EBMT Registry

Cellular therapy (CT) follow-up

Guide to the completion of the EBMT data collection form:

CT_FU_v2.2

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EBMT Registry

EBMT Clinical Research & Registry Department

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Introduction

Please make sure you have already checked the **Introduction to the EBMT Registry Completion Guidelines** document latest version available under *Manuals and Reference Documents* section on EBMT website.

Cellular therapies

Day 100, 6 Months, Annual & Unscheduled Follow-Up

The Cellular Therapy (CT) follow-up form must be submitted online into the EBMT Registry database within 100 days, 6 months and annually post-CT or at time of patient death, whichever occurs first.

Some sections of this form are relevant and should be submitted on a particular follow-up only. If so, it is mentioned in the subtitle of the respective section. Otherwise (if no instruction as to what follow-up period the section covers), the questions of the section should be completed for every follow-up: Day 100, 6 Months, Annual and Unscheduled follow-up.

Subsequent HCT/CT

In case a patient proceeds to a subsequent HCT/CT between time points (Day 100, 6 Months, Annual), the data collection form (DCF) form sequence will start over again with another Day 0 form associated with the treatment (e.g. HCT, CT). Before starting over, a follow-up should be reported prior to the preparative regimen for the subsequent HCT/CT, to capture any events that occurred between the last reported follow-up post-CT and before the subsequent treatment.

Survival status

Date of follow-up

Report the date of this follow-up. If the patient died before the specific time point, enter the date of death. If the patient was lost to follow-up, enter the last contact date the patient was alive.

Survival status

Indicate if the patient is last known to be **Alive** or **Dead** on the date of follow-up previously noted. If the patient is lost to follow-up, tick the box for **Lost to follow-up**. If the patient died, please complete the section on cause of death (question 34).

Assessment period covered by this report

Indicate which assessment period covers this report based on the time period in relation to the CT infusion date. You can select between the following:

- **Day 100:** 100 days post-CT. The data on this assessment should reflect the patient's status on the day the patient was last seen, closest to 100 days post-CT. If the patient died within 100 days, the data from the last date the patient was seen alive can be used.
- **6 months:** 6 months post-CT. The data on this assessment should reflect the patient's status on the day the patient was last seen, closest to 6 months post-CT. If the patient died within 6 months, the data from the last date the patient was seen alive can be used.
- **Annual or unscheduled follow-up** post-CT.
    - Annual follow-up: In principle each CT patient should receive a yearly follow-up after the CT. When reporting the annual follow-up in the Registry the follow-up that falls closest to the anniversary (yearly interval) of the CT should be reported.
    - Unscheduled follow-up: This form can also be used to report a follow-up that occurred outside of the scheduled follow-ups for a CT patient. For example, due to a death of a patient after 6 months post-CT or patient proceeding to a subsequent CT/HCT. If a patient proceeds to a subsequent HCT/CT then a follow-up should be reported prior to the preparative regimen for the subsequent HCT/CT, to capture any events that occurred in between.

Main cause of death

Report only one main cause of death, even if it was considered to be a combination of various causes. If the cause of death is not known, select **Unknown**.

The following main causes of death can be reported (check only one):

- **Relapse or progression/persistent disease**;
- **Secondary malignancy**;
- **Cellular therapy-related** - death caused by complications or infections after cellular therapy (specify details in the question ***Select treatment related cause***);
- **HCT-related** - death caused by complications or infections after transplant (specify details in the question ***Select treatment related cause***).
- **Gene therapy related** - death caused by complications after GT (specify details in the question ***Select treatment related cause)***.
- **IST-related** - death caused by complications or infections after IST, for patients with Bone Marrow Failure only. Specify details in the question ***Select treatment related cause.***

If none of the suggested answer options match, tick the box **Other** and specify the cause of death in the textbox in English .

Select treatment related cause

In case of Cellular therapy- or HCT-related or Gene-therapy or IST-related cause of death, specify if the cause of death was related to, select all that apply:

- **Graft versus host disease (GvHD);**
- **Non-infectious complication;**
- **Infectious complication.**

Infectious complication

If the cause of death was related to an infectious complication, select the type(s) of infections that apply:

- **Bacterial infection;**
- **Viral infection;**
- **Fungal infection;**
- **Parasitic infection;**
- **Infection with unknown pathogen.**

Please note that the new core Data Collection Forms (DCFs) do not have the category *"rejection/poor graft function or failure"* as contributory cause of death (previously in MEDs-A and B (auto, allo and disease-specific forms) since the cause of death following a graft failure is generally an infection.

Was an autopsy performed?

Select **Yes** if an autopsy was performed and select **No** if no autopsy was performed. If it is not known whether an autopsy was performed, select **Unknown**.

Best Response

This section should be completed only for Day 100 and 6 Months follow-up and will be disabled for all subsequent reporting periods. This section is not applicable for patients receiving CT for Inborn errors indication diagnosis.

Best clinical/biological response after this CT

Report the patient's best response achieved after CT but before any subsequent treatment, even if the patient got worse again afterwards. Please refer to Appendix 1 on the form to select the best response that is appropriate for the diagnosis of the patient. This includes the response observed before any subsequent treatment. If the best response after the CT has not been evaluated, select **Not evaluated**. If the best response after the HCT is unknown, select **Unknown.**

For Cell therapy given as treatment of a primary disease, the best response only has to be completed for the 100 days and 6 months follow-up. The disease specific options for the best response can be found in appendix 1 of the form.

The response must be assessed prior to additional non-planned disease treatment.

For the six-month form, copy the best response that was reported with the Day 100 form, unless a better disease response to CT is achieved during the six-month reporting period.

Example 1: A recipient with B-Cell Non Hodgkin Lymphomas is in *Chemorefractory relapse or progression, including primary refractory disease* at CT, achieves a CR during the first 100 days, and then progresses during the six-month reporting period. The best response to CT occurred in the 100 days reporting period and should be reported as "CR" on both Day 100 and 6 Months form. See table 1:

Table 1. Example of reporting the best response 1.

Assessment period	**Current disease status**	**Best clinical/biological response**	**Date response evaluated**
D0 form	Chemorefractory relapse or progression, including primary refractory disease	-	-
Day 100 form	CR	CR	Date of sample/image that first confirmed CR
6 Months form	Relapsed	CR	Date of sample/image that first confirmed CR (same as reported with d100 form)

Example 2: A recipient with B-cell acute lymphoblastic leukaemia is in CR at CT, maintains the response after transplant, and then relapses within the six-month reporting period. The best response to CT would be reported as "CCR" for all subsequent reporting periods. See table 2:

Table 2. Example of reporting the best response 2.

Assessment period	**Current disease status**	**Q4.1 Best clinical/biological response**	**Q5. Date response evaluated**

D0 form	CR	-	-
Day 100 form	CR	CCR	Date of sample/image that first confirmed a continued CR
6 Months form	Relapsed	CCR	Date of sample/image that first confirmed a continued CR (same as reported with d100 form)

Example 3: A recipient with multiple myeloma goes to CT having established a PR prior to CT and maintains the response throughout the 100-day reporting period. During the six-month reporting period, the recipient achieves a CR. The best response to CT occurred in the six-month reporting period. See table 3:

Table 3. Example of reporting the best response 3.

Assessment period	**Current disease status**	**Q4.1 Best clinical/biological response**	**Q5 Date response evaluated**
D0 form	Chemorefractory relapse or progression, including primary refractory disease	-	-
Day 100 form	PR	PR	Date of sample/image that first confirmed PR
6 Months form	CR	CR	Date of sample/image that first confirmed CR

Date best response first observed

Report the date the best response to the CT was first observed. The response date is the date that the sample or image was taken for assessing the response.

For the six-month form, copy the date reported with the Day 100 form, unless a better disease response to CT is achieved during the six-month reporting period. If the date is unknown, select **Unknown**.

Treatment of complication derived from a previous transplant/cellular therapy

If the indication for this CT was the treatment or prevention of complications (derived from a previous transplant/cellular therapy or expected from a subsequent transplant/cellular therapy), then select per *GvHD*, *Graft failure*, *Immune reconstitution* or *Infection* whether they have been:

- **Resolved;**
- **Improved;**
- **No response;**
- **Progressed;**
- **Not evaluated.**

GvHD

- **Resolved**: complete resolution of aGvHD manifestation;
- **Improved**: improvement of one stage in the severity of skin, liver and/or GI aGvHD, except improvement to stage 0, without deterioration in any other organ;
- **No response**: persistence of the same stage of aGvHD in all organs;
- **Progressed**: worsening of aGvHD of at least 1 stage in at least one organ;
- **Not evaluated**.

Graft failure

- **Resolved**;
- **Improved**;
- **No response**;
- **Progressed**;
- **Not evaluated**.

Immune reconstitution

- **Resolved**;
- **Improved**;
- **No response**;
- **Progressed**;
- **Not evaluated**.

Infection

- **Resolved**: Undetectable infection;
- **Improved**: Decrease in infectious burden without resolution;

- **No response**: stable infection;
- **Progressed**: worsening of the infection;
- **Not evaluated**.

Recovery

This section should be submitted for Day 100 follow up and 6 Months follow up. If the recovery occurred before 100 days and was reported at Day 100 follow-up the section can be skipped at 6 Months follow-up.(For (ANC) recovery and Platelet reconstitution)

Absolute neutrophil count (ANC) recovery (neutrophils ≥ $0.5x10^9$ cells/L)

Absolute neutrophil count (ANC) recovery is considered to take place when the number of neutrophils in the patient's peripheral blood rises to at least $0.5x10^9$ cells/L. Please note this is regardless of the use of growth factors and neutrophils level should be confirmed by three consecutive laboratory values obtained on different days.

Answer **No** if:

- An autologous reconstitution has taken place.
- The stem cell source is either PB or BM and the ANC <$0.5x10^9$ cells/L by Day +28.
- The stem cell source is CB and the ANC <$0.5x10^9$ cells/L by Day +42

Answer **Yes** if the absolute count of neutrophils post-CT is higher or equal to $0.5x10^9$ cells/L for 3 laboratory values.

If the absolute count of the patient's neutrophils was never below $0.5x10^9$ cells/L, the answer **Never below** must be chosen instead of answer **Yes.**

Mark the ANC as **Unknown** if it was not assessed post-CT.

Date of the last assessment

Indicate the date of the last assessment of the patient's neutrophils level.

Date of ANC recovery

The date to be entered is the first date out of the 3 consecutive neutrophil counts above $0.5x10^9$ cells/L were recorded on different days. This date must be at least 7 days after the last transfusion containing neutrophils.

Platelet reconstitution (platelets ≥$20x10^9$ cells/L)

Indicate whether or not there was platelet reconstitution achieved that is confirmed by 3 consecutive blood tests where absolute count of platelets is ≥$20x10^9$ cells/L. All dates should reflect no transfusions in the previous 7 days.

Answer No if the platelet count was <20x10^9 cells/L or if platelet transfusions were administered in the previous 7 days.
Answer Yes if the platelet count ≥ 20x10^9 cells/L was achieved and sustained for 3 consecutive laboratory values, obtained on different days without platelet transfusions administered in the previous 7 days.

Answer **Never below**, if the recipient's platelets never dropped below 20x10^9 cells/L at any time post-HCT and a platelet transfusion was never required. If the recipient's platelet count drops below 20x10^9 cells/L and/or the recipient received a platelet transfusion even once, do not use this option. This option is only applicable in the 100 day follow-up reporting period.

Answer **Unknown** if recipient's platelets were not assessed post-CT.

Date of the last assessment

If platelet reconstitution was not achieved, indicate the date of the last assessment of the patient's platelets level.

Date of platelet reconstitution

If platelet reconstitution was achieved, the date to be entered is the first date out of the 3 consecutive platelets counts ≥ 20x10^9 cells/L checked on different days and after 7 days without platelet transfusion. Mark as **Date unknown** if it is confirmed by medical record that patient achieved platelet reconstitution but the exact date of the first test with platelets counts ≥ 20x10^9 cells/L is not known.

Date of the last platelet transfusion

Indicate the date when the patient received the latest platelet infusion within the 100 day follow-up period; or mark it as **Not applicable** (not transfused) or **Date unknown.**

Was B-cell count monitored during this follow up period?

If B-cell count was not monitored after cellular therapy, select **No.**

If B-cell count was monitored after cellular therapy, select Yes and report if there was a B-cell recovery. If it is not known if there was B-cell recovery, select Unknown.

Generally CD19+ cells are monitored but other B-cell markers may be assessed.

Date of the last assessment

If there was no B-cell recovery answer **No** and report the **date of the last assessment**.

Date of the first B-cell recovery

If there was B-cell recovery observed, answer **Yes** and report the date of the first B-cell recovery. If the date of recovery was reported on the last follow-up , this can be skipped.

Current haematological findings

Report results of haematological investigation in the follow up period. If haematological values were assessed multiple times in the current reporting period, report the most recent (closest to the date of this follow-up) value. Carefully check in which unit the data should be reported.

- **Hb (haemoglobin):** Report the haemoglobin (Hb) level in grams per decilitre (g/dL). If the level was not evaluated, Select **Not evaluated**. If the haemoglobin level is not known, select **Unknown**.
- **Platelets:** Report the count of platelets in 10^9 cells/L. If it was not evaluated, select **Not evaluated**. If the amount is unknown, select **Unknown**.
    - Also specify if p**latelets were transfused within 7 days before the blood count assessment** by answering **Yes** (if transfused), **No** (not transfused), or marking **Unknown**, if it is not known.
- **White blood cells:** Report the amount of white blood cells in 10^9 cells/L. If it was not evaluated, select **Not evaluated**. If the amount is unknown, select **Unknown**.
- **Lymphocytes:** Report the percentage (%) of lymphocytes. If it was not evaluated, select **Not evaluated**. If the amount is unknown, select **Unknown**.
- **Neutrophils:** Report the percentage (%) of neutrophils. If it was not evaluated, select **Not evaluated**. If the amount is unknown, select **Unknown**.

