UKALL14

Case Report Form (CRF) Completion Guidelines

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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 specified 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 it is not possible to fax urgent CRFs, they may be sent via email. When emailing forms, such as the randomisation for study entry CRFs, 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 6799860). 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 If data are submitted on a superseded CRF, the site will be asked to resubmit the data on the current version.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 (e.g. significantly out-of-range values) or inconsistent with the protocol.

Data Clarification Forms (DCFs) will be generated on a regular 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 very much easier for you to do this (e.g. if there are multiple discrepancies to be resolved on the same CRF).

CRFs for Randomised patients (*14-1-XXX or 14-2-XXX*)

CRF Name	Current Version (date)	Use From Date
Registration	6.0 (27 Nov 15)	14 Dec 15
Cytogenetics	3.0 (3 May 13)	May 13
Induction Treatment – Phase 1	3.0 (20 Apr 15)	20 Apr 15
Induction Treatment – Phase 2	3.0 (20 Apr 15)	20 Apr 15
Post Induction Treatment Allocation (PITA)	2.0 (20 Apr 15)	20 Apr 15
Post Induction Registration – Maintenance	2.0 (20 Apr 15)	20 Apr 15
Post Induction Registration - Transplant	2.0 (20 Apr 15)	20 Apr 15
Intensification	2.0 (20 Apr 15)	20 Apr 15
Consolidation	2.0 (20 Apr 15)	20 Apr 15
Maintenance	1.0 (8 Dec 10)	Dec 10
Transplant Conditioning (RIC/MAC) Palifermin ODMQ Transplant Day 100 GvHD Graft Failure Post-Transplant Assessment	2.0 (20 Apr 15)	20 Apr 15
Treatment Summary	4.0 (27 Nov 15)	14 Dec 15
Annual Follow-up (Not in CR after Phase 2)	2.0 (20 Apr 15)	20 Apr 15
Annual Follow-up (Relapse/Secondary Malignancy)	2.0 (20 Apr 15)	20 Apr 15
Annual Follow-up (Long)	2.0 (20 Apr 15)	20 Apr 15
Late Effects (replaces 2 Year Additional Follow-Up)	1.0 (10 Mar 16)	21 Mar 16
Relapse	2.0 (19 Apr 11)	Apr 11
Death	3.0 (27 Nov 15)	14 Dec 15
Second Cancer	2.0 (20 Apr 15)	20 Apr 15
Lost to Follow-up	3.0 (27 Nov 15)	14 Dec 15
Centre Transfer	3.0 (10 Mar 16)	21 Mar 16
Adverse Events – Induction Phase 1	3.0 (27 Nov 15)	14 Dec 15
Adverse Events – Induction Phase 2	3.0 (27 Nov 15)	14 Dec 15
Adverse Events – Intensification	3.0 (27 Nov 15)	14 Dec 15
Adverse Events – Consolidation	3.0 (27 Nov 15)	14 Dec 15
Adverse Events – Transplant	3.0 (27 Nov 15)	14 Dec 15
Adverse Event of Special Interest	1.0 (27 Nov 15)	14 Dec 15
Informed Consent for Constitutional DNA	1.0 (27 Nov 15)	14 Dec 15

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: Randomised patients (*14-1-XXX or 14-2-XXX*)

Registration Form at Study Entry	
Required for:	**When/How to Submit:**
All eligible patients	*Fax* Randomisation must be performed before phase 1 begins. Complete the registration form to randomise the patient. Randomisation requests received after 4pm may not be processed until the next business day. *Email (if fax not available)* If sending randomisation requests by email, patient identifiable information (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	This page must contain complete and accurate site contact details to ensure CTC staff can communicate with research staff at the registering site throughout the patient registration/randomisation process. The research contact, pharmacy contact and consultant listed must all be on the delegation log to carry out the appropriate trial tasks.
Page 1 – Patient Details	
Steroid pre-phase start date	This can be before the date of registration.
Proposed start date of Induction Phase 1	This must be on or after the date of registration. • Please allow up to 2 hours for registrations to be processed • Registrations received after 4pm may not be processed until the next working day
Page 2 - Eligibility Checklist	
Eligibility confirmed by treating clinician	This is only required if the Hep B core antibody (HBcAb) viral serology test result is **positive** (the box marked with an *).
Page 5 – Haematology & Biochemistry	
Date of Haematology	Please provide results of blood test prior to starting steroid pre-phase. Other hospitals may need to be contacted to obtain this information.
White Blood Cell (WBC) Count	This should be the presenting white cell count. *It is essential that this result is from a test taken before the steroid pre-phase started.*
Date of Biochemistry	Please provide results of blood test prior to starting steroid pre-phase. Other hospitals may need to be contacted to obtain this information.
% Bone Marrow Blasts	This result is required in order to confirm trial eligibility. *If these results are pending or unobtainable, an anonymised diagnostic report must be submitted with the randomisation form to confirm the diagnosis of ALL.*
Page 6 – Liver Function Tests	
Date of Liver Function Tests	Please provide results of blood test prior to starting steroid pre-phase. Other hospitals may need to be contacted to obtain this information.

