CT follow-up

Guide to the completion of the EBMT data collection form:

CT_FU_ v1.0

22 August 2023

EBMT Registry

EBMT Clinical Research & Registry Department

Co-funded by the European Union

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CT follow-up

The CT follow-up form may be filled in paper version and 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.

1. 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.

2. Survival status:

Indicate if the patient is last known to be **Alive** or **Dead**. If the patient is lost to follow-up, tick the box for **Lost to follow-up**.

3. Assessment period covered by this report:

Indicate which assessment period covers this report. You can select between the following:

- **Day 100:** 100 days post CT;
- **6 months:** 6 months post CT;
- **Annual or unscheduled follow-up** post CT.

Best Response

This section (questions 4-5) should be completed only for Day 100 and 6 Months follow-up and will be disabled for all subsequent reporting periods.

4. Best clinical/biological response after this cellular therapy:

4.1. If the indication for this CT was the <u>treatment of a primary disease</u>, select the best response to the cellular therapy observed before any subsequent treatment:

- **Continued complete remission (CCR):** for recipients who were already in CR at CT**;**
- **Complete remission (CR)**: the status of disease at CT was not CR, but the status of the disease after CT is CR**;**
- **Partial remission;**
- **No response / Stable disease / No change;**
- **Disease progression.**

If the best response to CT was not evaluated (for instance, if the patient died before 100 days after CT, without being re-staged), select **Not evaluated**. If the best response is not known, select **Unknown**.

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:

Reporting 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	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)

Table 1, example of reporting the best response 1

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:

Reporting 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)

Table 2, example of reporting the best response 2

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:

Reporting 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

Table 3, example of reporting the best response 3

4.2. 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; or**
- **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.

5. Date response evaluated:

Report the date the best response to the cellular therapy was evaluated. 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. See examples in 4.1 If the indication was the treatment of a primary disease.

Recovery

6. 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.

6.1. Date of the last assessment:

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

6.2. 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.

7. 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.

7.1. Date of the last assessment:

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

7.2. Date of platelet reconstitution:

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.

7.3. Date of the last platelet transfusion:

Indicate the date when the patient received the latest platelet infusion within the 100 day follow-up period.

8. Was B-cell count monitored after CT?

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

If there was B-cell recovery observed, answer **Yes** and report the date of the first B-cell recovery.

If it is not known if there was B-cell recovery, select **Unknown**.

Current haematological findings

Report results of haematological investigation in the follow up period. Carefully check in which unit the data should be reported.

8. Haematological findings:

8.1. 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.

8.2. 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**.

8.2.1. Also specify if platelets 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.

8.3. 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.

8.4. Lymphocytes:

Report the percentage (%) of lymphocytes. If it was not evaluated, select Not evaluated. If the amount is unknown, select Unknown.

8.5. Neutrophils:

Report the percentage (%) of neutrophils. If it was not evaluated, select **Not evaluated**. If the amount is unknown, select **Unknown**.

Complications since the Last Report

GvHD

This section (questions 9 - 9.3.7) shall be completed only if the patient received an allogeneic HCT.

9. 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. If it did not occur select **No** and proceed to the next section.

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 standardized terminology (2).

9.1. Did the patient receive a systemic immunosuppressive treatment for GvHD?

Indicate if the patient received a systemic immunosuppressive treatment for GvHD. If the answer is Yes, specify also:

9.1.1. Date treatment started:

Report here the date the systemic immunosuppressive treatment for GvHD started**.**

9.1.2. Immunosuppression ongoing:

Indicate whether systemic immunosuppressive treatment for GvHD is still ongoing as per the date of this follow-up report. Mark as **Unknown** if this is not known.

9.2. Acute GvHD:

Indicate if aGvHD occurred.

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.

9.2.1. Date of onset:

If aGvHD occurred, report here the date of onset.

9.2.2. Maximum observed organ severity score:

Select for each organ listed in the table the observed severity score. If another site was also affected, answer **Yes** in **Other site affected** and specify this site in the text field in English.

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
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 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 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)

9.2.3. Overall maximum grade observed:

Select the overall maximum grade that was observed. If it is not known which overall maximum grade was observed, select **Unknown**.