Extended dataset

Antimicrobial prophylaxis

Did the patient receive antimicrobial prophylaxis?

Indicate if the patient received any type of prophylaxis.

If yes, what type of prophylaxis?

Check all types of prophylaxis the patient received.

Antibacterial

Antibiotic

Check all types of antibiotics that were administered as prophylaxis.

Phase

Only for the Day 100 Follow-Up:

Select the phases (**pre-engraftment**, **post-engraftment**) during which the antibiotic was administered. If administered during the post-engraftment phase, indicate whether it was given only during post-engraftment, or whether it was a continuation from pre-engraftment into post-engraftment, or stopped during pre-engraftment and then restarted during post-engraftment. Select **unknown** if you do not know during what phase(s) the antibiotic was given.

Response for Follow-Ups after Day 100:
Indicate whether the antibacterial prophylaxis was **started during this follow-up period**, or whether it is a **continuation from the previous follow-up period**. If started during this follow-up period, indicate the start date or select **unknown** if you do not know the start date.

Final date the antibacterial prophylaxis was discontinued

Report the date the patient last received any type of antibacterial prophylaxis, or select **unknown** if you do not know the final date antibacterial prophylaxis was administered, or select **ongoing** if the patient is still receiving antibacterial prophylaxis.

Antiviral

Did the patient receive cytomegalovirus (CMV) prophylaxis during this follow-up period?

Indicate if any type of CMV prophylaxis has been administered.

Which drugs were used?

Check all types of drugs that have been administered as CMV prophylaxis.

Final date CMV prophylaxis was discontinued

Report the date the patient last received any type of CMV prophylaxis, or select **unknown** if you do not know the final date CMV prophylaxis was administered, or select **ongoing** if the patient is still receiving any type of CMV prophylaxis.

Did the patient receive prophylaxis for varicella-zoster virus (VZV) or herpes simplex virus (HSV) with either acyclovir or valacyclovir during this follow-up period?

Indicate if either acyclovir or valacyclovir has been administered as VZV or HSV prophylaxis.

Final date VZV or HSV prophylaxis was discontinued

Report the date the patient last received either acyclovir or valacyclovir as VZV or HSV prophylaxis, or select **unknown** if you do not know the final date either acyclovir or valacyclovir was last administered as VZV or HSV prophylaxis, or select **ongoing** if the patient is still receiving either acyclovir or valacyclovir as VZV or HSV prophylaxis.

Did the patient receive rituximab or another anti-CD20 monoclonal drug as prophylaxis for Epstein-Barr virus post-transplant lymphoproliferative disorder (EBV-PTLD) during this follow-up period?

Indicate if any anti-CD20 monoclonal drug, including rituximab, has been administered as EBV-PTLD prophylaxis.

Did the patient receive prophylaxis for hepatitis B (HBV) during this follow-up period?

Indicate if any type of HBV prophylaxis has been administered.

Which drugs were used?

Check all types of drugs that have been administered as HBV prophylaxis.

Final date HBV prophylaxis was discontinued

Report the date the patient last received any type of HBV prophylaxis, or select **unknown** if you do not know the final date HBV prophylaxis was administered, or select **ongoing** if the patient is still receiving any type of HBV prophylaxis.

Antifungal

Antifungal

Check all types of antifungals that have been administered as prophylaxis.

Phase

Only for the Day 100 Follow-Up:

Select the phases (**pre-engraftment**, **post-engraftment**) during which the antifungal was administered. If administered during the post-engraftment phase, indicate whether it was given only during

post-engraftment, or whether it was a continuation from pre-engraftment into post-engraftment, or stopped during pre-engraftment and then restarted during post-engraftment. Select **unknown** if you do not know during what phase(s) the antifungal was given.

Response for Follow-Ups after Day 100:

Indicate whether the antifungal prophylaxis was **started during this follow-up period**, or whether it is a **continuation from the previous follow-up period**. If started during this follow-up period, indicate the start date or select **unknown** if you do not know the start date.

Final date the antifungal prophylaxis was discontinued

Report the date the patient last received any type of antifungal prophylaxis, or select **unknown** if you do not know the final date antifungal prophylaxis was administered, or select **ongoing** if the patient is still receiving antifungal prophylaxis.

Did the patient receive prophylaxis for *Pneumocystis jirovecii* pneumonia (PJP)during this follow-up period?

Indicate if any type of PJP prophylaxis has been administered.

Which drugs were used?

Check all types of drugs that have been administered as PJP prophylaxis.

Final date prophylaxis was discontinued

Report the date the patient last received any type of PJP prophylaxis, or select **unknown** if you do not know the final date PJP prophylaxis was administered, or select **ongoing** if the patient is still receiving PJP prophylaxis.

Pre-emptive viral therapy

Did the patient receive pre-emptive therapy for a viral infection during this follow-up period?

Indicate if the patient received pre-emptive therapy for any virus.

If yes, for what virus?

Indicate whether the patient has received pre-emptive therapy for CMV and/or EBV.

Specify the pre-emptive therapy for each CMV episode that occurred during this follow-up period

Repeat the questions below for each CMV episode to reflect all episodes that occurred.

CMV treatment start date

Report the date the patient first received any type of pre-emptive therapy for CMV.

Antiviral(s) used

Check all types of antivirals that have been administered as pre-emptive therapy for CMV.

Was this episode of CMV infection due to a resistant CMV strain?

Indicate if the CMV strain causing this CMV episode was identified to be of a drug-resistant phenotype with viral genetic mutations decreasing susceptibility to one or more antiviral drugs, or select **unknown** if you do not know if it was a resistant CMV strain.

Specify the pre-emptive therapy for each EBV episode that occurred during this follow-up period

Repeat the questions below for each EBV episode to reflect all episodes that occurred.

EBV treatment start date

Report the date the patient first received any type of pre-emptive therapy for EBV, or select unknown if you do not know the date.

Antiviral(s) used

Check all types of antivirals that have been administered as pre-emptive therapy for EBV.

Complications since the Last Report - GvHD

This section shall be completed only if the patient ever received an allogeneic HCT or a cell therapy of allogeneic origin prior to this CT. Do not report complications that were resolved before this cellular therapy. Do not report complications that were previously reported as resolved, unless they recurred.

Did graft versus host disease (GvHD) occur?

This question only needs to be answered if the patient ever received an allogeneic HCT or a cell therapy of allogeneic origin. Select **Yes** if GvHD occurred/were ongoing/resolved in this follow up period. If it did not occur select **No** and proceed to the next section. If this information is unavailable, select **Unknown**.

Graft-versus-host disease (GvHD) refers to a clinical syndrome caused by the response of transplanted donor allogeneic cells to histocompatibility antigens expressed on tissues of the transplantation recipient. Acute GvHD refers to the appearance of an allogeneic inflammatory response in exclusively three organs: the skin (inflammatory maculopapular erythematous skin rash), the liver (hyperbilirubinemia due to cholestatic jaundice), and the gastro-intestinal (GI) tract (upper and/or lower GI tract manifestations). The diagnosis must occur in the absence of manifestations of cGvHD and should ideally be supported by positive histological findings. cGvHD is based on either the presence of specific diagnostic signs or distinctive signs accompanied by additional confirmation (e.g. biopsy or other objective diagnostic test) in at least one target organ (skin & appendages, mouth, eyes, genitalia, oesophagus, lungs and muscles & fascia). Detailed definitions are described in the 2014 NIH Consensus (1) and 2018 EBMT—NIH—CIBMTR Task Force statement on standardised terminology (2).

Did the patient receive a systemic/immunosuppressive treatment for GvHD during this follow-up period?

Indicate **Yes** if the patient received a systemic/immunosuppressive treatment for GvHD in this follow up period, and indicate **No** if the patient did not receive a systemic/ immunosuppressive treatment for GvHD. If the information is unavailable, select **Unknown**. In case of No and Unknown, proceed to the next section: Complications since the last report - Non-infectious complications.

If the answer is **Yes**, specify also details in the subsequent questions:

Started in this follow-up period

Select this option if systemic/immunosuppressive treatment for GvHD starts during this follow-up. and report the **Date treatment started**: report here the date the systemic/immunosuppressive treatment for GvHD started**.** If the date is not known, select **Unknown.**

Ongoing since previous follow-up

Select this option if systemic/immunosuppressive treatment for GvHD started in a previous follow-up period and it was ongoing in this follow-up period. The details on whether the systemic/immunosuppressive treatment for GvHD stopped or not in the current follow up period should be reported in the subsequent question.

Treatment stopped

Report if systemic/immunosuppressive treatment for GvHD stopped during this follow-up. Mark **Unknown** if this information is unavailable. If the answer is Yes, specify also the **Stop date of treatment (**during this follow-up) or mark the date as **Unknown** if this date is unavailable.

Did acute GvHD occur?

Indicate if aGvHD occurred/were ongoing/resolved in this follow up period (including ongoing aGvHD first reported in a previous FU).

Acute graft versus host disease (aGvHD) is a consequence of donor T-cells recognizing the patient's antigens as foreign. It usually consists of dermatitis, hepatitis, and gastroenteritis. Although it usually develops within the first 100 days, it can also appear later on.

If the information is unavailable, select **Unknown**.

Started in this follow-up period

Select this option if aGvHD started during this follow-up and report the **date of onset** in the subsequent question. If the date is not known, select **Unknown.**

Ongoing since previous follow-up

Select this option if aGvHD started in a previous follow-up period and was ongoing in this follow-up period. The details on whether the aGvHD was resolved or not in the current follow up period should be reported in the subsequent question ***aGvHD resolved***.

Maximum observed organ severity score during this period

Select for each organ listed in the table the observed severity score during this follow up period. If another site was also affected, answer **Yes** in **Other site affected** and specify this site in the text field in English. Report **Unknown** if this information is unavailable. Select **Not evaluated** if aGvHD was not assessed.

The maximum grade for acute graft versus host disease (aGvHD) is defined according to the stages presented by the skin, liver, lower and upper GI tracts and can be found in table 4.

Organ	Stage	Description
Skin	0	No rash attributable to acute GvHD
	1	Skin rash < 25% body surface
	2	Skin rash 25-50% body surface
	3	Skin rash >50% body surface
	4	Generalized erythroderma (> 50% BSA) plus bullous formation and desquamation >5% of BSA

Organ	Stage	Description
Liver	0	Total serum bilirubin < 34 µmole/L (< 2 mg/dL)
	1	Total serum bilirubin 34–50 µmole/L (2 to 3 mg/dL)
	2	Total serum bilirubin 51–102µmole/L (3.1 to 6 mg/dL)
	3	Total serum bilirubin 103–255 µmole/L (6.1 to 15 mg/dL)
	4	Total serum bilirubin >255 µmole/L (> 15 mg/dL)
Lower GI tract (Lower gut)	0	Diarrhea < 500 mL/day or<3 episodes/day for adults or diarrhea <10 mL/kg/day or <4 episodes/day for children
	1	Diarrhea 500–999 mL/day or 3–4 episodes/day for adults or diarrhea 10–19.9 mL/kg/day or 4–6 episodes/day for children
	2	Diarrhea 1000–1500mL/day or 5–7 episodes/day for adults diarrhea 20–30 mL/kg/day or 7–10 episodes/day for children
	3	Diarrhea >1500 mL/day or >7 episodes/day for adults or diarrhea > 30 mL/kg/day or >10 episodes/day for children
	4	Severe abdominal pain with or without ileus or grossly bloody stools (regardless of stool volume)
Upper GI tract (Upper gut)	0	No or intermittent anorexia or nausea or vomiting
	1	Persistent anorexia or nausea or vomiting

Table 4. aGvHD grading system per organ (2).

Overall maximum grade observed during this period

Select the overall maximum grade that was observed during this follow up period. If it is not known which overall maximum grade was observed, select **Unknown**. Select **Not evaluated** if aGvHD was not assessed.

The overall grade (or the stage of skin, liver and gut) should be mentioned in the patients' file. If not clearly stated, ask the treating physician. You should report the maximum grade seen during the relevant period being studied as calculated from table 5.

Table 5. Overall maximum grade for aGvHD (2).

Grade							
1	Skin stage 1 or 2	AND	Liver stage 0	AND	Upper gut stage 0	AND	Lower gut stage 0
2	Skin stage 3	AND/ OR	Liver stage 1	AND/ OR	Upper Gut stage 1	AND/ OR	Lower gut stage 1
3	Any skin	AND	Liver stage 2 or 3	AND/ OR			Lower gut stage 2 or 3
4	Skin stage 4	OR	Liver stage 4	OR			Lower gut stage 4

Steroid-refractory acute GvHD

Indicate if the patient experienced steroid-refractory acute GvHD (answer **Yes** and provide details in subsequent questions) or not (answer **No**). Select **Unknown** if this information is not available.

Steroid refractory aGvHD is defined in the EBMT handbook (3) as: “Failure to respond to standard steroid doses (defined as progression within 3–5 days of starting treatment or an incomplete response by 7–14 days) or recurrence after initial dose reduction (steroid dependence)”.

Started in this follow-up period

Select this option if the patient experienced steroid-refractory acute GvHD and it started during this follow-up. Report also Date of onset (the date when steroid-refractory aGvHD started) or If the date is not known, select **Unknown.**

Ongoing since previous follow-up

Select this option if the patient experienced steroid-refractory acute GvHD that started in a previous follow-up period and was still ongoing in this follow-up period.

aGvHD resolved

If acute GvHD was resolved in this follow-up period, answer **Yes** and specify the **Date of aGvHD resolution** (the date on which aGvHD resolved completely) in this follow up period or mark the date as **Unknown**.

