ACUTE PROMYELOCYTIC LEUKAEMIA – Spanish Protocol AIDA regimen (AML17 protocol)

Prior to treatment

- Assess cardiac function by history & examination, ECG and CXR. If there is evidence of cardiac disease, prior anthracyclines or patient > 70yrs formal assessment of cardiac function by MUGA scan may be indicated – *discuss with consultant.*
- Check recent liver & renal function tests – anthracycline dose reduction may be indicated in these cases or 'Spanish protocol' may be inappropriate – *discuss with consultant*
- If appropriate discuss possibility of pregnancy with female patients and need for contraception with both male and female patients. Discuss risk of infertility - offer semen cryopreservation to males
- A central venous line, e.g Hickman, Groshong, PICC, should not be inserted until all haemostatic abnormalities have resolved
- Tissue typing ie HLA typing should be performed on all patients before starting this protocol. Send 5mls EDTA (blue tube) to both Manchester & Sheffield. The Manchester request form is a small postcard sized request form. The Sheffield request form is a National Blood Service request form 3A. Request both class I & II on all patients unless absolutely clear not ever planning an allogeneic transplant, in which case simply request a class I from Sheffield and no sample to Manchester.
- The Specialist Registrar must personally see these samples before they are sent to the lab. Do not assume these samples have been taken & sent to the lab; it the Specialist Registrar's responsibility to make absolutely sure these samples have been taken correctly before induction chemotherapy.
- Written consent

All-trans retinoic acid therapy (ATRA)

- Starting on day 1 of induction chemotherapy all patients should receive ATRA *(Tretinoin)* 45mg/m^2/day divided into two daily doses (*10mg capsules*) until CR is reached.
- If WBC at presentation is >10 x10^9/L prophylaxis against the retinoic acid syndrome must be started with dexamethasone 10mg 12-hourly. This can given orally if there is no vomiting

Course 1	Idarubicin 12mg/m^2 IV in 100ml Nsaline over 20mins	days 2,4,6, and 8. Give all 4 doses one day earlier if presenting WCC >10
	ATRA 45mg/m^2 /day PO as two equally divided doses until CR (round to nearest 10mg) – prescribe as Tretinoin	
Start courses 2, 3 and 4 when neutrophils >1.0 and platelets >100. All should be given on the Day Unit as out-patient treatment		
Course 2	Idarubicin 5mg/m^2 IV in 100ml Nsaline over 20mins	days 1,2,3 and 4 - so start this on a Monday
	ATRA 45mg/m^2/day PO on days 1 -15 (round to nearest 10mg) – prescribe as Tretinoin	
Course 3	Mitoxantrone 10mg/m^2 IV in 100ml Nsaline over 30mins	days 1,2,3,4 and 5 – so start this on a Monday
	ATRA 45mg/m^2/day PO on days 1 -15 (round to nearest 10mg) – prescribe as Tretinoin	
Course 4	Idarubicin 12mg/m^2 IV in 100ml Nsaline over 20mins	day 1 only
	ATRA 45mg/m^2/day PO on days 1 -15 (round to nearest 10mg) – prescribe as Tretinoin	

Prophylaxis for acute emesis	Ondanestron 8mg bd on each day of chemotherapy
Other medication	Allopurinol 300mg od for each day of chemotherapy; rasburicase may be required if WCC >10 – *discuss with consultant*. This only applies for course 1 when there is the potential for tumour lysis syndrome. Corsodyl 10ml qds mouthwash Norethisterone 5mg tds for menstruating females Posaconazole tablets 300mg bd for 1 day then 300mg od Stop when neutrophils >1.0 for 2 consecutive days. This only applies for course 1. Ciprofloxacin 500mg bd unless on IV antibiotics. Start when neutophils <1.0. Stop when neutrophils >1.0 for 2 consecutive days. This only applies for course 1. Aciclovir or co-trimoxazole is not routinely required GCSF is not usually required following any of these courses

Retinoic acid (differentiation) syndrome

- This is a major cause of mortality in patients treated with ATRA. The patient may have unexplained fever, weight gain, respiratory distress, interstitial pulmonary infiltrates, and pleural or pericardial effusions. Usually there is also hyperleucocytosis but the syndrome may occur at any level of WBC.
- At the earliest suspicion of the ATRA syndrome *discuss the case with the consultant*. Administer dexamethasone 10mg 12-hourly IV until disappearance of symptoms and signs and for a minimum of 3 days. The decision to continue or discontinue ATRA depends on the severity of the differentiation syndrome and this should be made by a consultant.

Pseudotumour cerebri

- This may develop in patients under 20years of age. It presents with headaches, nausea, vomiting and visual disturbances. *Discuss with the consultant* and temporarily stop ATRA.

Hepatotoxicity

- This is defined as: an increase in serum bilirubin, AST/ALT, or alkaline phosphatase >5 times the normal upper level. This requires a temporary suspension of the ATRA.
- If hepatoxicity persists following discontinuation of ATRA, the Idarubicin doses should not be changed on the AIDA arm.
- As soon as the symptoms and the patient‘s clinical condition improves, treatment with ATRA will be resumed at 50% of the previous dose during the first 4 days when serum bilirubin, AST/ALT or alkaline phosphatase are reduced to <4 times the normal upper level. Thereafter, in absence of worsening of the previous toxicity, ATRA should be resumed at full dosage.
- In case of reappearance of signs and symptoms of ATRA toxicity, the drug must be discontinued indefinitely during induction therapy.

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