UKALL14

Case Report Form (CRF) Completion Guidelines for 'Registration Only' patients

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General Instructions

The Principal Investigator (PI) is responsible for the quality of the data reported on the CRFs.

Each CRF must be signed and dated by an individual authorised by the PI to perform this trial activity as documented on the site's delegation log.

CRFs should be completed as soon as possible after the scheduled visit and submitted to the CTC according to the submission schedule.

Original CRFs do not need to be sent to the CTC. Submit CRFs by either post or fax or as directed in the submission schedule below. CRFs marked as *urgent* must be faxed.

If faxing urgent CRFs is not possible they may be sent via email. When emailing forms, such as the registration for study entry CRF, patient identifiable information (e.g. NHS number, day and month of birth) on the form must be redacted before it is emailed to ctc.ukall14@ucl.ac.uk. The identifiable information should then be provided to CTC via telephone. The un-redacted form must then be posted to the CTC

Lists of CRFs flagged as overdue will be sent to sites on a routine basis to assist site staff to track their patients' progress through the trial treatment.

Corrections to entries

If an error is made, draw a single line through the item, write the correct entry on an appropriate blank space near the original data point on the CRF. All changes, including the addition of new information, must be initialled and dated.

Do NOT:

Obscure the original entry
Try to correct/modify the original entry
Use Tippex or other correction fluid

Review of CRF

Before sending a CRF to the CTC please review it to confirm:

- The current version of each CRF has been used. If data are submitted on a superseded CRF, the site will be asked to resubmit the data on the current version.
- All patient identifiers are written on every page of the CRF. If they are not, the site will be asked to update and resubmit the CRF.
- The CRF is signed and dated. If it is not, the site will be asked to update and resubmit the CRF.
- All changes, including the addition of new data to previously submitted CRFs, have been initialled and dated. If they are not, the site will be asked to resubmit the CRF.
- All entries are clear and legible. Please avoid the use of abbreviations and acronyms.
- All questions have been answered, if any data are *unobtainable*, report this using the following options:
    - Not Evaluable (NE): If a test has been done but the results are not interpretable (e.g. sample haemolysed or clotted)
    - Not Recorded (NR): If a test has been done but the result has not been documented
    - Not Done (ND): If a test has not been done, please provide the reason the test was not done
    - Not Applicable (NA): If a value is not required for this patient, please provide the reason why the value is not applicable
    - Not Known (NK): only if every effort to obtain the data has been exhausted.

Partial dates

If an exact date is not known, please report the dates to the closest estimate month (i.e. NK/06/2000), year (i.e. NK/NK/2010) or between two dates (i.e. 10/12/2010 to 03/04/2011). If a partial date is reported and it is reasonably expected that a date should be obtainable (e.g. during trial treatment), a query will be raised to confirm the actual date cannot be obtained.

Data Discrepancies

CRFs received at the CTC will undergo various checks and all data will be entered into a trial database. Data discrepancies will be raised where data are missing, ambiguous, illegible, illogical, suspected to be incorrect (i.e. out-of-range values) or inconsistent with the protocol.

Data Clarification Forms (DCFs) will be generated on a routine basis and sent to sites according to the trial specific schedule. Please write the discrepancy response on the DCF in the outcome box provided. It is not necessary to send updated amended CRF pages to the UCL CTC unless specifically requested to do so within the text of the query or if it is considerably easier for you to do this (e.g. if there are multiple discrepancies to be resolved on the same CRF).

CRFs for 'Registration only' patients (*14-3-XXX*)

CRF Name	Current Version (date)	Use From Date
'Registration only' Sub-study Entry form	1.0	01 Dec 17
'Registration only' Induction Treatment form	1.1	20 Mar 18
'Registration only' Post-Induction Chemotherapy form	1.1	20 Mar 18
'Registration only' Transplant to D100 form	1.0	18 Jan 18
'Registration only' GvHD form	1.0	18 Jan 18
'Registration only' Annual follow-up form	1.0	18 Jan 18
Relapse	2.0 (19 Apr 11)	Apr 11
Death	3.0 (27 Nov 15)	14 Dec 15
Lost to Follow-up	3.0 (27 Nov 15)	14 Dec 15
Centre Transfer	3.0 (10 Mar 16)	21 Mar 16

There are no safety reporting requirements for 'Registration only' Sub-study patients, and therefore AEs, SAEs and pregnancy reports are not required.