Answer No if acute GvHD was resolved in this follow-up period.

If it is unknown whether aGvHD resolved, mark **Unknown**.

Did chronic GvHD occur during this follow-up period?

Indicate if chronic GvHD occurred/were ongoing/resolved in this follow up period (including ongoing cGvHD first reported in a previous FU).

Answer **No** if the patient has never had an episode of cGvHD in this follow up period. If the information is unavailable, select **Unknown**.

If the answer is **Yes**, specify also:

Started in this follow-up period

Select this option if cGvHD started during this follow-up and report the **Date of onset (**the date when cGvHD started) or if the date is not known, select **Unknown.**

Ongoing since previous follow-up

Select this option if cGvHD started in a previous follow-up period and was ongoing during this follow-up period. The details on whether the cGvHD was resolved or not in the current follow up period should be reported in the subsequent question ***aGvHD resolved***.

Maximum NIH score during this period

Indicate if the maximum NIH score during this period was **Mild**, **Moderate** or **Severe**. If the score is unknown, select **Unknown**. Select **Not evaluated** if cGvHD was not assessed

The NIH scoring system was first published in 2005 and was updated in 2014 and 2022. As described in the 2014 Diagnosis and Staging Working Group report (1), eight classical organs or sites (skin, mouth, eyes, lungs, musculoskeletal system, gastrointestinal tract, genitourinary tract, and liver) are considered for calculating global score.

Elements included in the proposed global scoring include both the number of organs or sites involved and the severity score within each affected organ. Indicate the maximum NIH score during this period, as per the results of these measurements. Instructions for physicians on assessing the NIH score can be found in the EBMT handbook (1,4) or table 6.

Mild cGvHD	1 or 2 organs involved with no more than score 1 AND Lung score 0
Moderate cGvHD	3 or more organs involved with no more than score 1 OR At least 1 organ (not lung) with a score of 2 OR Lung score 1
Severe cGvHD	At least 1 organ with a score of 3 OR Lung score of 2 or 3

Table 6. Assessing the maximum NIH score (1).

In 2022 the NIH consensus (5) recognized atypical manifestations of chronic GvHD, which should be placed in the section 'other' below the list of organs involved. Atypical manifestations do not contribute to the global severity score.

Date maximum NIH score

Report the date the maximum NIH score was observed in this follow-up period. If the date is not known, mark **Unknown**.

Maximum observed organ severity score

Select for each organ in the table the observed severity score. If another site was affected, answer **Yes** in **Other site affected** and specify this site in the text field. Select **Not evaluated** if cGvHD was not assessed.

Use the NIH scoring system as described in Chronic GvHD.

Steroid-refractory chronic GvHD

Indicate if the patient experienced steroid-refractory chronic GvHD. Steroid refractory cGvHD is defined as "progression of cGvHD while on prednisone at ≥1 mg/kg/day for 1 to 2 weeks or stable GvHD on ≥0.5 mg/kg/day (or 1 mg/kg every other day) of prednisone for 1 to 2 months" (2). Mark **Unknown** if this information is not available.

If the answer is **Yes**, specify details in the subsequent questions.

Started in this follow-up period

Select this option if steroid-refractory cGvHD started during this follow-up period and report the **Date of onset (**the date when steroid-refractory cGvHD started) or If the date is not known, select **Unknown.**

Ongoing since previous follow-up

Select this option if steroid-refractory cGvHD started in a previous follow-up period ans was ongoing in this follow-up period.

cGvHD resolved

Report whether chronic GvHD was resolved in this follow up period or not. If it is unknown whether cGvHD resolved, mark **Unknown**.

If the answer is **Yes**, specify the **Date of cGvHD resolution** or if the date is unavailable, select **Unknown**.

Was overlap syndrome observed (features of both chronic and acute GvHD)

If overlap syndrome was observed, select **Yes**. If overlap syndrome was not observed, select **No**. Mark **Unknown** if this information is unavailable.

Complications since the last report - Non-infectious complications

Do not report complications that were resolved before this cellular therapy.

Do not report complications that were previously reported as resolved, unless they recurred.

Did non-infectious complications occur during the follow-up period?

If no other non-infectious complication than GvHD occurred during the follow-up period or if the complication was grade 1 or 2, select **No** and proceed to the next section.

If non-infectious complications (other than GvHD) occurred/were ongoing/resolved in this follow-up period answer **Yes** taking into account the complication CTCAE grade (if applicable) as follows:

- The following complications should be reported if present regardless of the Maximum grade observed:
    - Cytokine release syndrome (CNS),
    - IEC-associated neurotoxicity syndrome (ICANS),
- The other complications listed in the table should be considerate for reporting with a CTCAE grade of at least 3 or up.

For adverse events not listed in the table but observed with CTCAE grade of at least 3, they should be considerate while answering this question and for reporting in the relevant **Other** text field. Consult with Appendix 4 in the paper form which non-infectious complications should not be reported even for grades 3 and 4.

If a grading is dependent on hospitalisation but the patient was an inpatient at the time of onset, the centre will make the interpretation. If the patient had been an out-patient and the severity was such that the patient would have been hospitalised, grading will be selected accordingly.

Adverse event observed during this period

Specify for each adverse event listed whether it was observed or not in this follow-up period. Follow instruction on the minimas CTCAE grate to consider the complication for reporting. The CTCAE gradings (v5) can be found on the website of the NIH (6). If the status of the adverse event is unknown, select **Unknown.** The list of adverse events includes the following:

- **Cytokine release syndrome (CRS);**
- **IEC-associated neurotoxicity syndrome (ICANS);**
- **Other neurotoxicity;**
- **Macrophage activation syndrome (MAS);**
- **Secondary haemophagocytic lymphohistiocytosis;**
- **Organ toxicity: skin;**

- **Organ toxicity: liver;**
- **Organ toxicity: lung;**
- **Organ toxicity: heart;**
- **Organ toxicity: kidney;**
- **Organ toxicity: gastrointestinal;**
- **Other organ toxicity;**
- **Tumour lysis syndrome;**
- **B-cell aplasia;**
- **Bone marrow aplasia;**
- **Hypogammaglobulinemia;**
- **Exacerbation of existing neurological disorder;**
- **Other complication.**

Example 1: A recipient with B-cell acute lymphoblastic leukaemia receives a CT on January 1st 2021 and develops a grade 1 CRS on January 3rd 2021. The patient is not treated during the reporting period and the CRS is not resolved at the moment of Day 100 assessment. The CRS develops to grade 2 within the six-month reporting period, the patient receives treatment and the CRS is resolved at the 6 months assessment. See table 7:

Reporting period	**Current adverse event**	**10.1 Adverse event**	**10.2 Maximum grade observed**	**10.3 Onset date**	**10.4 Treated**	**10.5 Resolved**
Day 100 form	CRS – present grade 1	Present	Grade 1 (ASTCT)	03-01-2021	No	No
6 Months form	CRS – present, develops into grade 2, resolved after 5 months	Present	Grade 2 (ASTCT)	03-01-2021	Yes	Yes
Annual FU	CRS – absent	Absent	-	-	-	-

Table 7. CRS assessment.

Event newly developed or ongoing since previous assessment

If you are reporting 6 months or annual follow-up, indicate if the adverse event **newly developed** in the follow-up period (i.e. started since the last follow-up event was reported and was not present at previous follow-up) or if it was **Ongoing since previous assessment** (i.e. the adverse event was reported at a previous follow-up and is still present at this follow-up).

Maximum grade observed

Select for each adverse event the maximum grade that was observed in the reporting period. If the grade is unknown, select **Unknown**. If not otherwise specified, CTCAE grading system is to be used (6).

For the following complications please use ASTCT Consensus Grading scale (Lee 2019) (https://www.astctjournal.org/article/S1083-8791(18)31691-4/fulltext):

- Cytokine release syndrome (CRS): is a non–antigen specific toxicity that occurs as a result of high-level immune activation;
- IEC-associated neurotoxicity syndrome (ICANS).

If for some reason it is not possible to use this grading system, please select the appropriate scale from the list (see Grading system question below).

There is no maximum grade to be indicated for bone marrow aplasia, hypogammaglobulinemia and B-cell aplasia.

Grading system

If Cytokine release syndrome (CRS) and/or IEC-associated neurotoxicity syndrome (ICANS) marked as observed during this follow-up period, specify the Grading system used for assessment by selecting one of the answer options:

- ASTCT consensus (Lee 2019)
- CTCAE
- Lee 2014
- MDACC
- Other; specify it in the text field.

B-cell aplasia

If B-cell aplasia is reported as Complication observed during this follow-up period -Yes, specify the **% B-cells** or mark it as **Not evaluated**.

B-cell aplasia is a condition characterised by extremely low B-cell counts.

Hypogammaglobulinemia

If **hypogammaglobulinemia** is reported as **Observed during this follow up period,** specify also the following details:

Was it also present at time of the cellular therapy?

Answer **No, occurred after the cellular therapy**, if the patient had no hypogammaglobulinemia at time of this cellular therapy.

Answer **Yes**, if the patient had hypogammaglobulinemia at time of this cellular therapy and report **Was it worsened by the cellular therapy** or not.

Specify (Indicate CTCAE term)

If **Exacerbation of existing neurological disorder** or **Other complication** is reported as **Observed during this follow up period, s**pecify the CTCAE term.

Consult with Appendix 4 in the paper form which non-infectious complications should not be reported even for grades 3 and 4.

Onset date

For each adverse event occurred in this follow up period (only if newly developed) , indicate the onset date of the event. Report the onset date when the adverse event was first observed during this follow-up period. If the complication has been reported in a previous follow-up form and was not resolved at that follow-up, leave this field empty.

Resolved

Report for each adverse event if the complication was resolved in this follow-up period (answer **Yes** and specify the **Stop date** it was resolved or mark the date as **Unknown**) or not (answer **No** if it is still ongoing). Use the **Unknown** answer option if there is no information on whether the complication was resolved or not**.**

Complications since the last report - Infectious complications

Do not report infections that were already reported as resolved on the previous assessment and did not reoccur.

Did infectious complications occur during the follow-up period?

Answer **Yes** if any infectious complications occurred/were ongoing/resolved in this follow up period (including any ongoing infectious complication first reported in a previous FU) during the follow-up period, select **No** and proceed to the next section.

Infections already reported on the previous follow-up need to be taken into account while reporting since they continued into this follow-up period. In this case, please make sure to report the current state in the current follow up period (e.g. clinical implications/localization/resolution).

Infections already resolved at the previous follow-up do not need to be reported, unless a reactivation occurred.

Please note that the following infections do NOT need to be reported:

- Minor ophthalmologic bacterial infections (e.g. conjunctivitis treated topically; blepharitis treated topically; stye treated topically)
- External otitis treated topically
- Otitis media treated with oral antibiotics
- Isolated lip herpes simplex
- Bacterial tonsillitis or pharyngitis treated orally
- Laryngitis without viral identification managed at home by inhalations or without any intervention
- Upper respiratory tract infection (URTI) without viral/bacterial identification managed at home
- Bilateral cervical lymph node enlargement concurrent with URTI that resolved without specific treatment, together with the resolution of URTI
- Local superficial wound infection resolved under topical antibiotics (including impetigo)
- Minor skin bacterial infections (e.g. folliculitis; acne)
- Minor fungal skin infection (e.g. candidal intertrigo treated topically)
- Diaper rash treated with local antifungals
- Candidal balanitis treated topically
- Vaginal candidiasis treated topically or with a single oral dose
- Asymptomatic bacteriuria due to a pathogen not multi-resistant
- Single low urinary tract infection treated orally without need for hospitalisation
- Phlebitis following peripheral intravascular infusion that resolved after intravascular removal without treatment with antibiotics
- Any isolate that is considered part of the normal flora of the place (oral cavity, vagina, skin, stools) except if it carries an antimicrobial resistance that has clinical implications (induce isolation precautions or a pathogen-directed therapy)
- Positive culture without clinical implications (i.e. symptoms/signs of disease; administration of pathogen-directed therapy; isolation precautions or surveillance)

Bacterial infection

Indicate if the patient had a bacterial infection in the follow-up period after the treatment (after lymphodepleting/conditioning regimen) took place. Report here only bacterial infections with microbiological documentation, otherwise they shall be reported as infection with unknown pathogen.

New or ongoing

Indicate if the patient had a **Newly developed** bacterial infection or if it was **Ongoing since previous assessment**.

Start date

Only if newly developed bacterial infection, report the date a first positive blood or other relevant culture or diagnostic sample was obtained. In case a diagnostic sample was obtained with a delay since the symptoms of infection started – report here the date when symptoms attributable to this infection started (e.g. patient with pneumonia, urine test for legionella was sent after a few days and the test result was positive).

In case an infection was found for the first time at autopsy, use the date of death, unless you can identify the date when the symptoms attributable to this infection were reported for the first time.

If the start date was already reported on the previous follow-up form (with the **Ongoing since previous assessment** option selected), the start date does not need to be reported again and this field shall be left blank.

Type of bacteria

Select the type of bacteria by marking if it is '**Gram-positive**', '**Gram-negative**' or **'Other'** (see the list in Appendix 1 of the form or available in the database).

Pathogen

Select the bacterium that caused the infection from the list in Appendix 2 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the 'Gram-positive bacteria other spp', 'Gram-negative bacteria other spp' or 'Bacteria other' option and enter its name in a textbox. Always report the full name of the bacterium.

