Chemotherapy Protocol

ACUTE MYELOID LEUKAEMIA

AMSACRINE-CYTARABINE-ETOPOSIDE

In-Patient Regimen

Regimen

- Acute Myeloid Leukaemia – InP-Amsacrine-Cytarabine-Etoposide (MACE)

Indication

- Consolidation therapy for AML in remission or salvage

Toxicity

Drug	Adverse Effect
Amsacrine	Nausea, mucositis, alopecia, hepatotoxicity, cardiac toxicity (as for anthracyclines, the risk of arrhythmias is increased by hypokalaemia)
Cytarabine	Nausea, vomiting, diarrhoea, fever, rash, itching, anorexia, oral and anal inflammation or ulceration, hepatic dysfunction, ocular pain, foreign body sensation, photophobia and blurred vision, dizziness, headache, confusion, cerebellar toxicity, myalgia and bone pain
Etoposide	Nausea, mucositis and alopecia, anaphylactic reactions

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

Monitoring

Drugs

- U&Es, LFTs and FBC prior to starting a cycle of treatment
- Prior to starting treatment consider an ECG, ECHO or MUGA scan if there is a cardiac history, the patient is elderly or has a previous history suggestive of potential cardiac disease.

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.

Discuss all dose reductions with the relevant consultant.

Haematological

In general the treatment can proceed if the neutrophils are greater than $1x10^9$/L and the platelets are greater than $100x10^9$/L. Always' check with the relevant consultant.

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

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units/L	Dose (% of original dose)
Amsacrine	greater than 34		N/A	60%
Cytarabine	greater than 34		N/A	50% Escalate doses in subsequent cycles in the absence of toxicity
Etoposide	26-51		60-180	50%
	greater than 51		greater than 180	Clinical decision

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Amsacrine	less than 60	75%
Cytarabine	less than 60	60%
	less than 45	50%
	less than 30	Discuss with consultant
Etoposide	15-50	75%
	less than 15	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.

Regimen

1 cycle will be set in ARIA

Cycles should proceed when there is neutrophil and platelet recovery.

Drug	Dose	Days	Administration
Amsacrine	100mg/m^2	1, 2, 3, 4, 5	Intravenous infusion in 500ml glucose 5% over 60 minutes
Cytarabine	200mg/m^2	1, 2, 3, 4, 5	Intravenous infusion in 1000ml sodium chloride 0.9% over 22 hours
Etoposide	100mg/m^2	1, 2, 3, 4, 5	Intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes

Dose Information

- Amsacrine will be dose banded according to the national dose bands (5mg/ml)
- Cytarabine will be dose banded according to the national dose bands (20mg/ml)
- Etoposide will be dose banded according to the agreed bands

Administration Information

Extravasation

- Amsacrine - vesicant
- Cytarabine – neutral (irritant in large volumes)
- Etoposide - irritant

Other

- Amsacrine must not be infused in sodium chloride 0.9% as precipitation or flocculation occurs. The line should be flushed with glucose 5% before and after administration of amsacrine.

Additional Therapy

This is an inpatient regimen please ensure all supportive 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

- Aciclovir 400mg twice a day until neutrophils are greater than 1x10^9/L

- Antifungal prophylaxis according to consultant choice until neutrophils are greater than $1x10^9$/L.
- 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 – X71.2
- Delivery – X72.1

References

1. Hann IM, Stevens RF, Goldstone AH et al. Randomized comparison of DAT versus ADE as induction chemotherapy in children and younger adults with acute myeloid leukemia. Results of the Medical Research Council's 10th AML trial (MRC AML10). Adult and Childhood Leukaemia Working Parties of the Medical Research Council. Blood 1997; 89(7): 2311-8.

REGIMEN SUMMARY

InP-Amsacrine-Cytarabine-Etoposide (MACE)

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, 2, 3, 4, 5

1. Warning – Check supportive medicines prescribed
   Administration Instructions
   - ondansetron 8mg twice a day oral or intravenous for 7 days
   - metoclopramide 10mg three times a day when required for nausea oral or intravenous
   - aciclovir 400mg twice a day oral
   - antifungal prophylaxis according to consultant choice

     Always refer to the patient schedule for supportive treatments and fluids

2. Amsacrine 100mg/m^2 intravenous infusion in 500ml glucose 5% over 60 minutes
   Administration Instructions
   Amsacrine must not be infused in sodium chloride 0.9% as precipitation or flocculation occurs. The line should be flushed with glucose 5% before and after administration of amsacrine.

3. Cytarabine 200mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 22 hours

4. Etoposide 100mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	March 2017	New protocol	Dr Deborah Wright 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.