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.

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

Table 5, overall maximum grade for aGvHD (2)

9.2.4. Steroid-refractory acute GvHD:

Indicate if the patient experienced steroid-refractory acute GvHD or not. 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)".

9.2.5. Date of aGvHD resolution:

If the acute GvHD resolved, please report the date on which it was thought to have resolved completely. If it is still ongoing, select **Ongoing**.

9.3. Chronic GvHD:

Indicate if chronic GvHD occurred or not.

Answer **No** if the patient has never had an episode of cGvHD.

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

9.3.1. Date of onset:

If cGvHD occurred, report here the date of onset.

9.3.2. 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**.

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.

9.3.3. Date maximum NIH score:

Report the date the maximum NIH score was observed.

9.3.4. 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.

Use the NIH scoring system as described in 9.3.2.

9.3.5. 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).

9.3.6. Date of cGvHD resolution:

Report the date of cGvHD resolution. If it is not resolved yet, select **Ongoing**.

9.4. 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**.

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.

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

If no other non-infectious complication than GVHD did occur during the follow-up period, select **No** and proceed to the next section. If non-infectious complications occurred, select **Yes** and report in the table below. If the status of the adverse event is unknown, select Unknown.

For adverse events not listed in the table, specify them in the **Other** text field.

10.1. Adverse event observed:

Specify for each adverse event listed whether it was **Present** or **Absent**. If the status of the adverse event is unknown, select **Unknown.**

If the adverse event was diagnosed and reported in a previous reporting period, and the symptoms continue into this reporting period, indicate **Present**.

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

10.1.1. If **hypogammaglobulinemia** is reported as Present**,** specify also the following details:

Was it also present at time of the cellular therapy?

Answer **No**, 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 if it was worsened by cellular therapy or not.

10.2. 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.bbmt.org/article/S1083-8791(18)31691-4/fulltext#seccesectitle0014):

- 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 scale, please select appropriate scale from the list.

For **B-cell aplasia**, a condition characterised by extremely low B-cell counts, indicate the percentage of B-cells or mark as **Not evaluated**, if the percentage was not assessed.

There is no maximum grade to be indicated for bone marrow aplasia and hypogammaglobulinemia.

10.3. Onset date:

Report the onset date when the first symptoms of the adverse event was observed.

If the adverse event was diagnosed in a previous reporting period, and the symptoms continue into this reporting period, and the date has already been reported, copy the date reported previously.

10.4. Treated:

Report for each adverse event whether it was treated (answer **Yes**) or not (answer **No**). If it is not known if the adverse event was treated or not, select **Unknown**.

10.5. Resolved:

Report for each adverse event if it has been resolved (answer **Yes**) or not (answer **No**). If it is not known if the adverse event has been resolved or not, select **Unknown**.

Infectious complications

11. Did infectious complications occur during the follow-up period?

Answer **yes**, if any infectious complications occurred during the follow-up period, which includes previously unreported infections and reactivation of previously resolved infections.

Answer **no**, if no infectious complications occurred during the follow-up period, or if the infectious complication occurred in the previous follow-up period and remained or was resolved in this follow-up period.

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 hospitalization
- 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)

12. 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.

12.1. Start date

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.

12.2. 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).

12.3. Pathogen

Select the bacterium that caused the infection from the list in Appendix 1 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the '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.

12.4. Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark unknown if it is not possible to identify. Clinical implications are at least one of the following: symptomatic infection in the relevant organ/system, the need for pathogen-directed therapy, or the need for the isolation precautions for infections.

12.4.1. Infection with clinical implications, yes:

Select the clinical implication(s) of the infection from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;
- Isolation precautions.

12.5. Localisation (CTCAE term)

Select the CTCAE term for the infection from the list in Appendix 2 of the form or available in the database.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and must be reported!