Please note that some bacteria appear several times but with the emphasis on their resistance pattern. If relevant susceptibility data is unavailable, 'Gram-positive bacteria other spp' or 'Gram-negative bacteria other spp' can be selected (e.g. in case of *Pseudomonas* without information on carbapenem susceptibility (meropenem, imipenem or doripenem) choose 'Gram-negative bacteria other spp'). For *Staphylococcus aureus*: if vancomycin susceptibility is unavailable, but it is methicillin-susceptible (can appear as "oxacillin"), it should be reported as '*Staphylococcus aureus* MSSA (methicillin-susceptible)'. For '*Staphylococcus aureus* MRSA (methicillin-resistant)', indicate whether the vancomycin susceptibility was not tested, or whether it was VISA (vancomycin-intermediate) or VRSA (vancomycin-resistant) based on the minimum inhibitory concentration (MIC) for vancomycin falling within the range noted in the Appendix.

Common commensals (most commonly coagulase-negative Staphylococci, *Micrococcus* spp., *Bacillus* spp., *Propionibacterium* spp.) should be reported only if there are at least two positive blood cultures.

Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark unknown if it is not possible to identify. Infection with clinical implications is at least one of the following: symptomatic infection in the relevant organ/system, or infection that requires pathogen-directed therapy.

Infection with clinical implications: Yes

Select all clinical implications of the infection during this follow-up period that apply from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;

Localisation (adapted from CTCAE terms)

Select the localisation for the infection from the list in Appendix 3 of the form or available in the database.

In the appendix, we include both **general localisation** as part of the core dataset and **detailed localisation** as part of the extended dataset. If the more specific localisation is known, please report the **general localisation** and, if requested in the extended dataset, further specify by providing the **detailed localisation**. If only the higher-level localisation is known, report only the core dataset general localisation.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and at least 1 location involved during this follow-up period must be reported.

The localisations used in the current form are adapted from CTCAE version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

If the clinical information available does not specify the localisation of the infection, probably the infection was asymptomatic and will not have to be reported. Otherwise, the symptoms should guide the choice.

Intravascular catheter-related infection

Indicate if the infection was related to a central venous catheter (CVC). Please note that bacteraemia can be CVC-related or not CVC-related. The definition for the CVC-related bacteremia requires one of the following:

- The same organism (genus, species, and susceptibility pattern) growing from at least 1 percutaneous blood sample culture and from the catheter tip (e.g. two coagulase- negative Staphylococci, but different species, such as *Staphylococcus capitis* and *Staphylococcus epidermidis*, or two *Staphylococcus epidermidis* with completely different susceptibilities are not the same).
- 2 blood samples for culture are obtained (1 from a catheter hub and 1 from a peripheral vein) that meet CVC-related bacteraemia criteria for differential time to positivity (DTP): growth of microbes from blood obtained through the catheter hub being detected at least 2 hours before microbial growth is detected in blood samples obtained from a peripheral vein (7).

If the infection was related to an intravascular catheter (answered **Yes**), **specify** the details by selecting the type of CVC infection from the list in Appendix 3 or available in the database.

Resolved

Indicate if the infection was resolved during the follow-up period (answer **Yes**) or not (answer **No**). By resolved it is understood that the patient is free of symptoms/signs of this infection or symptoms/signs of this infection are under control, and negative diagnostic tests were obtained in case the investigation was repeated, and the relevant imaging is compatible with expected improvement.

Mark the field as **Unknown** if there is not information on whether the infection was resolved or not.

Contributory cause of death

In case the patient is deceased, indicate if the infection contributed to death.

If there was more than one bacterial infectious complication during the follow-up period, repeat these questions for the subsequent infection. Copy and fill-in the table as many times as possible.

Viral infection

Indicate if the patient had a viral infection in the follow-up period after the treatment (after lymphodepleting/conditioning regimen) took place. Report here only infections with microbiological documentation, otherwise they shall be reported as infection with unknown pathogen.

New or ongoing

Indicate if the patient had a **Newly developed** viral infection or if it was **Ongoing since previous assessment**.

Start date

Only if newly developed infection, report the date a first positive viral test (usually PCR or antigen) was obtained. In case a diagnostic sample was obtained with a delay since the symptoms of infection started – report here the date when symptoms attributable to this infection started (e.g. patient with encephalitis, with a positive PCR in cerebrospinal fluid done 10 days after symptoms started).

In case an infection was found for the first time at autopsy, use the date of death, unless you can identify the date when the symptoms attributable to this infection were reported for the first time.

In case the start date was already reported on the previous follow-up form (with the **Ongoing since previous assessment** option selected), the start date does not need to be reported again and this field should be left blank.

Pathogen

Select the virus that caused the infection from the list in Appendix 2 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the 'Viruses other' option and enter its name in a textbox. Always report the full name of the virus.

If the pathogen was CMV/EBV: was this infection a reactivation?

Answer **Yes**, if the patient's serology tests (CMV IgG, EBNA, EBV IgG) were positive before the treatment (start of lymphodepleting/conditioning regimen) took place or if the patient has been reported to have previously had an active CMV/EBV infection.

Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark unknown if it is not possible to identify. Infection with clinical implications is at least one of the following: symptomatic infection in the relevant organ/system, or infection that requires pathogen-directed therapy.

Infection with clinical implications: Yes

Select all clinical implications of the infection during this follow-up period that apply from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;

Localisation (adapted from CTCAE terms)

Select the localisation for the infection from the list in Appendix 3 of the form or available in the database.

In the appendix, we include both **general localisation** as part of the core dataset and **detailed localisation** as part of the extended dataset. If the more specific localisation is known, please report the **general localisation** and, if requested in the extended dataset, further specify by providing the **detailed localisation**. If only the higher-level localisation is known, report only the core dataset general localisation.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and at least 1 location involved during this follow-up period must be reported.

When EBV DNA is detected in the blood—which constitutes the vast majority of EBV detections—you can report the localization as viremia/DNAemia by selecting from the blood infections group.

The localisations used in the current form are adapted from CTCAE version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

If the clinical information available does not specify the localisation of the infection, probably the infection was asymptomatic and will not have to be reported. Otherwise, the symptoms should guide the choice.

Resolved

Indicate if the infection was resolved during the follow-up period. By resolved it is understood that the patient is free of symptoms/signs of this infection or symptoms/signs of this infection are under control, and negative diagnostic tests were obtained in case the investigation was repeated, and the relevant imaging is compatible with expected improvement.

Contributory cause of death

In case the patient is deceased, indicate if the infection contributed to death.

If there was more than one viral infectious complication during the follow-up period, repeat these questions for the subsequent infection. Copy and fill-in this table as many times as necessary.

Fungal infection

Indicate if the patient had a fungal infection in the follow-up period after the treatment (after lymphodepleting/conditioning regimen) took place. Report here only infections with microbiological documentation, otherwise they shall be reported as infection with unknown pathogen.

New or ongoing

Indicate if the patient had a **Newly developed** bacterial infection or if it was **Ongoing since previous assessment.**

Start date

Only if newly developed infection, report the date a first positive culture, PCR test or galactomannan test was obtained, or the pathogen was first identified by its typical appearance in the tissue/specimen material. In case a diagnostic sample was obtained with a delay since the symptoms of infection started – report here the date when symptoms attributable to this infection started, or when this is not known, the date of the first imaging (e.g. CNS, lungs, or liver/spleen imaging for instance in hepatosplenic candidiasis in a patient with persistent fever and negative blood cultures).

In case an infection was found for the first time at autopsy, use the date of death, unless you can identify the date when the symptoms attributable to this infection were reported for the first time.

In case the start date was already reported on the previous follow-up form (with the **Ongoing since previous assessment** option selected), the start date does not need to be reported again and this field should be left blank.

Type of fungi

Select the type of fungal infection by marking if it is 'Yeasts' or 'Moulds'.

Pathogen

Select the fungus that caused the infection from the list in Appendix 2 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the 'Yeasts other' or 'Moulds other' option and enter its name in a textbox. Always report the full name of the fungus. Please note that there is an option for mould infection diagnosed based on positive galactomannan only without additional microbiological confirmation.

Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark unknown if it is not possible to identify. Infection with clinical implications is at least one of the following: symptomatic infection in the relevant organ/system, or infection that requires pathogen-directed therapy.

Infection with clinical implications: Yes

Select all clinical implications of the infection during this follow-up period that apply from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;

Localisation (adapted from CTCAE terms)

Select the localisation for the infection from the list in Appendix 3 of the form or available in the database.

In the appendix, we include both **general localisation** as part of the core dataset and **detailed localisation** as part of the extended dataset. If the more specific localisation is known, please report the **general localisation** and, if requested in the extended dataset, further specify by providing the **detailed localisation**. If only the higher-level localisation is known, report only the core dataset general localisation.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and at least 1 location involved during this follow-up period must be reported.

The localisations used in the current form are adapted from CTCAE version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

If the clinical information available does not specify the localisation of the infection, probably the infection was asymptomatic and will not have to be reported. Otherwise, the symptoms should guide the choice.

Intravascular catheter-related infection

Indicate if the infection was related to a central venous catheter (CVC). Please note that fungemia can be CVC-related or not CVC-related. The definition for the CVC-related fungemia requires one of the following:

- The same organism (genus, species and susceptibility pattern) growing from at least 1 percutaneous blood sample culture and from the catheter tip
- 2 blood samples for culture are obtained (1 from a catheter hub and 1 from a peripheral vein) that meet CVC-related fungemia criteria for differential time to positivity (DTP): growth of fungi from blood obtained through the catheter hub being detected at least 2 hours before fungal growth is detected in blood samples obtained from a peripheral vein (7).

If the infection was related to an intravascular catheter, **specify** details by selecting the type of CVC infection from the list in Appendix 4 or available in the database.

Resolved

Indicate if the infection was resolved during the follow-up period. By resolved it is understood that the patient is free of symptoms/signs of this infection or symptoms/signs of this infection are under control,

and negative diagnostic tests were obtained in case the investigation was repeated, and the relevant imaging is compatible with expected improvement.

Contributory cause of death

In case the patient is deceased, indicate if the infection contributed to death.

If there was more than one fungal infectious complication during the follow-up period, repeat these questions for the subsequent infection. Copy and fill-in this table as many times as necessary.

Parasitic infection

Indicate if the patient had a parasitic infection in the follow-up period after the treatment (after lymphodepleting/conditioning regimen) took place. Report here only infections with microbiological documentation, otherwise they shall be reported as infection with unknown pathogen.

New or ongoing

Indicate if the patient had a **Newly developed** parasitic infection or if it was **Ongoing since previous assessment**.

Start date

Only if newly developed infection, report the date a first positive antigen or DNA test was obtained or the first positive microscopic examination was performed. In case a diagnostic sample was obtained with a delay since the symptoms of infection started – report here the date when symptoms attributable to this infection started, or when this is not known, the date of the first imaging (e.g. CNS imaging for instance in Toxoplasmosis).

In case an infection was found for the first time at autopsy, use the date of death, unless you can identify the date when the symptoms attributable to this infection were reported for the first time.

In case the start date was already reported on the previous follow-up form (with the **Ongoing since previous assessment** option selected), the start date does not need to be reported again and this field should be left blank.

Type of parasite

Select the type of parasitic infection by marking if it is ‘Protozoa’ or ‘Helminths’.

Pathogen

Select the parasite that caused the infection from the list in Appendix 2 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the ‘Protozoa other

spp' or 'Other helminths' option and enter its name in a textbox. Always report the full name of the parasite.

Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark unknown if it is not possible to identify. Infection with clinical implications is at least one of the following: symptomatic infection in the relevant organ/system, or infection that requires pathogen-directed therapy.

Infection with clinical implications: Yes

Select all clinical implications of the infection during this follow-up period that apply from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;

Localisation (adapted from CTCAE terms)

Select the localisation for the infection from the list in Appendix 3 of the form or available in the database.

In the appendix, we include both **general localisation** as part of the core dataset and **detailed localisation** as part of the extended dataset. If the more specific localisation is known, please report the **general localisation** and, if requested in the extended dataset, further specify by providing the **detailed localisation**. If only the higher-level localisation is known, report only the core dataset general localisation.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and at least 1 location involved during this follow-up period must be reported.

The localisations used in the current form are adapted from CTCAE version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

If the clinical information available does not specify the localisation of the infection, probably the infection was asymptomatic and will not have to be reported. Otherwise, the symptoms should guide the choice.

Resolved

Indicate if the infection was resolved during the follow-up period. By resolved it is understood that the patient is free of symptoms/signs of this infection or symptoms/signs of this infection are under control,

and negative diagnostic tests were obtained in case the investigation was repeated, and the relevant imaging is compatible with expected improvement.

Contributory cause of death

In case the patient is deceased, indicate if the infection contributed to death.

If there was more than one parasitic infectious complication during the follow-up period, repeat these questions for the subsequent infection. Copy and fill-in this table as many times as necessary.

Infection with unknown pathogen

Indicate if the patient had an infection with unknown pathogen in the follow-up period after the treatment (after lymphodepleting/conditioning regimen) took place.

Use this section to report clinical infections without microbiological documentation, like pneumonia, cellulitis, typhlitis, etc.

New or ongoing

Indicate if the patient had a **Newly developed** infection with unknown pathogen or if it was **Ongoing since previous assessment**.

Start date

Only if newly developed infection, report the date the first signs or complaints were recorded or the first positive radiology was obtained. In case an infection was found for the first time at autopsy, use the date of death, unless you can identify the date when the symptoms attributable to this infection were reported for the first time.

In case the start date was already reported on the previous follow-up form (with the **Ongoing since previous assessment** option selected), the start date does not need to be reported again and this field should be left blank.

Infection with clinical implications

Infection with clinical implications is at least one of the following: symptomatic infection in the relevant organ/system, or infection that requires pathogen-directed therapy. Since an infection with an unknown pathogen always has clinical implications to be reported, the 'Infection with clinical implications, yes' field always has to be filled in.

