Treatment non-HCT/CT/GT/IST therapy

Guide to the completion of the EBMT data collection form:

Treatment for diagnosis_v1.1

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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.

Treatment non-HCT/CT/GT/IST

The treatment for diagnosis form should be filled and submitted online in the EBMT Registry database whenever there is an instruction to complete the "Treatment - non-HCT/CT/IST/GT" form on the diagnosis, main treatment or follow-up form. The purpose of this form is to report pre-HCT/CT lines of treatment or additional lines of treatment given during the follow-up period post main treatment. The treatments can include chemotherapy or any other intervention (radiotherapy, surgery). The form should be completed only if the treatment was given for the disease that was the indication for the HCT, CT, GT or IST and for the following reasons: induction, bridging, relapse, progression, maintenance/preventive treatment, or consolidation.

This form is to be submitted as core data if the instruction to complete the "Treatment - non-HCT/CT/IST/GT" form belongs to the core dataset. Then it is a mandatory data for completion and currently covers the following cases:

Lymphomas	all pre-HCT/CT lines of treatment
Chronic Leukaemias (CML and CLL)	all pre-HCT/CT lines of treatment
Cellular Therapy	all pre-CT lines of treatment for all malignant indication diagnoses and Immunoglobulin-related Amyloidosis
HCT Day 100 Follow-up	all post-HCT lines of treatment for all malignant indication diagnoses and Immunoglobulin-related Amyloidosis

HCT Annual/Unscheduled Follow up	all post-HCT lines of treatment administered during the follow-up period for all malignant indication diagnoses and Immunoglobulin-related Amyloidosis

If the instruction is marked as an extended dataset then the form is volunteer for submission. Currently it covers the following cases:

Chronic Leukaemias (PLL and Other Chronic Leukaemias)	all pre-HCT/CT lines of treatment
Plasma Cell Neoplasms	all pre-HCT/CT lines of treatment
MDS/MPN overlap syndromes	all pre-HCT/CT lines of treatment
Myeloproliferative Neoplasms (MPN)	all pre-HCT/CT lines of treatment
Myelodysplastic Neoplasms (MDS)	all pre-HCT/CT lines of treatment

This form captures information about one line of treatment. For every new line - a new form should be filled in and submitted. One line of treatment covers all cycles of the same drugs/regimen given in the same period with the same reason, and within the same disease status of the patient. The line of treatment can include chemotherapy and/or any other intervention (radiotherapy, surgery). The form should be completed if the treatment was given for the disease that was the indication for the HCT, CT, GT or IST. The form can be registered before, between or after the main treatment (HCT, CT, GT or IST). The main reason for the line of therapy can be: induction, bridging, relapse, maintenance/preventive treatment, or consolidation.

Example of mantle cell lymphoma, a typical first line treatment is alternating RCHOP and RDHAP for 6 cycles (3 each) then autotransplant then Rituximab maintenance. There is no separate evaluation of the response to RCHOP and that of RDHAP. Here, the different cycle ofR-CHOP and R-DHAP before the transplant are considered as 1 lin, the 1st line of treatment

Other EBMT DCFs will reference the current form to mark what information and at which time point of the patient's treatment history should be submitted through the non-HCT/CT/GT/IST form for either core or extended data.

Mobilisation, the preparative regimen (conditioning/lymphodepletion) and GvHD preventive treatment should be reported in the HCT/CT/GT-related forms. GvHD treatment and treatment of infectious and non-infectious complications should not be reported through the current form.

The Treatment for diagnosis form includes the following main sections:

1. Treatment;
2. Chemotherapy / Drug Regimen;
3. Interventions;
4. Response To This Line Of Treatment.

Allogeneic and Autologous HCT, Cellular therapy, Gene therapy and IST (for bone marrow failure syndromes) should **not** be reported through this form.

Date treatment started

Report the date when this line of treatment started.

Diagnosis for which this treatment was given

Enter the indication diagnosis for this line of treatment. Make sure the indication diagnosis has been registered in EBMT Registry first, using the relevant indication diagnosis form.

During online data entry the indication diagnosis must be selected from the drop-down list of all registered indication diagnoses for this patient.

Line of treatment

Report the chronological number of the line of treatment.