The CTCAE version that was used for the current form is version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

12.6. Intravascular catheter-related infection

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

- The same organism 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 bacteremia criteria for quantitative blood cultures: a colony count of microbes grown from blood obtained through the catheter hub being at least 3-fold greater than the colony count from blood samples obtained from a peripheral vein
- 2 blood samples for culture are obtained (1 from a catheter hub and 1 from a peripheral vein) that meet CVC-related bacteremia 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
- 2 quantitative blood cultures of samples are obtained through 2 catheter lumens, with the colony count for the blood sample drawn through one lumen being at least 3-fold greater than the colony count for the blood sample obtained from the second lumen (7).

12.6.1. Specify

If the infection was related to an intravascular catheter, select the type of CVC infection from the list in Appendix 3 or available in the database.

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

If there was more than one bacterial infectious episode during the follow-up period, repeat these questions for the subsequent infection.

13. 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.

13.1. Start date

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.

13.2. Pathogen

Select the virus that caused the infection from the list in Appendix 1 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the 'Other' option and enter its name in a textbox. Always report the full name of the virus.

13.2.1. If the pathogen was CMV/EBV: was this a primary infection in a previously seronegative patient?

Answer yes, if the patient's serology tests (CMV IgG, EBNA, EBV IgG) and (if taken) PCR tests were negative before the treatment (start of lymphodepleting/conditioning regimen) took place.

13.3. Infection with clinical implications

Indicate if the infection had clinical implications (or not), or mark unknown if it is not possible to identify. Clinical implications are at least one of the following: symptomatic infection in the relevant organ/system, the need for pathogen-directed therapy, or the need for the isolation precautions for infections.

13.3.1. Infection with clinical implications, yes:

Select the clinical implication(s) of the infection from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;
- Isolation precautions.

13.4. Localisation (CTCAE term)

Select the CTCAE term for the infection from the list in Appendix 2 of the form or available in the database.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential must be reported!

The CTCAE version that was used for the current form is version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

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

If there was more than one viral infectious episode during the follow-up period, repeat these questions for the subsequent infection.

14. 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.

14.1. Start date

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.

14.2. Type of fungi

Select the type of fungal infection by marking if it is yeasts or moulds.

14.3. Pathogen

Select the fungus that caused the infection from the list in Appendix 1 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the ‘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.

14.4. Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark unknown if it is not possible to identify. Clinical implications are at least one of the following: symptomatic infection in the relevant organ/system, the need for pathogen-directed therapy, or the need for the isolation precautions for infections.

14.4.1. Infection with clinical implications, yes:

Select the clinical implication(s) of the infection from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;
- Isolation precautions.

14.5. Localisation (CTCAE term)

Select the CTCAE term for the infection from the list in Appendix 2 of the form or available in the database.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and must be reported!

The CTCAE version that was used for the current form is version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

14.6. 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 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 quantitative blood cultures: a colony count of fungi grown from blood obtained through the catheter hub being at least 3-fold greater than the colony count from blood samples obtained from a peripheral vein
- 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
- 2 quantitative blood cultures of samples are obtained through 2 catheter lumens, with the colony count for the blood sample drawn through one lumen being at least 3-fold greater than the colony count for the blood sample obtained from the second lumen (7).

14.6.1. Specify

If the infection was related to an intravascular catheter, select the type of CVC infection from the list in Appendix 3 or available in the database.

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

If there was more than one fungal infectious episode during the follow-up period, repeat these questions for the subsequent infection.

15. 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.

15.1. Start date

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.

15.2. Type of parasite

Select the type of parasitic infection by marking if it is protozoa or helminths.

15.3. Pathogen

Select the parasite that caused the infection from the list in Appendix 1 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the ‘Other’ option and enter its name in a textbox. Always report the full name of the parasite.

15.4. Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark unknown if it is not possible to identify. Clinical implications are at least one of the following: symptomatic infection in the

relevant organ/system, the need for pathogen-directed therapy, or the need for the isolation precautions for infections.

15.4.1. Infection with clinical implications, yes:

Select the clinical implication(s) of the infection from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;
- Isolation precautions.

15.5. Localisation (CTCAE term)

Select the CTCAE term for the infection from the list in Appendix 2 of the form or available in the database.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and must be reported!

The CTCAE version that was used for the current form is version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

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

If there was more than one parasitic infectious episode during the follow-up period, repeat these questions for the subsequent infection.