Registration Form at Study Entry	
Page 7 – Medical History	
Does the patient have a significant medical history or baseline symptoms?	Include *significant* pre-existing medical conditions and *all* baseline symptoms including symptoms related to the diagnosis of ALL. (e.g.: anaemia, neutrophil count decreased, etc.)
Severity Grade	This is only required for conditions which are ongoing.
Page 8 – Informed Consent	
Date PIS given to patient	Please state the date the patient information sheet was given to the patient. Please annotate the CRF accordingly if this is the case.
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.
Date Part 2 of the Consent Form signed	If the patient has signed part 2 of the consent form (optional), enter the date the form was signed
Name of person taking consent	This person must be on the site delegation log and authorised to carry out this trial activity.
Page 9 – Informed Consent for Constitutional DNA (Optional) *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.
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 randomisation CRF is signed-off by a person listed on the delegation log for that task

Cytogenetics Form	
Required for:	**When/How to Submit:**
All registered patients ***All patients who have relapsed***	By post or fax: - Within 2 weeks of registration/randomisation. - As soon as possible following relapse.
Date of Diagnosis or Relapse sample	Please enter the date on which the sample(s) was taken
Date of cytogenetic analysis	Please enter the date that each of these tests were reported locally
Date of FISH	
Date of Molecular Genetic testing	

Induction Treatment – Phase 1 Form	
Required for:	**When/How to Submit:**
Any patient who received any Induction Phase 1 treatment	By post or fax within 30 days following the completion of Induction Phase 1 treatment.
Page 1 – Steroid Pre-phase	
Pre-phase given according to protocol schedule	Confirm if given without alteration from protocol schedule and provide number of days steroids were given.
Page 2 - Phase 1 Induction - Standard Therapy	
Date Phase 1 induction started	Please enter the date that phase 1, day 1 chemotherapy was given.
Page 3 - Phase 1 Induction - B Lineage/Rituximab Randomisation	
BSA (m^2)	This should be the BSA used to calculate the dose given.
Rituximab Dose (mg)	Do not leave blank, write 0 if dose of this IMP has been completely omitted. [NB: All doses of IMPs given or not given must be explicitly documented in order to facilitate safety reporting and trial analysis.]
Reduction	A dose *reduction* has occurred if the patient has received less than 375mg/m^2 for any reason
Reason for reduction/delay/omission	If any doses of the IMP have been reduced/delayed/omitted due to toxicity (adverse event), ensure this reason matches data on the Adverse Event CRF for this phase of treatment. If any dose has been reduced/delayed/omitted to prevent toxicity, please annotate the form accordingly.
Page 4 – Oncaspar (Pegylated-Asparaginase)	
BSA (m^2)	This should be the BSA used to calculate the dose given.
Oncaspar Dose (IU)	Do not leave blank. Write 0 if day 4 and/or day 18 dose has been completely omitted. [NB: All doses of IMPs given or not given must be explicitly documented in order to facilitate safety reporting and trial analysis.]
Reduction	A dose *reduction* has occurred if patient received less than 1000 IU/m^2 for any reason.
Reason for reduction/delay/omission	If any doses of the IMP have been reduced/delayed/omitted due to toxicity (adverse event), ensure this reason matches data on the Adverse Event CRF for this phase of treatment. If any dose has been reduced/delayed/omitted to prevent toxicity, please annotate the form accordingly. *If Erwinase has been given in place of Oncaspar following hypersensitivity reaction, report this as an omission.*
Erwinase	This section should be completed if Erwinase has been given in place of Oncaspar following hypersensitivity reaction.
Page 6 - Response Assessment	
Date of Response Assessment	Please enter the date of the end of phase response assessment (e.g. bone marrow aspirate). If performed more than 35 days after day 1 of induction phase 1, please annotate the form to explain the reason for the delay.
Number of days in hospital	This is the number of days the patient has been an in-patient between phase 1, day 1 and the end of phase assessment.

