NCRI AML17 Trial

SECTION B

INDUCTION CHEMOTHERAPY (Courses 1 and 2)

INSTRUCTIONS

Note: This section is for both AML and APL patients.

(1) Administer Course 1 in accordance with the randomisation assigned and Protocol guidelines (see Protocol Section 9, AML or Section 19, APL).

(2) Investigators will be informed within 10 days whether a patient is eligible for the CEP-701 randomisation. If eligible, patients should be consented using PIS 4.

(3) Following recovery from course 1, assess response by performing a bone marrow aspirate. If hypocellular, repeat after 7-10 days. Marrow response must be recorded on the web-based CRF.

(4) After recording marrow response, clinicians will be informed if the patient is high risk. Such patients are eligible for the High Risk Randomisation (Protocol Section 11). Initiate a search for an allogeneic stem cell donor

(5) Patients with core binding factor leukaemia should receive course 2 of allocated treatment and will then be eligible for the 3 vs 4 course randomisation. Some of these patients will already have entered the CEP-701 randomisation, in which case they should continue irrespective of whether allocated 3 or 4 courses. If a CBF patient did not receive Mylotarg in course 1 they should be randomised to receive 3mg/m^2 or 6mg/m^2 on day 1 of course 2.

(6) All patients who are not high risk should receive course 2 of allocated treatment.

(10) Please enter this form on the online web entry system, or return it to the AML17 Trial Office, Wales Cancer Trials Unit, 6th Floor, Neuadd Meirionnydd, Heath Park, Cardiff CF14 4YS.

INDUCTION CHEMOTHERAPY (Courses 1 and 2)

Patient's initials:: ..... Sex:..... Date of birth: ...../...../.....

Hospital: ..... Hospital No.: .....

Consultant: ..... AML17 Trial No.: .....

I INDUCTION CHEMOTHERAPY: Randomised to:

AML :

ADE ☐ DA ☐ Mylotarg 3mg/m^2 ☐ Mylotarg 6mg/m^2 ☐

APL :

AIDA ☐ ATO/ATRA ☐

II CHEMOTHERAPY RECEIVED

COURSE	**1**	**2**
Date Started		
Was the scheduled drug and dose given?	YES ☐ NO ☐	YES ☐ NO ☐
If NO to scheduled drug/dose, please describe actual treatment including drugs and doses		

Was Mylotarg given? YES ☐ NO ☐ If YES, state date given: ……/……/……

Was the scheduled dose given? YES ☐ NO ☐

If NO to scheduled dose, what dose was given and what was the reason for the dose alteration?

……

……

III RESPONSE TO INDUCTION

Marrow Examinations (if initial marrow not assessable and repeat taken, please give details of both marrows):

After	**Course 1**	Repeat if necessary	**Course 2**	Repeat if necessary
Date				
Cellularity (1=hypo, 2=normo, 3=hyper)				
Blasts %				
Marrow Response				

Responses: **CR:** <5% leukaemic cells in cellular marrow; **PR**: 5-15% leukaemic cells in cellular marrow.

RD: >15% leukaemic blast cells; **NA:** Not assessable (e.g. hypoplastic marrow)

NCI CTC Toxicity Grading

NB: No toxicity = 0

GRADE	1	2	3	4
Nausea/ Vomiting	Nausea	Transient vomiting	Vomiting requiring therapy	Intractable vomiting
Alopecia	Minimal hair loss	Moderate, patchy alopecia	Severe alopecia	Total alopecia
Oral	Soreness/erythema	Erythema, ulcers, can eat solids	Ulcers, requires liquid diet	Feeding not possible
Diarrhoea	Transient <2 days	Tolerable but ≥2 days	Intolerable, requiring therapy	Haemorrhagic dehydration
Cardiac Function	Asymptomatic but abnormal cardiac sign	Transient symptomatic dysfunction: no therapy required	Symptomatic dysfunction, responsive to therapy	Symptomatic dysfunction, not responsive to therapy
*Liver Function: AST	>Upper limit normal to 2.5 x normal	>2.5 x normal to 5.0 x normal	>5.0 x normal to 20.0 x normal	>20.0 x normal
ALT	>Upper limit normal to 2.5 x normal	>2.5 x normal to 5.0 x normal	>5.0 x normal to 20.0 x normal	>20.0 x normal
Bilirubin	>Upper limit normal to 1.5 x normal	>1.5 x normal to 3.0 x normal	>3.0 x normal to 10.0 x normal	> 10.0 x normal
*Renal Function: Creatinine	>Upper limit normal to 1.5 x normal	>1.5 x normal to 3.0 x normal	>3.0 x normal to 6.0 x normal	>6.0 x normal
Proteinuria	1+ or <0.3 g% or < 3g/L	2-3+ or 0.3-1.0 g% or 3-10 g/L	4+ or > 1.0 g% or >10 g/L	nephrotic syndrome
Haematuria	micro only	gross, no clots	gross + clots	requires transfusion
Sensory Neuropathy	Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function	Sensory alteration or paresthesia (including tingling), interfering with function but not interfering with ADL	Sensory alteration or paresthesia interfering with ADL	Disabling

*To grade liver, renal toxicity use the maximum level reached after each Course.