General reminders

- ***Sign and date all CRF forms before faxing or emailing***
- ***Read through the general guidance notes present on CRFs in conjunction with Completion Guidelines***
- ***Original copies of CRFs do not need to be sent to UCL CTC, faxing or emailing copies is accepted***

Submission Schedule and Key Points: 'Registration only' patients (*14-3-XXX*)

'Registration only' Sub-study Entry Form	
Required for:	**When/How to Submit:**
All eligible 'registration only' patients	*Fax* Patients must be registered before starting phase 1 induction. Registration requests received after 4pm may not be processed until the next business day. *Email (if fax not available)* If sending 'registration only' study entry requests by email, patient identifiable information (i.e. NHS number, day and month of birth) on the form must be redacted before it is emailed to ctc.ukall14@ucl.ac.uk. The identifiable information should then be provided to CTC via telephone (0207 679 9860). **The un-redacted form must then be posted to the CTC**
Fax Cover Sheet	
Site contact details	Please provide complete and accurate site contact details to ensure CTC staff can contact the site if there are any queries. The research contact and consultant must be on the delegation log to carry out the appropriate trial tasks.
Page 2 - Eligibility Checklist	
Inclusion criteria	The answers to the questions must all be Yes
Exclusion criteria	The answers to the questions must all be No. Hepatitis testing is not mandatory, however if it is performed locally as standard, a positive test result will render the patient ineligible for the trial.
Page 5 – Haematology & Biochemistry	
Date of Haematology	Please provide results of blood tests prior to starting the steroid pre-phase.
White Blood Cell (WBC) Count x109/L	Please provide results of blood tests prior to starting the steroid pre-phase.
% Bone Marrow Blasts	If these results are pending or unobtainable, an anonymised diagnostic report confirming ALL must be submitted with the registration form.
Page 6 – Informed Consent	
Date PIS given to patient	Please state the date PIS was given.
Version Number Patient Information Sheet	Please state the version used.
Date patient signed Part 1 of the Consent Form	Please state the date the ICF was signed. Patients should be given 24 hours to read, consider and discuss the PIS and then consent taken the following day. If it is not possible to wait 24 hours due to urgency of treatment, consent may be taken the same day, but the investigator must follow up with the patient at a later stage to confirm they are still happy to continue, with the discussion and consent documented in patient notes. If this is the case please annotate the form accordingly, and send details of date consent was re-confirmed via email.
Version Number of Consent Form	Please state the version used.
Page 7 – Informed Consent for Constitutional DNA (Optional), Genetic Testing: Buccal swab collection: Consent for constitutional DNA samples can be obtained at any time during the trial	
Date PIS given to patient	Please state the date the 'Additional Genetic Testing Buccal swab PIS' was given to the patient. If not yet given, the patient can still enter trial – please annotate form accordingly.

‘Registration only’ Sub-study Entry Form	
Date patient signed ‘Genetic Testing Buccal Swab Consent form’	Please provide the date patient signed the Genetic Testing Buccal Swab ICF. If consent is pending, please annotate the form accordingly.
Version Number Patient Information Sheet	Please state the version used.
Version Number of Consent Form	Please state the version used.
CRF sign-off	Please ensure the registration CRF is signed-off by a person listed on the delegation log for that task