Induction Treatment – Phase 2 Form	
Required for:	**When/How to Submit:**
Any patient who received any Induction Phase 2 treatment	By post or fax within 30 days following the completion of Induction Phase 2 treatment.
Page 1 - Phase 2 Induction - Standard Therapy	
Date Phase 2 induction started	Please enter the date that phase 2, day 1 chemotherapy was given.
Page 2 - Phase 2 Induction - T Lineage/ Nelarabine Randomisation:	
Did the patient have unresolved Grade 2 or greater neurotoxicity at the end of Phase 2?	If the answer to this question is yes, ensure this matches data on the Adverse Event CRF for this phase of treatment.
If yes, was Nelarabine omitted?	If the answer to this question is yes, no further data on this page are required.
BSA (m^2)	This should be the BSA used to calculate the dose given.
Nelarabine Dose (g)	Do not leave blank, write 0 if dose of this IMP has been completely omitted. [NB: All doses of IMPs given or not given must be explicitly documented in order to facilitate safety reporting and trial analysis.]
Reduction	A dose *reduction* has occurred if the patient received less than 1.5g/m^2 for any reason.
Reason for reduction/delay/omission	If any doses of the IMP have been reduced/delayed/omitted due to toxicity (adverse event), ensure this reason matches data on the Adverse Event CRF for this phase of treatment. If any dose has been reduced/delayed/omitted to prevent toxicity, please annotate the form accordingly.
Date of response assessment	Please enter the date of the end of phase response assessment (e.g. bone marrow aspirate). If performed more than 35 days after day 1 of induction phase 2, please annotate the form to explain the reason for the delay.
Number of days in hospital	This is the number of days the patient has been an in-patient between phase 2, day 1 and the end of phase assessment.
Remission Status	If the patient is not in Complete Remission (CR) at this time point but *was* in CR at the end of Phase 1 Induction, please submit a Relapse Form. <u>Annual Follow-Up Forms:</u> If remission has not yet been achieved, i.e. the patient was not in CR at Phase 1 or at time of Phase 2 Response Assessment, please use the Annual Follow-up Form headed 'Not in CR after Phase 2'. If the patient was in CR at the end of Phase 1 Induction, please use the Annual Follow-up Form headed 'Relapse/Second Cancer'.

Post Induction Treatment Allocation (PITA) Form

It is essential that this CRF is submitted for *all patients who are in CR at the end of Induction Phase 2.*
Answer the questions and follow the arrows in the flowchart accordingly. The answer to all other questions is N/A (not applicable)
Don't forget the 'completed by' field on this CRF is on page 3 – often missed.

Required for:	**When/How to Submit:**
All patients in CR at the end of Induction Phase 2	*Urgent Fax/Email* As soon as possible following the completion of Induction Phase 2 treatment **but not before the completion of any ongoing donor search*.* If a patient is not in CR at the end of Induction Phase 2 – please submit a Treatment Summary CRF as soon as possible.
Fax Cover Sheet	
Site contact details	This page must contain complete and accurate site contact details to ensure CTC staff can communicate with research staff at the participating hospital site.
Page 1	
Does the patient have a sibling donor?	This question can only be answered accurately once tissue typing tests of all eligible siblings has been completed. If a search for a matched sibling donor was not carried out, this should be reported as Not Done (ND).
Is a protocol* donor available?	This question can only be answered accurately once the search for a suitable donor has been completed. If a search for a suitable unrelated donor was not carried out, this should be reported as Not Done (ND).
*Protocol donor (section 5.6.1) *Standard risk patients with a sibling donor* *Any high risk patient with an *8/8 MUD donor* *Patients with High Risk cytogenetics and/or MRD (post induction phase 2) with a 7/8 MMUD **or** cord blood*	
Page 2	
This page is only required for high risk patients who do not have a suitable protocol donor *or* standard risk patients who are not continuing to maintenance treatment.	
Page 3	
This page is only required for patients with suitable protocol donor but who do not fulfil the eligibility criteria for transplant for any reason; e.g.: clinical decision, patient choice	

Post Induction Registration – Maintenance Form

It is essential that this CRF is submitted for *all patients who have been allocated to Maintenance Treatment.* This group *does not include* patients who have received interim chemotherapy prior to Transplant.

