EBMT

European Society for Blood and Marrow Transplantation

Cellular Therapy Forms Manual

A guide to the completion of the EBMT Cellular Therapy Forms

Introduction

This document contains information on how to complete the latest versions of the EBMT Cellular Therapy data collection forms as published on the EBMT website:

- EBMT Registry 55 Cellular Therapy Form – Pre-Infusion Registration
- EBMT Registry 56 Cellular Therapy Form – Day 0
- EBMT Registry 57 Cellular Therapy Form – Day 100, 6 Months & Annual Follow-Up

It is preceded by the definition of Cellular therapy and information on when a new registration should be submitted to the EBMT. For general information on how to register data please visit https://www.ebmt.org/registry/how-use-registry

For downloads of the Cellular Therapy Forms and manual please go to https://www.ebmt.org/registry/data-collection

For information on submitting data directly to the EBMT Registry using Castor software please refer to: https://www.ebmt.org/registry/cellular-therapy-data-collection-castor

Updated manuals are available to download from the above link. We are grateful for any feedback as to its content (clarity of the definitions, omissions, insufficient background or excessive verbosity, etc.). Please send all comments to the EBMT Cellular Therapy helpdesk at cellulartherapyhelpdesk@ebmt.org.

Cellular therapy registry

The EBMT Registry aims to collect data on advanced cellular therapies used for treatment other than hematopoietic stem cell transplantation (HSCT) as well as data on the clinical characteristics and outcome of the treated patients. Advanced cellular therapies belong to the group of advanced therapy medicinal products (ATMP) which are defined as medicines for human use that are based on genes, tissues or cells.

Advanced cellular therapies can be infused individually, sequentially or in combination with other treatments, including HCST. The Cellular Therapy Form design takes advantage of pre-existing data collection forms and rules for reporting to the EBMT Registry; however, it can be used independent of whether the patient has received some form of cell transplant previously or not.

Background

The therapeutic potential of ATMPs like cytotoxic T-cells, tumour vaccines and mesenchymal stem cells (MSCs) is undergoing extensive clinical testing in areas such as cancer, tissue repair and immunomodulation (regenerative medicine and immunotherapy). While some ATMPs are already on the market, additional ATMPs may soon become available to treat patients suffering from autoimmune, neurologic and hematologic disorders, heart disease and or other diseases.

Pharma companies are currently developing ATMPs made of living hematopoietic cells that may be genetically engineered in vitro e.g. in order to express the wild-type form of a gene that is mutated in the patient, or to generate a fully artificial molecule such as chimeric antigen receptor (CAR), allowing for improved recognition of target antigens. The latter is used to generate CAR-T cell therapies.

Although these therapies may be promising and prove to be of clinical use, clinical trials are often small with a limited Follow-Up time. The detection of long-term beneficial effects, as well as late and rare side effects would require a large number of patients followed over many years.
The EBMT Registry collects data on patients treated with these novel cellular therapies to allow for analyses of their risk and benefits.

Currently the EBMT Registry only collects information on advanced cellular therapies in the context of - HSCT/CT treatments in haematology and oncology, either as treatment of the primary disease (e.g. leukaemia, MPD, MDS, lymphoma etc), or treatment of associated complications (supportive care, immune modulation etc) Please contact cellulartherapyhelpdesk@ebmt.org if you want to register an advanced cellular therapy use for a non-oncologic/haematologic diagnosis.

Registration of new Cellular Therapy treatments

The Cellular Therapy Form consists of three sub-forms: Pre-Infusion Registration (including Disease Classification Sheets), Day 0 and Follow-Up. The Day 0 form should be registered in the EBMT Registry database straight after the CT infusion. The Follow-Up should be recorded at 100 days, 6 months, 1 year after the treatment date and then annually or at time of death, whichever occurs first.

If the patient had a previous Cellular Therapy or a stem cell transplant please make sure that this previous treatment is registered and that the latest Follow-Up was recorded using appropriate Follow-Up forms before proceeding. This is so we can capture relapse data and other events between the transplant/advanced cellular therapy.

The centre should not fill in the Pre-Infusion Registration form if:

- the centre only acts as a referral centre.
- the centre is only involved in following the patient after therapy which has been performed elsewhere.
- the cell collection has been performed at this centre but the infusion has been performed elsewhere.
- the cells are non-substantially modified hematopoietic cells and the treatment qualifies as HSCT as defined in the MED-AB Forms Manual; in this case submit the HSCT MED-AB data collection forms https://www.ebmt.org/registry/data-collection.
- the treatment is an Autologous Stem-Cell-Based Gene Therapy for Inherited Disorders. In this case submit MED-AB data collection form for Inherited Disorders which contains an extended genetic manipulation section.

- used to report donor lymphocyte infusions (DLIs). The Cellular Therapy Form should not be used at all. DLIs can be reported using standard HSCT MED-A or MED-B Follow-Up forms.

How many Cellular Therapy Forms should be submitted?
To understand how many forms need to be filled in, consult the flowchart in Appendix A. Additionally, the following definitions are important:

- Cellular therapy treatment: the infusion of one or more units with one indication as selected on the form, where the total units infused are separated by less than 100 days.
- Cellular therapy infusion unit: an infusion unit is a product consisting of one or more bags with the same type of manipulated cells, from the same donor (one) and with a unique batch or product number. If different manipulated cell types were used, cells from multiple donors or there are different identification codes for multiple bags, these are regarded as different infusion units.
- Cellular therapy infusion episode: the infusion of one or more units on one day. If the cellular therapy infusion units were infused over multiple days, this is regarded as multiple infusion episodes.

Timing
Disease Classification Sheet. All information contained in the Pre-Infusion Registration form (incl. Disease Classification Sheet unless the cellular therapy was given for a complication) must be recorded in the EBMT Registry database as soon as the centre emits the order for the cellular therapy to the market authorisation holder or the patient undergoes cell collection to procure the starting material.
All information contained in the Day 0 form must be recorded in the EBMT Registry database as soon as possible after the first cellular therapy infusion.
No items can be left blank unless specifically stated in the definition. If the item is marked as "unknown", you might be asked for this information again at the time of data quality checks.

Follow-up
Follow-up should be submitted 100 days, 6 months, 1 year after the initial cell infusion and then annually. For each patient only one Follow-Up needs to be submitted per timepoint regardless of the number of cellular therapies and/or HSCT the patient may have received.
If a patient had a previous HSCT, Follow-Up forms for CT only should be used to report follow-up.

Dates
If the exact date of an event is unknown, the following system must be used:

- If only the exact day is unknown, use the first day of the month to report the date, for example: 01-05-2020
- If both the day and month are unknown, use the first of January to report the date, for example: 01-01-2020

Form layout

The data collection on cellular therapy is divided into three forms:

- EBMT Registry 55 Cellular Therapy Form – Pre-Infusion Registration
- EBMT Registry 56 Cellular Therapy Form – Day 0
- EBMT Registry 57 Cellular Therapy Form – Day 100, 6 Months & Annual Follow-Up

In addition to timepoint-specific questions, every section consists of patient identifiers and the survival status at that time point.

Pre-Infusion Registration
The Pre-Infusion Registration covers diagnosis, details about the planned treatment and the planned cellular therapy product(s).

Day 0
The Day 0 form covers previous therapies, the patient's status at cellular therapy including comorbidities, details about the cellular therapy infusion unit(s) and the infusion episode(s).

Follow-Ups
The Follow-Up form should be re-used for day 100, 6 months and annual follow-up. For patients that are not part of post-authorisation studies, the EBMT requests follow-up data at the following intervals:

- Every year if the patient was transplanted less than 10 years ago
- Every 2 years if the patient was transplanted between 10 and 20 years ago
- Every 5 years if the patient was transplanted more than 20 years ago

For patients in post-authorisation studies, annual follow-ups should be completed every year for up to 15 years after the cellular therapy.
The Follow-Up form covers haematologic recovery, response to the cellular therapy, haematological findings, complications, possible additional treatments, disease status, hospital admissions, pregnancy (outcomes) and persistence of infused cells.

Informed consent

Was the patient asked to consent to data submission?
Indicate whether the patient or their legal guardians were asked if they consent to sharing their data with EBMT.
If the answer to this question is 'no', no further data entry can take place.

Date of informed consent
Indicate the date informed consent was given (by signing an informed consent form) by the patient or their legal guardians. Report the date as year/month/day.

Is your centre using the new EBMT consent form?
Indicate whether your centre is using the EBMT consent form.

Did the patient consent to data sharing with health authorities and/or researchers?
Indicate whether the patient or their legal guardians consent to having their pseudonymized data shared with health authorities and/or researchers

Did the patient consent to data sharing with Health Technology Assessment bodies?
Indicate whether the patient or their legal guardians consent to having their pseudonymized data shared with Health Technology Assessment bodies (a public organisation that provides recommendations on medicines and other healthcare interventions that can be paid for or reimbursed).

Did the patient consent to data sharing with Market Authorisation Holders?
Indicate whether the patient or their legal guardians consent to having their pseudonymized data shared with Market Authorization Holders (e.g.: Pharmaceutical Companies).

Did the patient consent to their medical records being reviewed?
Indicate whether the patient or their legal guardians consented to allow monitors to review their pseudonymized medical records.

Centre identification

EBMT Centre Identification Code (CIC)
Every centre that is submitting data to the EBMT receives a CIC, which is populated automatically in ProMISe when a user selects the corresponding centre during data entry.
This item is essential for correct registration of your data.

Hospital
Enter the name of the hospital where the treatment took place.

Unit name
Enter the name of the unit of the hospital where the treatment took place.
Entering this information is important if a centre has more than one unit reporting independently to the EBMT. Ensure that the same name is used in the future.

Unit or team type
Enter the type of the unit or team responsible for the treatment (i.e. Paediatric Haematology, Haematology, Oncology, Rheumatology, etc.). If the field would be a replication of the unit name above, the unit/team type does not need to be filled in.

Contact person
Provide the name of the person responsible for updating or correcting the data recorded in the EBMT Registry database.

Patient data

EBMT Registry Unique Identification Code
This number is a unique number assigned to a patient by ProMISe, also known as IDAA.

IMPORTANT NOTE: All data for a patient should be entered using the same Identification Code. **The number in Castor should be identical to the number in ProMISe.**
This includes subsequent transplants and cellular therapies.

Patients transferred to other centres for further treatment must always keep their original Identification Code. If a patient had a prior treatment elsewhere please use the data access request form in the link below to request access to their existing Identification Code:
Patient Given Previous Treatment in Other Centre.pdf

Date of this report
If data is being entered directly from the patient notes, the 'date of this report' is the date the data is being entered into the registry database. If the data is filled in on a paper form first and then into the registry database, the 'date of this report' is the date the paper form was filled in. This date will remain unchanged regardless of how much more data is added to the patient record in the future.

Hospital unique patient number or code
Number/code used by the treating centre to uniquely identify this patient. This item is compulsory. It must be unique in the centre, and should be sufficient to identify the patient within the hospital environment. The number should not be liable to change. If a patient receives a second treatment, no new number should be assigned: the same unique number for this patient should be used when registering subsequent cell infusions and/or HSCTs.

Other type of patient identification codes
If the centre uses any other identification codes for the patient, this can be entered here. This item is optional.

Initials (first name(s) - surname(s))
Enter the initial of the first name of the patient followed by the initial of the surname of the patient. Make sure there is consistency in the way the identification of the patient is given to ensure the record can always be traced even if the patient remains anonymous.

Date of birth
Enter the patient's exact date of birth.

Sex
Indicate the patient's sex at birth.

ABO group and Rh factor
Select the patient's blood group and rhesus factor status from the dropdown menu.

Indication for cellular therapy

Main indication
Select the indication for the cellular therapy treatment. The treatment can be aimed at one or more indications.

Treatment of a primary disease:
Select this option if the treatment was for a primary disease or disorder. Do not select diseases the patient may have had in the past, unless the procedure being reported is meant to treat these diseases.

After entering the main indication diagnosis, the Disease Classification Sheet corresponding to the main indication needs to be completed. During data entry it can be indicated whether the disease was of secondary origin.

In each Disease Classification Sheet there is a section for sub-classification and disease status specific to the respective diagnosis. Please, use the Med-AB Forms Manual for information on how to complete Disease Classification Sheets.

Treatment or prevention of complications:
Select this if the therapy was prescribed for the treatment or prevention of complications including infections.

Both:
If the treatment was for both, the primary disease and (prevention of) complications, select 'Both, treatment of primary disease and complications'.

If this cellular therapy is prescribed after a previous HSCT, the original treatment must be registered first using the HSCT Med-AB data collection forms https://www.ebmt.org/registry/data-collection.
If the patient and/or the relevant treatment of that patient has not yet been registered, the patient and the relevant treatment must be registered before adding the Cellular Therapy Form.

Date of diagnosis
If the patient is being treated for a primary disease, enter the date of diagnosis of the disease for which the patient is being treated.
If the indication for the treatment is a transformed disease or is a secondary malignancy that does not constitute a relapse of the primary disease, enter date of transformation, not the diagnosis date of the original disease.

Basic information on the planned cellular therapy

Clinical setting (tick only 1 box)
Select only one option.

As per marketing approval / Standard of care / Institutional guidelines:
Select this option if the patient is treated with cellular therapy according to the centre's standard of care policies.

Hospital exemption:
Select if the patient is treated with cellular therapy manufactured under the hospital exemption rule. The hospital exemption rule is a provision under which some cellular therapy products can be manufactured by academic or commercial facilities, and administered to patients either as orphan treatment where no equivalent commercial product is available or in the context of early clinical trials designed to provide proof-of-concept information. By definition any approved product already placed on the market cannot be manufactured in the context of the hospital exemption.

Compassionate use / accelerated access:
Select this option if the patient is treated under compassionate use. These are regulatory provisions under which a cellular product can be administered to a specific patient outside of a clinical trial, upon request and approval from regulatory agencies. Regulations may vary from country to country and some countries may not provide such opportunities. In case of doubt, please check with a clinician in the treating centre.

Investigational drug product (DP) / Clinical trial:
Tick this box if the patient is enrolled in a clinical trial, whether academia-sponsored or industry-sponsored.

If the product was administered in a clinical trial setting or as an investigational product, the following information needs to be reported:

Phase
Indicate the phase of the clinical trial.

Blind trial
Indicate if this is a blind trial. This is a trial where neither the treating doctor nor the patient knows which of the treatments offered in the trial is being given (e.g. placebo vs active substance).

Randomised trial
Indicate if the treatment is allocated randomly to the trial subjects.

Eudract number
Number given to the trial when registered with the European Clinical Trials Database

USA CT number
USA clinical trials number, only applicable to trials (also) conducted in the US. If the clinical trial number (NCT number) is not clearly documented, it can be looked up using the 'Find a Study' feature on www.clinicaltrials.gov

UMIN CT number
Japanese clinical trials number, only applicable to trials (also) conducted in Japan.

Cell origin
Indicate whether the cells infused were collected from the patient (autologous) or from another person (allogeneic).

Autologous:
The cells were collected from the patient who later received their own cells back.

Allogeneic:
The patient received a cellular therapy product prepared from cells collected from another person. Additionally, report if the donor was a new donor or an existing donor. If the donor was unknown or no data was available, skip the 'Donor' page.

Note: in case a product has been manufactured from hematopoietic cells collected from the recipient of an allogeneic cell transplant, after donor hematopoietic chimerism was established, the final product may contain cells of donor origin; however, the starting material is autologous in nature, thus select "Autologous".

Donor

Date of Birth/Age at time of donation
Fill in the donor's exact date of birth or their age at the time of donation (if the date of birth is not available).

Sex of Donor
Select the donor's sex at birth.

Donor ID given by centre
Indicate the donor ID that was assigned to the donor by the treating centre.

Global registration identifier for donors
Fill in the 19-character global registration identifier for donors (GRID) that was assigned to the donor. More information on the GRID, can be found here:https://wmda.info/professionals/optimising-search-match-connect/why-global-identifier/.

Donor ID given by the Donor Registry or Cord Blood Bank
Enter the identification code that was assigned to the donor by the donor registry or cord blood bank

ION code of the Donor Registry or Cord Blood Bank
Fill in the Issuing Organisation Number (ION) of the donor registry or cord blood bank. If the code is unknown, it can be found using https://share.wmda.info/display/WMDAREG/Database.

EuroCord code for the Cord Blood Bank
If cord blood was used for cellular therapy, fill in the EuroCord code.

Name of Donor Registry or Cord Blood Bank
Enter the name of the donor registry or cord blood bank, and full donor centre (if applicable).

Planned cellular therapy infusion products

If more than one cellular product was planned for infusion, replicate this section for every product.

Multiple cellular infusion products are defined as:

- Products that get different batch numbers after manipulation
- Products taken from multiple donors

If none of the above are applicable for the product, the section only needs to be filled in once.

Is the planned cell infusion product a commercial product?
If the product is manufactured by a pharmaceutical company after market authorization was obtained, the product is considered to be a commercial product. If the product was made by the hospital or administered before market authorization, the product is not commercial.

Is it planned to manufacture more than one cell infusion unit?
If manufacturing of only one unit is planned, select no.
If according to the definition above multiple cellular infusion units are planned, select yes and fill in the number of different cell infusion units that are planned to be manufactured.

Name of the manufacturer
Select the name of the facility which manufactured the infusion product (pharmaceutical or biotech company, cell processing laboratory or another site). If the manufacturer's name is not on the list, select 'other' and specify the name.

Name of the product
Select the product name. If the product name is not on the list, select 'other' and specify the name.

Tissue source
Select the tissue from which the cells were collected, for example, bone marrow or tumour.

Collection procedure
Date of the 1st collection
The collection date is the date when the actual cell collection (apheresis) started, independent of whether a preparatory regimen was necessary or not. Report the date of the first collection.

Number of collections
Report the number of occasions when cells were collected from the donor or patient. Include only those collections that were used for this particular cellular therapy product.