‘Registration only’ Induction Treatment Form	
Required for:	**When/How to Submit:**
Any ‘registration only’ patient who received Phase 1 or Phase 2 Induction treatment. Complete one form for each induction cycle given	By post or fax within 30 days following the completion of the relevant Induction treatment phase.
Page 1 – Induction treatment	
Date treatment phase started	Provide date first dose of treatment was given for the relevant induction phase.
Which treatment regimen was followed?	Enter the code for the most closely followed regimen, irrespective of any dose reductions, delays or omissions. If a drug routinely used within a certain regimen was omitted, the intended regimen should still be chosen.
Phase of induction treatment	Please specify the phase of induction patient started.
Has the patient been given rituximab?	Enter yes or no for all patients. If yes provide number of doses.
Philadelphia status	Please complete for all patients. If positive provide details of TKI treatment.
Local assessment of remission history	Confirm if patient has achieved first remission, and give the date this was identified. If patient is in CR after phase 1 the date can be left blank when completing form at end of phase 2, but please annotate that patient was in CR after phase 1.
Response Assessment	Provide date of bone marrow examination used to assess response; specify cellularity grade & percentage of blasts to confirm outcome
Remission status	Confirm current remission status. If first remission has ever been achieved and the patient is no longer in remission, please submit a Relapse Form.
Page 2 – Response Assessment	
Haematology Assessment	Performed at end of relevant induction phase, once all treatment for that regimen has been given and counts recovered.
Treatment plan	Indicate the next plan of action for first line ALL treatment following the induction phase just given. If first line treatment is discontinued, provide the date the final dose of first line treatment was given. Ensure that other CRFs (e.g. relapse form) are completed and submitted as directed on CRF. The CRF also gives guidance on what CRF is due next.

‘Registration only’ Post-Induction Chemotherapy Form	
Required for:	**When/How to Submit:**
‘Registration only’ patients who do not have a transplant at any time during first line treatment for ALL	By post or fax within 30 days of completing any cycle of post-induction chemotherapy treatment e.g.: - End of intensification - End of all cycles of consolidation - Interim maintenance therapy - Every 3 months during maintenance
Page 1 – Post-Induction treatment	
Date treatment phase started	Date of first dose of block of treatment covered by the form
Which post-induction treatment regimen was followed?	Enter the code for the most closely followed regimen, irrespective of any dose reductions, delays or omissions. If a drug routinely used within a certain regimen was omitted, the intended regimen should still be chosen.
Treatment phase	Enter the code for the block of treatment covered by the form. For consolidation, enter number of cycle’s patient received in total. For maintenance, enter the month at time of form completion, e.g. for months 1-3 of maintenance, write “3”.
Has the patient been given rituximab?	Enter yes or no for all patients. If yes provide number of doses given.
Philadelphia status	Please complete for all patients. If positive provide details of TKI treatment.
Local assessment of remission history – *complete only if CR1 reached during treatment block*	Only complete this section if CR1 has not been reported on a previous CRF
Treatment plan	Indicate the next plan of action for first line ALL treatment following the treatment block that has just been given. If first line treatment is discontinued, provide the date the final dose of first line treatment was given. Ensure that other CRFs (e.g. relapse form) are completed and submitted as directed on CRF. The CRF also gives guidance on what CRF is due next.

‘Registration only’ Transplant to D100 Form	
Required for:	**When/How to Submit:**
Any ‘registration only’ patient who has a transplant as part of first line treatment for ALL	Do not complete or send this form until D100 has passed. By post or fax within 30 days of Day 100 visit. If patient has relapsed or died prior to D100, submit a death/relapse form as applicable.
Page 1 - Transplant & conditioning	
Treatment patient received between end of induction and beginning of transplant conditioning	Answer yes or no for each of the phases given. Provide number of cycles of consolidation or number of months of maintenance, if applicable.
Source of donor cells	Give details of the donor source, type of conditioning and dates of conditioning for all patients.
Conditioning drugs given	Indicate yes or no for all drugs listed. If conditioning drug(s) not listed please add to CRF.
Did patient receive TBI?	Enter yes or no for all patients. If yes, provide details.
Page 2 – Day 100 post transplant assessment.	

‘Registration only’ Transplant to D100 Form	
Date of Day 100 assessment	State the date of the patient’s D100 post-transplant hospital visit. This should be as near as possible to the actual D100 point. If patient has died/relapsed prior to reaching D100 submit a death form and relapse form as applicable. Date of assessment to be recorded as n/a if patient died
GvHD	If GvHD has occurred, please complete and submit a GvHD form for each episode.