Required for:	**When/How to Submit:**
All patients allocated to Maintenance Chemotherapy	*Urgent Fax/Email* As soon as possible following the completion of Induction Phase 2 treatment **but not before the completion of any ongoing donor search*.* Registration should be completed before Intensification Treatment begins. Registration requests received after 4pm may not be processed until the next business day.
Fax Cover Sheet	
Site contact details	This page must contains complete and accurate site contact details to ensure CTC staff can communicate with research staff at the registering site throughout the registration process.
Page 1	
Confirmation of Registration to Maintenance	Confirmation of the registration to maintenance will be sent by fax and email using the details provided on the cover sheet.

Post Induction Registration – Transplant Form

It is essential that this CRF is submitted for *all patients who have been allocated to Transplant Treatment.* If the patient is moving to a different trial participating site for transplant, the research teams at both hospitals will need to work together to capture and report trial data throughout this phase of treatment; the CTC will make every effort to co-ordinate between the two sites wherever possible.

Required for:	**When/How to Submit:**
All patients allocated to Stem Cell Transplant	*Urgent Fax/Email* As soon as possible following the completion of a successful donor search. Registration should be completed before Conditioning Treatment begins. Registration requests received after 4pm may not be processed until the next business day.
Fax Cover Sheet	
Site contact details	This page must contain complete and accurate site contact details to ensure CTC staff can communicate with research staff at the registering site throughout the registration process.
Page 1	
Over 40 years of age *(This is an assessment of the patient's risk of relapse due to age)*	If the patient was greater than 40 (i.e.: has past their 41st birthday), at the time of study entry, the answer to this question is YES
Page 4	
Transplant Registration/Randomisation	Confirmation of the registration to transplant will be sent by fax and email using the details provided on the cover sheet.

Intensification Treatment Form	
Required for:	**When/How to Submit:**
Any patient who received any Intensification Treatment	By post or fax within 30 days following the completion of Intensification Treatment.
Page 1	
Did the patient receive intensification/CNS prophylaxis?	If the patient received any intensification treatment, including patients who had a cycle of intensification treatment before proceeding to transplant, the answer to this question is Yes. If the patient did not receive any intensification treatment, no further data are required.
Date Intensification started	Please enter the date that intensification day 1 chemotherapy was given.
Was treatment given according to protocol schedule?	If all IMPs and Non-IMPS in this treatment phase were given without delay, reduction or omission, the answer to this question is Yes. If there were any delays, reductions or omissions during this treatment phase, the answer to this question is No. Please report the reason for the delay, reduction or omission in the table provided.
Page 2	
BSA (m^2)	This should be the BSA used to calculate the dose given.
Oncaspar Dose (IU)	Do not leave blank, write 0 if dose of this IMP has been completely omitted. [NB: All doses of IMPs given or not given must be explicitly documented in order to facilitate safety reporting and trial analysis.]
Reduction	A dose *reduction* has occurred if the patient received less than 1000IU/m^2 for any reason
Reason for reduction/delay/omission	If any doses of the IMP have been reduced/delayed/omitted due to toxicity (adverse event), ensure this reason matches data on the Adverse Event CRF for this phase of treatment. If any dose has been reduced/delayed/omitted to prevent toxicity, please annotate the form accordingly. *If Erwinase has been given in place of Oncaspar following hypersensitivity reaction, report this as an omission.*
Erwinase	This section should be completed if Erwinase has been given in place of Oncaspar following hypersensitivity reaction.