A line of treatment covers all cycles of the same drugs/regimen given in the same period with the same reason, and within the same disease status of the patient.

If a new line of treatment is initiated, a new form should be completed, so all separate lines are represented individually on the patient timeline.

The counting starts from 1 after diagnosis and continues after the main treatment. Main treatments such as HCT or CT are counted as one line of treatment (e.g., HCT + conditioning regimen or CT + lymphodepleting).

Reason for this line of treatment

Select the main indication for this line of treatment by marking the option:

- Induction;
- Bridging;
- Relapse;
- Progression
- Maintenance / preventive treatment;

- Consolidation;
- Other; specify.

If the answer option Maintenance / preventive treatment is selected, report the type of relapse prevention in the following subquestion.

Type of relapse prevention

For Maintenance/ preventive Treatment for Leukemias and , Plasma Cell Neoplasm, please specify 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 **MRD positive**. If the MRD assay cannot detect malignant cells mark it as **MRD negative**. Mark it as **MRD unknown** if MRD status evaluation was not carried out.

Chemotherapy / Drug Regimen

Chemotherapy/Drugs

If the patient received chemotherapy or drugs, answer **Yes** and provide details in the subsequent questions.

Answer **No**, if the patient did not receive any chemotherapy or drugs in this line of treatment.

Select **Unknown** if there is no information on whether the patients received any chemotherapy or drugs in this line of treatment.

Start date

Report the start date of the chemotherapy or drug regimen in this line of treatment. Mark as **Unknown** if the date is not available.

Treatment stopped

Report if the line of treatment was stopped and provide details in subsequent questions. If treatment has not stopped at time of reporting make sure to update this data field in the EBMT Registry whenever the treatment ends.

Mark as **Unknown** if there is no information whether treatment stopped or not.

End date

Report the end date of the chemotherapy or drug regimen in this line of treatment. If multiple drugs were given, report the end date of the last administered drug.

Mark as **Unknown** if the end date is not available.

Reason for treatment withdrawal

For Chronic Lymphocytic Leukaemia, if the treatment ended, report the reason for the treatment withdrawal by selecting one of the answer options:

- Planned withdrawal
- Toxicity
- Progression or insufficient response
- Other reason; specify.

Mark this field as **Unknown** if there is no information about the reason for the chemotherapy or drug regimen withdrawal.

Extended dataset

For Acute Leukaemia and for Lymphoma

Chemo/Drug regimen

Specify all the names of the chemotherapy or drugs used in this line of treatment. Please consult the LIST OF CHEMOTHERAPY DRUGS/AGENTS AND REGIMENS on the EBMT website for drugs/regimens names and synonyms.

Number of cycles

Specify the number of cycles prescribed as per protocol.

Number of days per cycle

Specify the number of days prescribe per cycles as per protocol.

Daily dose (extended question only for Acute Leukaemia)

Specify the daily prescribed drug dose as per protocol in mg/m2, mg/Kg, mg, or mg/mL.

Intrathecal therapy *(extended question only for Acute Leukaemia)*

For patients with Acute Leukaemia as indication for the HCT/CT, if at least one of the drugs has been administered by Intrathecal injection, please report if by answering **Yes** to the question Intrathecal therapy**.** If none of the drugs has been administered by intrathecal injection, tick **No**. Mark as **Unknown** if there is no information on whether the patient received intrathecal therapy or not.

Drugs that may be administered by intrathecal injection for acute leukaemia are Cytarabine, Methotrexate and Corticosteroid(hydrocortisone). They are usually used for prevention in patients who had previous CNS involvement or at risk of CNS relapse.

Chemo/Drug regimen

Specify all the names of the chemotherapy or drugs used in this line of treatment. Please consult the LIST OF CHEMOTHERAPY DRUGS/AGENTS AND REGIMENS on the EBMT website for drugs/regimens names and synonyms.

Interventions

Radiotherapy

If the patient received radiotherapy including irradiation, answer **Yes** and provide details in the subsequent questions.

Answer **No**, if the patient did not receive any radiotherapy in this line of treatment.

Select **Unknown** if there is no information on whether the patients received or not any radiotherapy in this line of treatment.

Start date

Report the start date of the radiotherapy including irradiation in this line of treatment. Mark as **Unknown** if the date is not known.