Diagnosis

If the indication for cellular therapy was a primary disease, complete the relevant Disease Classification Sheets. Further information on how to complete the forms can be found in the MEDAB manual: https://www.ebmt.org/sites/default/files/2020-12/MED-ABFormsManual.pdf.
Certain items have to be entered into ProMISe.
This concerns:

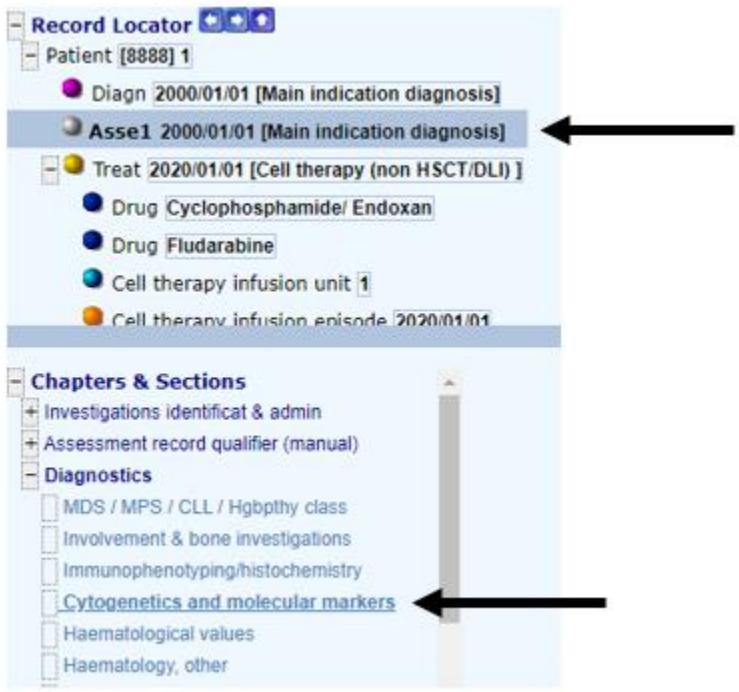
- Cytogenetic abnormalities
- Molecular markers,
- White blood cell counts for acute leukaemia

- International prognostic index (IPI) and KI-67 (proliferation index) for non-Hodgkin B-cell lymphomas
- Grade and stage for multiple myeloma and non-graft treatments that preceded the cellular therapy

Cytogenetics, molecular markers and immunophenotyping

Step 1: Turning off the Dynamic Item Filter

Go to the Diagnostics chapter of the Main indication diagnosis assessment. Continue to the 'Cytogenetics and molecular markers' section:



At the top of the screen, in the menu where the 'Exit' button is, you see an icon of a sheet of paper with binoculars:

Click this. It will turn off the Dynamic item Filter, which makes all items in ProMISe visible. The small number will change from 80 to 0.

You will notice the following expansion of the 'Cytogenetics and molecular markers' chapter:

Assessment(1)	value	label
CIC	8888	8888
Patient	1	1
Assessment date	2000/01/01 00:00	2000/01/01 (exact)
Diagnostics		
MDS / MPS / CLL / Hgbpthy class		
Involvement & bone investigations		
Disease involvement / metastasis		
Size of largest mass		
Immunophenotyping/histochemistry		
Immunophenotyping done?		
Cytogenetics and molecular markers		
Chromosome analysis		
Molecular or other type of markers		
Haematological values		
Haematology, other		
Biochemistry		
LDH levels		

Before

Assessment(1)	value	label
CIC	8888	8888
Patient	1	1
Assessment date	2000/01/01 00:00	2000/01/01 (exact)
Diagnostics		
MDS / MPS / CLL / Hgbpthy class		
Involvement & bone investigations		
Immunophenotyping/histochemistry		
Immunophenotyping done?		
CD4+ PLL Immunophenotyping		
CD8+ PLL Immunophenotyping		
Source for immunophenotyping		
Positive immunohistochemistry		
Cytogenetics and molecular markers		
Chromosome analysis		
Technique used for cytogenetics		
Complex karyotype: Are there 3 or more abnormalities		
Monosomal karyotype		
Number metaphases with abnormalites		
Number metaphases examined		
VH gene status		
VH3-21 status		
Chromosomal breakage test *(for Fanconi only)*		
Molecular or other type of markers		
Haematological values		
Haematology, other		
Biochemistry		

After

Step 2: Entering the relevant overarching data

Not all of the items that were added to the table are relevant. In the image below, the questions that need to be answered are indicated with an arrow. The first one is ‘Immunophenotyping done?’, where it needs to be filled in if an immunophenotyping test was performed. After that, move on to ‘Chromosome analysis’. Answer here if the cytogenetics were normal, abnormal, not evaluated or if it is unknown if a cytogenetics analysis was performed. Next, add the technique that was used for the analysis and if there were 3 or more abnormalities noted.

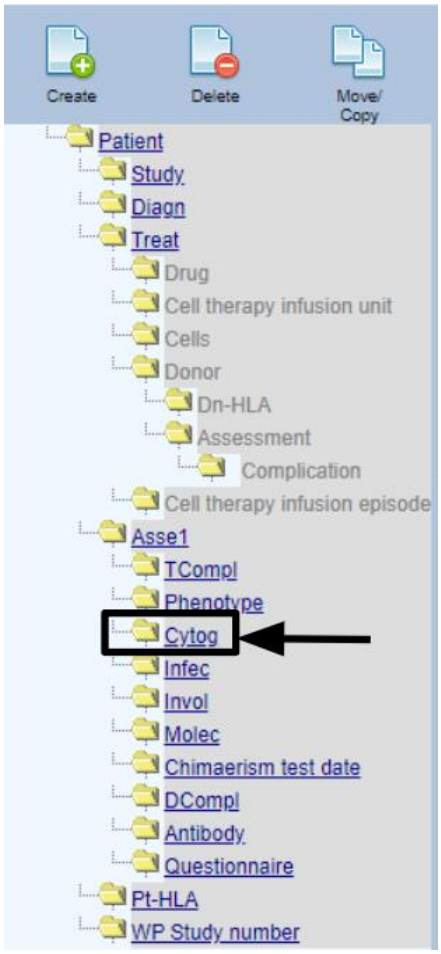
Assessment(1)	value	label
CIC	8888	8888
Patient	1	1
Assessment date	2000/01/01 00:00	2000/01/01 (exact)
Diagnostics		
MDS / MPS / CLL / Hgbpthy class		
Involvement & bone investigations		
Immunophenotyping/histochemistry		
→ Immunophenotyping done?		
CD4+ PLL Immunophenotyping		
CD8+ PLL Immunophenotyping		
Source for immunophenotyping		
Positive immunohistochemistry		
Cytogenetics and molecular markers		
→ Chromosome analysis		
→ Technique used for cytogenetics		
→ Complex karyotype: Are there 3 or more abnormalities		
Monosomal karyotype		
Number metaphases with abnormalites		
Number metaphases examined		
VH gene status		
VH3-21 status		
Chromosomal breakage test *(for Fanconi only)*		
→ Molecular or other type of markers		
Haematological values		
Haematology, other		
Biochemistry		

Skip the next questions until the ‘Molecular or other type of markers’. Here, fill in if molecular markers were present, absent, not evaluated or if it was unknown if an assessment was performed.

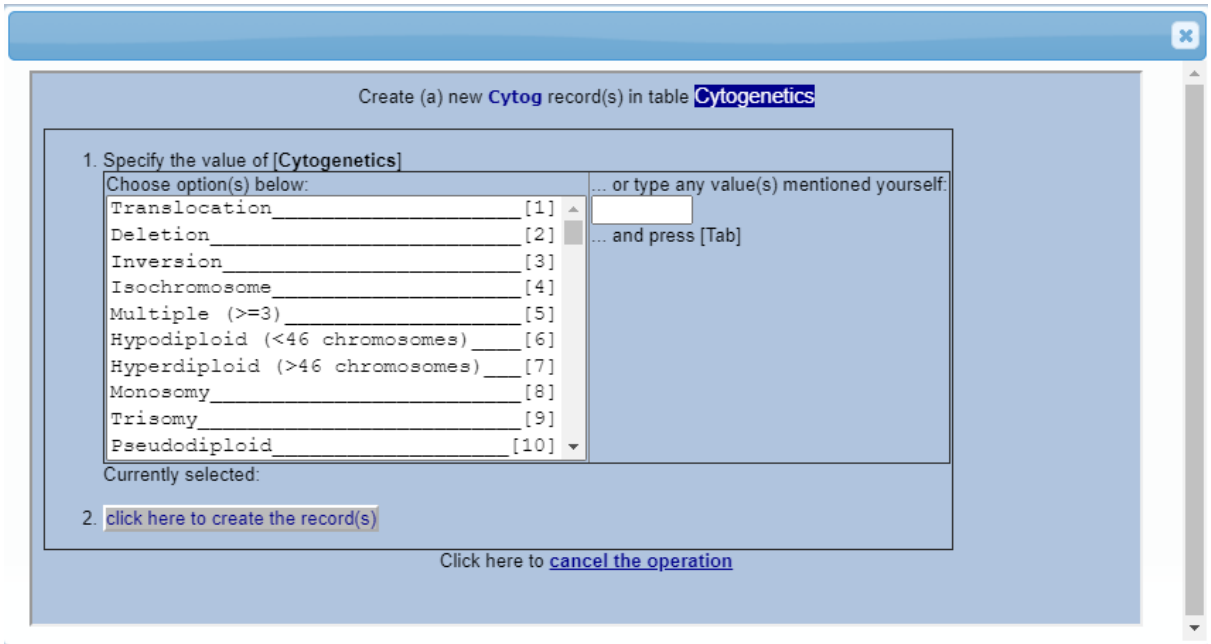
Cytogenetic abnormalities

After completing step 1 and 2, the cytogenetic abnormalities need to be added to the assessment record. Click ‘Create’ in the menu above the patient history:

A long list of items that you can add appears (image *). Keep in mind this only appears if you have the **diagnosis assessment** selected.



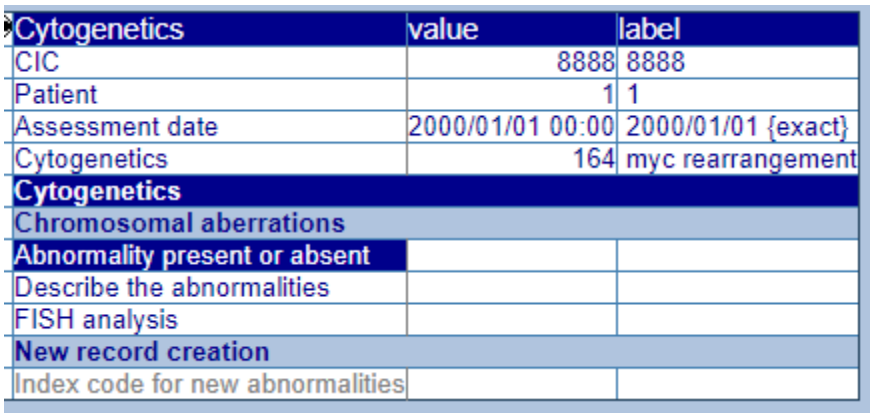
Choose ‘Cytog’ from the list below ‘Assessment’. A popup will appear in the screen, where all cytogenetic abnormalities that can be entered into ProMISe are listed:



To quickly get to the abnormality you are looking for, type in the first letter. Press that letter again to get to the right option. You can also type in the number in the box on the right side if you know the number of the abnormality. Common abnormalities for lymphoma and B-cell ALL are summarised in the table below.

	Abnormality	ProMISe Code
DLBCL	t(2;8)	161
	t(8;14)	162
	t(8;22)	163
	t(14;18)	114
	myc rearrangement	164
	BCL-2 rearrangement	165
	BCL-6 rearrangement	166
B-cell ALL	t(9;22)	101
	11q23	108
	t(4;11)	102
	Hyperdiploidy (>46 chromosomes)	6
	t(5;14)(q31;q32)	153
	t(1;19)	116
	Trisomy 8	117

After you select the correct abnormality from the list, press 'Click here to create the record(s)'. You will be sent to a new table in ProMISe, which looks like this:

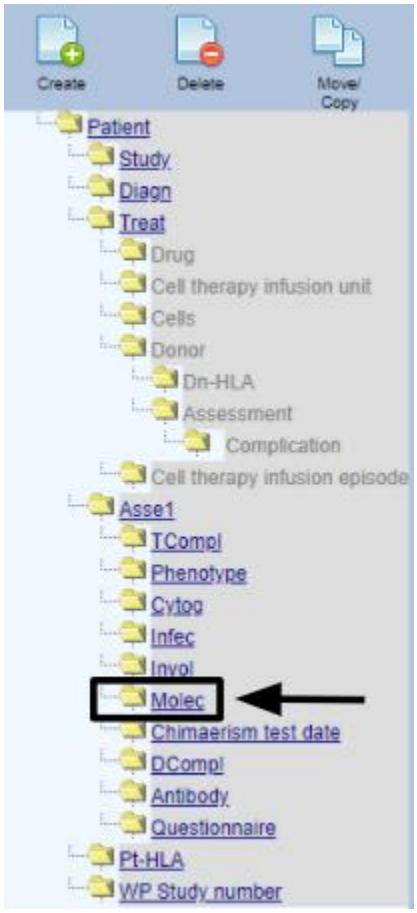


Cytogenetics	value	label
CIC	8888	8888
Patient	1	1
Assessment date	2000/01/01 00:00	2000/01/01 {exact}
Cytogenetics	164	myc rearrangement
Cytogenetics		
Chromosomal aberrations		
Abnormality present or absent		
Describe the abnormalities		
FISH analysis		
New record creation		
Index code for new abnormalities		

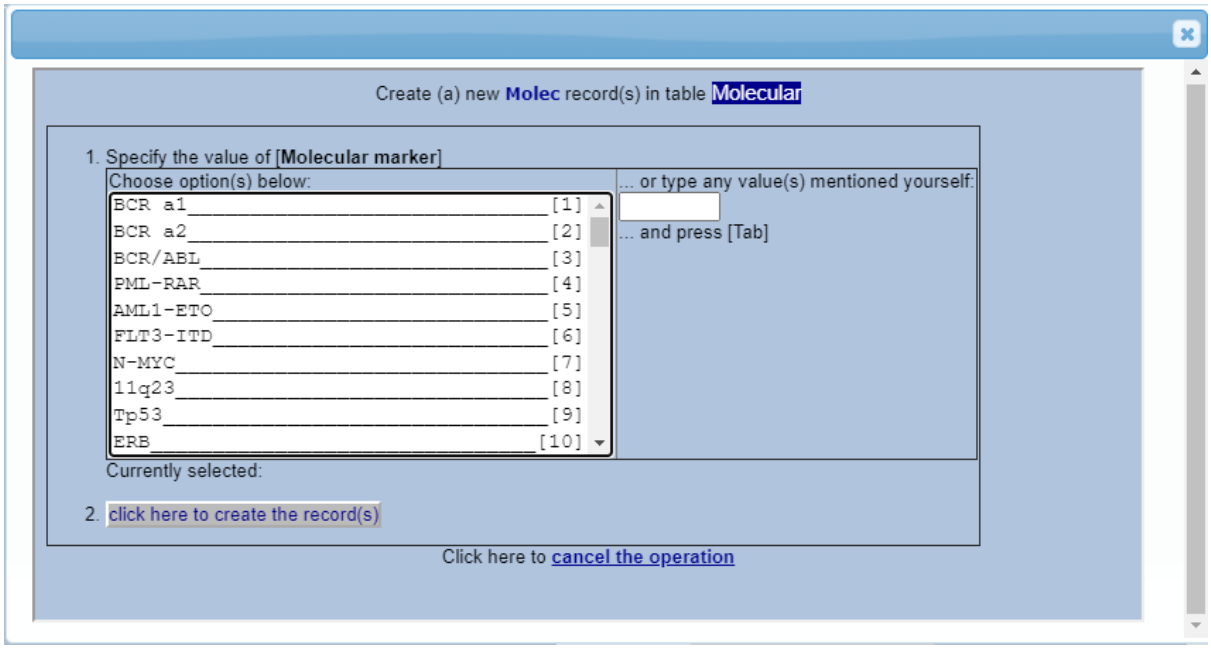
The only thing that needs to be entered is the first item, 'Abnormality present or absent'. Except for when you chose 'Other abnormality' or 'Full Karyotype', then you also need to fill in 'Describe the abnormalities'.
As many cytogenetic abnormalities as necessary can be added.

Molecular markers

After completing step 1 and 2 ,again select the diagnosis assessment. Click ‘Create’ in the menu above the patient history: choose ‘Molec’ from the list below ‘Assessment’.



A popup will appear in the screen, where all molecular markers that can be entered into ProMISe are listed:



To quickly get to the marker you are looking for, type in the first letter. Press that letter again to get to the right option. You can also type in the number in the box on the right side if you know the number of the marker. Common markers for lymphoma and B-cell ALL are summarised in the table below.

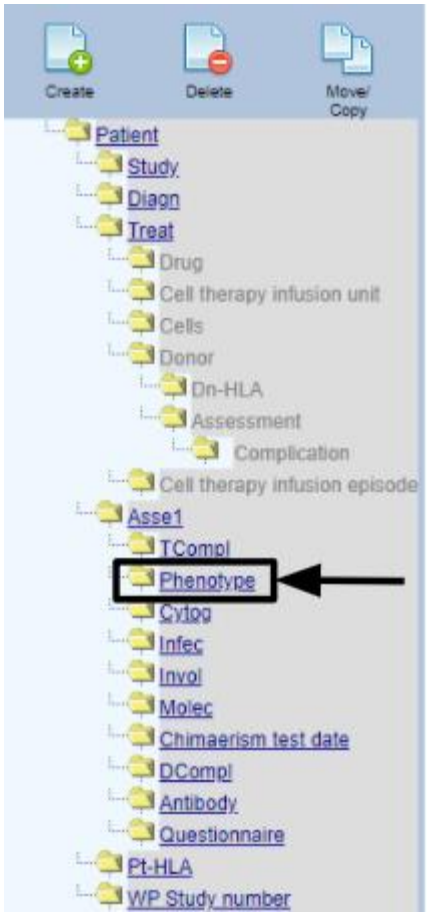
	Marker	**ProMISe Code**
DLBCL	myc	42
	BCL-2 rearrangement	43
	BCL-6 rearrangement	44
B-cell ALL	BCR-ABL	3
	MLL-rearrangement/mutation	100
	AFF1(AF4)-MLL	35
	MLLT1(ENL)-MLL	25
	MLLT3(AF9)-MLL	22
	TEL(ETV6)-AML1(RUNX1)	36
	IL3-IGH	37
	TCF3-PBX1	38
	IKZF1 (IKAROS)	39
	NOTCH1 & FBXW7	40

The only thing that needs to be entered is the first item, Molecular marker present or absent'. Except for when you chose 'Other', then you also need to fill in 'Other molecular marker, specify'.