Infection with clinical implications: Yes

Select all clinical implications of the infection that apply from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;

Localisation (adapted from CTCAE terms)

Select the localisation for the infection from the list in Appendix 3 of the form or available in the database.

In the appendix, we include both **general localisation** as part of the core dataset and **detailed localisation** as part of the extended dataset. If the more specific localisation is known, please report the **general localisation** and, if requested in the extended dataset, further specify by providing the **detailed localisation**. If only the higher-level localisation is known, report only the core dataset general localisation.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and at least 1 location involved during this follow-up period must be reported.

The localisations used in the current form are adapted from CTCAE version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

If the clinical information available doesn't specify the localisation of the infection, probably the infection was asymptomatic and will not have to be reported. Otherwise, the symptoms should guide the choice.

Intravascular catheter-related infection

Indicate if the infection was related to a central venous catheter (CVC). For example, a purulent infection of the exit site or tunnel, without isolation of pathogen.

If the infection was related to an intravascular catheter, **specify** details by selecting the type of CVC infection from the list in Appendix 4 or available in the database.

Infection resolved

Indicate if the infection was resolved during the follow-up period. By resolved it is understood that the patient is free of symptoms/signs of this infection or symptoms/signs of this infection are under control, and the relevant imaging is compatible with expected improvement.

Contributory cause of death

In case the patient is deceased, indicate if the infection contributed to death.

If there was more than one infectious complication with an unknown pathogen during the follow-up period, repeat these questions for the subsequent infection. Copy and fill-in this table as many times as necessary.

Extended dataset

SARS-CoV-2 related question

Did the patient receive a vaccination against SARS-CoV-2 during this follow-up period?

Indicate if the patient received a vaccination against SARS-CoV-2 in the follow-up period after the CT treatment took place.

Number of doses

Report how many doses of the SARS-CoV-2 vaccine the patient has received.

Date of last dose

Report the date the patient received their last dose of the SARS-CoV-2 vaccine.

Secondary Malignancies and Autoimmune Disorders

Did a secondary malignancy or autoimmune disorder occur?

Answer **No** if no secondary malignancy or autoimmune disorder occurred or if the secondary malignancy or autoimmune disorder was already reported in the previous CT follow-up form.

Answer **Yes** if secondary malignancy or autoimmune disorder occurred and it has not been reported with a CT follow-up form yet. The secondary malignancy can be any disease for which the patient had not been diagnosed before the CT. Do not include relapse, progression or transformation of the same disease subtype.

Answer **Unknown** if there is no information on whether secondary malignancy or autoimmune disorder occurred or not.

If Yes is selected, select what type of secondary malignancy occurred in the checkbox

- Iatrogenic disease in relation with treatments administered prior to cellular therapy cells indication and administration (i.e. cytotoxic agents, targeted therapies, immunotherapies, radiation therapy, etc.);
- Transformation of engineered immune effector cells through insertional mutagenesis or other mechanisms.

Further details on secondary malignancy or autoimmune disorder

Report, if applicable, the further details on secondary malignancy or autoimmune disorder.

Date of diagnosis

Report the date of diagnosis of secondary malignancy/autoimmune disorder.

Histologic type

If applicable, report the histologic type.

Location

If applicable, report where the secondary malignancy or autoimmune disorder occurred.

Secondary malignancy material preserved

Answer **Yes** if secondary malignancy material was preserved. Answer **No** if secondary malignancy material was not preserved. If it is not known if secondary malignancy material was preserved or not, select **Unknown**.

Concomitant PBMCs preserved

Answer **Yes** if concomitant peripheral blood mononuclear cells (PBMCs) were preserved. Answer **No** if concomitant PBMCs were not preserved. If it is not known if concomitant PBMCs were preserved or not, select **Unknown**.

Was this disease an indication for a subsequent HCT/CT/IST?

If the answer is **No**, complete the respective non-indication diagnosis form.

If the answer is **Yes**, complete the relevant indication diagnosis form.

Persistence of the infused cells

Was persistence of the infused cellular products assessed since the last follow-up?

Answer **No** if persistence of the infused cellular products has not been assessed since the last reported follow-up and proceed with the next section. Answer **Yes** if tests to detect the persistence of the infused cells have been performed since the last reported follow-up and provide details in subsequent questions. If it is not known, select **Unknown**.

Date of the last assessment

If a test was performed, indicate the date of the last test before the follow-up assessment that is being reported. If it is not known, select **Unknown**.

Source of cells used for testing

Report the source of cells that was used to assess the persistence of the infused cellular product:

- **Bone marrow,**
- **Peripheral blood,**
- **Tumour**.

If another source of cells was used for testing, select **Other** and specify the source of cells in the text field.

Technique used for testing

Indicate the technique that was used to assess the persistence of the infused cellular product:

- **Molecular (PCR),**
- **Flow Cytometry,**
- **Chimerism,**
- **Imaging,**
- **Immunohistochemistry**.

If another technique was used for testing, select **Other** and specify technique used in the text field.

Were immune effector cells (IEC) detected

Select **Yes** if immune effector cells (IEC) were detected. Select **No** if immune effector cells were not detected.

Last Disease Status – Additional Assessments

Disease burden

LDH level

Indicate if the LDH level was **Normal, Elevated**, or if it was **Not evaluated**. If the LDH was assessed multiple times in the current reporting period, report the most recent value. If the LDH level is not known, select **Unknown**.

Inflammatory state (C-reactive protein [CRP] concentration)

Indicate if the C-reactive protein [CRP] concentration was **Normal, Elevated**, or if it was **Not evaluated**. If the CRP was assessed multiple times in the current reporting period, report the most recent value. If the CRP level is not known, select **Unknown**.

Maximum CRP concentration:

If C-reactive protein [CRP] concentration was Elevated, report the **maximum CRP concentration** and specify the units used: if it is **mg/dL** or **mg/L**.

Date of C-reactive protein level assessment

Report the date of C-reactive protein level assessment.

Additional treatments

Include only systemic treatments designed to consolidate the anti-tumour activity of CT cells, prevent relapse (i.e. administration of immune checkpoint inhibitors) or treat complications. Do not include supportive care, including anti-infectious agents.

Indicate only treatments that have not been reported at previous CT follow-up(s).

Did the patient undergo additional treatment during or immediately after this cellular therapy or since the last follow-up?

Select **No** if the patient did not undergo additional treatment during or after this cellular therapy since the last follow-up.

Select **Yes** if the patient did undergo additional treatment and newly started in this follow-up period complete the **"Treatment non-HCT/CT/GT/IST"** form.

Select **Unknown** if it is unknown if the patient underwent additional treatment.

Additional cell infusions

Did the patient receive additional cell infusions?

If the patient received additional cell infusions, excluding a new HCT and/or CT treatment, select **Yes** and proceed to the next question. If the patient did not receive additional cell infusions, select **No**.

For this question, it does not matter if it was a boost or DLI. This can be clarified in the next questions.

If answered Yes, the following should be taken into account:

If the cells were infused with the aim of improving chimaerism, or preventing or treating relapses, it most likely was a DLI. The treating physician knows the aim of the infusion. In rare cases, the aim can be as for a boost and a DLI. In this case boost should be selected and the cell infusion sheet for DLI should be completed.

Is this cell infusion an allogeneic boost?

If the cell infusion was an allogeneic boost, select **Yes**. Otherwise select **No**.

An allogeneic boost is an infusion of cells from the same donor without conditioning, with no evidence of graft rejection. A boost is infused with the aim of providing enough hematopoietic cells to have an effect on engraftment.

If cells are not from the same donor (in the case of inborn errors) OR there is conditioning (chemo and/or TBI), then it is considered to be a genuine transplant.

Date of the allogeneic boost

If applicable, report here the date the allogeneic boost took place.

Is this cell infusion an autologous boost?

If the cell infusion was an autologous boost answer **Yes** and proceed to the question below. If it was not an autologous boost, select **No**.

Autologous boost is infusion of pre-collected and stored autologous stem cells without conditioning.

Date of the autologous boost

If applicable, report here the date the autologous boost took place.

Note: If this cell infusion is not a boost, attach the Cell Infusion (CI) sheet available in Appendix 4, completing as many sheets as episodes of cell infusion that took place during this follow-up period; then continue with questions below.

Did the patient receive subsequent HCT (either at your or another centre)?

If the patient received subsequent HCT, either at your or another centre, select **Yes** and make sure that this subsequent treatment is registered using the appropriate HCT form before proceeding.

If the patient did not receive subsequent HCT, select **No**.

Did the patient receive subsequent CT (either at your or another centre)?

If the patient received subsequent CT, either at your or another centre, select **Yes** and make sure that this subsequent treatment is registered using the appropriate CT form before proceeding.

If the patient did not receive subsequent CT, select **No**.

Reason for subsequent CT

If the patient received subsequent CT, select the reason a subsequent CT was required by choosing among the following answer options:

- Primary failure;
- Consolidation;

- Mitigation of side effects.

Hospital Admission

This section should be submitted only for the Day 100 and 6 Months follow-ups.

Was inpatient admission and care needed since the last follow-up?

If the patient did not require inpatient admission or care since the last follow-up, select No and proceed to the next question.

If inpatient admission and care was needed since the last follow-up, select **Yes** and report the **number of days** the patient was admitted in the hospital. This question concerns readmission after the patient was already discharged from hospital after conditioning therapy and cell infusion. If it is a planned admission for the procedure itself, it shall not be reported.

If it is unknown if inpatient admission and care was needed since the last follow up, select Unknown.

Was the patient transferred to the intensive care unit (ICU) since the last follow-up?

If the patient was not transferred to the ICU since the last follow-up, select **No**. If the patient was transferred to the ICU after the last follow-up, select **Yes** and report the **number of days the patient spent in the ICU.** If the patient was transferred to the ICU within the admission of conditioning and cell infusion, the answer should be **Yes**.

If it is not known whether the patient was transferred to ICU or not since the last follow-up, select **Unknown**.

Relapse, Progression, Recurrence of disease or Significant Worsening

This section is not relevant if CT was for Inborn Errors indication diagnosis.

Was there a relapse, progression, recurrence of disease or significant worsening of organ function related to the primary disease after HCT?

Indicate if there was a relapse,progression, recurrence or significant worsening of organ function related to the primary disease after CT detected by any method. If multiple instances of relapse, progression, recurrence of disease or significant worsening took place in this follow-up period, report all instances. When filling this question in the EBMT registry, click the **add** button as many times as necessary for reporting all instances. ('+ Add' on the EBMT Registry.) If the answer is **No,** proceed to the next section.

Type

Report if a **relapse or recurrence of disease** is reported, or a **(continuous) progression or significant worsening**.

Date of relapse/progression/recurrence/worsening

Report the date of the relapse/progression/recurrence/significant worsening since CT. If the date is not known, select **unknown**.

Malignant disorders only

Type of relapse/progression

For Malignant disorders only report the type of relapse/progression: answer **Yes** next to Medullary and/or Extramedullary to report that there was this type of relapse/progression observed; answer **No** next to indicated involvement types to mark that it was not observed. Use **Unknown** answer option to indicate that there is no information for this involvement type.

Medullary involvement. Indicate if the marrow or blood were affected by the disease. Please be aware that although the vast majority of acute leukaemias involve the invasion of the bone marrow by blasts, there are cases where blast invasion is only found in organs other than the bone marrow (e.g. choromas).

Medullary relapse is when malignant cells are only found in the bone marrow. In case of extramedullary relapse, malignant cells are found in sites other than the bone marrow, such as soft tissues or organs.

Extramedullary involvement. Extramedullary involvement (EMI) refers to disease cells found in organs or tissue outside the blood or bone marrow. The most common sites of extramedullary disease are the central nervous system (CNS), skin and ovaries/testes.

Involvement at time of relapse (If the relapse was extramedullary or both medullary and extramedullary)

If the relapse/progression was extramedullary or both medullary and extramedullary, report per each of the site listed, if **Skin**, **CNS** (central nervous system) or **Testes/Ovaries** were involved at time of relapse. Also indicate if any **Other** site was involved. If yes, specify this in the textfield in English.

CD19 expression at relapse after CT

For Precursor lymphoid neoplasms only, indicate if CD19 expression at relapse after CT was **Absent**, **Present** or if it is **Unknown**.

Patient status

Performance status at the last assessment (check only one)

Select one answer to indicate the performance score system used to calculate the performance status at cellular therapy follow-up:

- Karnofsky;
- Lansky;
- ECOG.

Report the score that reflects the performance status at the current follow-up. It is not necessary to fill in both the Karnofsky/Lansky and ECOG score, one is sufficient. Descriptions of the Karnofsky score system can be found in table 8, Lansky in table 9 and the ECOG score system can be found in table 10.

Karnofsky scale

Score	Performance Status
100	Normal, no complaints or evidence of disease
90	Able to perform normal activity; minor signs and symptoms of disease
80	Able to perform normal activity with effort; some signs and symptoms of disease
70	Cares for self, unable to perform normal activity or to do active work
60	Requires occasional assistance but is able to care for most of own needs
50	Requires considerable assistance and frequent medical care
40	Requires special care and assistance; disabled
30	Hospitalisation indicated, although death not imminent; severely disabled
20	Hospitalisation necessary; active supportive treatment required, very sick
10	Fatal processes progressing rapidly; moribund
0	Dead

Table 8. Karnofsky scoring system for adult patients.

Lansky scale

Score	Performance Status
100	Fully active, normal

Score	Performance Status
90	Minor restrictions in physically strenuous activity
80	Active, but tires more quickly
70	Both greater restriction of and less time spent in play activity
60	Up and around, but minimal active play; keeps busy with quieter activities
50	Gets dressed but lies around much of the day, no active play but able to participate in all quiet play and activities
40	Mostly in bed; participates in quiet activities
30	In bed; needs assistance even for quiet play
20	Often sleeping; play entirely limited to very passive activities
10	No play; does not get out of bed
0	Unresponsive

Table 9. Lansky scoring system for paediatric patients.