Treatment stopped

Report if the radiotherapy including irradiation was stopped and if **Yes** provide details when. If treatment has not stopped at time of reporting make sure to update this data field in the EBMT Registry whenever the radiotherapy including irradiation ends.

Mark as **Unknown** if there is no information whether treatment stopped or not.

End date

Report the end date of the radiotherapy including irradiation in this line of treatment.

Mark as **Unknown** if the date is not available.

Splenic irradiation

For patients with Myeloproliferative neoplasms as indication for the HCT/CT, report if the patient received splenic irradiation in this line of treatment by answering **Yes** (and providing details in the subsequent questions) or **No**. Mark as **Unknown** if there is no information on whether the patient received splenic irradiation or not.

If patient received splenic irradiation

Splenic irradiation, or splenic radiation therapy, is a radiation therapy directly aimed at the spleen. It aims to reduce the spleen size in the case of splenomegaly, to relieve discomfort for patients.

Total prescribed radiation dose as per protocol

If splenic irradiation was performed, specify the total prescribed radiation dose as per protocol in Gy. Mark this field as **Unknown** if there is no information on the total prescribed radiation dose.

Number of fractions

If splenic irradiation was performed, specify the number of fractions. Mark this field as **Unknown** if there is no information on the number of fractions.

Number of radiation days

If splenic irradiation was performed, specify the number of radiation days. Mark this field as **Unknown** if there is no information on the total number of radiation days (for example, if it is ongoing).

Surgery

If the patient underwent surgery as part of this line of treatment, answer **Yes** and provide details in the subsequent questions.

Answer **No**, if the patient did not undergo surgery as part of this line of treatment.

Select **Unknown** if there is no information on whether the patients underwent surgery or not as part of this line of treatment.

Date

If the patient underwent surgery, report the surgery date. Mark as **Unknown** if the surgery date is not known.

Surgery type

If the patient underwent surgery, indicate the surgery type by selecting one of the answer options:

- Splenectomy;

- Other; specify.

Mark as **Unknown** if the surgery type is not known.

Repeat the questions for all interventions used in this line of treatment.

Response To This Line Of Treatment (Disease Specific)

Response assessment date

Report the date the best response was assessed. Mark as **Unknown** if the date of assessment is not known.

Complete only the subsequent question that is relevant for the indication diagnosis for this treatment. Note that there are different best responses for the different diseases. For all diseases the options **Unknown** and **Not evaluated** can be selected. In the EBMT Registry, the system will only show the relevant options and question(s).

Acute leukaemias (AML, PLN, Other)

Select the response from the following list, consult with criteria described in table 1:

- Complete remission (CR)
- Not in complete remission

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

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 1. Acute leukaemias response.

Minimal residual disease (MRD)

Report the MRD status of acute leukaemia according to the guidelines provided below.

Chronic leukaemias (CML, CLL, PLL, Other)

Chronic Myeloid Leukaemia (CML)

Select the response from the list:

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

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

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

If the response was chronic phase (CP) also indicate:

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 3. 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 3. 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 3. 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 3. Definitions of haematological, cytogenetic and molecular remission for patients in chronic phase.

Chronic Lymphocytic Leukaemia (CLL), Prolymphocytic Leukaemia(PLL) and other chronic leukaemias

Select the response from the list according to the criteria provided in tables 4-7:

- Complete Remission (CR)

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

If the 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 4. Response evaluation according to 2018 iwCLL criteria.

*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.

Disease status or best response	
Complete Remission (CR)	See table 4 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 4 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 (SD)	See table 4 for detailed criteria. All of the criteria have to be met. Constitutional symptoms alone do not define PD.
Progression	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.

Table 5. Additional clarifications for Chronic lymphocytic leukaemias disease status classification.

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 6. 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 6 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 6 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 6 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 7. 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)

Report the MRD status of chronic leukaemia according to the guidelines provided below.

Plasma cell neoplasms (PCN)

Select the response from the list according to the criteria provided in table 8:

- 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 response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

	Response
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 8. Plasma cell neoplasms response.

Number

Select the number of the status.

Leukaemias (AL, CLL) and PCN

Minimal residual disease (MRD)

For patients in complete remission (CR) or stringent complete remission (sCR), specify the MRD, by selection one of the answer options below:

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. If the MRD status is not known, mark as **Unknown**.