Date of Complete Marrow Response (if applicable): ...../...../.....

Reason for failure to achieve CR:

☐ Inadequate trial of chemotherapy — death before chemotherapy started.

☐ Induction death — death due to infection, haemorrhage or other treatment-related cause.

☐ Resistant disease — no effect on blasts or regenerating population predominantly blasts.

☐ Partial remission — maximum reduction in marrow blasts achieved was down to 5-15%.

☐ Any other reason – please specify ……

IV TOXICITY

COURSE	**Course 1**			**Course 2**		
Date of neutrophil recovery to>1.0x10^{9}/l*†						
Date of platelet recovery to >50 x 10 ^{9}/l*						
Date of platelet recovery to >100 x 10 ^{9}/l*						
Non-haematological toxicity‡ (WHO grade: see facing page)	Grade (0=no toxicity)	Date grade started	Date grade stopped	Grade (0=no toxicity)	Date grade started	Date grade stopped
Nausea/vomiting	.....	.....	.....	.....	.....	.....
Alopecia	.....	.....	.....	.....	.....	.....
Oral	.....	.....	.....	.....	.....	.....
Diarrhoea	.....	.....	.....	.....	.....	.....
Cardiac function	.....	.....	.....	.....	.....	.....
Liver toxicity**:						
AST	.....	.....	.....	.....	.....	.....
ALT	.....	.....	.....	.....	.....	.....
Bilirubin	.....	.....	.....	.....	.....	.....
Renal toxicity:**						
Creatinine	.....	.....	.....	.....	.....	.....
Proteinuria	.....	.....	.....	.....	.....	.....
Haematuria	.....	.....	.....	.....	.....	.....
Other (Specify: .....)	.....	.....	.....	.....	.....	.....

* Please state if not recovered before next course (or death)
† If duration of neutropenia exceeds 42 days,please complete an SAE form
** Maximum grade after each course
‡ If grade 3 or 4 please complete an SAE form

V SUPPORTIVE CARE REQUIREMENTS

COURSE	Course 1	Course 2
Units of blood	.....	.....
Units of platelets	.....	.....
Number of days on i.v. antibiotics	.....	.....
Total number of days in hospital	.....	.....
Date first discharged (please state if not discharged)	.....	.....

VI CEP-701 RANDOMISATION

Complete for patients eligible for CEP-701 randomisation

Was patient randomised: YES ☐ NO ☐

If NO, please give reason:

☐ Patient died before randomisation point

☐ Patient refusal.

☐ Other (please specify) .....

VII APL TREATMENT

COURSE	Course 1	Course 2
QT prolongation?	YES ☐ NO ☐	YES ☐ NO ☐
Other arrhythmias?	YES ☐ NO ☐	YES ☐ NO ☐
Sensory neuropathy (Max grade)	.....	.....
Peak WBC ($x10^9$/l)	.....	N/A
Date of peak WBC	.....	N/A
Was mylotarg treatment given?	YES ☐ NO ☐	N/A
Were prophylactic steroids used?	YES ☐ NO ☐	N/A
Differentiation syndrome?	YES ☐ NO ☐	N/A
Tumour lysis syndrome?	YES ☐ NO ☐	N/A

If the answer is YES to any of the above please give details

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VIII TISSUE TYPING OF SIBLINGS

Has tissue typing of siblings been done? NO ☐ YES ☐

If **NO**: Reason why not: No siblings ☐

Patient not high risk ☐

Too old/unfit for allo-SCT ☐

Died/relapsed before done ☐

Other ☐ Specify: .....

If **YES**: Reason: To search for potential allo-SCT donor ☐

Other ☐ Specify: .....

Tissue typing laboratory: .....

Result: HLA-matched sibling ☐ No HLA-matched sibling ☐ Pending ☐

IX TRANSPLANT ARRANGEMENTS

Is the patient scheduled for transplant? NO ☐ YES ☐

If **YES**, please give:

Approx. date: …...../…...../…....

Type of transplant: Standard Allo ☐ Mini Allo ☐ Other ☐ Specify: .....……

X IF DEATH OCCURS: Date: ...../...../.....

Principal cause(s): Infection ☐ Haemorrhage/CVA ☐ Resistant disease ☐

Cardiac ☐ Renal ☐ Hepatic ☐ Pulmonary ☐ Other ☐ ……..……(specify)

Please state circumstances of death or enclose copies of all relevant reports (e.g. letter to GP):

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XI IF RELAPSE or t-MDA/AML:

Relapse ☐ t-MDS/AML ☐ Date of event: ...../...../.....

Please complete a relapse form following treatment for relapse

Please enter data online at http://aml17.cardiff.ac.uk or return when complete to: AML17 Trial Office, Wales Cancer Trials Unit, 6th Floor, Neuadd Meirionnydd, Heath Park, Cardiff CF14 4YS.