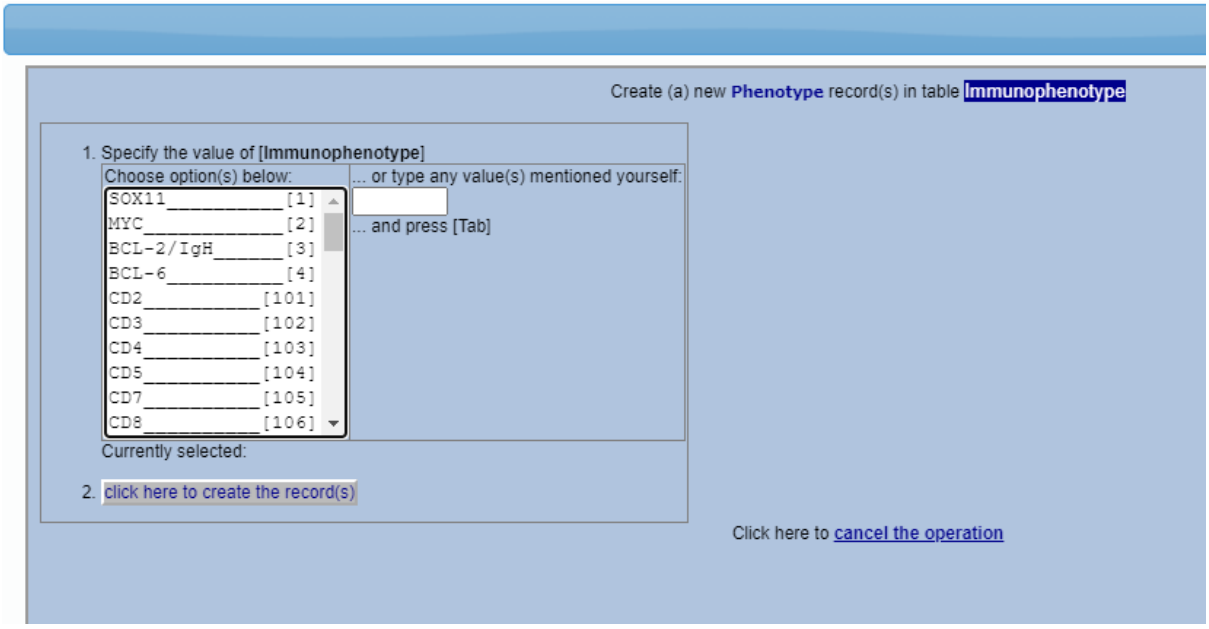
Molecular	value	label
CIC	8888	8888
Patient	1	1
Assessment date	2000/01/01 00:00	2000/01/01 {exact}
Molecular marker	100	MLL rearrangement/mutation, any
Molecular biology		
Molecular markers		
Molecular marker present or absent?		
Other molecular marker, specify		
New record creation		
Index code for new marker		

As many molecular markers as necessary can be added.

After completing step 1 and 2 ,again select the diagnosis assessment. Click ‘Create’ in the menu above the patient history: choose ‘Phenotype’ from the list below ‘Assessment’.



A popup will appear in the screen, where all immunophenotypes that can be entered into ProMISe are listed:



To quickly get to the phenotype you are looking for, type in the first letter. Press that letter again to get to the right option. You can also type in the number in the box on the right side if you know the number of the phenotype. Common phenotypes for lymphoma are summarised in the table below.

	Phenotype	**ProMISe Code**
DLBCL	MYC	2
	BCL-2 rearrangement	3
	BCL-6 rearrangement	4

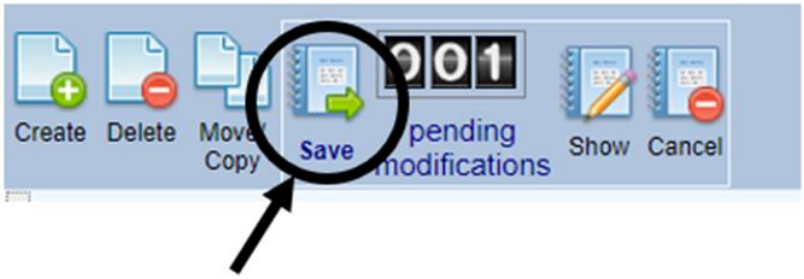
The only thing that needs to be entered is the first item, 'Immunophenotype present or absent'. Except for when you chose 'Other', then you also need to fill in 'Other immunophenotype, specify'.

Phenotype		
Phenotype		
Immunophenotype present or absent		
Other immunophenotype: specify		
% of this phenotype		
New record creation		
Index code for new phenotype		

As many phenotypes as necessary can be added.

Finishing

After you have added all the necessary information about cytogenetic abnormalities, molecular markers and/or the immunophenotype, the patient record can be saved. Click 'Save' next to the modifications counter above the patient record.

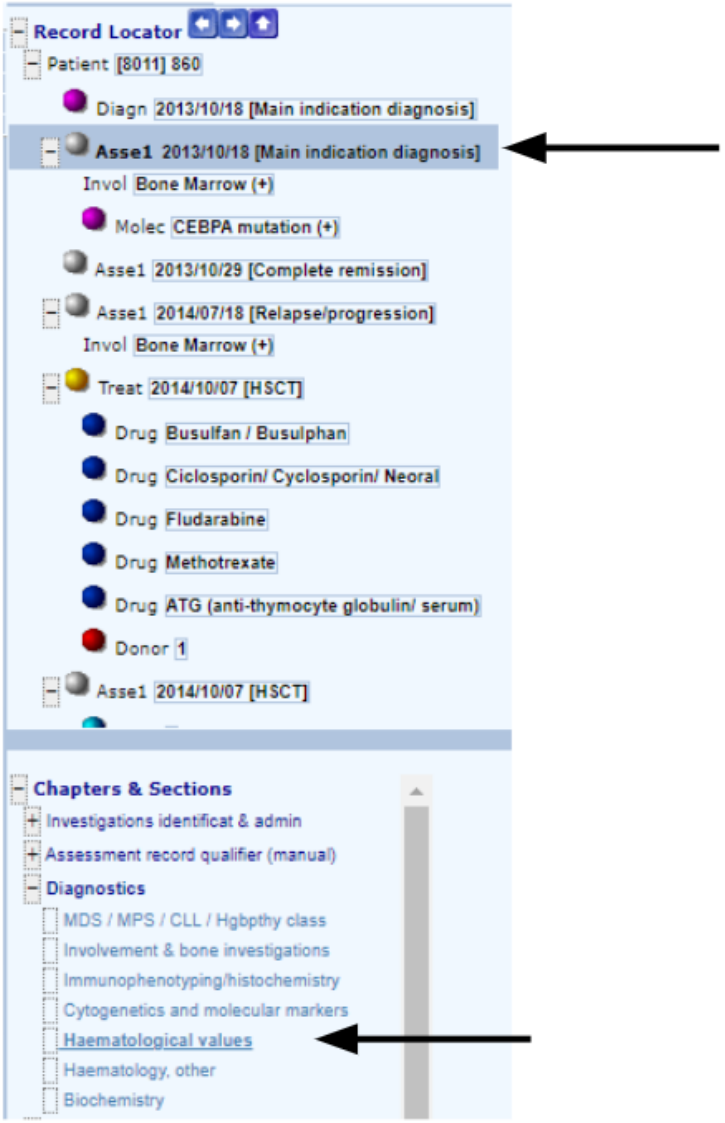


After the information has been entered and the record has been saved, turn the dynamic item filter back on by clicking on the paper with the binoculars again:

The number next to the binoculars will go back from 0 to 80 (depending on the table that is opened). The dynamic item filter is now turned on. This is the final step.

Entering the white blood cell count at diagnosis

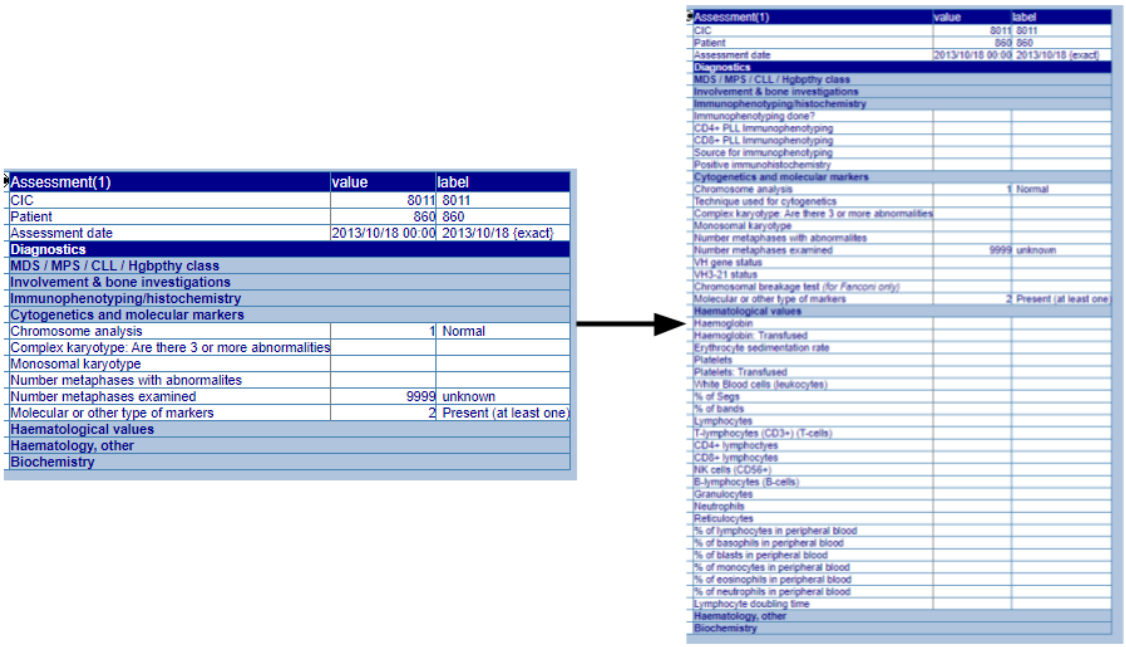
Step 1: Turning off the Dynamic Item Filter
Go to the Diagnostics chapter of the Main indication diagnosis assessment. Continue to the 'Haematological values' section:



At the top of the screen, in the menu where the 'Exit' button is, you see an icon of a sheet of paper with binoculars:

Click this. It will turn off the Dynamic item Filter, which makes all items in ProMISe visible. The small number will change from 80 to 0.

You will notice the following expansion of the ‘Haematological values’ chapter:



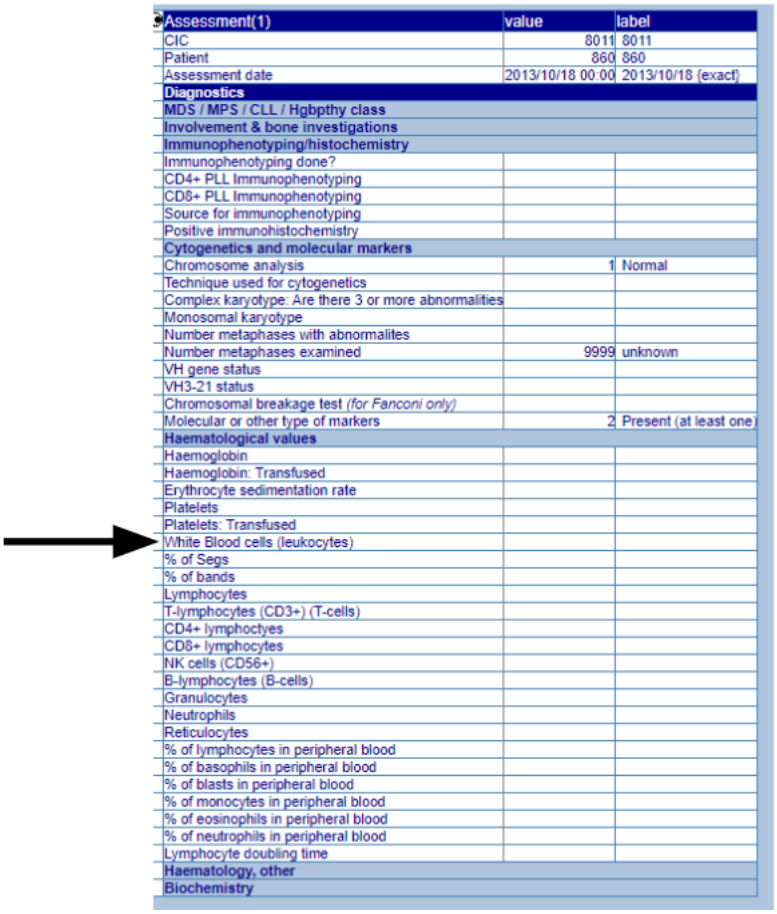
Assessment(1)	value	label
CIC	8011	8011
Patient	860	860
Assessment date	2013/10/18 00:00	2013/10/18 (exact)
Diagnostics		
MDS / MPS / CLL / Hgbpthy class		
Involvement & bone investigations		
Immunophenotyping/histochemistry		
Cytogenetics and molecular markers		
Chromosome analysis	1	Normal
Complex karyotype: Are there 3 or more abnormalities		
Monosomal karyotype		
Number metaphases with abnormalites		
Number metaphases examined	9999	unknown
Molecular or other type of markers	2	Present (at least one)
Haematological values		
Haematology, other		
Biochemistry		

Assessment(1)	value	label
CIC	8011	8011
Patient	860	860
Assessment date	2013/10/18 00:00	2013/10/18 (exact)
Diagnostics		
MDS / MPS / CLL / Hgbpthy class		
Involvement & bone investigations		
Immunophenotyping/histochemistry		
Immunophenotyping done?		
CD4+ PLL Immunophenotyping		
CD8+ PLL Immunophenotyping		
Source for immunophenotyping		
Positive immunohistochemistry		
Cytogenetics and molecular markers		
Chromosome analysis	1	Normal
Technique used for cytogenetics		
Complex karyotype: Are there 3 or more abnormalities		
Monosomal karyotype		
Number metaphases with abnormalites		
Number metaphases examined	9999	unknown
VH gene status		
VH3-21 status		
Chromosomal breakage test *(for Fanconi only)*		
Molecular or other type of markers	2	Present (at least one)
Haematological values		
Haemoglobin		
Haemoglobin: Transfused		
Erythrocyte sedimentation rate		
Platelets		
Platelets: Transfused		
White Blood cells (leukocytes)		
% of Segs		
% of bands		
Lymphocytes		
T-lymphocytes (CD3+) (T-cells)		
CD4+ lymphoctyes		
CD8+ lymphocytes		
NK cells (CD56+)		
B-lymphocytes (B-cells)		
Granulocytes		
Neutrophils		
Reticulocytes		
% of lymphocytes in peripheral blood		
% of basophils in peripheral blood		
% of blasts in peripheral blood		
% of monocytes in peripheral blood		
% of eosinophils in peripheral blood		
% of neutrophils in peripheral blood		
Lymphocyte doubling time		
Haematology, other		
Biochemistry		

Before **After**

Step 2: entering the relevant data

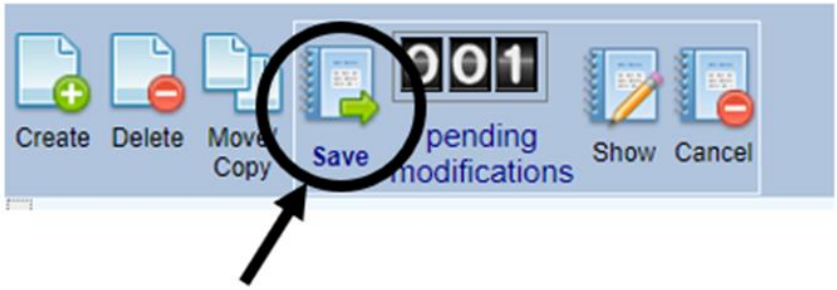
Not all of the items that were added to the table are relevant. In the image below, only the question that needs to be answered is the one indicated with an arrow. The question is ‘White blood cells (leukocytes)’:



Assessment(1)	value	label
CIC	8011	8011
Patient	860	860
Assessment date	2013/10/18 00:00	2013/10/18 (exact)
Diagnostics		
MDS / MPS / CLL / Hgbpthy class		
Involvement & bone investigations		
Immunophenotyping/histochemistry		
Immunophenotyping done?		
CD4+ PLL Immunophenotyping		
CD8+ PLL Immunophenotyping		
Source for immunophenotyping		
Positive immunohistochemistry		
Cytogenetics and molecular markers		
Chromosome analysis	1	Normal
Technique used for cytogenetics		
Complex karyotype: Are there 3 or more abnormalities		
Monosomal karyotype		
Number metaphases with abnormalites		
Number metaphases examined	9999	unknown
VH gene status		
VH3-21 status		
Chromosomal breakage test *(for Fanconi only)*		
Molecular or other type of markers	2	Present (at least one)
Haematological values		
Haemoglobin		
Haemoglobin: Transfused		
Erythrocyte sedimentation rate		
Platelets		
Platelets: Transfused		
White Blood cells (leukocytes)		
% of Segs		
% of bands		
Lymphocytes		
T-lymphocytes (CD3+) (T-cells)		
CD4+ lymphoctyes		
CD8+ lymphocytes		
NK cells (CD56+)		
B-lymphocytes (B-cells)		
Granulocytes		
Neutrophils		
Reticulocytes		
% of lymphocytes in peripheral blood		
% of basophils in peripheral blood		
% of blasts in peripheral blood		
% of monocytes in peripheral blood		
% of eosinophils in peripheral blood		
% of neutrophils in peripheral blood		
Lymphocyte doubling time		
Haematology, other		
Biochemistry		

Finishing

After the information about the white blood cell count at diagnosis has been added, the patient record can be saved. Click ‘Save’ next to the modifications counter above the patient record.