16. 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, etc.

16.1. Start date

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.

16.2. Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark unknown if it is not possible to identify. Clinical implications are at least one of the following: symptomatic infection in the relevant organ/system, the need for pathogen-directed therapy, or the need for the isolation precautions for infections.

16.2.1. Infection with clinical implications, yes:

Select the clinical implication(s) of the infection from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;
- Isolation precautions.

16.3. Localisation (CTCAE term)

Select the CTCAE term for the infection from the list in Appendix 2 of the form or available in the database.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and must be reported!

The CTCAE version that was used for the current form is version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

16.4. 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.

16.4.1. Specify

If the infection was related to an intravascular catheter, select the type of CVC infection from the list in Appendix 3 or available in the database.

16.5. 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.

If there was more than one infectious episode with an unknown pathogen during the follow-up period, repeat these questions for the subsequent infection.

SARS-CoV-2 related questions

17. Did the patient receive a vaccination against SARS-CoV-2 after HCT?

Report if the patient received at least one vaccination dose against SARS-CoV-2 after the treatment (after lymphodepleting/conditioning regimen) took place.

17.1. Number of doses

If the patient received a vaccination against SARS-CoV-2 after the treatment (after lymphodepleting/conditioning regimen) took place, report the number of doses that were administered after the treatment.

17.2. Date of the last dose

If the patient received a vaccination against SARS-CoV-2 after the treatment (after lymphodepleting/conditioning regimen) took place, report the date the last dose was administered.

18. Did the patient have a SARS-CoV-2 infection after HCT (positive PCR or antigen test)?

Answer **Yes** to this question if the patient had a SARS-CoV-2 infection which was confirmed by PCR or an antigen test after the treatment (after lymphodepleting/conditioning regimen) took place, either symptomatic or asymptomatic.

18.1. Date

Report the date the patient tested positive for SARS-CoV-2 after the treatment (after lymphodepleting/conditioning regimen) took place.

If there was more than one episode (new confirmed infection at least ≥ 90 days after the clearance of the previous one or at any time if evidence of a different variant), report the subsequent dates the patient tested positive after the treatment (after lymphodepleting/conditioning regimen) took place.

Secondary Malignancies and Autoimmune Disorders

19. Did a secondary malignancy or autoimmune disorder occur?

If the secondary malignancy or autoimmune disorder was already reported in the previous CT follow-up form, answer **No**.

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.

19.1. 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.

19.2. Further details on secondary malignancy or autoimmune disorder:

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

19.3. Date of diagnosis:

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

19.4. Histologic type:

If applicable, report the histologic type.

19.5. Location:

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

19.6. 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**.

19.7. 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**.

19.8. 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

20. 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**.

20.1. 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.

20.2. 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,** or
- **Tumour**.

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

20.3. 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,** or
- **Immunohistochemistry**.

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

20.4. Were immune effector cells (IEC) detected:

Select **Yes** if immune effector cells were detected by the relevant technique. Select **No** if immune effector cells were not detected.

Last Disease Status – Additional Assessments

21. Disease burden:

21.1. LDH level

Indicate if the LDH level was **Normal, Elevated**, or if it was **Not evaluated**. If the LDH level is not known, select **Unknown**.

21.2. 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 LDH level is not known, select **Unknown**.

21.2.1. If it was Elevated

Report the **maximum CRP concentration** and specify the units used: if it is **mg/dL** or **mg/L**.

21.3. Date of C-reactive protein level assessment:

Report the date of C-reactive protein level assessment.

Post-therapy Treatment

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).

22. 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 report the date it started. Select **Unknown** if it is unknown if the patient underwent additional treatment.

22.1. Date started

Report here the date the additional disease treatment started.

23. 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 question 23.1. If the patient did not receive additional cell infusions, select **No**.

23.1. 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.

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.

23.2. Is this cell infusion an autologous boost?

If the cell infusion was an autologous boost answer **Yes** and proceed to question 24.3. If it was not an autologous boost, select **No**.

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

23.3. Date of the boost:

If applicable, report here the date the 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.