‘Registration only’ GvHD Form *N.B. We strongly recommend this form is completed in discussion with a clinician.*	
Required for:	**When/How to Submit:**
Any ‘registration only’ patient who experiences GvHD	Send by post or fax. Complete form for each new or worsening episode as possible following confirmation of GvHD at any time. Assessment of GvHD should take place as a minimum on D100 and at subsequent annual follow-up visits.
Page 1 – GvHD Assessment	
Date of onset	This date is the initial date of onset for an episode of GVHD. This date does not change if an episode worsens.
Date of assessment	This date must reflect the date when patient was assessed for presence of new episode(s)/ update of existing episode(s).
Acute GvHD	If acute GvHD is present use modified Glucksberg scoring system (see protocol appendix 6). Give the grade for all organs listed and calculate grade. If patient is experiencing chronic GvHD annotate this section as n/a.
Chronic GvHD	If chronic GvHD is present refer to the classification scheme for chronic GVHD in protocol appendix 6. Give the involvement for all organs listed. If patient is experiencing acute GvHD annotate field with n/a.

‘Registration only’ Annual Follow-up Form	
Required for:	**When/How to Submit:**
All ‘registration only’ patients	Send by post or fax. If patient has died/relapsed prior to reaching the next follow-up timepoint submit a death form and/or relapse form as applicable. Within 30 days of each annual assessment carried out on the anniversary of the date patient stops first line treatment.
Page 1 – Annual follow-up Assessment	
Date of Assessment	Enter the date of the clinic visit where the patient was seen, or the date of other contact with the patient. Date of assessment to be recorded as n/a if the patient died during the past year.
Local assessment of remission history	Only complete this section if CR1 has not been reported on an earlier form. If CR1 previously reported, please annotate accordingly.
Patient Status	- If patient has died, ensure a death form is completed and submitted as directed on the CRF - If patient has relapsed, ensure a relapse form is completed and submitted as directed on CRF.

‘Registration only’ Annual Follow-up Form	
Further treatment	If patient has received any second line treatment since stopping the first line treatment or since last annual follow-up visit, ensure details of all treatment started has been added.
Page 2 – Annual follow-up Assessment (Transplant patients only)	
Donor Lymphocyte infusion & GvHD	This page only needs completing for transplant patients. Enter n/a if patient has not had a transplant. For transplant patients provide details of DLI, if given, along with the reason(s) and confirm if GvHD has been experienced, sending in a GvHD CRF where applicable

The following forms are identical to the randomised patients, and instructions for completion remain unchanged:

Relapse Form	
Required for:	**When/How to Submit:**
Any patient who has relapsed	*Urgent Fax/Email* As soon as possible following the confirmed date of relapse. Complete all sections of the form, and please remember to send a relapse BM (or peripheral blood if WCC >30 x 10^9/l) sample to the MRD lab (protocol section 8.1.2).

Death Form	
Required for:	**When/How to Submit:**
Any patient who has died	*Urgent Fax/Email* Within 7 calendar days of becoming aware of the death.
Was there evidence (bone marrow, peripheral blood, CNS, other) of ALL at the time of death?	The purpose of the question is to confirm if the patient was in remission at the time of death. Complete all sections in light of most recent assessment closest to the time of death; - If not yet confirmed in CR 1, answer = yes - If relapsed & in CR 2 is not yet confirmed, answer = yes - If recent tests (visits) show in CR (& no suspicion of relapse), answer = no
Was this death exempt from SAE Reporting?	-- Answer No -- SAEs are not collected for ‘Registration only’ patients.

Lost to Follow Up Form	
Required for:	**When/How to Submit:**
Any patient who is lost-to-follow up or who has withdrawn trial consent completely; i.e. for any future follow up data to be sent to the CTC	By post or fax as soon as possible after patient is confirmed as being lost to follow up.
Lost to Follow Up	A patient should only be considered lost to follow up after every effort has been made to locate and make contact, e.g. by contacting their local hospital and/or GP. Indicate status of the patient: - Complete section A if patient is lost to follow-up - Complete section B if patient has wholly or partially withdrawn consent & state which areas consent is withdrawn.

Centre Transfer Form	
Required for:	**When/How to Submit:**
Any patient whose care – including follow up - transferred from one trial centre to another at any point.	By post or fax as soon as possible after transfer has been arranged. Complete all sections to ensure that data are collected from, and related correspondence is directed to, the appropriate site.

CRF Flowchart – 'Registration only' patients (*14-3-XXX)*