After the information has been entered and the record has been saved, turn the dynamic item filter back on by clicking on the paper with the binoculars again:

The number next to the binoculars will go back from 0 to 80 (depending on the table that is opened). The dynamic item filter is now turned on. This is the final step.

Entering IPI and KI-67

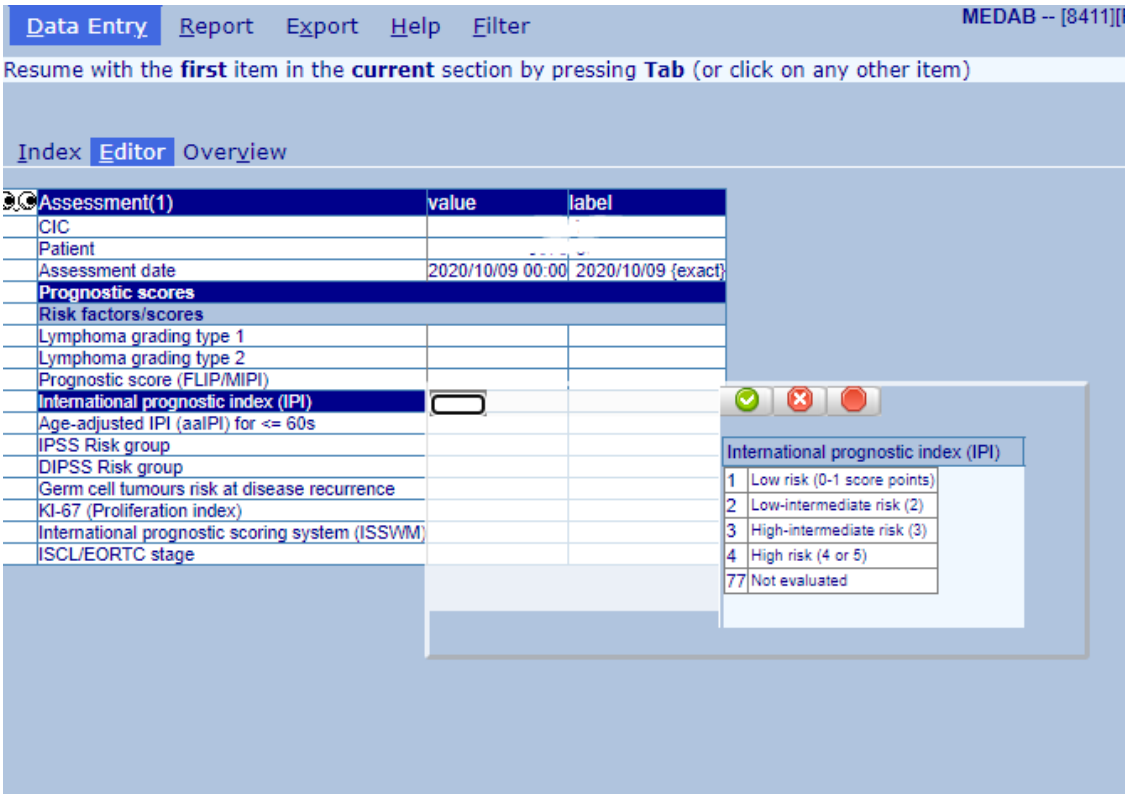
[1] Turning off the Dynamic Item Filter
Go to the Diagnostics chapter of the Main indication diagnosis assessment. At the top of the screen, in the menu where the ‘Exit’ button is, you see an icon of a sheet of paper with binoculars:

Click this. It will turn off the Dynamic item Filter, which makes all items in ProMISe visible. Make sure the number next to the binoculars is ‘0’.

Entering International prognostic index (IPI)

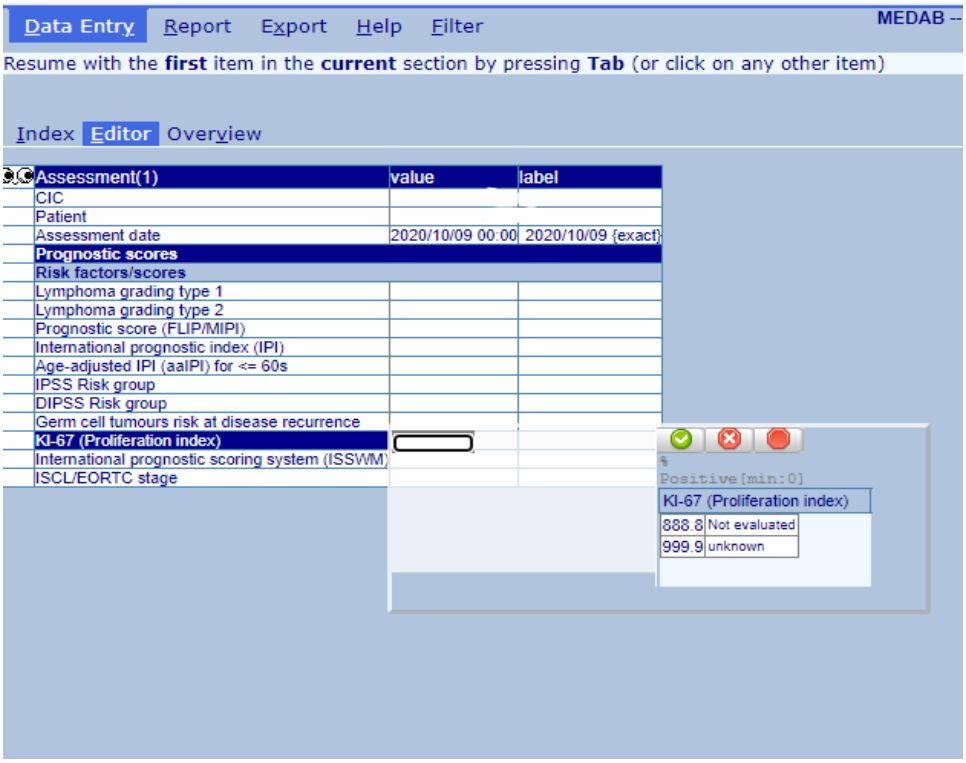
Go to the **‘Assessment’** of the **main indication diagnosis** go to **‘Prognostic scores’ -> ‘Risk index’**

The following screen will appear. Complete the **'International Prognostic Index'**



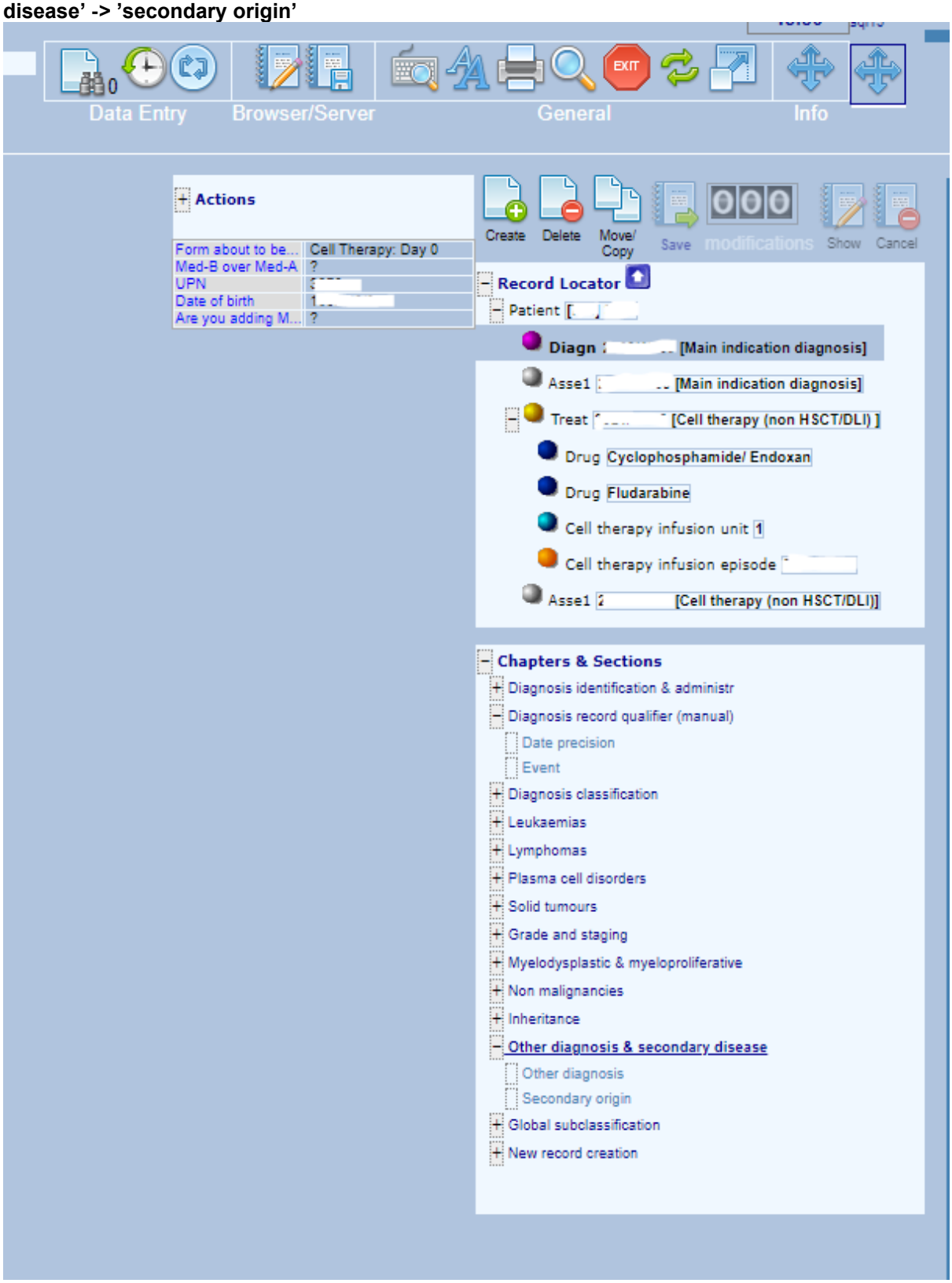
Entering KI-67 (Proliferation index)

In the same screen as above complete the **'KI-67 (Proliferation index)'**. Add a percentage or otherwise unknown/not evaluated.

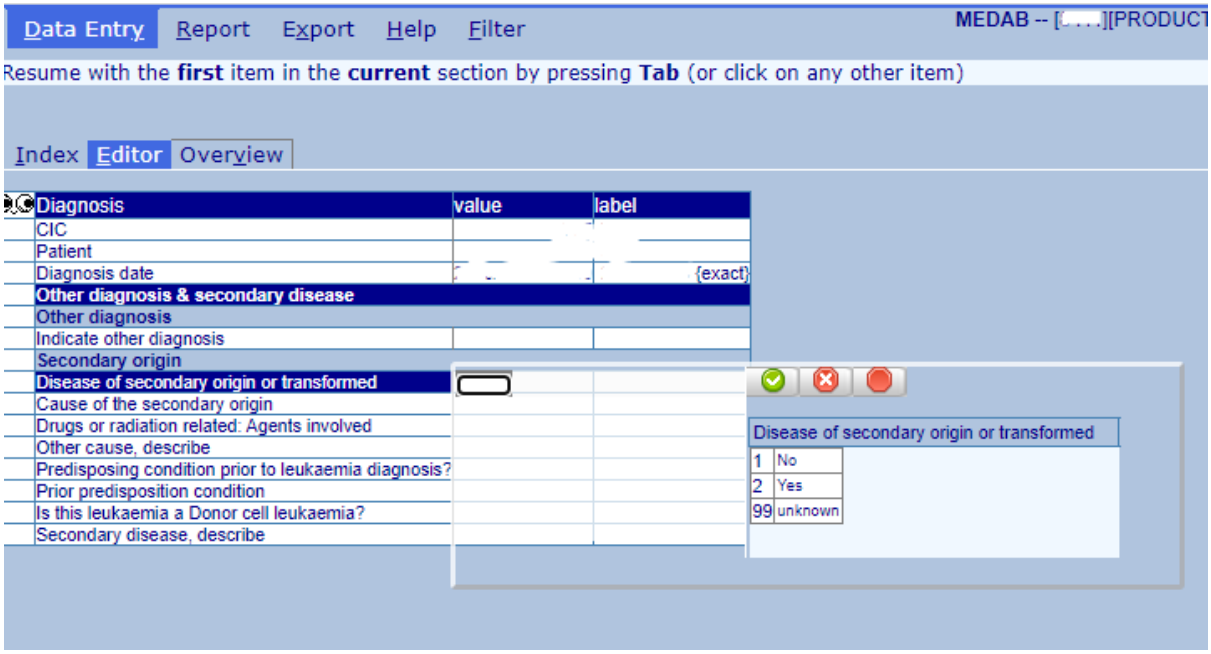


Entering if disease was of secondary origin or transformed

Go to the **'Diagn'** of the **main indication diagnosis** go to **'Other diagnosis and secondary disease' -> 'secondary origin'**



The following screen will appear:



Complete **Disease of secondary origin or transformed**

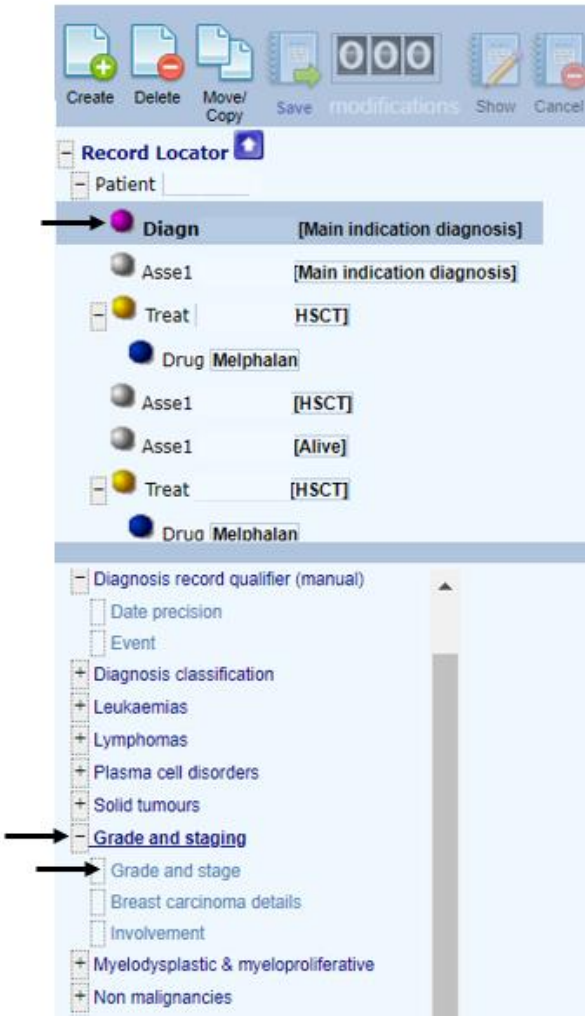
Note: In case the disease is of secondary origin or transformed from another disease, please enter this disease also in the Registry as a (non-indication) **diagnosis**.

Entering MM Grading

[1] Turning off the Dynamic Item Filter
Go to the Diagnostics chapter of the Main indication diagnosis assessment. At the top of the screen, in the menu where the 'Exit' button is, you see an icon of a sheet of paper with binoculars:

Click this. It will turn off the Dynamic item Filter, which makes all items in ProMISe visible. Make sure the number next to the binoculars is '0'.