ECOG scale

Grade	Performance Status
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

Table 10. ECOG scoring system.

Pregnancy after cellular therapy

Complete only for 6 Months and Annual/Unscheduled Follow-Up.

Has a patient become pregnant or impregnated another person since the last follow-up?

If the patient has not become pregnant or has not impregnated another person 6 months post CT or since the last follow-up, select **No** and proceed to the next section.

Extended dataset
Was there an attempted pregnancy since the last follow-up?
Indicate if there was an attempted pregnancy since the last follow-up select **Yes, No or Unknown.**

If the patient has become pregnant or has impregnated another person 6 months post CT or since the last follow-up select **Yes** and provide details in the question below. Select Unknown if it is not known.

Did the pregnancy result in a live birth?

If the patient has become pregnant or has impregnated another person since the last follow-up, answer **Yes**. If the pregnancy resulted in a live birth, indicate the **Year of birth** and **Month of birth** of the child, or mark the date **Unknown** if the date is not available.

Answer **No** if pregnancy did not result in a live birth and indicate the **Date of spontaneous or induced termination** (YYYY/MM/DD) or mark the date as **Unknown**. In case of multiple spontaneous or induced terminations, report the date of the first such event.

Select **Still pregnant at time of follow-up** if the patient/the person they impregnated was still pregnant at the time of the follow-up.

If there is no detailed information about the pregnancy and whether or not it resulted in a live birth, select **Unknown**.

If multiple pregnancies occurred in the follow-up period, the live birth should be prioritised in reporting, in the absence of the live birth, ongoing pregnancy should be prioritised: if one pregnancy resulted in live birth and another not, report the live birth only; if there occurred any terminated pregnancy and the other pregnancy is ongoing as of this follow-up date, select *Still pregnant at time of follow-up* answer option.

Extended dataset
Conception method
Indicate which conception method was used for the pregnancy that resulted in live birth. Select **Natural, Assisted** or **Unknown**

Disease Status (Disease specific)

This section is not applicable for patients with Inborn Errors indication diagnosis.

Disease status at his follow-up or at time of death

Indicate the disease status at this follow-up or at time of death corresponding to indication diagnosis by selecting from the list provided in Appendix 1.

The disease status is split into disease specific sections:

- Acute Leukaemias
- Chronic Leukaemias
- Plasma Cell Neoplasms (Pcn)
- Mpn, Mds, Mds / Mpn Overlap Syndromes
- Lymphomas
- Solid Tumours
- Bone Marrow Failure Syndromes (Bmf) Including Aplastic Anaemia (Aa)
- Autoimmune Disorders
- Haemoglobinopathies
- Other Diagnosis.

The instructions for completing appendix 1 can be found in appendix 1 of this document.

Appendix 1 - Disease specific best response and disease status

The disease status and best response are split into disease specific sections which can be found in appendix 1 of the follow-up form. This section is separated into disease status for:

- Acute leukaemias;
- Chronic leukemias;
- Plasma cell neoplasms;
- MPN, MDS, MDS/MPN overlap syndromes;
- Lymphomas;
- Solid tumours;
- Bone marrow failure syndromes (BMF) including aplastic anaemia (AA);
- Autoimmune disorders;
- Haemoglobinopathies;
- Other diagnoses.

Acute leukaemias

This section is applicable to acute myeloid leukaemias (AML), precursor lymphoid neoplasms (PLN) and other acute leukaemias.

Acute leukaemias disease status or best response

Select the disease status or best response from the following list, consult with criteria described in the table 5:

- Complete remission (CR);
- Not in complete remission.

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively. If reporting the disease status, also indicate the minimal residual disease (MRD) status.

Disease status or best response	
Complete remission (CR) is defined as meeting all of the following response criteria for at least four weeks: ● <5% leukemic blasts in the bone marrow ● No blasts with Auer rods (applies to AML only) ● No extramedullary disease (e.g., CNS, soft tissue disease)	**Not in complete remission:** In accordance with the defined criteria for complete remission (CR), a patient would not attain complete remission if they do not fulfil at least one of the complete remission criteria.

Table 11. Acute leukaemias disease status or best response.

Minimal residual disease (MRD)

Only for the disease status section, report the MRD status of acute leukaemia according to the guidelines provided below.

Chronic leukaemias

The chronic leukaemias section is split into chronic myeloid leukaemia (CML) and chronic lymphocytic leukaemia (CLL), prolymphocytic leukaemia (PLL) and other chronic leukaemias.

Chronic myeloid leukaemia disease status or best response

Select the disease status or best response from the list:

- Chronic phase (CP) and type of remission (haematological, cytogenetic, molecular)
- Accelerated phase
- Blast crisis

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Disease status or best response		
Chronic phase (CP)	**Accelerated phase (AP)**	**Blast crisis (BC)**
• None of the features of accelerated phase or blast crisis	• Bone marrow or peripheral blood blasts 10%-19% • Peripheral blood basophils ≥ 20% • Presence of additional clonal cytogenetic abnormality in Ph+ cells (ACA)[a]	• Bone marrow or peripheral blood blasts ≥ 20% • Extramedullary blast proliferation (myeloid sarcoma) • Presence of morphologically apparent lymphoblasts (>5%) warrants consideration of lymphoblastic crisis

Table 12. International Consensus Classification (ICC) criteria for Chronic Myeloid Leukaemias.

[a]Second Ph, trisomy 8, isochromosome 17q, trisomy 19, complex karyotype, or abnormalities of 3q26.2.

Number

If the disease status or best response was chronic phase (CP), accelerated phase or blast crisis, select the number of this status.

If the disease status or best response was chronic phase (CP) also indicate Haematological remission, Cytogenetic remission, Molecular remission below

Haematological remission

If the patient was in Chronic phase (CP), report if haematological remission was achieved (answer Yes), or not achieved (answer No) according to the criteria provided in table 13. Answer Not evaluated if it was not evaluated or Unknown if it cannot be verified if it was evaluated or not.

Cytogenetic remission

If the patient was in Chronic phase (CP), report if cytogenetic remission was achieved (answer Yes), or not achieved (answer No) according to the criteria provided in table 13. Answer Not evaluated if it was not evaluated or Unknown if it cannot be verified if it was evaluated or not.

Note: A patient in cytogenetic remission must be in haematological remission but could still present a molecular relapse. This is because the cytogenetic technique has a higher resolution than haematological measurements but lower resolution than molecular methods.

Molecular remission

If the patient was in Chronic phase (CP), report if molecular remission was achieved (answer Yes), or not achieved (answer No) according to the criteria provided in table 13. Answer Not evaluated if it was not evaluated or Unknown if it cannot be verified if it was evaluated or not.

Note: A patient in molecular remission must also be in cytogenetic and haematological remission. This is because molecular techniques have a higher resolution than both haematological and cytogenetic measurements.

Disease status or best response (only CP)		
Haematological remission	**Cytogenetic remission**	**Molecular remission**
Haematological remission is defined by a patient meeting all of the following: ● WBC < 10 x 10^9 /L ● Haemoglobin > 11.0 g/dL ● Platelet Count < 450 x 10^9 /L ● Normal Differential (<1% precursor cells) ● No palpable splenomegaly ● No extramedullary disease	Cytogenetic remission is defined by: ● 0% t(9;22) positive metaphases together with haematological remission ● A minimum of 20 analysable metaphases must be assessed for appropriate evaluation of a cytogenetic remission. Remission should be confirmed with repeated cytogenetic analysis within 4 to 12 weeks	Molecular remission is defined by: ● Cells with the BCR::ABL1 fusion protein are not detectable, in the peripheral blood and /or the bone marrow, by an assay with a sensitivity to allow detection of one t(9;22) positive cell in 10^5 to 10^6 RT-PCR cells. The result should be confirmed by two consecutive tests done at least 4 weeks apart.

Table 13. Definitions of haematological, cytogenetic and molecular remission for patients in chronic phase.

Minimal residual disease (MRD)

Only for disease status section report the MRD status of chronic myeloid leukaemia according to the guidelines provided below.

Chronic lymphocytic leukaemia (CLL), prolymphocytic leukaemia (PLL) and other chronic leukaemias disease status or best response

Select the disease status or best response from the list according to the criteria provided in tables 14-17:

- Complete Remission (CR)
- Partial Remission (PR)
- Progression
- Stable Disease (SD)

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Group	Parameter	Complete Remission (CR)	Partial Remission (PR)	Stable Disease (SD)	Progressive Disease (PD)
A	Lymph nodes	None ≥1.5 cm	Decrease ≥50% (from baseline)*	Change of −49% to +49%	Increase ≥50% from baseline or from response
	Liver and/or spleen size†	Spleen size <13 cm; liver size normal	Decrease ≥50% (from baseline)	Change of −49% to +49%	Increase ≥50% from baseline or from response
	Constitutional symptoms	None	Any	Any	Any
	Circulating lymphocyte count	Normal	Decrease ≥50% from baseline	Change of −49% to +49%	Increase ≥50% over baseline
B	Platelet count	≥100 × 10^9/L	≥100 × 10^9/L or increase ≥50% over baseline	Change of −49 to +49%	Decrease of ≥50% from baseline secondary to CLL
	Haemoglobin	≥11.0 g/dL (untransfused and without erythropoietin)	≥11 g/dL or increase ≥50% over baseline	Increase <11.0 g/dL or <50% over baseline, or decrease <2 g/dL	Decrease of ≥2 g/dL from baseline secondary to CLL
	Marrow	Normocellular, no CLL cells, no B-lymphoid nodules	Presence of CLL cells, or of B-lymphoid nodules, or not done	No change in marrow infiltrate	Increase of CLL cells by ≥50% on successive biopsies

Table 14. Response evaluation according to 2018 iwCLL criteria.

Disease status	
Complete Remission (CR)	See table 8 for detailed criteria. All of the criteria have to be met. But: ● If a patient has all CR criteria but has persistent cytopenia, the patient can be considered as a CR as an adaptation of these guidelines. ● If a patient has all criteria of a CR but bone marrow evaluation has not been performed (even with persistent cytopenia), the patient can be considered as a CR as an adaptation of these guidelines.
Partial Remission (PR)	See table 8 for detailed criteria. At least 2 of the parameters of group A and 1 parameter of group B need to improve if previously abnormal; if only 1 parameter of both groups A and B is abnormal before therapy, only 1 needs to improve. Clinical (palpation) evaluation only without CT-scan (or alternate imaging), according to routine practice, is accepted.
Stable Disease (no change, no response/loss of response)	See table 8 for detailed criteria. All of the criteria have to be met. Constitutional symptoms alone do not define PD.
Relapse (untreated)	Evidence of PD in a patient who has previously achieved the criteria of a CR or PR for 6 months or more after the last dose of CLL therapy.
Progressive disease (PD)	At least 1 of the criteria of group A or group B has to be met. Sequential imaging is not warranted in CLL outside clinical trials and is not required for the EBMT Registry.
Never treated	No treatment was given.

Table 15. Additional clarifications for Chronic lymphocytic leukaemias disease status classification.

*Sum of the products of 6 or fewer lymph nodes (as evaluated by CT scans and physical examination in clinical trials or by physical examination in general practice).

†Spleen size is considered normal if <13 cm. There is not a firmly established international consensus of the size of a normal liver; therefore, liver size should be evaluated by imaging and manual palpation. For the EBMT Registry, clinical (palpation) evaluation only without CT-scan (or alternate imaging), according to routine practice, is accepted.

Group	Parameter	CR (all met)	PR (≥2 in A and ≥1 in B)	SD (all met)	PD (≥1 in A or B met)
A	Lymph nodes	long-axis diameters to <1.0 cm	Decrease ≥30% in SLD	Change of − <30% to + ≤20%	Increase >20% in SLD
	Spleen†	Spleen size <13 cm	Decrease ≥50% in vertical length beyond normal from baseline	Change of −49% to +49% beyond normal from baseline	Increase ≥50% in vertical length beyond normal from baseline
	Constitutional symptoms	None	Any	Any	Any
	Circulating lymphocyte count	<4 × 10^9/L	≤30 × 10^9/L and decrease ≥50% from baseline	>30 × 10^9/L or change of −49% to +49%	Increase ≥50% from baseline
	Marrow	T-PLL cells <5% of mononuclear cells	Any	Any	Any
	Any other specific site involvement*	None	Any	Any	Any
B	Platelet count	≥100 × 10^9/L	≥100 × 10^9/L or increase ≥50% from baseline	Change of −49% to +49%	Decrease of ≥50% from baseline
	Haemoglobin	≥11.0 g/dL (untransfused)	≥11 g/dL or increase ≥50% from baseline	<11.0 g/dL or <50% from baseline, or change <2 g/dL	Decrease of ≥2 g/dL from baseline
	Neutrophils	≥1.5 × 10^9/L	≥1.5 × 10^9/L or increase ≥50% from baseline	Change of −49% to +49%	Decrease of ≥50% from baseline

Table 16. T-PLL response evaluation according to the T-PLL consensus criteria.

SLD: sum of long-axis diameters of up to 3 target lesions

*Pleural or peritoneal effusion, skin infiltration, central nervous system involvement.

† For the EBMT Registry, clinical (palpation) evaluation only without CT-scan or alternate imaging, according to routine practice, is accepted.