24. Did the patient receive subsequent HCT?:

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

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

25. Radiotherapy:

If the patient received radiotherapy, select **Yes**. If the patient did not receive radiotherapy, select **No**. Select **Unknown** to mark that there is no information if the patient received radiotherapy or not.

26. Drugs/chemotherapy:

If the patient did not receive any drugs or chemotherapy, select **No** and proceed to 'Relapse/progression or significant worsening', starting at question 27.

If the patient did receive any drugs or chemotherapy, select **Yes** and complete the table by listing all chemotherapy/drugs given during one line of treatment. Report as many lines of treatment as applicable answering questions 26.1- 26.5.

26.1. Drug/regimen used:

Indicate here which drugs/regimens were given per each line of treatment. Please consult the List of Chemotherapy Drugs, Agents and Regimens on the EBMT website for drugs/regimens names.

26.2. Start date:

Report the start date of each line of treatment when the drug(s)/regimen(s) were given.

26.3. Reason:

Indicate reason(s) the drug(s) was/were given for:

- **Prophylaxis/preventive** reasons,
- **Relapse**,
- **Maintenance,**
- **Consolidation** reasons,
- **Non-infectious complications**, or
- **Infectious complications**.

If the drug/regimen was given, because of another reason which is not listed, select **Other** and specify the reason in the textbox.

26.4. Response to this line of treatment:

Report the response to this line of treatment by selecting one of the options:

- **Continued complete remission (CCR)**
- **Complete remission (CR)**
- **Partial remission**
- **No response / Stable disease / No change**
- **Disease progression**

If it was not evaluated, select **Not evaluated**. If it is unknown what the response was to this line of treatment, select **Unknown**.

26.5. Response assessment date:

Report the response assessment date.

27. Did the patient receive subsequent cellular therapy (either at your or another centre)?

Answer **No** if the patient did not receive subsequent cellular therapy, either at your or another centre. If the patient did receive subsequent cellular therapy, answer **Yes** and select the reason for subsequent CT.

If the patient had a subsequent cellular therapy (which was not part of this cellular therapy), this subsequent treatment should be registered using a new CT treatment form as a new cellular therapy treatment.

28. Is the patient receiving any medication not related to cell therapy or its indications?

If the patient received any medication not related to cellular therapy or its indications, select **Yes**. If the patient received medication related to cellular therapy or its indications, or if the patient did not receive any medication, select **No**. Select **Unknown** if it's not known if the patient received any medication or not and if it was related to cell therapy or its indications or not.

Hospital Admission

This section should be submitted only for Day 100 and 6 Months Follow-Up.

29. 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.**

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

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

Relapse/Progression or Significant Worsening

31. Was there a relapse/progression or significant worsening of organ function related to the primary disease after HCT?

Indicate if there was a relapse/progression or significant worsening of organ function related to the primary disease after CT detected by any method. If the answer is **Yes**, proceed to questions

31.1. - 31.5. If the answer is **No,** proceed to the next section. If it was a continuous progression, select **Continuous progression since CT**.

31.1. Number of relapses/progressions since CT:

Report here the number of relapses and/or progressions since CT this follow up is related to.

31.2. Date of first relapse/progression:

Report the date of the first relapse/progression since the CT.

31.3. Date of subsequent relapse/progression:

If there were multiple relapses/progressions, also report the date of subsequent relapses/progressions. If more than 2 relapses/progressions occurred, copy/duplicate and fill-in this section as many times as necessary.

31.4. Type of relapse:

This question only needs to be answered for malignancies (inborn errors, haemoglobinopathies and autoimmune disorders are not considered malignant disorders). In case of relapse, specify the type of relapse by indicating if it was **Medullary only**, **Extra-medullary only** or **Both medullary and extra-medullary**. If the type of relapse is unknown, select **Unknown**.

31.5. Involvement at time of relapse (If the relapse was extra-medullary or both medullary and extra-medullary):

Report for each area of involvement, which are **Skin**, **CNS** (central nervous system), **Testes/Ovary, Other,** if it was involved at time of relapse answer **Yes**, or answer **No** if it was not involved. If answering Yes for the **Other,** specify it in the text field.