Consolidation Treatment Form	
Required for:	**When/How to Submit:**
Any patient who received any Consolidation Treatment	By post or fax within 30 days following the completion of Cycle 4 Consolidation Treatment. (One CRF for all 4 cycles)
Page 1	
Date cycle 1 started	Please enter the date that consolidation cycle 1, day 1 chemotherapy was given.
Page 2	
BSA (m^2)	This should be the BSA used to calculate the dose given.
Oncaspar Dose (IU)	Do not leave blank, write 0 if dose of this IMP has been completely omitted. [NB: All doses of IMPs given or not given must be explicitly documented in order to facilitate safety reporting and trial analysis.]
Reduction	A dose *reduction* has occurred if the patient received less than 1000IU/m^2 for any reason

Consolidation Treatment Form	
Reason for reduction/delay/omission	If any doses of the IMP have been reduced/delayed/omitted due to toxicity (adverse event), ensure this reason matches data on the Adverse Event CRF for this phase of treatment. If any dose has been reduced/delayed/omitted to prevent toxicity, please annotate the form accordingly. *If Erwinase has been given in place of Oncaspar following hypersensitivity reaction, report this as an omission.*
Erwinase	This section should be completed if Erwinase has been given in place of Oncaspar following hypersensitivity reaction.
Page 4	
Date cycle 2 started	Please enter the date that consolidation cycle 2, day 1 chemotherapy was given. If more than 22 days after the start of consolidation cycle 1, please provide a reason for the delay.
Page 5	
Date cycle 3 started	Please enter the date that consolidation cycle 3, day 1 chemotherapy was given. If more than 22 days after the start of consolidation cycle 2, please provide a reason for the delay.
Page 6	
BSA (m2)	This should be the BSA used to calculate the dose given.
Oncaspar Dose (IU)	Do not leave blank, write 0 if dose of this IMP has been completely omitted. [NB: All doses of IMPs given or not given must be explicitly documented in order to facilitate safety reporting and trial analysis.]
Reduction	A dose *reduction* has occurred if the patient has received less that 1000IU/m^2 for any reason
Reason for reduction/delay/omission	If any doses of the IMP have been reduced/delayed/omitted due to toxicity (adverse event), ensure this reason matches data on the Adverse Event CRF for this phase of treatment. If any dose has been reduced/delayed/omitted to prevent toxicity, please annotate the form accordingly. If Erwinase has been given in place of Oncaspar following hypersensitivity reaction, report this as an omission.
Erwinase	This section should be completed if Erwinase has been given in place of Oncaspar following hypersensitivity reaction.
Page 7	
Date cycle 4 started	Please enter the date that consolidation cycle 4, day 1 chemotherapy was given. If more than 43 days after the start of consolidation cycle 3, please provide a reason for the delay.

Maintenance Treatment Form	
Required for:	**When/How to Submit:**
Any patient who received any Maintenance Treatment	By post or fax within 30 days of each 3 month treatment cycle (3 – 24 months post-transplant)
Date of assessment	The date should be approximately 3 months after the previous date of assessment unless a delay to treatment has been reported.
Month of assessment	This must correspond with the date of assessment provided

TRANSPLANT FORMS: NB there are multiple CRFs within the transplant package

1. Non-Myeloablative Conditioning Regimen Form (1 Page)

Required for:	When/How to Submit:
Any patient who received any Conditioning Treatment	By post or fax within 30 days following the completion of Conditioning Treatment.
Daily Dose	Dose should be reported in the units specified or, the units must be provided.
If the regimen given differs from the protocol in drugs, doses or schedule, please annotate the CRF accordingly. The reason for the deviation from protocol guidance also needs to be clearly documented.	

2. Myeloablative Conditioning Regimen Form (2 Pages)

Required for:	When/How to Submit:
Any patient who received any Conditioning Treatment	By post or fax within 30 days following the completion of Conditioning Treatment.
Daily Dose	Dose should be reported in the units specified or, the units must be provided.
If the regimen given differs from the protocol in drugs, doses or schedule, please annotate the CRF accordingly. The reason for the deviation from protocol guidance also needs to be clearly documented.	

3. Palifermin Form (1 Page)

N.B. palifermin randomisation closed in April 2016 but some forms may still be due

Required for:	When/How to Submit:
All patients randomised for Palifermin Treatment	By post or fax within 30 days following the completion of Conditioning Treatment.
Palifermin Dose (mcg)	Do not leave blank. Write 0 if dose of this IMP has been completely omitted.
Reduction	A dose *reduction* has occurred if the patient received less than the protocol specified dose for their treatment arm (180mcg/kg or 60mcg/kg) for any reason
Reason for reduction/delay/omission	If any doses of the IMP have been reduced/delayed/omitted due to toxicity (adverse event), ensure this reason matches data on the Adverse Event CRF for this phase of treatment. If any dose has been reduced/delayed/omitted to prevent toxicity, please annotate the form accordingly.

