Chemotherapy Protocol

ACUTE MYELOID LEUKAEMIA

Ambulatory Regimen

AmB - DA (3+8) CADD–Cytarabine-Daunorubicin

Regimen

- Acute Myeloid Leukaemia – AmB - DA (3+8) CADD – Cytarabine-Daunorubicin

Indication

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

- Patient fulfils criteria for ambulatory care.

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

- Blood pressure, fluid balance and weight throughout and immediately after the 6 day administration period.

- 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 echocardiogram 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.

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

This regimen should be given after a cycle of DA (3+10). Day one begins when the neutrophil are equal to or greater than $1x10^9$/L and the platelet count is equal to or greater than $80x10^9$/L.

Drug	Dose	Days	Administration
Cytarabine	100mg/m^2 twice a day	1, 2, 3, 4, 5, 6, 7, 8	Intravenous bolus via CADD pump in 125ml sodium chloride 0.9%
Daunorubicin	50mg/m^2	1, 3, 5	Intravenous infusion in 100ml sodium chloride 0.9% over 60 minutes or as a slow intravenous bolus over 20 minutes

Dose Information

- Cytarabine will be dose banded according to the national dose bands (100mg/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 600mg/m^2 or 400mg/m^2 in patients with cardiac dysfunction or who have been exposed to extensive pelvic radiation

Administration Information

Extravasation

- Daunorubcin – vesicant
- Cytarabine – neutral (irritant in large volumes)

Other

- Each CADD pump will contain 8 doses (16 doses are required in total which is equal to two pumps). The quantity in the pump will be equal to 800mg/m$^{2.}$ This is to be diluted with sodium chloride 0.9% 125ml (15ml per dose plus a 5ml overage). The first dose will be administered on the evening of day 1. This will mean the pump will be changed on day 5 after the morning dose has been administered.

Additional Therapy

- Antiemetics

  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, 8 oral

- Aciclovir 400mg twice a day oral
- Mouthwashes according to local or national policy on the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Coding

- Procurement – X70.4
- Delivery – N/A

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.

REGIMEN SUMMARY

AmB - DA (3+8) CADD – Cytarabine-Daunorubicin

Day 1

1. Ondansetron 8mg oral or intravenous

2. Daunorubicin 50mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 60 minutes
   Administration Instructions
   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. Cytarabine 100mg/m^2 intravenous bolus twice a day via CADD pump in 125ml sodium chloride 0.9%
   Administration Instructions
   Each CADD pump will contain 8 doses (16 doses are required in total which is equal to two pumps). The quantity in the pump will be equal to 800mg/m^2. This is to be diluted with sodium chloride 0.9% 125ml (15ml per dose plus a 5ml overage). The first dose will be administered on the evening of day 1. This will mean the pump will be changed on day 5 after the morning dose has been administered.

Take Home Medicines (day 1 only)

4. Metoclopramide 10mg three times a day when required oral

5. Ondansetron 8mg twice a day starting on the evening of day one of the cycle for 8 days oral

6. Aciclovir 400mg twice a day for 28 days

Day 3

7. Warning – Check ondansetron
   Administration Instructions
   Please check the patient has taken a dose of ondansetron prior to the administration of daunorubicin. If the patient has forgotten administer ondansetron 8mg oral or intravenous

8. Daunorubicin 50mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 60 minutes
   Administration Instructions
   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.

Day 5

9. Warning – Check ondansetron
   Administration Instructions
   Please check the patient has taken a dose of ondansetron prior to the administration of daunorubicin. If the patient has forgotten administer ondansetron 8mg oral or intravenous

10. Daunorubicin 50mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 60 minutes
    Administration Instructions
    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.

11. Cytarabine 100mg/m^2 intravenous bolus twice a day via CADD pump in 125ml sodium chloride 0.9%

Administration Instructions

Each CADD pump will contain 8 doses (16 doses are required in total which is equal to two pumps). The quantity in the pump will be equal to 800mg/$m^{2.}$ This is to be diluted with sodium chloride 0.9% 125ml (15ml per dose plus a 5ml overage). The first dose will be administered on the evening of day 1. This will mean the pump will be changed on day 5 after the morning dose has been administered.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	July 2017	New protocol	Dr Deborah Wright Pharmacist	Dr Chris Dalley 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 Hospitals 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.