31.6. CD19 expression at relapse after CT:

In case of Precursor lymphoid neoplasms only, select if CD19 expression at relapse after cellular therapy was **Present** or **Absent**. Or if status is unknown, select **Unknown.**

Patient status

32. 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;** or
- **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	Hospitalization indicated, although death not imminent; severely disabled
20	Hospitalization 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

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.

33. Has 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 since the last follow-up, select **No** and proceed to the next section. If the patient has become pregnant or has impregnated another person since the last follow-up select **Yes** and provide details in question 33.1. Select **Unknown** if it is not known.

33.1. Did the pregnancy result in a live birth?

If the pregnancy resulted in a live birth, answer **Yes.** Answer **No** if pregnancy did not result in a live birth. Select **Still pregnant at time of follow-up** if the patient/the person they impregnated was still pregnant at the time of follow-up. If there is no information about the pregnancy and whether or not it resulted in a live birth, select **Unknown**.

Cause of Death (if patient died)

34. Main cause of death:

Check only one main cause that applies. In case of doubt, consult a physician. If none of the answers in the table match, tick the box **Other** and specify it. 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 (answer question 34.1);
- **HCT-related** - death caused by complications or infections after transplant (answer question 34.1).

34.1. Select treatment related cause:

In case of Cellular therapy- or HCT-related cause of death, specify if the cause of death was related to:

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

34.1.1. 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.**

Last disease status

ACUTE LEUKAEMIAS
Other Acute Leukaemias - Last Disease Status

35. Status:

Indicate the status of the acute leukaemia disease at the time of the last assessment that is being reported. Options are:

- **Primary induction failure** - choose this answer if despite treatment patient has never achieved a complete remission.
- **Relapse (1st, 2nd, 3rd or higher) -** chose this option if > 5% blasts in the bone marrow after a period of Complete remission.
- **Complete haematological remission (CR)** choose this option if for at least 4 weeks:
  - < 5% blasts in the bone marrow
  - No blasts with Auer rods (applies to AML only)
  - Normal maturation of all cellular components in the bone marrow
  - No extramedullary disease (e.g., CNS, soft tissue disease)
  - Transfusion independent

35.1. Number:

In case of complete haematological remission, report the ordinal number of this CR by choosing one of the following options:

- **1st;**
- **2nd;**
- **3rd or higher.**

35.2. Cytogenetic remission:

In case of complete haematological remission, specify if cytogenetic remission was achieved (answer **Yes**) or not (answer **No**).

Or indicate if it was **Not evaluated** or **Unknown**. Mark as **Not applicable** if no abnormalities were detected prior to this time point.

Cytogenetic remission (complete): 0% positive metaphases together with haematological remission.

NOTE: 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.

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

35.3. Molecular remission:

In case of complete haematological remission, specify if molecular remission was achieved (answer **Yes**) or not (answer **No**).

Or indicate if it was **Not evaluated** or **Unknown**. Mark as **Not applicable** if no abnormalities were detected prior to this time point.

Molecular remission: cells with the BCR/ABL 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.

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.

35.4. Relapse:

Report the numerical order of this relapse: means the ordinal number of relapse that occurred after the first CR has been achieved. Choose one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

36. Status:

Indicate the status of the chronic myeloid leukaemia disease at the time of the last assessment that is being reported. Options are:

- **Chronic phase (CP)**
- **Accelerated phase**
- **Blast crisis**

36.1. Number (for chronic phase):

For patients in chronic phase (CP), report the ordinal number of this CP by choosing one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

36.2. Haematological remission:

Complete remission (CR) is defined as no blast cells in the peripheral blood and no more than 5% blasts in the bone marrow. CR requires that bone marrow biopsy has been done, otherwise it cannot be evaluated. This definition is related to the **haematological remission** if type of remission is not specified.

The above must be accompanied by sufficient cellularity and signs of regeneration of normal cellularity. If the bone marrow is aplastic, even in the absence of blasts (hypoplasia without blasts), it cannot be considered a CR but should be reported as “Other”.

36.3. Cytogenetic remission

For patients in chronic phase (CP), specify if cytogenetic remission was achieved (answer **Yes**) or not (answer **No**).