4. Oral Daily Mucositis Questionnaire (1 Page per Day)

Required for:	When/How to Submit:
All patients randomised for Palifermin Treatment	Within 30 days following the completion of Conditioning Treatment.

THESE QUESTIONNAIRES CAN NOT BE COMPLETED RETROSPECTIVELY

It is essential that this questionnaire is complete by all patients participating in the Palifermin randomisation from the date of admission until D28 or date of discharge (whichever is sooner).

If the patient is moving to a different trial participating site for transplant, the research teams at both hospitals will need to work together to capture and report trial data throughout this phase of treatment; the CTC will make every effort to co-ordinate between the two sites wherever possible.

****UPDATE palifermin trial arm closed April 2016 and no further palifermin treatment is given therefore these forms are longer in use****

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5. Transplant Form (1 Page)

Required for:	When/How to Submit:
Any patient who received donor stem cells	By post or fax within 30 days following Transplant Day 0.
Type of donor	This must match the donor type reported on the Post Induction Treatment Allocation CRF. If a 9/10 matched donor is used, please specify if this is equivalent to an 8/8 match or a 7/8 match.

6. Day 100 Form (2 Pages)

Required for:	When/How to Submit:
Any patient who received donor stem cells	By post or fax within 30 days following the Day 100 assessment.
Page 1	
Day 100	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.
Graft failure	If the patient's neutrophils and/or platelets did not recover to the required levels, please complete and submit a graft failure form.
Page 2	
If ITU admission was required, was this exempt from SAE reporting? *The purpose of this question is to confirm if an SAE report is/was required. Please refer to SAE reporting time frames, exemptions and flowchart in protocol section 12.2.2.*	Any adverse event that is life-threatening or results in prolonged hospitalisation is defined as serious. ITU admissions are often associated with life-threatening events or prolonged hospitalisations. If, in the investigator's opinion, an ITU admission that occurred was not serious, the rationale should be clearly documented in the source data at site. If the answer to this question is NO, please cross-check against the SAE records for this patient to confirm that an SAE has already been submitted. If not submitted we recommend contacting the CTC immediately to discuss prior to completing an SAE

7. GvHD Form (2 Pages)

Required for:	When/How to Submit: ***N.B. We strongly recommend this form is completed in discussion with a clinician.***
Any patient who experiences GvHD	By post or fax as soon as possible following confirmation of GvHD. One CRF for each episode. 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 then 3 monthly for 2 years following transplant (as per protocol schedule of assessments, appendix 12), or if there is a significant development.
Page 1	
Date of onset of this episode	For a worsening episode of GvHD this date must match the date of onset as given on the initial/previous form.

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Has this episode of GvHD resolved?	If No, please submit an updated CRF when the episode has resolved (don't forget to initial and date all changes).
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.

8. Graft Failure Form (1 Page)

Required for:	**When/How to Submit:**
Any patient with confirmed graft failure	By post or fax as soon as possible following confirmation of graft failure.

TRANSPLANT FORMS

9. Post-Transplant Assessment Form (1 Page per Visit)

Required for:	When/How to Submit:
Any patients who receives donor stem cells	By post or fax within 30 days of each 3 monthly assessment (6 – 24 months post-transplant)
Date of assessment	Date of assessment should reflect the date of the patient's clinic visit. Enter as n/a if patient died during the 3-month period. This is the date of assessment at the end of each 3 month period following transplant. The first date should be approximately 6 months after Day 0; all subsequent assessment dates should be 3 months after the previous date of assessment.
Month of assessment	This must correspond with the date of assessment provided
Patient status	If patient has relapsed or died prior to this assessment, submit a death/relapse form as applicable.
Has the patient been given DLI? If yes, please enter DLI details below:	Please provide the details of any DLI doses the patient has been given since the previous assessment.
Has the patient experienced GvHD since last assessment?	This refers to NEW episodes of GvHD. Please also complete a GvHD form for any new episodes of GvHD Please note that if an episode GvHD has been ongoing since the last post-transplant assessment, the answer to this question should be 'no'. Please ensure that the GvHD form from the ongoing episode is updated with any new information (such as date of resolution).