Entering grade and staging for Multiple Myeloma patients
Go to the Main indication diagnosis record. Open the section Grade and staging



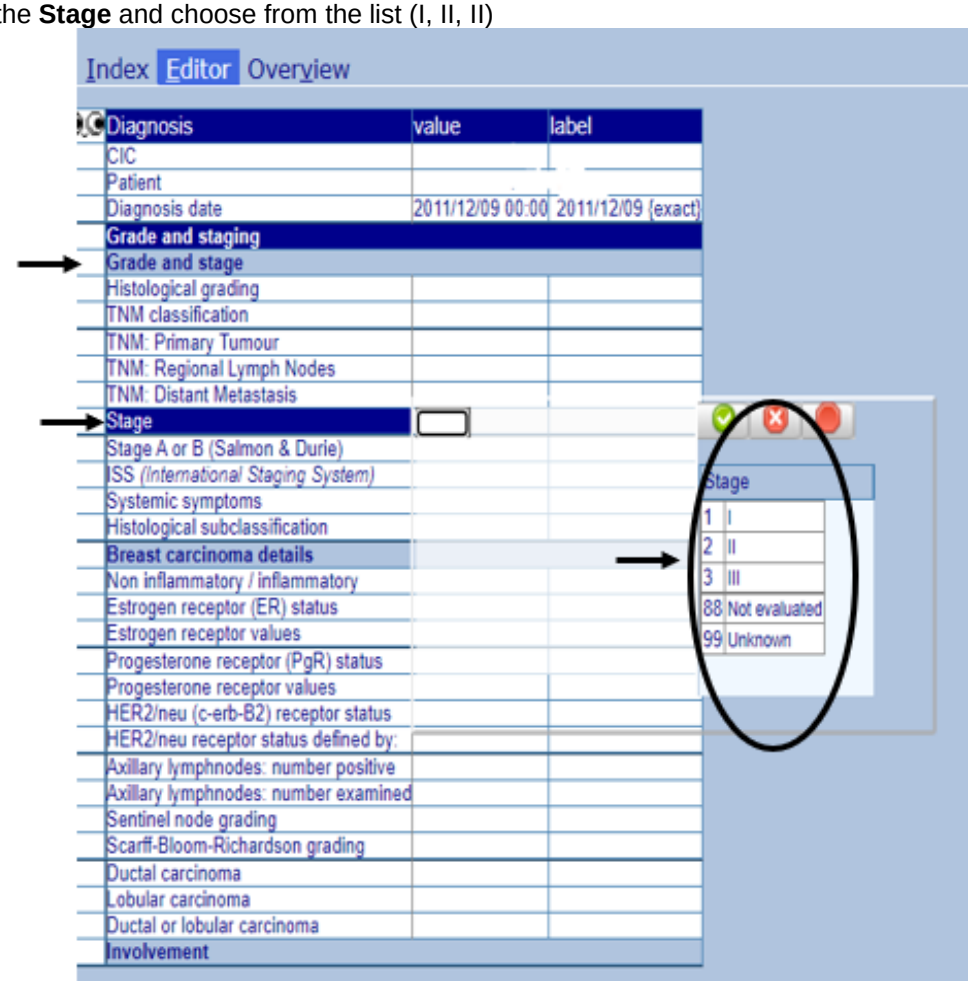
The following screen will appear.
For entering the Salmon and Durie stage please complete both the Stage and the number:

Staging at diagnosis:

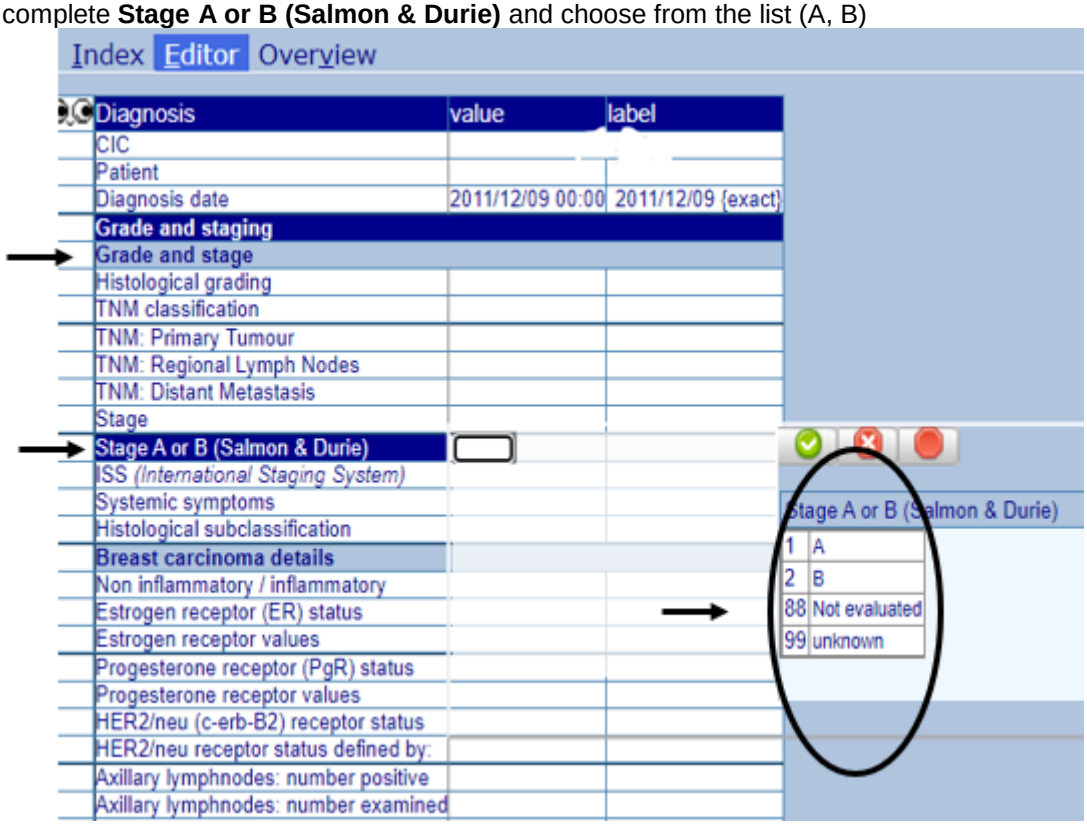
Salmon & Durie staging for multiple myeloma:
(Please tick both columns.)

Stage	Symptoms
☐ I	☐ A
☐ II	☐ B
☐ II	

Complete the **Stage** and choose from the list (I, II, II)



Then complete **Stage A or B (Salmon & Durie)** and choose from the list (A, B)

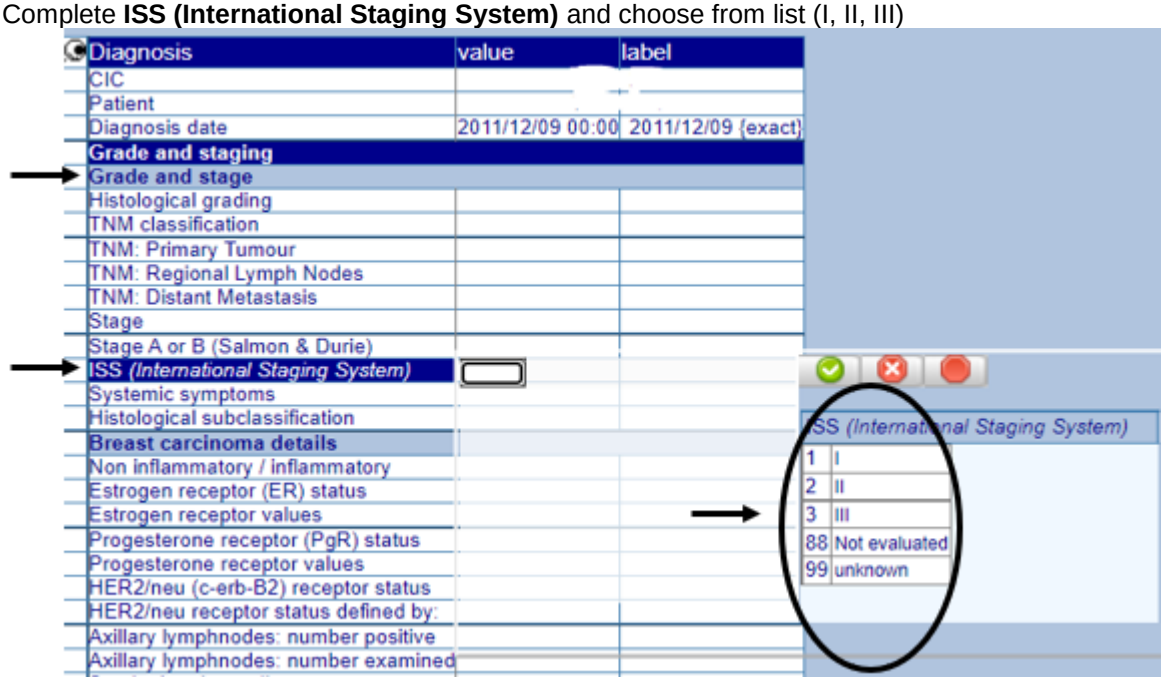


For the ISS:

ISS STAGE:

Stage	β2-µglob (mg/L)	Albumin (g/L)
☐ I	< 3.5	> 35
☐ II	< 3.5 OR 3.5 ≤ 5.5	< 35 any
☐ III	> 5.5	any

Complete **ISS (International Staging System)** and choose from list (I, II, III)



Entering non-graft treatments

[1] Turning off the Dynamic Item Filter

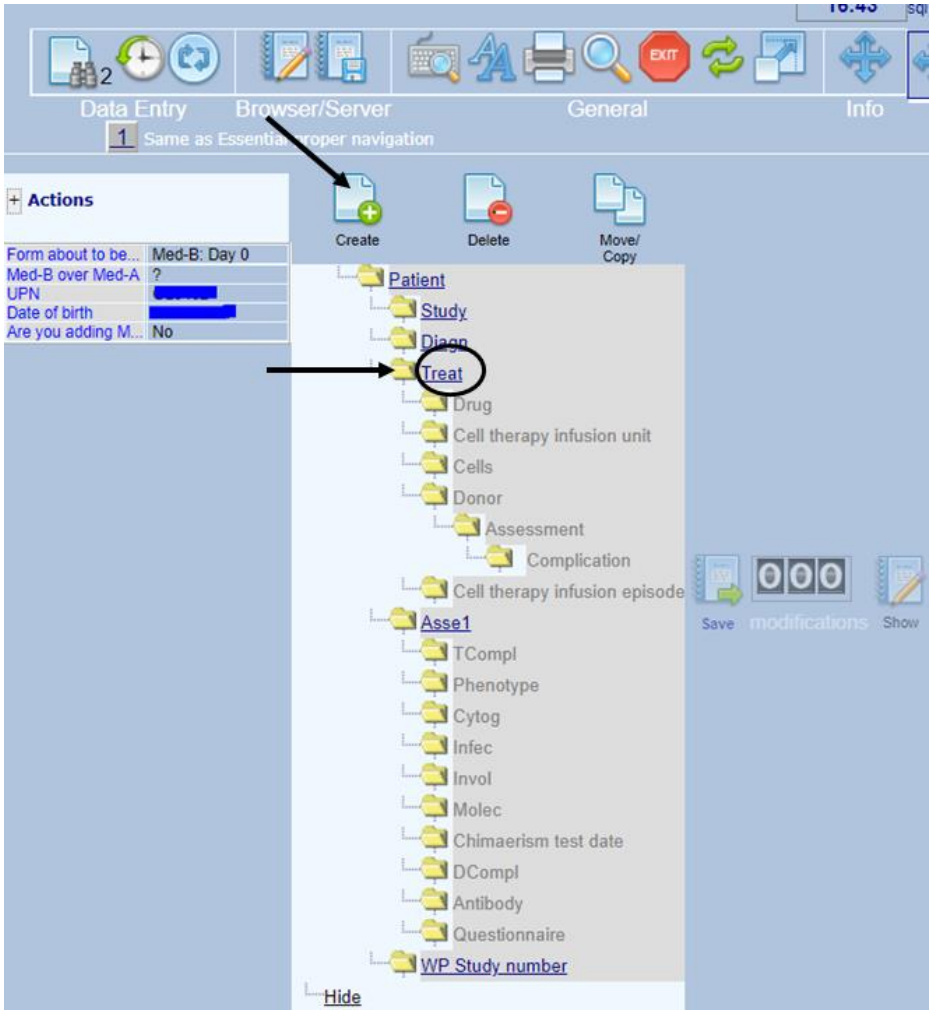
Go to the Diagnostics chapter of the Main indication diagnosis assessment. At the top of the screen, in the menu where the 'Exit' button is, you see an icon of a sheet of paper with binoculars:

Click this. It will turn off the Dynamic item Filter, which makes all items in ProMISe visible. Make sure the number next to the binoculars is '0'.

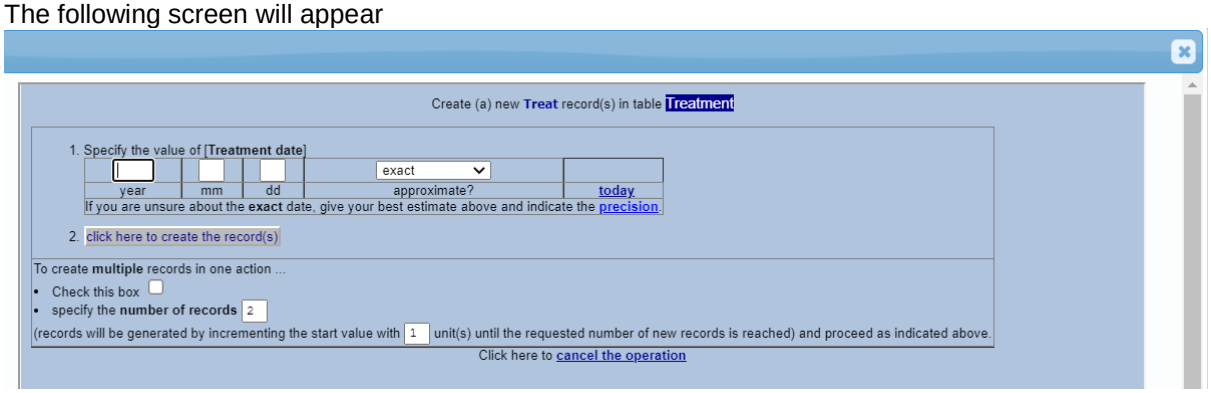
Entering pre-treatments

When the patient has had a previous non-graft treatment (e.g. chemo) for their Lymphoma, Leukaemia or Multiple Myeloma please enter these drug(s) and/or regimen(s) in Promise.

Press **Create** and then **Treat**

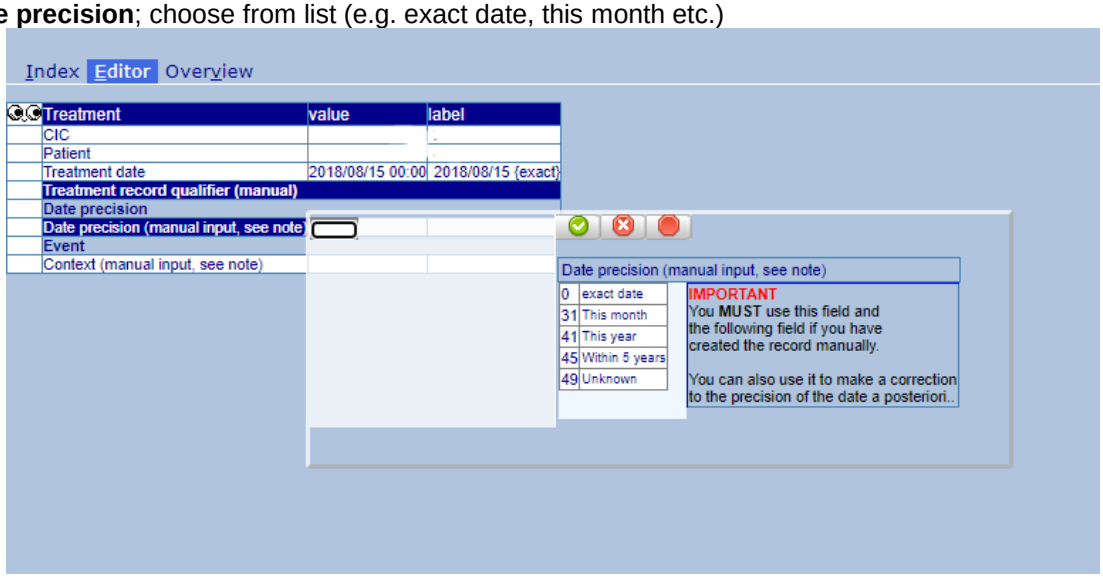


The following screen will appear

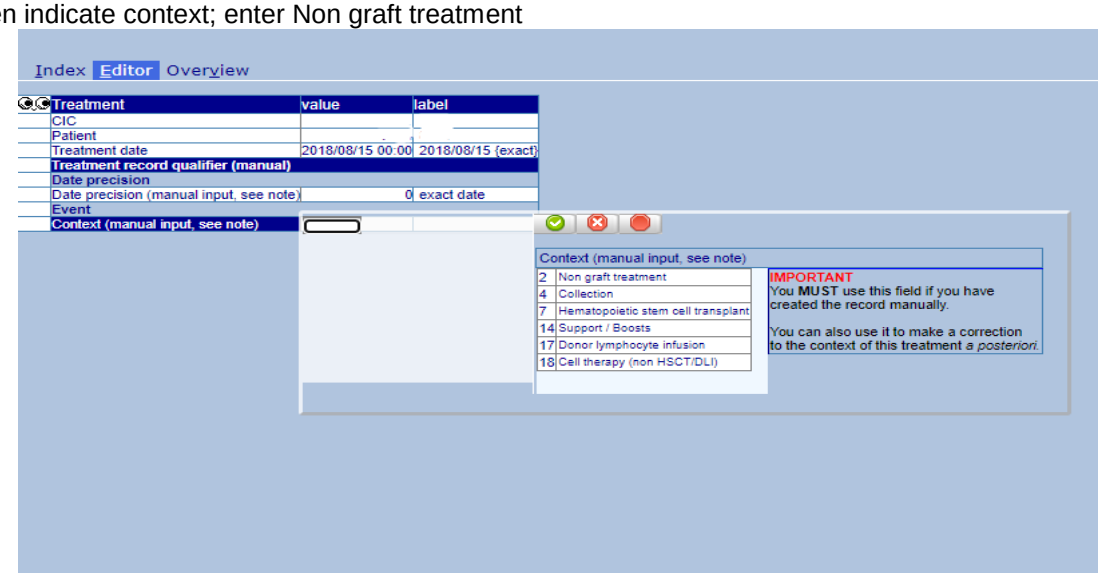


Enter start date of drug (regimen) given: year / month/ day and click on **click here to create record**

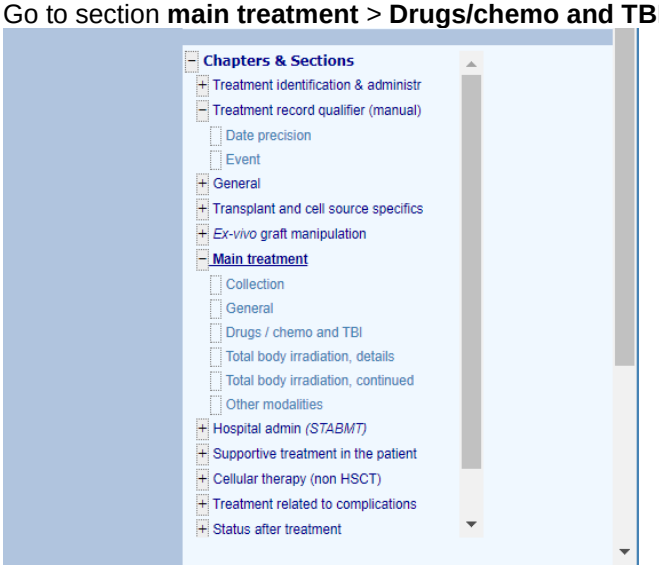
The following screen will appear.
Date precision; choose from list (e.g. exact date, this month etc.)