Or indicate if it was **Not evaluated** or **Unknown**. Mark as **Not applicable** if no abnormalities were detected prior to this time point.

36.4. Molecular remission:

For patients in chronic phase (CP), specify if molecular remission was achieved (answer **Yes**) or not (answer **No**).

Or indicate if it was **Not evaluated** or **Unknown**. Mark as **Not applicable** if no abnormalities were detected prior to this time point.

36.5. Number (for accelerated phase):

For patients in accelerated phase, report the ordinal number of this accelerated phase status by choosing one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

36.6. Number (for blast crisis):

For patients with blast crisis, report the ordinal number of this blast crisis status by choosing one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

CHRONIC LEUKAEMIAS
Chronic Lymphoid Leukaemias (CLL) - Last Disease Status

37. Status:

Indicate the status of the chronic lymphoid leukaemias at the time of the last assessment that is being reported. Options are:

- **Complete remission (CR)**
- **Partial remission (PR)**
- **Stable disease (SD)**
- **Relapse (untreated)**
- **Progressive disease (PD)**
- **Never treated**

37.1. Minimal residual disease (MRD) (by FACS or PCR):

Only applicable if chronic leukaemias status is complete remission or partial remission. Select if MRD status was **Negative** or **Positive**. If MRD status was not been evaluated, select **Not evaluated**.

CHRONIC LEUKAEMIAS
Prolymphocytic and Other Chronic Leukaemias (PLL & Other) Last Disease Status

38. Status:

Indicate the status of prolymphocytic or other chronic leukemias disease at the time of the last assessment that is being reported. Options are:

- **Complete remission (CR)**
- **Partial remission (PR)**
- **Stable disease (SD)**
- **Relapse (untreated)**
- **Progressive disease (PD)**
- **Never treated**

LYMPHOMAS
All Lymphomas - Last Disease Status

39. Technique used for disease assessment:

39.1. CT scan done:

Indicate if CT scan was done or not.

39.2. PET

Indicate if PET scan was **Negative** or **Positive**. If PT scan was not evaluated, select **Not evaluated**.

40. Status:

Indicate the status of the lymphoma disease at the time of the last assessment that is being reported. Options are:

- **Never treated**
- **Complete remission (CR).**
  - Specify also if CR was **Unconfirmed** *(CRU* = complete response with persistent scan abnormalities of unknown significance)* or **Confirmed.**
- **Partial response (PR) with or without a prior CR**
- **Stable disease**
- **Untreated relapse from a previous CR / untreated progression from a previous PR.** Specify also if the relapse was verified using histopathology by answering **Yes** or **No** in **Histopathological verification of relapse** field.
- **Chemorefractory relapse or progression, including primary refractory disease.** Specify also if the relapse was verified using histopathology by answering **Yes** or **No** in **Histopathological verification of relapse** field.
- **Disease status unknown or Not evaluated/Not evaluable**

MYELODYSPLASTIC SYNDROMES (MDS) -
Last Disease Status

41. Status:

Indicate the status of the MDS disease at the time of the last assessment that is being reported. Options are:

- **Primary refractory phase (no change)**
- **Complete remission (CR)**
- **Improvement but no CR**
- **Relapse after CR**
- **Progression/Worsening**
- **Never treated (supportive care or treatment without chemotherapy)**

41.1. Number (for complete remission):

Only applicable if the answer to question 41 is **Complete remission**, report the ordinal number of this CR by choosing one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

41.2. Number (for relapse after CR):

Only applicable if the answer to question 41 is **Relapse after CR**, report the ordinal number of this relapse after CR by choosing one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

COMBINED MYELODYSPLASTIC SYNDROMES/MYELOPROLIFERATIVE NEOPLASMS (MDS/MPN) - Last Disease Status

42. Status:

Indicate the status of the MDS/MPN disease at the time of the last assessment that is being reported. Options are:

- **Primary refractory phase (no change)**
- **Complete remission (CR)**
- **Improvement but no CR**
- **Relapse after CR**
- **Progression/Worsening**
- **Never treated (supportive care or treatment without chemotherapy)**