Disease status: additional clarifications	
Complete Remission (CR)	See table 10 for detailed criteria. All of the criteria have to be met, however a few exceptions are possible: ● If a patient has all CR criteria but has persistent cytopenia, the patient can be considered as being in CR as an adaptation of these guidelines. ● If a patient has all criteria of CR but bone marrow evaluation has not been performed (even with persistent cytopenia), the patient can be considered as being in CR as an adaptation of these guidelines.
Partial Remission (PR)	See table 10 for detailed criteria. At least 2 of the parameters of group A and 1 parameter of group B need to improve if previously abnormal; if only 1 parameter of both groups A and B is abnormal before therapy, only 1 needs to improve. Clinical (palpation) evaluation only without CT-scan (or alternate imaging), according to routine practice, is accepted.
Stable Disease (no change, no response/loss of response)	See table 10 for detailed criteria. All of the criteria have to be met.
Relapse (untreated)	Evidence of PD in a patient who has previously achieved the criteria of a CR or PR for 6 months or more after the last dose of CLL therapy.
Progressive Disease (PD)	At least 1 of the criteria of group A or group B has to be met. Sequential imaging is not warranted in CLL outside clinical trials and is not required for the EBMT Registry. Constitutional symptoms alone do not define PD.

Table 17. Additional clarifications for T-PLL disease status classification.

Progression sensitivity

If the disease status or best response was progression, indicate if the progression was **resistant** to the last chemotherapy regimen the patient received, or if it was **sensitive**. If this is not known, select **unknown**.

Minimal residual disease (MRD)

Only for disease status section report the MRD status of chronic lymphocytic leukaemia according to the guidelines provided below.

Plasma cell neoplasms

Disease status or best response

Select the disease status or best response from the list according to the criteria provided in table 18:

- Complete remission (CR)
- Stringent complete remission (sCR)
- Very good partial remission (VGPR)
- Partial remission (PR)
- Stable disease (no change, no response/loss of response)
- Progression
- Relapse

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Disease status	
Complete remission (CR)	Absence of detectable monoclonal immunoglobulin in serum and monoclonal light chains in the urine by immunofixation. The detection of monoclonal immunoglobulin, even at low levels which are too weak to quantitate, is not a CR. • <5% of plasma cells in bone marrow aspirate • Disappearance of any soft tissue plasmacytomas. • No increase in size or number of lytic lesions if assessed (radiographic studies are not mandatory) If any of the above investigations have not been done, even if the others are indicative of a CR, the status should be registered as VGPR. Where CR has already been attained (bone marrow evaluation included) it may not be necessary to do a bone marrow evaluation again to confirm that the patient is still in CR (all other criteria confirming CR). Therefore, the patient is still in CR.

Stringent complete remission (sCR)	All of the following: • CR as defined above • normal free light (FLC) chain ratio • Absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence
Very good partial remission (VGPR)	One or more of the following: • Serum and urine M-protein detectable by immunofixation but not on electrophoresis • >=90% reduction in serum M-protein plus urine M-protein level <0.1g/ per 24h In addition, there must be no increase in size or number of lytic lesions if assessed (radiographic studies are not mandatory) If any of the above investigations have not been done, even if the others are indicative of a VGPR, the status should be registered as PR.
Partial remission (PR)	All of the following: • >50% reduction in serum M-protein plus reduction in 24h urinary M-protein by >=90% or to <0.2g/ per 24h. • A reduction of more than 50% in the size of soft tissue plasmacytomas if present at pre-treatment • No increase in size or number of lytic lesions if assessed (radiographic studies are not mandatory) In the absence of measurable serum and urine M-protein, the following criteria applies: • A decrease in the difference between involved and uninvolved free light chain (FLC) of more than 50% If the FLC assay cannot be measured, the following criteria apply: • >=50% reduction in plasma cells provided baseline bone marrow plasma cell percentage was >=30% • A reduction of more than 50% in the size of soft tissue plasmacytomas if present at pre-treatment
Stable disease(no change, no response/loss of response)	Does not meet the criteria for CR, VGPR, PR or progressive disease (includes the old Minimal response (MR) criteria)

Progression	One or more of the following: • Increase of 25% or more in measurable monoclonal immunoglobulin in serum and urine (absolute increase must be >=0.5g/dL). This is not applicable to light chain myelomas • Increase of 25% or more in urinary light chains (absolute increase must be >=0.2g/ per 24h) • An increase of 25% or more in bone marrow plasma cells (absolute % must be >=10%) • Increase of old/appearance of new osteolytic bone lesions on x-ray • Appearance of soft tissue plasmacytoma • Development of hypercalcemia (corrected serum calcium >11.5 mg/dL or 2.65 mmol/L) that can be attributed solely to the plasma cell disorder In the absence of measurable serum and urine M-protein, the following criterium applies: • An increase of 25% or more in the difference between involved and uninvolved free light chain (absolute increase must be >0.01g/dL from nadir) .
Relapse	Clinical relapse requires one or more of the following criteria: • Direct indicators of increasing disease and/or end organ dysfunction (CRAB features) related to the underlying clonal plasma-cell proliferative disorder. • Development of new soft tissue plasmacytomas or bone lesions • Increase of 50% (and at least 1 cm) in the size of existing plasmacytomas or bone lesions. • Hypercalcemia (> 11.5 mg/dL) • Decrease in haemoglobin of > 2 g/dL • Rise in serum creatinine by 2 mg/dL or more

Table 18. Plasma cell neoplasms disease status or best response.

Number

For patients in Complete remission (CR), Stringent complete remission (sCR), Very good partial remission (VGPR), Partial remission (PR) or Relapse, select the number of the status or mark it as Unknown.

Was the patient on dialysis during this follow-up period?

for PCN Disease Status, report whether the patient was on dialysis during this follow-up period. Select **Unknown** if this information is unavailable. If the answer is Yes, provide details in sub-questions.

Started in this follow-up period

Select this option if dialysis started during this follow-up period. and specify the **Start date** of dialysis. If the start date is not known, select **Unknown.**

Ongoing since previous follow-up

Select this option if dialysis started during a previous follow-up period and was still ongoing during this follow-up.

Did dialysis stop?

Report whether dialysis was stopped during this follow-up. Select **Unknown** if this information is unavailable. If the answer is Yes, specify the **End date** of the dialysis. If the dialysis stopped but the end date is not known, select **Unknown**.

Minimal residual disease

Complete this section only if the patient disease status is reported for patients with an AL, CLL or a plasma cell neoplasm diagnosis.

If the patient is in haematologic CR, but has evidence of disease by more sensitive assessments including molecular, flow cytometry or cytogenetic methods, mark it as **Positive**. If the MRD assay cannot detect malignant cells mark it as **Negative**. Mark it as **Not evaluated** if MRD status evaluation was not carried out during the follow-up period.

Positive minimal residual disease

If there was positive minimal residual disease, indicate if this was **increasing**, **stable** or **decreasing**. If the level is not known, select **unknown**. A change in MRD should be confirmed within 4 weeks, in a second consecutive sample, preferably with a BM sample. The definitions are as follows:

- **Increasing** (>1 $\log_{10}$ increase between any 2 positive samples measured in the same tissue (PB or BM));
- **Stable** (<1$\log_{10}$ between any 2 positive samples measured in the same tissue (PB or BM));
- **Decreasing** (>1 $\log_{10}$ decrease between any 2 positive samples measured in the same tissue (PB or BM)).

Date MRD status evaluated

Report the date the MRD status was evaluated. If the date is not known, select **unknown**.

Sensitivity of MRD assay

Select the appropriate sensitivity of the MRD assay from the list.

Method used

Select the most sensitive method that was used to assess the MRD status.

Myeloproliferative neoplasms (MPN), Myelodysplastic neoplasms (MDS), MDS/MPN overlap syndromes

Disease status or best response

Select the disease status or best response from the list according to the criteria provided in the corresponding tables 19-21:

- Complete remission (CR).
- Improvement but no CR
- Primary refractory phase (no change)
- Relapse
- Progression/worsening

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

MPN Disease status or best response	
Complete remission (CR)	The 4 following criteria must be true: 1. Resolution of disease-related symptoms and signs including palpable hepatosplenomegaly 2. Haemoglobin (Hb) ≥ 10g/dL, platelet ≥ 100 ×10^9/L and neutrophils ≥ 1 × 10^9/L 3. <2% immature myeloid cells (<5% in splenectomized patients) 4. Normal bone marrow histology and fibrosis grade no higher than 1
Improvement but no CR	Requires one criterion in absence of progression: 1. Hb increase of 2g/dL or transfusion independence 2. Spleen reduction of 50% 3. 100% increase in platelet count and absolute platelet count of at least 50 × 10^9/L 4. 100% increase in absolute neutrophil count (ANC) and an ANC of at least 0.5 × 10^9/L
Primary refractory phase (no change)	Treatment with intent to achieve remission was given, but no remission was achieved.

Relapse	Loss of complete remission.
Progression/Worsening	Requires one of the following: 1. Progressive splenomegaly 2. Leukaemic transformation (increase of peripheral blood blast percentage of at least 20%)

Table 19. MPN disease status or best response.

MDS Disease status or best response	
Complete remission (CR)	For patients with MDS with increased blasts: Complete remission was achieved if marrow blast count was below 5% and normalisation of peripheral blood counts was observed for at least 4 weeks. For patients with other types of MDS: normalisation of PB counts.
Improvement but no CR	**1) Haematological response (in patients with cytopenia)** ● If haemoglobin < 11g/dl, erythroid response (>11 g/dl); ● If platelets <100g/l, platelet response (>100 g/l); ● If neutrophils < 1g/l, neutrophil response (>1g/l); ● If >0% peripheral blasts, response when 0% peripheral blood blasts; ● If transfusion dependant (red blood cells), independence of transfusion achieved (8 weeks without transfusions); ● If transfusion dependant (platelets), independence of transfusion achieved (8 weeks without transfusions) **2) Marrow blast response (in patients with increased marrow blasts):** A decrease of 50% in marrow blasts, but still >5% marrow blasts.
Primary refractory phase (no change)	Treatment with the intent to achieve remission was given, but no remission was achieved.
Relapse	Loss of complete remission.
Progression/ Worsening	More blasts in BM than before treatment.

Table 20. MDS disease status or best response.

MDS/MPN Disease status or best response	
Complete remission (CR)	Marrow blast count < 5% and a normalisation of peripheral blood counts was observed for at least 4 weeks.
Improvement but no CR	Bone marrow blasts decreased by ≥ 50% after pre-treatment but still > 5%. All CR criteria were abnormal before treatment.
Primary refractory phase (no change)	Treatment with intent to achieve remission was given, but no remission was achieved.
Relapse	Loss of complete remission.
Progression/Worsening	Higher blast count in the BM and/or PB than before treatment. Worsening of cytopenias (anaemia and/or thrombocytopenia). Progression from the MD- to the MP-variant of CMML.

Table 21. MDS/MPN disease status or best response.

Number

If the disease status or best response was complete remission (CR) or relapse, select the number of this status.

Lymphomas

Disease status or best response

Select the disease status or best response from the list according to the criteria provided in table 22:

- Chemorefractory relapse or pression, including primary refractory disease
- Complete remission (CR)
- Partial remission
- Stable disease (no change, no response/loss of response)
- Untreated relapse (from a previous CR) or progression (from a previous PR)

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Disease status or best response		
Complete remission (CR)	Complete absence of disease, no signs or symptoms of the original disease.	Confirmed (Only applicable if the Complete Remission was evaluated by CT-scan or MRI methods.)
		Unconfirmed (Only applicable if the Complete Remission was evaluated by CT-scan or MRI methods.)
Partial response (PR) with or without prior CR	Reduction in the disease of 50% or more	
Stable disease (no change, no response/loss of response)	Less than 50% reduction in the disease burden.	

Untreated relapse from previous CR/untreated progression from previous PR	Worsening of the disease status in patients in PR or re-appearance of the lymphoma in patients in CR, such as: recurrence of disease or systemic symptoms (B-symptoms), patient remains untreated after the relapse or progression.
Chemorefractory relapse or progression, including primary refractory disease	Does not present any of the features of any type of remission after treatment.

Table 22. Lymphomas disease status or best response.

Complete remission: confirmed

Indicate if the complete remission was **confirmed** or **unconfirmed**. Unconfirmed means a complete response with persistent scan abnormalities of unknown significance. If it is not known if the complete remission was confirmed, select **unknown**.