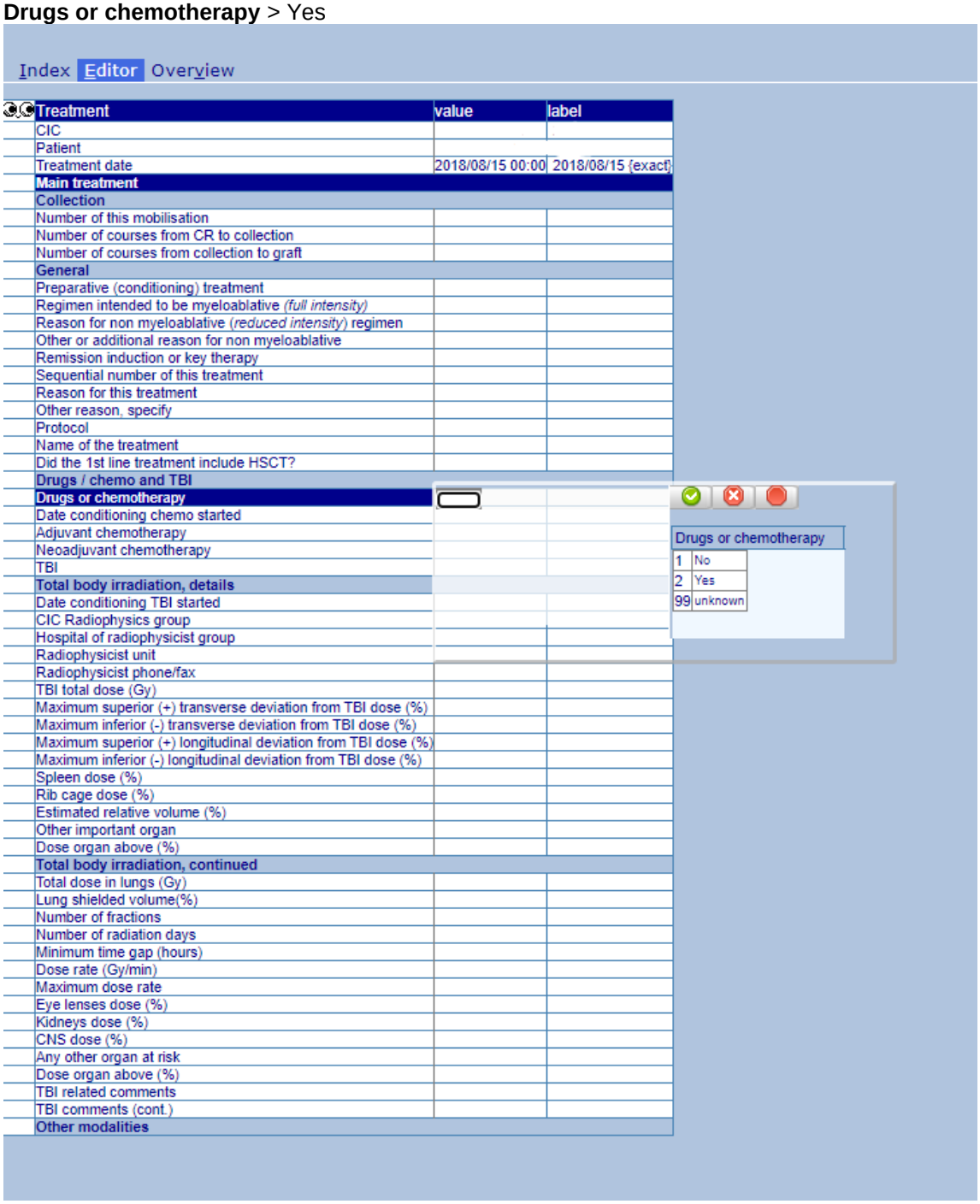
Then indicate context; enter Non graft treatment



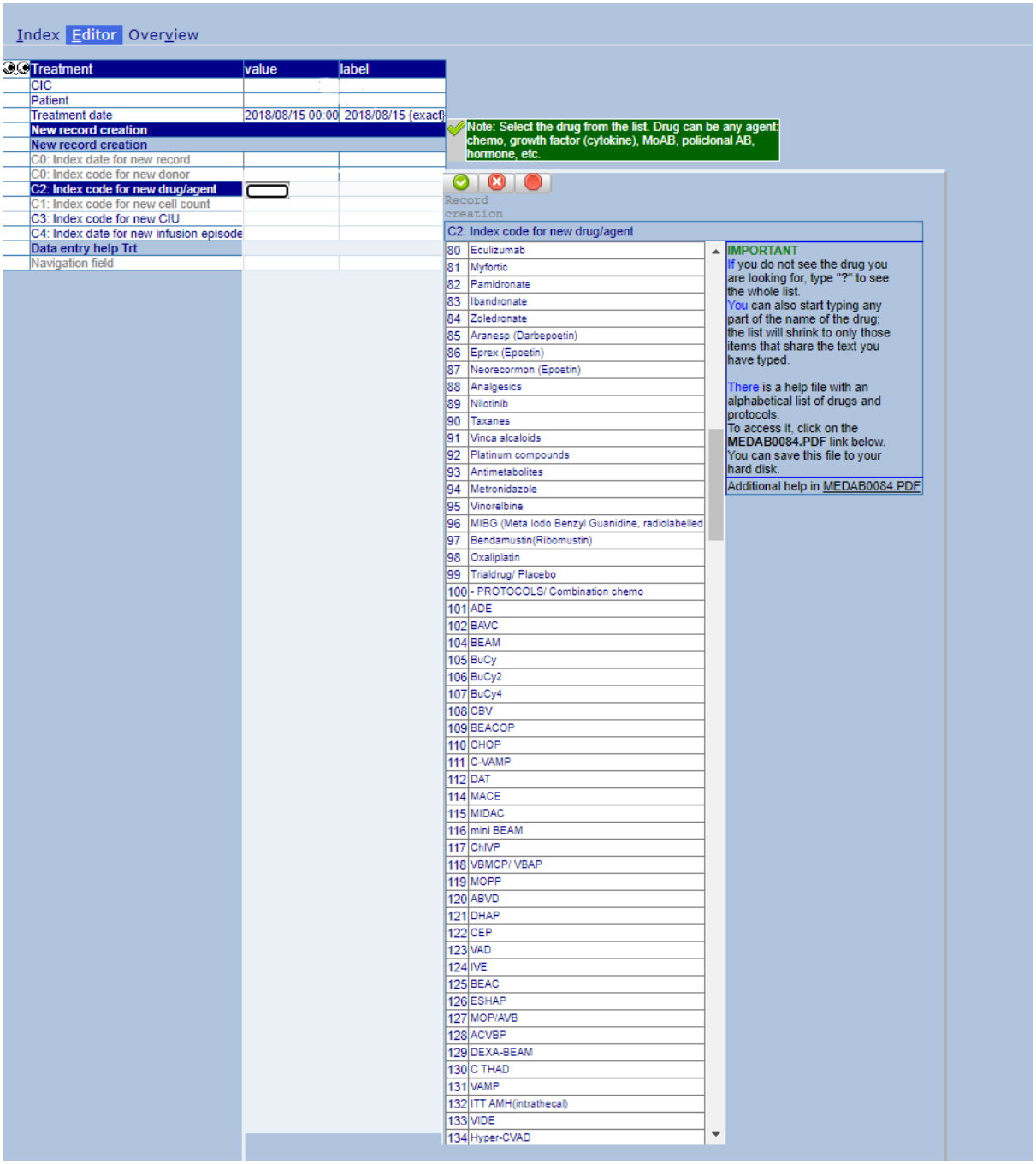
Go to section **main treatment** > **Drugs/chemo and TBI**



Drugs or chemotherapy > Yes



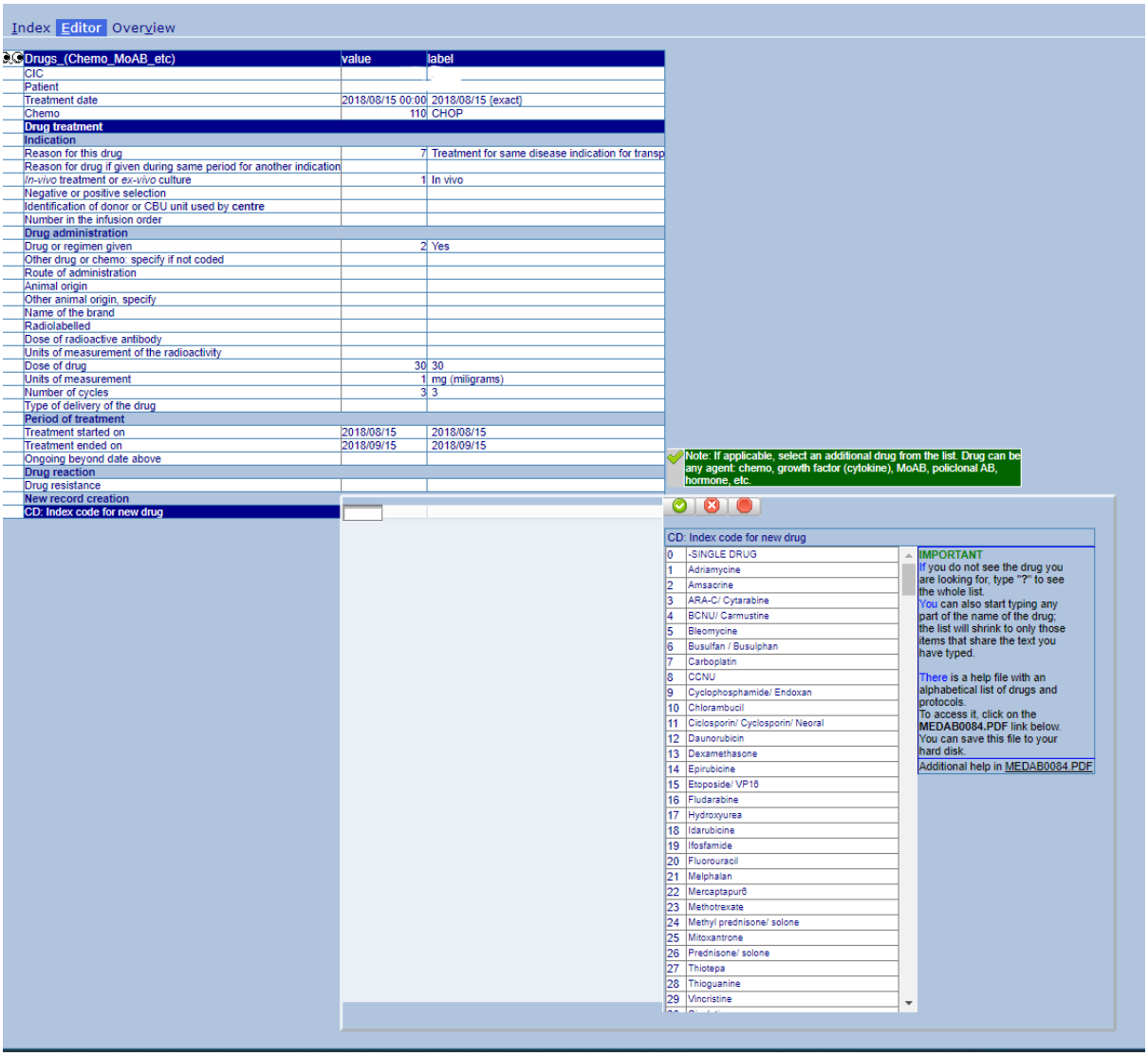
The following screen will appear. Select the drug or regimen from the list



When drug is created complete the following sections:

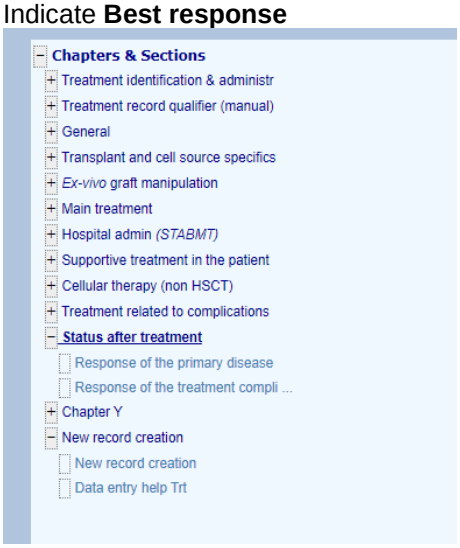
- Reason for this drug
- Dose
- Units
- Number of cycles
- Start date
- Stop date

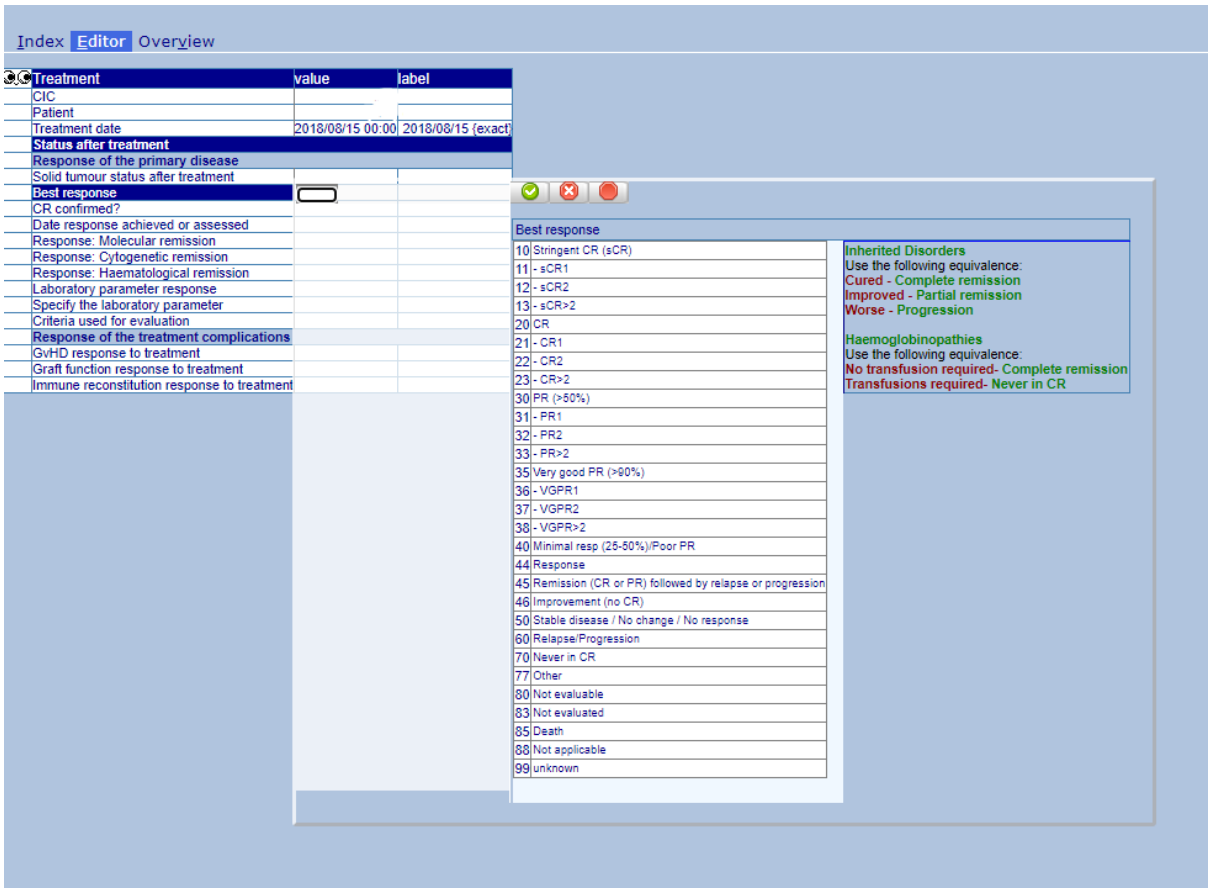
If another drug has been given as part of the line of treatment please enter new drug (1).
If no other drug is given please indicate No More [code 888]



Indicate best response for this treatment

Go to **status after treatment** > **response of the primary disease**
Indicate **Best response**





Day 0

Patient identification

Person responsible for filling in the form
Enter the name of the person who filled in the form. This can be the same person as who is entering the data into the registry database. If the form was printed out and filled in by someone else, report this person's name.

Date of this report
If data is being entered directly from the patient notes, the 'date of this report' is the date the data is being entered into the registry database. If the data is filled in on a paper form, the 'date of this report' is the date the form is filled in. This date will remain unchanged regardless of how much more data is added to the patient record in the future.

Previous therapies given before transplant/CT

Previous therapies refer to any treatment that is given for the indication (disease/complication) before the cellular therapy. Only therapies given for the diagnosis that is the main indication for cellular therapy should be reported. Please note that not only treatments before HSCT should be reported, but also treatments that are given between HSCT and cellular therapies

Has the information requested in this section been submitted with a previous HSCT/Cellular Therapy registration for this patient?
If the information on previous therapies has not been submitted yet, answer ‘no’ and continue with this section. If the information has been submitted, select ‘yes’ and continue with the Cellular Therapy section.

Was the patient treated before this cellular therapy procedure?
If the patient was not treated, select ‘no’ and continue with the next section of the form.
If the patient has been treated for the diagnosis that is the main indication for this cellular therapy, select ‘yes’, report the starting date and the sequential number of this treatment.

Chemotherapy/drugs given?
Indicate if the patient has been treated with chemotherapy or drugs in previous therapies. If this is not the case, select ‘no’ and skip the table with treatment lines.
If therapies were given, select ‘yes’ and provide the requested details in the table.

List all chemotherapy/drugs given during one line of treatment
All lines of chemotherapies and drugs that were given to the patient for the main indication diagnosis for cellular therapy should be listed in the table.