Treatment Summary Form

Required for:	When/How to Submit:
All registered patients	By post or fax within 30 days of completing final UKALL14 trial treatment. Please note that UKALL14 treatment is not complete until the end of Maintenance Treatment or the 24 month post-transplant assessment period.
Completed all trial treatment	A patient is considered to have completed all trial treatment if they have reached the end of 24 months of maintenance treatment or the 24 month post-transplant assessment period during 1st Complete Remission
Date most recent UKALL14 trial treatment (including any given during 24 month post-SCT follow-up):	Please enter the date on which the last dose of trial treatment was given. Please note that 'trial treatment' refers to any treatment given to the patient (e.g. backbone NIMP chemotherapy) not just IMP doses. If the patient has stopped trial treatment early due to relapse or death, this date must be on or before the date of relapse/death.
Reason for stopping trial treatment early	If the patient has stopped trial treatment early due to relapse or death, please don't forget to submit the Relapse or Death CRF.

Annual Follow-up Forms

If patient has relapsed or died prior to date of follow-up, submit a death/relapse form as applicable. No need to complete the form if patient has died before reaching the assessment timepoint.
It is essential that an Annual Follow-up CRF is submitted every year for all surviving patients on, or near, the anniversary of the last trial treatment date.
If a patient moves to a new location, including out of the UK, event (relapse) and outcome (survival) data must still be submitted.
There are three different Annual Follow-up CRFs – the type required is determined by the patient's status and progress through the trial.

Scenario 1: Not in CR after Phase 2

Required for:	When/How to Submit:
Any surviving patients who did not reach complete remission (CR) at any time during Induction Treatment including patients who stopped trial treatment early at the end of Induction Phase 1 due to refractory disease.	By post or fax within 30 days of every annual assessment carried out on the anniversary of the last trial treatment.

Scenario 2: Relapse/Second Cancer

Required for:	When/How to Submit:
Any surviving patients who have relapsed or been diagnosed with a second cancer	By post or fax within 30 days of each annual assessment carried out on the anniversary of the last trial treatment.

Scenario 3: Annual Follow-Up (2 Pages)

Required for:	When/How to Submit:
Any surviving patients in first CR and not diagnosed with a second cancer	By post or fax within 30 days of each annual assessment carried out on the anniversary of the last trial treatment.

The following guidance should be used to assist in completion of annual follow up forms: *Page 1 – Annual follow-up Assessment*	
Date of Assessment (all follow up forms)	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 reporting past year.
Patient Status (all follow up forms)	- 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.
Further treatment (all follow up forms)	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.
Remission status (not in CR after phase 2 form only)	Only complete this section if CR1 has not been reported on an earlier form. If CR1 previously reported, please annotate accordingly.
Full blood count (annual follow up form)	Please enter results on, or as close as possible, to the clinic visit. If taken on a different date to the clinic visit (date of assessment), please annotate the CRF accordingly.
Avascular necrosis (annual follow up form)	Answer yes or no, and provide details as applicable
Serious cardiac problems (annual follow up form)	Answer yes or no, and provide details as applicable

Annual Follow-up Forms	
Employment status (annual follow up form)	Answer yes or no, and provide details as applicable
Second cancer (annual follow up form)	Answer yes or no, and complete and submit a second cancer form if applicable
Remission status (not in CR after phase 2 form only)	Only complete this section if CR1 has not been reported on an earlier form. If CR1 previously reported, please annotate accordingly.

Late Effects Form (replaces 2 Year Additional Follow Up)	
This CRF includes the General Health Questionnaire [GHQ-12] which cannot be completed retrospectively. Please remember to hand this to the patient at their clinic visit.	
Required for:	**When/How to Submit:**
All surviving patients	By post or fax within 30 days of the late effects assessment timepoint (see Protocol section 8.3.) - In patients who completed trial treatment this will be 2 years after completing maintenance or the 24 month post-transplant assessment period - In patients who stop trial treatment early, this will be 4.5-5 years after trial registration

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? *The purpose of this question is to confirm that an SAE report was not required to report this death. Please refer to SAE reporting time frames, exemptions and flowchart in protocol section 12.2.2.*	Any adverse event that results in death is, by definition, serious. However, section 12.2.2 outlines circumstances where events are exempt from SAE reporting. These include disease-related deaths and deaths due to adverse events that were **not** temporally and causally related to the study IMPs. Please check section 12.2.2 carefully when completing this section of the CRF. If there is any doubt about whether a death needs reporting as an SAE, please contact the CTC on ctc.ukall14@ucl.ac.uk.

