes

Administration Instructions

Alternatively, daunorubicin can be administered as a slow intravenous bolus over 20 minutes, according to local practice. Whatever the mode of administration, the final concentration of daunorubicin **must not** exceed 1mg/mL.

17. Warning – Cytarabine is TWICE a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

18. Cytarabine 100mg/m² intravenous bolus twice a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

Day 6, 7, 8, 9, 10

19. Warning – Check supportive medicines prescribed

Administration Instructions

- metoclopramide 10mg three times a day when required oral or intravenous
- ondansetron 8mg twice a day on days 1, 2, 3, 4, 5, 6, 7 oral or intravenous
- aciclovir 400mg twice a day oral
- discuss the need and choice of antifungal with a consultant
- allopurinol 300mg once a day for 7 days oral or rasburicase infusion
- gastric protection according to local policy

20. Warning – Cytarabine is TWICE a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

21. Cytarabine 100mg/m² intravenous bolus twice a day

Administration Instructions

The doses must be given 12 hours apart. This may mean the administration of one dose on the evening of day one and one dose on the morning of day 11.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	June 2017	Administration instructions amended, references updated.	Eleanor Taylor Pharmacist	Robert Williams Pharmacist
1	April 2017	New protocol	Lucy Shade Pharmacist	Dr Deborah Richardson Consultant Haematologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
 NHS Isle of Wight
 Portsmouth Hospitals NHS Trust
 Salisbury NHS Foundation Trust
 University Hospital Southampton NHS Foundation Trust
 Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.