Drug/chemotherapy
Fill in the drug or chemotherapy per treatment line. In Castor, the same drug list as in ProMISe is available. If the applicable regimen (R-CHOP, R-DHAP, VRD, VBAP, VMCP, etc.) is available in the dropdown, the regimen should be selected. If the regimen is not available, report the regimen’s drugs individually.

Number of cycles
Report the number of drug or chemotherapy cycles that were given. Note: One ’line’ of chemotherapy usually consists of repeated or alternating cycles of drugs according to a certain schedule.

Date started
Report the date this line of treatment was started.

Date ended
Report the date this line of treatment ended.

Radiotherapy
Indicate if the patient underwent radiotherapy in the past.

Radiotherapy start and end date
If the patient received radiotherapy, provide the start and end date of the radiotherapy.

Other treatment
If the patient received any other kind of previous treatments that have not been registered yet, select ‘yes’ and specify the treatment.

Response to this line of treatment
Report the best response to each line of previous treatment using the section relevant for the main diagnosis the treatment was administered for. Copy the section as many times as necessary.

Patient status at cellular therapy

Performance score: type used
Indicate if the performance score at cellular therapy was calculated using the Karnofsky, Lansky or Eastern Cooperative Oncology Group (ECOG) scale.

Performance score: score
Select the score that reflects the performance status at cellular therapy.
It is not necessary to fill in both the Karnofsky/Lansky and ECOG score, one of them is sufficient.
Descriptions of the scores can be found in Appendix B.

Weight at time of cellular therapy
Report the patient's weight in kilograms. The value should represent the weight at the start of the cellular therapy.

Height at time of cellular therapy
Report the patient's height in centimetres. The value should represent the height at the start of the cellular therapy.

B-cell aplasia at the time of cellular therapy?
Report if B-cell aplasia (NCBI: "A condition characterised by extremely low B-cell counts." (1)) was present or absent at the time the infusion took place.

Percentage of B-cells
If B-cell aplasia was present, report the percentage of B-cells.

Disease status at cellular therapy
Select the appropriate disease status the patient is being treated for. For definitions of the different statuses, see the 'Definitions for Disease Status and Response by Disease' documents under 'Clinical Manuals & Reference Documents' on the EBMT data collection webpage.

Comorbidity index

Was there any clinically significant co-existing disease or organ impairment as listed below at the time of patient assessment prior to the preparative regimen?
Review the comorbidity index table on the form, and confirm if any of the listed items are present or not. If at least one comorbidity is present, the entire table needs to be completed.
The answers should represent the situation at the start of the preparative regimen (conditioning/lymphodepleting conditioning regimens) unless otherwise stated in the definitions below.
Ensure the answer 'Yes' is only given if the comorbid condition fits the definition found in the form itself.

Were there any additional major clinical abnormalities not listed above and present prior to the preparative regimen?
Specify other additional major clinical abnormalities present prior to preparative treatment not listed in the table above and present prior to the preparative regimen. Report only clinically relevant abnormalities.

Cellular therapy treatment

Was the cellular product infused during this treatment/procedure?
Indicate if the cells that were collected for manufacturing were infused to the patient. if yes, provide the 'Date of the first infusion'. If no infusion took place, provide the 'Reason why the treatment did not take place' by selecting the appropriate answer option

Reason why the treatment did not take place
If the cells were not infused, select the appropriate reason. If none of the answers are applicable, select 'other' and specify the reason. Continue with 'Date of last assessment'.

Date of the first infusion
If the infusion took place, report the date of the first cell infusion.

Date of last assessment
If the infusion did not take place, report the date the patient was last seen by the physician.

Cellular therapy infusion unit(s)

Was there more than one cell infusion unit administered during this treatment?
If according to the flowchart in Appendix A, more than one unit was infused, answer "Yes" here. Copy and fill in the 'Cellular therapy Infusion Unit – Description and Collection' section for each cell infusion unit that was administered.

Cellular therapy infusion units: description

Name of the manufacturer
Select the name of the facility which manufactured the infusion product (pharmaceutical or biotech company, cell processing laboratory or another site). If the manufacturer's name is not on the list, select 'other' and specify the manufacturer.

Name of the product
Select the product name. If the product name is not on the list, select 'other' and specify the product name.

Unique ID of the product
If a unique identification code is available (e.g. serial number), add this here.

Batch number
Report the batch number of the cell infusion unit, if applicable.

Identification of the cell infusion unit given by the centre
Report the cell infusion unit identification that was assigned to the unit by the treating centre. This information is mandatory if more than one cell infusion unit has been used in the same treatment. If there is only one cell infusion unit, enter '1' or any other identification codes the centre used to identify this specific cell infusion unit.

Was the product consistent with specification?
Indicate if the product was consistent with the specifications. Products that are out of specification did not meet the acceptance criteria set by the manufacturer. Consult the physician who approved the product for infusion in case of doubt.

Was the generated cellular product cryopreserved prior to infusion?
Select ‘yes’ if the cellular product has been cryopreserved (frozen at very low temperatures) prior to infusion at any time point between collection and infusion. If this was not the case, select ‘no’.

Cellular therapy infusion unit - manipulation

This section only needs to be filled in for non-commercial products. If the infused product is a commercial product, continue at ‘Therapy and Cell Infusion’.

Ex vivo manipulation of the product contained in the cellular therapy infusion unit
Indicate if the cells contained in the infusion unit were manipulated in a laboratory. E.g. selected, modified or genetically engineered.

Processing/Manufacturing facility
Indicate where the cell manipulation took place.

Gene manipulation
Select ‘no’ if the product was not genetically manipulated. If the product was genetically manipulated, select ‘yes’ and continue with the subsequent questions on manipulation.

Gene transfer
Indicate if gene transfer was used for gene manipulation.
This is a procedure by which newly acquired DNA is incorporated into the genome of the cell through either recombination or insertion.

Vector
If gene transfer was used, select the vector. If another vector was used, specify the type of vector used. Non-integrating vectors, including RNA electroporation, should also be listed here.

Transgene
If genes were inserted, tick the transgene and specify all targets. If TCR was used, specify the HLA element too. If another transgene was used than the ones listed, specify the type and name.

Gene editing
Indicate if the cells underwent a type of genetic engineering in which DNA is inserted or removed from a genome using artificially engineered nucleases. If gene editing was done, indicate the manipulated gene.

Manipulated gene
Select what genes were manipulated. If another gene was manipulated than the ones listed, specify the gene.

Other gene manipulation
Indicate if a different genetic manipulation not previously listed was used. If yes, specify the manipulation.

Recognition of a specific target/antigen
If the aim of the manipulation was the recognition of a specific target or antigen, tick all applicable targets listed. If it was another virus, fungus, or target, specify. If the target was a tumour or cancer antigen(s), specify all details.

Cell types
Select the cell types that were infused to the patient after apheresis.

Expansion
Indicate if expansion was performed. This is a procedure meant to increase the number of collected cells in the laboratory before infusion.

Activation
Indicate if activation was used. This procedure aims to induce new biological activity(ies) on treated cells.

Induced differentiation
Indicate if the cells were induced to differentiate into different cell types by contact with other cells or stimulation by differentiation inducing factors.

Therapy and cell infusion(s)

Chronological number of cellular therapy for this patient
Indicate the sequential cycle of this cellular therapy. HSCTs or DLIs should not be counted when defining the chronological number of cellular therapy.

Note: if the infusions are given more than 100 days apart, or if the indication for the cellular therapy has changed, the therapy should be considered a new treatment.

If this is not the first Cellular therapy treatment for this patient and the previous Cellular Therapy treatment cannot be registered, please indicate:

Same package/product as for the previous cellular therapy?
Indicate if the same cellular therapy infusion product is being used as for the previous treatment.

Date of last cellular therapy before this one
Report the start date of the most recent cellular therapy treatment.

Type of last cellular therapy before this one
Select the type of cellular therapy.

If the previous therapy was an allogeneic cellular therapy, answer the question about the donor.

Was the same donor used for all prior and current cellular therapy?
If the previous therapy was an allograft, indicate if the same donor has been used for all previous and current cellular therapies.

Was the last cellular therapy performed at another institution?
Report if the patient has received a treatment in another institution. If yes, fill in the subsequent questions.

CIC, name of institution and city
Indicate the other centre's CIC if known. If not known, provide the name of the institution and the city in which the centre is located.

Reason for the cellular therapy: treatment of a primary disease
If the therapy was given for the treatment of a primary disease, select the reason for cellular therapy.

Reason for the cellular therapy: complications:
If the therapy was given for the treatment of complications derived from a previous treatment, indicate if the treatment was related to:
- Graft versus host disease (GvHD)
- Graft function
- Immune reconstitution

Therapy & cell infusions preparative treatment

Did the patient receive preparative (lymphodepleting) treatment?
Indicate if the patient received lymphodepleting chemotherapy prior to the infusion of the cellular product.

In the event of the cellular therapy infusion unit being infused at the same time as an HSCT taking place, the HSCT conditioning/preparative treatment is not to be reported here. In these cases, the correct answer to the question Patient preparative treatment would be “No”.

If the patient received a lymphodepleting treatment, fill in the table.

Name of drug
Report all lymphodepleting drugs that the patient received in preparation for their cellular therapy. The same drug may have several different names depending on the country or product. Please consult the existing drug list (LIST OF DRUG NAMES & SYNONYMS) which can be found on the EBMT website: https://www.ebmt.org/ebmt/documents/med-ab-list-drug-names-and-synonyms
This document provides alternative names for many of the drugs in case the name cannot be found in the drop-down menu.

Important note: ‘Other’ should only be used if the drug or its synonym is not listed. In this case, the name of the drug should be given in full; do not use abbreviations.
If the patient received bridging therapy, this should be reported in ‘Previous therapies given before transplant/cellular therapy’.

Total prescribed cumulative dose
Indicate the total cumulative prescribed dose and the units in which the dose is given for each drug. Do not provide daily or weekly doses, but the final cumulative dose received by the time the regimen has ended.
For example, if the dose of a particular drug is 100 mg/m2 on days 1 and 2, then 100 mg/m2 x 2 days=200 mg/m2 and the dose to be entered should be 200 mg/m2.

Units
Select the units of the total prescribed cumulative dose. The units listed are those most commonly used. If the units used are different, try to convert the dose as necessary to one of the listed units.

Other type of treatment
Indicate here if any additional treatment was given, e.g.: radiotherapy, photopheresis or any other medical procedure.

Cell infusion episodes

Was there more than one cell infusion episode during this treatment or procedure?
If multiple cell infusions took place, answer “Yes” here. Copy and fill in the ‘Cell infusion episodes’-section for each cell infusion unit that was administered.

If two different cell infusion units are infused simultaneously or within a short interval (within hours), it is considered one cell infusion episode. If the same cell infusion unit is infused on two different days, it is considered two cell infusion episodes.

Number of infusion episodes
If multiple infusion episodes according to the definition above were part of the treatment, indicate the number of infusion episodes.

Cell infusion episode(s): description

Identification of the cell infusion unit given by the centre
If more than one cell infusion unit was administered, report the identification of the unit that was part of the infusion episode.

Date of cell infusion episode
Report the date of the first cellular therapy infusion of the treatment.
For patients receiving cellular therapy for a complication of HSCT, put the date of first cellular therapy treatment, not the date of HSCT.

Route of infusion
Indicate how the cells were infused to the patient.
If the route of infusion is not listed, select “Other route” and specify the infusion route.

Is the exact number of cells infused available?
If the exact number of cells that were infused is not available, select ‘no’. If the exact number is known, select ‘yes’ and fill in the subsequent questions.

Number of cells infused
If the number of cells infused was known, provide the total number of cells infused used during the infusion episode.

Units
If the number of cells infused was known, select the units for the number of cells that were infused.

Cell viability
Report the percentage of cell viability.

Combined /concomitant therapies planned before this cellular therapy to optimise efficiency?
Select ‘no’ if no combined or concomitant therapies were planned. If combined or concomitant therapies were planned, select ‘yes’ and specify the therapies.

Treatment given
Indicate if the combined or concomitant therapies were given simultaneously to the cellular therapy infusion or after the cellular therapy episode was finished.

Survival status

Indicate if the patient was alive on the scheduled date of cellular therapy infusion, even if the product was not infused. If the patient died between apheresis and cell infusion, provide the date of death. For further information on the causes of death, see ‘Survival status’.

If the patient died shortly after cell infusion, please provide as many details as possible on the Follow-Up form.

Follow-Up

Person responsible for filling in the form
Enter the name of the person who filled in the form. This can be the same person as who is entering the data into the system. If the form was printed out and filled in by someone else, report that person's name.

Date of this report
If data is being entered directly from the patient notes, the 'date of this report' is the date the data is being entered into the registry database. If the data is filled in on a paper form, the 'date of this report' is the date the form is filled in. This date will remain unchanged regardless of how much more data is added to the patient record in the future.

REMINDER NOTE:
If a patient had more than one type of main treatment (e.g. HSCT and Cellular Therapy) it is the responsibility of the centre that performed the most recent treatment (Cellular Therapy or HSCT) to follow-up on the patient. If the patient received both HSCT and CT treatments, the CT Follow-Up form should be filled in.

Recovery

Absolute neutrophil count (ANC) recovery
Indicate if there was ANC recovery. ANC recovery is defined as neutrophils ≥0.5x10^9 cells/L (observed in three consecutive measurements) before additional treatment. If this number was not reached, select 'no' and fill in the date of last assessment.
If the neutrophils never went below 0.5x10^9 cells/L, select 'never below'.

Date of ANC recovery
Enter the first date of 3 consecutive neutrophil counts ≥0.5x10^9 cells/L. This date must be at least 7 days after the last transfusion containing neutrophils.

Platelets ≥20x10^9 cells/L
Indicate if the platelets reached ≥20x10^9 cells/L (observed in three consecutive measurements). If this was not reached, select 'no'. If it was reached, select 'yes' and enter the date of platelet reconstitution. If the date is not available because the patient was discharged, select 'Date unknown; patient discharged before levels reached'. If the date is unknown because the patient was an out-patient, select 'date unknown; outpatient'. If the platelet count was never below 20x10^9 cells/L, select 'never below'

Date platelets ≥20x10^9 cells/L
Report the first date of 3 consecutive values of platelet counts ≥20x10^9 cells/L. This date must be at least 7 days after the last platelet transfusion.

Platelets ≥50x10^9 cells/L
Indicate if the platelets reached ≥50x10^9 cells/L. If this was not reached, select 'no'. If it was reached, select 'yes' and enter the date of platelet reconstitution. If the date is not available because

the patient was discharged, select ‘Date unknown; patient discharged before levels reached’. If the date is unknown because the patient was an out-patient, select ‘date unknown; outpatient’.
If the platelet count was never below 50x10^9 cells/L, select ‘never below’.

Date platelets ≥50x10^9 cells/L
Report the first date of 3 consecutive values of platelet counts ≥50x10^9 cells/L. This date must be at least 7 days after the last platelet transfusion.

Date last platelet transfusion
Report the last date the patient received a platelet transfusion within the follow-up period. If no platelet transfusion took place, select ‘not applicable’.

Response to cellular therapy

Best clinical/biological response after the entire cellular therapy treatment
Select the best response achieved since the cellular product was infused. This question is only relevant for day 100- and 6-months Follow-Up.
For example:

- If the patient achieves complete remission before day 100, enter complete remission at day 100- and 6-months Follow-Up (even if the patient relapses after; this question concerns the best response to the treatment).
- If the patient achieves partial remission before day 100, enter partial remission at day 100. If the response turns into complete remission after day 100, the best response at 6 months Follow-Up is complete remission.

See Med-AB Manual for HSCT for the definition of response in most primary diagnoses.

Date response evaluated
Report the date the best response was observed.

Last contact date for this report

Last contact date for this report
If the patient was alive, enter the date of the last assessment that was as close as possible to the date of the 1st infusion episode in this cellular therapy treatment +100 days, +6 months or + the years since infusion took place.
If no assessment was performed, for example because the patient was lost to follow-up, enter the last contact date after the infusion episode. If a patient died before the specific time point, enter the date of death.

Current haematological findings

Was a haematological investigation performed?
Indicate if a haematological investigation was performed. If this was done, select ‘yes’ and continue with the subsequent items. If not, select ‘no’ and continue at ‘Performance score’.

Hb
Report the haemoglobin level in grams per decilitre.

Platelets
Report the platelet count in 10^9 cells/L.

Were platelets transfused within 7 days before the date of test?
Indicate if the patient received a platelet transfusion within 7 days before the blood count was assessed.

White blood cells
Report the number of white blood cells per 10^9 cells/L.

Percentage lymphocytes
Report the percentage of lymphocytes

Percentage neutrophils
Report the percentage of neutrophils.

Percentage haematocrit
Report the percentage of haematocrit.

Were red blood cells transfused within 30 days before the date of test?
Indicate if the patient received a red blood cell transfusion within 30 days before the blood count was assessed.

B-cell aplasia since last assessment
Report if B-cell aplasia was present since the last assessment. If B-cell aplasia was present, report the % of B-cells. If B-cell aplasia was treated, report the treatment in the post therapy treatment table.

Percentage of B-cells
Report the percentage of B-cells.

Performance score

Performance score: type used
Indicate if the performance score at cellular therapy was calculated using the Karnofsky, Lansky or Eastern Cooperative Oncology Group (ECOG) scale. Descriptions of the scores can be found in Appendix B.

Performance score: score
Select the score that reflects the performance status at cellular therapy.
It is not necessary to fill in both the Karnofsky/Lansky and ECOG score, one of them is sufficient

Complications since the last report

GvHD

Did graft versus host disease occur?
If the patient did not have an episode of Graft versus Host Disease (GvHD), select ‘no’ and continue with the ‘Other complications’ section. If the patient has had GvHD since the last assessment, select ‘yes’.

Type of GvHD
Select the type of GvHD that was present since the last assessment. This can be acute or chronic GvHD only, or both.