Date MRD status evaluated

Report the date of MRD status evaluation.

Sensitivity of MRD assay

Report the sensitivity of MRD assay by choosing one of the given answer options, or mark **Other** checkbox and specify it.

Method used

Indicate if the MRD assessment was performed through **PCR**, **Flow cytometry** or **NGS** (Next Generation Sequencing). If another method was used, choose the **Other** option and specify it in the textbox.

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

Select the response from the list according to the criteria provided in the corresponding tables 9-11:

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

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

MPN 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 9. MPN response.

MDS 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 10. MDS disease status or best response.

MDS/MPN 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 11. 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

Select the response from the list according to the criteria provided in table 12:

- 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 response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Response		
Complete remission (CR)	Complete absence of disease, no signs or symptoms of the original disease.	Confirmed
		Unconfirmed
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 12. Lymphomas 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

Select the response from the list according to the criteria provided in table 13:

- 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.

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 13. Solid tumour response.

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

Other diagnosis

If the indication diagnosis for this treatment is was Other diagnosis, specify the response by selecting one of the answer options:

- **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 response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Appendix A - when to complete the non-HCT/CT/GT/IST treatment form

The non-HCT/CT/GT/IST treatment form is part of the core and extended dataset. For some diagnoses, it has to be completed as part of the core dataset. For other diagnoses it is only part of the extended dataset.

In the forms where it is part of the core dataset, and thus mandatory to fill, it is marked on the data collection forms as follows:

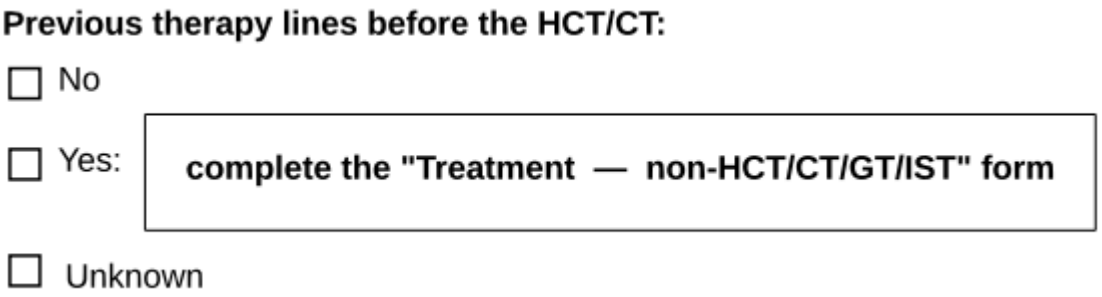

Figure 1. Example of remark where completing the non HCT/CT/GT/IST form is mandatory

Table 14 highlights for every data collection form, when the treatment non HCT/CT/GT/IST form has to be filled.

Form	When to complete	Remark
Acute leukaemias	Never	
Autoimmune disorders	Never	
Bone marrow failures incl. Aplastic Anaemia (AA)	Never	
Chronic leukaemias	Core	For PLL and Other chronic leukemias —-- Extended
Combined Myelodysplastic Syndrome / Myeloproliferative Neoplasm (MDS/MPN)	Extended	
Haemoglobinopathies	Never	
Inborn errors	Never	

Lymphomas	Core	
Myelodysplastic syndromes (MDS)	Extended	
Myeloproliferative neoplasms (MPN)	Extended	
Other indication diagnosis	Never	
Non-indication diagnosis	Never	
Plasma cell neoplasms (PCN)	Extended	
Solid tumours	Never	
Allogeneic HCT	Never	
Autologous HCT	Never	
Gene therapy	Never	
Cellular therapy	Core	
Immunosuppressive treatments (IST)	Never	
HCT follow-up D100	Core	Only if patient receives additional treatment for the disease (incl. relapse/progression)
HCT follow-up annual/unscheduled	Core	Only if patient receives additional treatment for the disease (incl. relapse/progression)
Gene therapy follow-up	Never	
Cellular therapy follow-up	Core	Only if patient receives additional treatment for the disease (incl. relapse/progression)
Immunosuppressive treatment day 100	Never	
Immunosuppressive treatment annual/unscheduled	Never	