42.1. Number (for complete remission):

Only applicable if the answer to question 42 is **Complete remission (CR)**, report the ordinal number of this CR by choosing one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

42.2. Number (for relapse after CR):

Only applicable if the answer to question 42 is **Relapse after CR**, report the ordinal number of this relapse after CR by choosing one of the following answer options:

- **1st;**

- **2nd;**
- **3rd or higher.**

MYELOPROLIFERATIVE NEOPLASMS (MPN) - Last Disease Status

43. Status:

Indicate the status of the MPN disease at the time of the last assessment that is being reported. Options are:

- **Primary refractory phase (no change)**
- **Complete remission (CR)**
- **Improvement but no CR**
- **Relapse after CR**
- **Progression/Worsening**
- **Never treated (supportive care or treatment without chemotherapy**

43.1. Number (for complete remission):

Only applicable if the answer to question 43 is **Complete remission**, report the ordinal number of this CR by choosing one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

43.2. Number (for relapse after CR):

Only applicable if the answer to question 43 is **Relapse after CR,** report the ordinal number of this CR by choosing one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

PLASMA CELL DISORDERS (PCD) incl. MULTIPLE MYELOMA (MM) - Last Disease Status

44. Status:

Indicate the status of the PCD incl. MM disease at the time of the last assessment that is being reported. Options are:

- **Never treated**
- **Stringent complete remission (SCR)**
- **Complete remission (CR)**
- **Very good partial remission (VGPR)**
- **Partial remission (PR)**
- **Relapse from CR (untreated)**

- **Progression**
- **Stable disease / No change**

44.1. Number:

This question is only applicable if the answer to question 44 is Stringent complete remission (SCR), Complete remission (CR), Very good partial remission (VGPR), Partial remission (PR) or Relapse from CR (untreated). Report the ordinal number of this status by choosing one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

SOLID TUMOURS - Last Disease Status

45. Status:

Indicate the status of the solid tumours disease at the time of the last assessment that is being reported. Options are:

- **Adjuvant**
- **Never treated (upfront)**
- **Stable disease/No response**
- **Complete remission (CR).**
  - Specify also if CR was **Unconfirmed** *(CRU* = complete response with persistent scan abnormalities of unknown significance)* or **Confirmed**.
- **1st partial response (PR1)**
- **Relapse**
- **Progressive disease (PD)**

45.1. Number (for complete remission):

This question is only applicable if answer to question 45 was **Complete remission (CR)**, report the ordinal number of this CR by choosing one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

45.2. Number (for relapse):

Only if answer to question 45 was **Relapse**, report the ordinal number of this relapse by choosing one of the following answer options:

- **1st;**
- **2nd;**
- **3rd or higher.**

45.3. Sensitivity to chemotherapy:

Only if answer to question 45 was **Relapse**, indicate how sensitive the patient was to chemotherapy. Choose between the following options:

- **Sensitive**;
- **Resistant;**
- **Untreated**.

BONE MARROW FAILURE SYNDROMES (BMF) incl. APLASTIC ANAEMIA (AA) - Last Disease Status

46. Status:

Indicate the status of the BMF incl. AA disease at the time of the last assessment that is being reported. Options are:

- **Stable disease/No response;**
- **Complete remission (CR);**
- **Partial remission;**
- **Relapse/Progression.**

HAEMOGLOBINOPATHIES - Last Disease Status

47. Transfusion status:

If there was no transfusion, select **No transfusion required**.

If there was a transfusion, select **Transfusion required** and report the date of the first transfusion.

OTHER DIAGNOSES - Last Disease Status

48. Status:

Report if the status of other diagnoses was:

- **Cured**,
- **Improved**,
- **Unchanged;** or
- **Worse**.

Cell Infusion Sheet

The following completion guidelines refer to the completion of appendix 4 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.

1. Chronological number of CI episode for this patient:

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

2. Date of the first infusion:

Report the date of the first infusion within this episode.

3. Number of infusions within 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.

4. Source of cells:

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

5. 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.

6. Disease status at time of this cell infusion:

Report the disease status at the time of this cell infusion. 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.

7. 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 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.

8. 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**.

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