Acute GvHD: maximum grade
Select the maximum grade of acute GvHD that was observed in the last period.
The maximum grade for acute graft versus host disease (aGvHD) is defined according to the stage presented by the skin, liver and/or gut.

The maximum grade seen during the relevant period being studied is calculated from the table below.

	skin stage	liver stage	upper gut stage	lower gut stage
grade 1	1 or 2 and	0 and	0 and	0
grade 2	3 or	1 or	1 or	1
grade 3		2 or 3 or		>1
grade 4	4 or	4		

The overall grade (or the stage of skin, liver and or gut) should be mentioned in the patients' file. If not clearly stated, ask your physician.

Acute GvHD: type
Indicate if this aGvHD episode is a new onset (first episode), recurrent (resolved since the last report and then recurred) or persistent (continuous since the last report).

Acute GvHD: date of onset
Indicate the onset date of the current aGvHD episode.

Acute GvHD: stage
Select the stage of GvHD per organ.

Organ	Stage	Definition
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 erythroderma
	4	Generalised erythroderma with bullous formation, often with desquamation
Liver	0	Bilirubin < 34 micromol/L
	1	Bilirubin 34-50 micromol/L
	2	Bilirubin 51-102 micromol/L
	3	Bilirubin 103-255 micromol/L
	4	Bilirubin > 255 micromol/L

Lower gut	0	No diarrhoea attributable to acute GVHD / diarrhea ≤ 500 mL/day
	1	Diarrhoea volume 501 - 1000 ml/day
	2	Diarrhoea volume 1001 - 1500 ml/day
	3	Diarrhoea volume > 1501 ml/day
	4	Severe pain with or w/o ileus
Upper gut	0	No persistent nausea or vomiting
	1	Persistent nausea or vomiting

Acute GvHD: related to cell therapy?
Indicate if the acute GvHD was related to the current Cellular therapy treatment.

Acute GvHD: resolved?
Indicate if the aGvHD was resolved completely before the last assessment date according to the form being completed.

Acute GvHD treatment
Report if this episode of acute GvHD was treated. If yes, indicate the drugs or therapies that were used to treat aGvHD.

Chronic GvHD: episode
Indicate which episode of chronic GvHD is being reported. If it was the first episode, select 'first episode'. If the chronic GvHD was resolved before but started again, select 'recurrence', if it has been ongoing select 'continuous since last reported episode'. If the chronic GvHD was present but resolved during the follow-up period, select 'yes, but resolved', if it was present, resolved and then recurred, select 'yes, but resolved and recurred again'.

Chronic GvHD: date of onset
Indicate the onset date of the current cGvHD episode.

Chronic GvHD: maximum extent during this period
Chronic GvHD is considered limited if it is present only in the liver and/or a localised area of the skin. If the cGvHD affects any other organ(s) or there is generalised skin involvement, it is considered to be extensive.

Chronic GvHD: maximum NIH consensus score during this period
Select the appropriate NIH score. The score should be calculated by the physician. If the score is not reported, select 'Not calculated'.

Toxicities (non-infectious)

For all complications:

- ➢ Report the date when the first symptoms of the complications were documented.
- ➢ Maximum grade – if the grade is requested, report the maximum grade which was observed during the last reporting period.
- ➢ Indicate if a complication was treated and if it resolved before the last assessment date.

Cytokine release syndrome (CRS)
Cytokine-associated toxicity, also known as cytokine storm, is a non–antigen specific toxicity that occurs as a result of high-level immune activation.

- ➢ Report the date when the first symptoms of the complications were documented.
- ➢ Maximum grade – report the maximum grade which was observed during the last reporting period.
- ➢ Indicate if CRS was treated and if it was resolved before the last assessment date.

Scale/criteria used to determine the grade of CRS
Select the grading system that was used to measure the extent of cytokine release syndrome. If a different grading system was used, select 'Other grading system' and specify which system was used.

Neurotoxicity
Indicate which symptoms of neurotoxicity were present by answering 'yes' or 'no' to each question. If a different symptom than the ones listed was present, use the 'Other' item and specify the symptom.

- Altered mental status
- Aphasia: note grade 3 dysphasia is defined as aphasia.
- Hemiparesis
- Seizure(s)
- Tremors
- Visual hallucinations
- Encephalopathy
- Cerebral oedema
- Other: If the recipient experienced a symptom of neurotoxicity not listed above, report here and specify the symptom including grade if applicable.

- ➢ Report the date when the first symptoms of the complications were documented.
- ➢ Maximum grade – if the grade is requested, report the maximum grade which was observed during the last reporting period.
- ➢ Indicate if a complication was treated and if it resolved before the last assessment date.

Grade 3-4 organ toxicity
- Grade 3: As defined by the CTCAE criteria, grade 3 toxicity represents severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care Activities of Daily Living (ADL), which refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.
- Grade 4: As defined by the CTCAE criteria, grade 4 toxicity represents life-threatening consequences where urgent intervention is indicated.

- ➢ Report the date when the first symptoms of the complications were documented.
- ➢ Maximum grade – if the grade is requested, report the maximum grade which was observed during the last reporting period.
- ➢ Indicate if a complication was treated and if it resolved before the last assessment date.

Tumour lysis syndrome
- ➢ Report the date when the first symptoms of the complications were documented.
- ➢ Maximum grade – if the grade is requested, report the maximum grade which was observed during the last reporting period.

- ➢ Indicate if a complication was treated and if it resolved before the last assessment date.

Bone marrow aplasia

- ➢ Report the date when the first data of the complication were documented.
- ➢ Indicate if a complication was treated and if it resolved before the last assessment date.

Hypogammaglobulinemia

Hypogammaglobulinemia refers to low levels of circulating gamma globulins, IgG immunoglobulins in the blood. Levels lower than 600mg/dL of circulating immunoglobulins are considered to be hypogammaglobulinemia in adult patients.

In paediatric patients aged 4 to 10 years, immunoglobulin levels lower than 500mg/dL are considered hypogammaglobulinemia. In children below the age of 4 years, hypogammaglobulinemia needs to be diagnosed on an individual basis by the treating physician.

If the hypogammaglobulinemia continues from a prior reporting period, report the original diagnosis date as the onset date.

Was hypogammaglobulinemia present before cellular therapy?

Indicate if hypogammaglobulinemia was present before the infusion episode took place.

If Yes, was it worsened by cellular therapy?

If hypogammaglobulinemia was present before the infusion episode, report if the immunoglobulin levels decreased after infusion.

Insertional mutagenesis

- ➢ Report the date when the first data of the complication were documented.
- ➢ Indicate if it resolved before the last assessment date.

Exacerbation of existing neurological disorder

- ➢ Report the date when the first symptoms of the complication were documented.
- ➢ Indicate if a complication was treated and if it resolved before the last assessment date.
- ➢ Specify the neurological disorder

Hemorrhagic stroke

- ➢ Report the date when the first symptoms of the complications were documented.
- ➢ Maximum grade – if the grade is requested, report the maximum grade which was observed during the last reporting period.
- ➢ Indicate if a complication was treated and if it resolved before the last assessment date.

Other toxicity/complications

If the patient developed other toxicities or complications than described on the form, report these here. Specify the complication as clearly as possible, in English.

- ➢ Report the date when the first symptoms of the complications were documented.
- ➢ Maximum grade – report the maximum grade which was observed during the last reporting period.
- ➢ Indicate if the complication was treated and if it resolved before the last assessment date.

Infectious complications

Each infectious episode should be reported separately. Indicate if the infection was present by answering ‘yes’ or ‘no’ to every question. After indicating which infections were present, fill in the table at the bottom of the page.
In the table the type of infection should be specified (using the names listed on the form), the location of infection if applicable, the onset date, pathogen, if the infection was treated and if it was resolved before the last assessment date.
Additionally, for virus reactivations report the highest copy number in copies/ml and the date the highest copy number was observed.

The Infectious Diseases Working Party (IDWP) has published the following document, which should be consulted before filling in these sections of the form:
https://www.ebmt.org/sites/default/files/migration_legacy_files/document/Infectious%20Diseases%20WP%20definitions%20and%20complications%20after%20SCT.pdf

Secondary malignancy

Did a secondary malignancy or autoimmune disorder occur?
If the patient developed a secondary disease or autoimmune disorder after the cell infusion, tick ‘yes’ and fill in the next questions. If not, select ‘no’ and continue at ‘Post therapy treatment’.

Diagnosis
Indicate the diagnosis of the secondary disease or autoimmune disorder as clearly as possible in English.

Date of diagnosis
Report the date of diagnosis.

Histologic Type
Report the histologic type of the secondary malignancy if applicable.

Location
Describe the location of the secondary malignancy if applicable.

Secondary malignancy material preserved
Report if material of the secondary malignancy was preserved.

Post therapy treatment

This section is for systemic treatments only. Treatment for acute GvHD should not be reported here but in the GvHD section.

Did the patient undergo additional treatment during or after the cellular therapy?
Indicate if the patient has received any medications in the last reporting period. This question concerns both treatment for the disease itself as for complications. If the patient received additional treatment, report the date the treatment started.

Indication for the treatment
Report the reason for the treatment which can be treatment for complications or treatment for the disease itself.

Date started
Report the start date of the treatment.

Date ended
Fill in the end date of the treatment. If the treatment is ongoing, tick the box for ‘ongoing at this date’.

Did the patient receive any other type of treatment?
If the patient received other types of treatment report these here.

Is the patient receiving any medication not related to cell therapy or its indications?
Indicate if the patient received medications that were not related to the cellular therapy or the disease that was the indication for the therapy.

First relapse or progression after CT

First Relapse or Progression or Significant worsening of organ function
Only answer this question if one of the indications for the cellular therapy is a primary disease or infection. Report the first relapse or significant worsening after cellular therapy.

Select ‘yes’ if there was an occurrence of new sites of disease, or the re-occurrence of disease or systemic symptoms (B symptoms) after having achieved a complete remission which lasted for 3 months or more.
Select ‘continuous progression’ if the CR lasted less than 3 months. Progression also describes any worsening of the disease status in patients previously assessed as not in CR.

1st relapse: means the first relapse that occurs after a first CR has been achieved. If the patient has never had a CR, the status of the disease cannot be relapse, but it can be progression.

Date of relapse
If the patient had a relapse of the primary disease, report the date the relapse was diagnosed.

Last disease status

Last disease status
Select the disease status that reflects the status at the time of last assessment that is being reported.

Histopathological verification of relapse
This question only needs to be answered for patients with a lymphoma diagnosis. Select if the relapse was verified using histopathology.

Transfusion status (for haemoglobinopathies)
Indicate if the patient required transfusions after the cellular therapy.

Disease burden: LDH level
Indicate if the LDH level was normal, elevated or not evaluated.

Disease burden: inflammatory state
Indicate if the C-reactive protein concentration was normal, elevated or not evaluated. If the level was elevated, report the maximum CRP concentration and unit.

Hospital admission

This section only needs to be completed for follow-up at day 100 and 6 months.

Was inpatient admission and care needed (not ICU)?
Report if the patient was admitted to the hospital for inpatient care since the last assessment.

Was the patient transferred to the Intensive Care Unit?
Report if the patient was transferred to the intensive care unit since the last assessment.

Pregnancy after cellular therapy

Has the patient or partner become pregnant after this cellular therapy?
Indicate whether a female patient or the female partner of a male patient has become pregnant since the patient underwent the treatment procedure. This includes all types of conception: natural and assisted.

Did the pregnancy result in live birth?
If a pregnancy occurred, indicate whether the pregnancy resulted in a live birth or not. If the pregnancy did not result in a live birth, complete the birth outcome. If the pregnancy did result in live birth, complete the newborn status and length of term.

Birth outcome
If the pregnancy did not result in live birth, report if this was because of stillbirth or an abortion.

New born status
If the pregnancy resulted in live birth, indicate if the newborn was healthy or affected by a disease. If the information is unknown or not provided, select ‘information not provided’.

Length of term
If the pregnancy resulted in live birth, report whether the pregnancy was full-term or the baby was born prematurely. If the information is unknown or not provided, select ‘information not provided’.

Persistence of infused cells

Were tests performed to detect the persistence of the cellular products during this period?
Select ‘yes’ if tests to detect the persistence of the infused cells were performed. If no tests were performed, select ‘no’ and continue with the next section.

Date of the last test
If a test was performed, indicate the date of the last test before the follow-up assessment that is being reported.

Source of cells
Select the source of cells that was used to assess the persistence of the infused cellular product.

Technique used
Select the technique that was used to assess the persistence of the infused cellular product.

Were cells detected?
State if the infused cells were detected by the relevant technique.

Survival status

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 ‘Check here if patient lost to follow-up’.

Main cause of death
Tick only one major cause of death. In case of doubt, check with the physician since this information is sometimes difficult to find in the patient’s file.

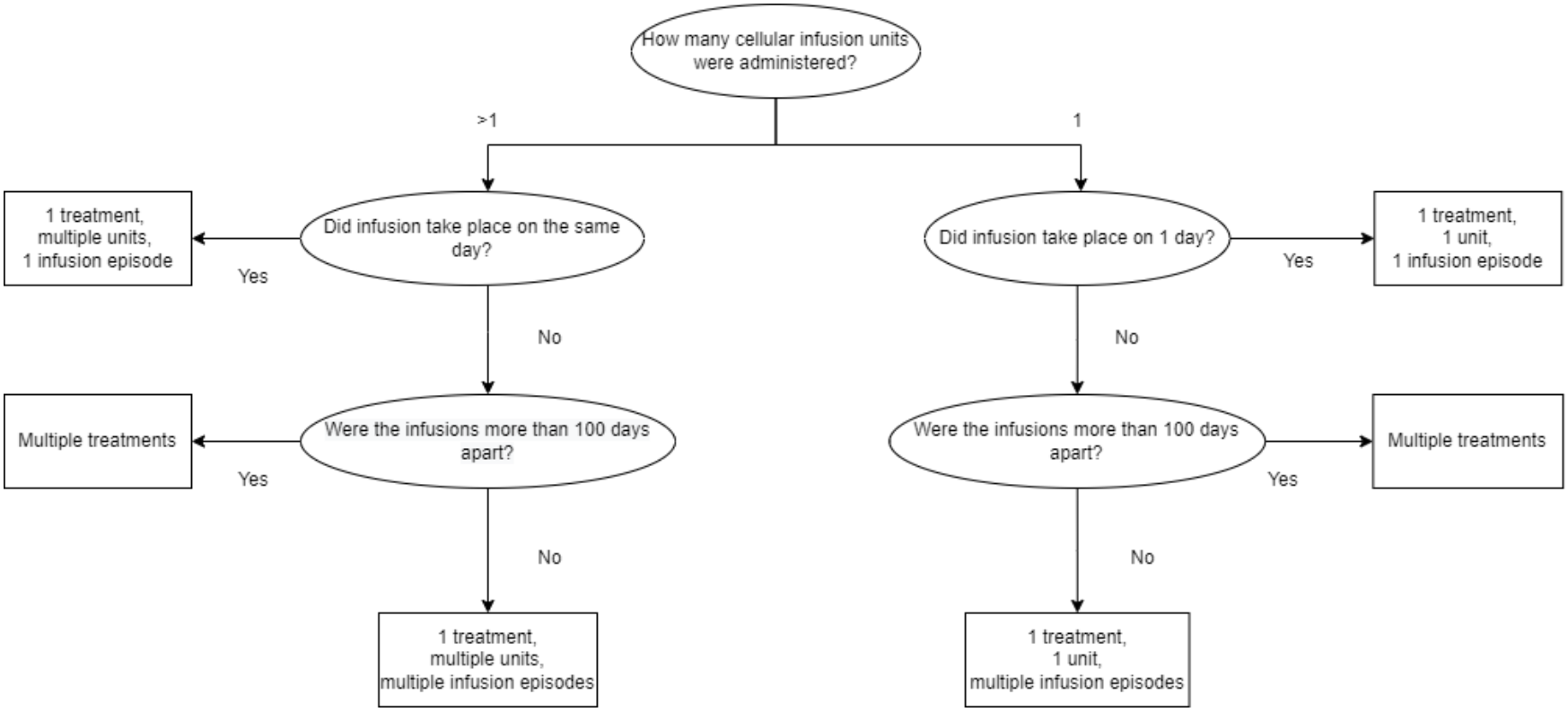
Contributory causes of death
In case contributory factors resulted in the death of the patient, tick all the relevant options from the ‘contributory causes of death’ list.

References

1. B-Cell Aplasia (Concept Id: C4552224) - MedGen - NCBI [Internet]. Ncbi.nlm.nih.gov. 2021 [cited December 2021]. Available from: https://www.ncbi.nlm.nih.gov/medgen/1702770
2. 1. ECOG Performance Status - ECOG-ACRIN [Internet]. ECOG-ACRIN. 2021 [cited December 2021]. Available from: https://ecog-acrin.org/resources/ecog-performance-status

Appendix A

Data entry flowchart



Appendix B

Karnofsky/ECOG scoring systems (2)

Score	Performance status: Karnofsky/Lansky
100	Normal, no complaints, no evidence of disease / Fully active, normal
90	Able to perform normal activity; minor signs and symptoms of disease / Minor restrictions in physically strenuous activity
80	Able to perform normal activity with effort; some signs and symptoms of disease / Active, but tires more quickly
70	Cares for self, unable to perform normal activity or to do active work / Both greater restriction of and less time spent in play activity
60	Requires occasional assistance but is able to care for most of own needs / Up and around, but minimal active play; keeps busy with quieter activities
50	Requires considerable assistance and frequent medical care / Gets dressed but lies around much of the day, no active play but able to participate in all quiet play and activities
40	Requires special care and assistance; disabled / Mostly in bed; participates in quiet activities
30	Hospitalization indicated, although death not imminent; severely disabled / In bed; needs assistance even for quiet play
20	Hospitalization necessary; active supportive treatment required, very sick / Often sleeping; play entirely limited to very passive activities
10	Fatal processes progressing rapidly; moribund / No play; does not get out of bed

Score	ECOG 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