Solid tumours

Disease status or best response

Select the disease status or best response from the list according to the criteria provided in table 23:

- Complete remission (CR)
- First partial remission
- Partial remission (PR)
- Progressive disease
- Relapse
- Stable disease (no change, no response/loss of response)

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Disease status or best response		
Complete remission (CR)	Disappearance of all target lesions and all non-target lesions and normalisation of tumour marker level.	**Unconfirmed** complete response with persistent scan abnormalities of unknown significance
		Confirmed CR with No abnormalities detected in scan
		Unknown if it is not known if the complete remission was confirmed, select unknown
First partial remission	The patient achieved a reduction in disease of > 30% or more for the first time ever, but did not achieve complete remission[a]	
Partial remission (PR)	The patient achieved partial remission not for the first time.	
Progressive disease (PD)	At least 20% increase in the sum of diameters of target lesions, in addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions is also considered progression).	
Relapse	Reappearance of disease in patients whose last disease status was complete remission.	**Sensitive:** patient achieves a reduction of >30% in the disease burden after treatment for this relapse.
		Resistant: patient has not achieved a reduction of more than 30% in the disease burden after treatment for this relapse.
		Unknown: if it is not known if the relapse was resistant or sensitive, select unknown.
Stable disease (no change, no response/loss of response)	Target Lesions: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum length diameters since the treatment started. Non-Target Lesions: Persistence of one or more non-target lesion(s) or/and maintenance of tumour marker level above the normal limits	

Table 23. Solid tumours disease status or best response.

a. As per RECIST 1.1 guidelines https://pubmed.ncbi.nlm.nih.gov/19097774/

Bone marrow failures (incl. AA)

Disease status or best response

Select the disease status or best response from the list according to the criteria provided in table 24:

- Complete remission (CR)
- Partial remission (PR)
- Haematological improvement (HI); NIH partial response
- Stable disease (no change, no response/loss of response)
- Relapse/Progression

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Disease status or best response	Severe aplastic anaemia	Moderate aplastic anaemia	Genetic BMF
Complete Remission (CR)	All of the following: ● No evidence of clonal evolution, by marrow cytogenetic and flow cytometry ● Peripheral blood counts: haemoglobin >10 gr/dL, absolute neutrophils >1.0 x 10^9/L, platelets >100 x 10^9/L	All of the following: ● No evidence of clonal evolution, by marrow cytogenetic and flow cytometry ● Peripheral blood counts: haemoglobin normal for age, absolute neutrophils >1.5 x 10^9/L, platelets >150 x 10^9/L	All of the following: ● Haemoglobin higher than the inferior limit according to age, transfusion independence. For age-related reference values ● Absolute neutrophils ≥1.5 × 10^9/L up to age 18 years, ≥1.8 × 10^9/L, in adults from 18 years ● Platelets >150 x 10^9/L, transfusion independence

Partial Remission (PR):	All of the following: • No evidence of clonal evolution, by marrow cytogenetic and flow cytometry • No longer meeting criteria for diagnosis of SAA • Transfusion independence (defined as no need of any PRBC or platelet transfusion) • Peripheral blood counts: haemoglobin >8 gr/dL, absolute neutrophils >0.5 x 10^9/L, platelets >20 x 10^9/	At least one of the following: • No evidence of clonal evolution, by marrow cytogenetic and flow cytometry • Transfusion independence (if previously required) doubling or normalisation of at least one cell line • Peripheral blood counts: haemoglobin >10 gr/dL, absolute neutrophils >1.0 x 10^9/L, platelets >100 x 10^9/L	All of the following: • Haemoglobin ≥8 <10 gr/dL, transfusion independence • Absolute neutrophils ≥0.5 <1.0 × 10^9/L • Platelets ≥20 <50 × 10^9/L, transfusion independence
Haematological improvement (HI); NIH partial response:	No longer meeting criteria for diagnosis of SAA, in absence of CR or PR	No longer meeting criteria for diagnosis of MAA or genetic BMF, in absence of CR or PR	One or two of the following: • Haemoglobin ≥8 <10 gr/dL, transfusion independence; or • Absolute neutrophils ≥0.5 <1.0 × 10^9/L; or • Platelets ≥20 <50 × 10^9/L, transfusion independence
Stable disease (no change,	Patients who have not achieved a CR, PR, HI, relapse or progression will be considered to have a stable disease.		

no response/loss of response)			
Relapse / Progression:	Any of the following events after a haematological response (CR or PR): ● Meeting again the criteria for SAA ● Requirement of transfusion support (if not due to independent medical conditions) ● Decrease in any of the peripheral blood counts as follows: Decrease to less than 50% of the medium sustained count during remission if: absolute neutrophils <1.0 x 10^9/L, platelets <50 x 10^9/L; or Or in any case if: absolute neutrophils <0.5 x 10^9/L , platelets <20 x 10^9/L The peripheral blood count decrease must be: ● Not due to any independent concomitant medical condition ● Demonstrated in at least 3 tests over a period of 2 weeks	After a haematological response (CR or PR), once again meeting the criteria for MAA	All of the following: ● Haemoglobin <8 gr/dL or transfusion dependence ● Absolute neutrophils <0.5 × 10^9/L ● Platelets <20 × 10^9/L or transfusion dependence

	• Not responding to re-introduction of low dose cyclosporin A		

Table 24. BMF (incl. AA) disease status or best response.

Did transfusions stop during the follow-up period?

If the disease status is reported for bone marrow failures, indicate if transfusions stopped since the last follow-up. If the patient was never transfusion dependent, select **patient was never transfusion dependent**.

If the transfusions are ongoing, select **no**. If the transfusions did stop, select **Yes** and complete the next questions. If the patient is transfusion independent and was transfusion dependent at a previous follow-up, select **ongoing transfusion independence since last follow-up**. If the transfusion status is not known, select **unknown**.

Did the patient return to transfusion dependency afterwards?

If the patient became transfusion independent since the last follow-up, but is back to needing transfusions within this follow-up period, select **yes**. If they continue to be independent of transfusions after stopping in this follow-up period, select **no**. If it is not known if the patient went back to needing transfusions, select **unknown**.

First transfusion date

If the patient stopped transfusions during the follow-up period but went back to being transfusion dependent, report the first transfusion date after the transfusion free period. If the date is not known, select **unknown**.

Autoimmune disorders

Disease status or best response

Select the disease status or best response from the list:

- **No evidence of disease**- the patient has achieved complete absence of disease, there are no signs or symptoms of the original disease described.
- **Improved**
- **Unchanged** - Patients who have not demonstrated complete absence of disease, improvement in symptoms, or deterioration of symptoms will be classified as **Unchanged**.
- **Worse**

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Haemoglobinopathies

The haemoglobinopathies section is split into thalassemia and sickle cell disease.

Thalassemia best response

Select the best response that was achieved since the main treatment:

- Transfusion independent
- Transfusions required

For clarification, transfusion independence is typically defined as going 8-12 weeks without needing transfusions, without a specific haemoglobin threshold.

If the best response is not known or was not evaluated, select **Unknown** or **Not evaluated**, respectively.

Date of last transfusion

If a patient reached transfusion independence, report the date of the last transfusion after main treatment the patient received. If the date is not known, select **Unknown**.

Date of first transfusion

If a patient still requires transfusions, report the date of the first transfusion the patient received after main treatment due to Haemoglobin deficiency (recurrence of disease). If the date is not known, select **Unknown**.

Thalassemia disease status

Patient requires transfusions during follow-up period

Indicate if the patient requires transfusions during follow-up period after haematopoietic recovery by selecting **No** or **Yes**.

Patient requires transfusions, Yes

If a patient is transfusion dependent indicate whether at this follow-up period the **Return to transfusion dependence after CT or transfusion free period** occurred or patient **Ongoing transfusion dependence since previous assessment.**

Date of first transfusion

If a patient has returned to transfusion dependence after main treatment or transfusion free period during this follow-up period, report the date of the first transfusion after main treatment or transfusion free period. If the date is not known, select **Unknown**. If a patient has ongoing transfusion dependence

since the previous assessment and the date was reported at the previous follow-up form, do not report the date here, the question will be disabled.

Number of units

Report the number of transfusion units patient received during this follow-up period. If the exact number is not known, select **Unknown**.

Did transfusions stop?

Indicate if the patient stopped receiving the transfusions. If the patient stopped transfusions and did not require more during this follow-up period, select **Yes.**

Date of last transfusion

If the patient stopped transfusions during the reporting period, provide the date when the last transfusion was administered. If it is not known, select **Unknown**.

Sickle cell disease best response

Select the best response that was achieved since the main treatment:

- No return of sickling episodes. Patients are considered to have no return of sickling episodes when they have shown an absence of recurrent sickle cell crises.
- Return of sickling episodes. When recurrent sickle cell crises reoccur.

If the best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Date of first episode

If a patient has returned to sickling episodes, report the date of the first episode after main treatment. If the date is not known, select **unknown**.

Sickling episodes occur during follow-up period

This should only be completed when reporting the disease status. Indicate if there were no more recurrent sickle cell episodes since the last follow-up by selecting **no**. If recurrent sickling episodes were present since the last follow-up, select **yes**. If it is not known if the sickling episodes returned, select **unknown**.

First return of sickling episodes after cellular therapy

Select this option if it is the first return of sickling episodes after CT.

Date of first episode (after cellular therapy)

If the sickling episodes reoccurred for the first time since the main treatment, report the date of the first sickling episode. If the date is not known, select **unknown**.

Ongoing presence of sickling episodes

Select this option if the sickling episodes have been ongoing since a previous follow-up period.

Number of SCD episodes (during follow-up)

If the sickling episodes first returned after main treatment or were ongoing from the previous follow-up, report the number of sickling episodes which occurred during this follow-up period. If the number is not known, select **unknown**.

Other diagnosis

Disease status or best response

Select the disease status or best response from the list:

- **No evidence of disease -** the patient has achieved complete absence of disease, there are no signs or symptoms of the original disease described.
- **Improved**
- **Unchanged -** Patients who have not demonstrated complete absence of disease, improvement in symptoms, or deterioration of symptoms will be classified as **Unchanged**.
- **Worse**

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Cell Infusion Sheet

The following completion guidelines refers to the completion of appendix 6 of the form, the cell infusion sheet.

Please report each cell infusion episode performed during the follow-up period in a separate cell infusion sheet, completing as many sheets as episodes of cell infusion that took place. Cell infusion treatment is often given as sequential cell infusions through a series of days or even weeks. In order to make the data comparable, one episode of cell infusion treatment (one "CI)" is defined as any number of cell infusions that take place for the same indication within 10 weeks from first to last infusion. If the indication for the treatment changes within the 10 weeks, that would be considered as 2 separate episodes of cell infusion (2 "CI"), with the 2nd episode starting on the 1st day infusions were given after the change in indication.

Do not use this cell infusion sheet for any boost. All boosts shall be registered inside the follow-up form.

Chronological number of CI episode for this patient

Report the chronological number of this cell infusion episode for this patient.

Date of the first infusion

Report the date of the first infusion within this episode.

Number of infusions within this episode (10 weeks)

Report the number of infusions within 10 weeks. Count only infusions that are part of the same regimen and given for the same indication.

Source of cells

Indicate if the source of cells are **allogeneic** and/or **autologous**, check all that apply.

Type of cells

Select the type of cells, check all that apply:

- **Lymphocytes (DLI);**
- **Mesenchymal;**
- **Fibroblasts;**
- **Dendritic cells;**
- **NK cells;**
- **Regulatory T-cells;**
- **Gamma/delta cells;**
- **Virus-specific T-cells.**

If the type of cells is **virus specific T-cells,** also specify the virus the T-cells were directed against.

If the type of cells is not listed, select **Other** and specify the type of cells in the text field.

Disease status at time of this cell infusion

Indicate the disease status at time of this cell infusion corresponding to indication diagnosis by selecting from the list provided in Appendix 1.

The disease status is split into disease specific sections:

- Acute leukemias;
- Chronic leukemias;
- Plasma cell neoplasms;
- MPN, MDS, MDS/MPN overlap syndromes;
- Lymphomas;
- Solid tumours;
- Bone marrow failure syndromes (BMF) including aplastic anaemia (AA);
- Autoimmune disorders;
- Haemoglobinopathies;
- Other diagnoses.

The instructions for completing appendix 1 can be found in appendix 1 of this document.

If the disease status has not been evaluated, select **Not evaluated**. Select **Unknown** if the disease status at the time of this cell infusion is not known.

Indication

Select all the indications for this cell infusion episode that apply:

- **Planned/protocol;**
- **Prophylactic;**
- **Treatment of acute GvHD;**
- **Treatment of chronic GvHD;**
- **Treatment PTLD, EBV lymphoma;**
- **Treatment for primary disease;**
- **Mixed chimaerism;**
- **Loss/decreased donor chimaerism;**
- **Treatment of viral infection other than EBV;**
- **Poor graft function;**
- **Infection prophylaxis.**

If the indication is not listed, select **Other** and specify it in the text field.

Acute GvHD - maximum grade *(after this infusion episode but before any subsequent cell infusion/HCT/CT):*

Indicate the maximum grade (Grade scale 0 - 4) of acute GvHD. If the grade is unknown but aGvHD is present, select **Present but grade unknown**.

Date Acute GvHD onset after cell infusion

Report the aGvHD onset date after the cell infusion. If the date is not known, select **unknown**.

Bibliography

1. Jagasia MH, Greinix HT, Arora M, Williams KM, Wolff D, Cowen EW, et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group report. Biol Blood Marrow Transplant [Internet]. 2015 Mar;21(3):389–401.e1. Available from: http://dx.doi.org/10.1016/j.bbmt.2014.12.001
2. Schoemans HM, Lee SJ, Ferrara JL, Wolff D, Levine JE, Schultz KR, et al. EBMT-NIH-CIBMTR Task Force position statement on standardized terminology & guidance for graft-versus-host disease assessment. Bone Marrow Transplant [Internet]. 2018 Nov;53(11):1401–15. Available from: http://dx.doi.org/10.1038/s41409-018-0204-7
3. Holler E, Greinix H, Zeiser R. Acute Graft-Versus-Host Disease. In: Carreras E, Dufour C, Mohty M, Kröger N, editors. The EBMT Handbook: Hematopoietic Stem Cell Transplantation and Cellular Therapies [Internet]. Cham (CH): Springer; Available from: http://dx.doi.org/10.1007/978-3-030-02278-5_43
4. Wolff D, Lawitschka A. Chronic Graft-Versus-Host Disease. In: Carreras E, Dufour C, Mohty M, Kröger N, editors. The EBMT Handbook: Hematopoietic Stem Cell Transplantation and Cellular Therapies [Internet]. Cham (CH): Springer; Available from: http://dx.doi.org/10.1007/978-3-030-02278-5_44
5. Cuvelier GDE, Schoettler M, Buxbaum NP, Pinal-Fernandez I, Schmalzing M, Distler JHW, et al. Toward a Better Understanding of the Atypical Features of Chronic Graft-Versus-Host Disease: A Report from the 2020 National Institutes of Health Consensus Project Task Force. Transplant Cell Ther [Internet]. 2022 Aug;28(8):426–45. Available from: http://dx.doi.org/10.1016/j.jtct.2022.05.038
6. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) [Internet]. 2021 [cited 2023 Mar 21]. Available from: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm
7. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis [Internet]. 2009 Jul 1;49(1):1–45. Available from: http://dx.doi.org/10.1086/599376