Second Cancer Form	
Required for:	**When/How to Submit:**
Any patient diagnosed with a second cancer	By post or fax as soon as possible following confirmed diagnosis of second cancer
Diagnosis	Relapsed ALL is not a second cancer

Lost to Follow Up Form	
Required for:	**When/How to Submit:**
Any patient who has been 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.

Adverse Events Form

There are five treatment phase specific Adverse Events CRFs. It is essential that an Adverse Event CRF is submitted for each phase of treatment the patient started.

1. Induction Phase 1

Required for:	When/How to Submit:
Any patient who received any Induction Phase 1 treatment	By post or fax within 30 days following the completion of Induction Phase 1 treatment.

2. Induction Phase 2

Required for:	When/How to Submit:
Any patient who received any Induction Phase 2 treatment	By post or fax within 30 days following the completion of Induction Phase 2 treatment.

3. Intensification

Required for:	When/How to Submit:
Any patient who received any Intensification Treatment	By post or fax within 30 days following the completion of Intensification Treatment.

4. Consolidation

Required for:	When/How to Submit:
Any patient who received any Consolidation Treatment	By post or fax within 30 days following the completion of Consolidation Treatment. (One CRF for all 4 cycles)

5. Transplant

Required for:	When/How to Submit:
Any patient who received donor stem cells	By post or fax within 30 days following Day + 30

Date of Onset	For events with an onset after study registration, please enter the date on which the patient first reported signs/symptoms. For events ongoing at the time of study registration, the onset date should be the date on which the event first increased in severity by one or more CTCAE grades.
Was the event serious?	Please refer to SAE reporting time frames, exemptions and flowchart in protocol section 12.2.2.If the answer to the question is 1 (Yes). Please cross-check against SAE records for this patient to confirm an SAE report has been submitted. If this event was serious but an SAE report was not required as per protocol exemptions, the answer to this question is 2 (Yes, but SAE report not required).

Adverse Event of Special Interest	
All thromboembolic events must be reported on either a Thromboembolic Event Urgent Event Form or on an SAE Report as appropriate.	
Required for:	**When/How to Submit:**
Use this form to report venous thromboembolisms occurring outside the SAE reporting window. (See Protocol section 12.2.2.1)	*Fax/Email* AEs of special interest must be reported within 7 calendar days of becoming aware of the event. *N.B. a thromboembolic event occurring during phase 1 is very likely to fall under the SAE reporting window. Refer to protocol section 12.2.2.1 or contact CTC if there is uncertainty.*

Informed Consent – Constitutional DNA (Consent is optional)	
Required for:	**When/How to Submit:**
Use this form to report information about consent for constitutional DNA studies and family history information for patients registered to UKALL14 prior to the implementation date of Protocol v7.0.	Send by post or fax. Consent for constitutional DNA can be obtained at any time during the trial. It is recommended to provide the PIS and obtain consent (if granted) at time of study entry, but this is not mandatory.
Page 1 – Informed Consent – Constitutional DNA	
General note:	This only needs to be completed for **either** the stored bone marrow sample **or** buccal swab. Please cross through the section that does not apply.
Date PIS given to patient	Please state the date on which the PIS (Stored Bone Marrow Sample) or PIS (Buccal Swab) was given to the patient
Date patients signed consent form	Please state the date on which the ICF (Stored Bone Marrow Sample) or ICF (Buccal Swab) was signed
Version Number Patient Information Sheet	Please state the version used.
Version Number of Consent Form	Please state the version used.
Name of person taking consent	This must be someone who is listed on the site delegation and who is authorised to carry out this trial activity.
Page 2 – Family history of cancer	
Have any of the patient's first degree relatives had cancer?	Answer yes or no for all patients, and provide details where applicable.

CRF Flowchart – Randomised patients (*14-1-XXX or 14-2-XXX*)