Immunosuppressive treatment (IST) day 100 follow-up

Guide to the completion of the EBMT data collection form: IST FU D100_v1

21 August 2023

EBMT Registry
EBMT Clinical Research & Registry Department
Table of Contents

Immunosuppressive treatment day 100 follow-up ................................................................. 4
  1. Date of follow-up: ........................................................................................................... 4
  2. Survival status: ............................................................................................................... 4
  3. Date of the last IST for this patient: ................................................................................. 4

Best response .......................................................................................................................... 4

  4. Best response after this IST: ......................................................................................... 4
  5. Date best response first observed: ................................................................................. 5

Transfusions since last IST episode ....................................................................................... 6

  6. RBC ................................................................................................................................. 6
  7. RBC irradiated .................................................................................................................. 6
  8. Platelets .......................................................................................................................... 6
  9. Platelets irradiated .......................................................................................................... 6

Secondary malignancies ....................................................................................................... 6

  10. Did a secondary malignancy or autoimmune disorder occur? .................................... 6
      10.1. Was this disease an indication for a subsequent HCT/CT/IST? ......................... 7

PNH Tests at this Follow-Up .................................................................................................. 7

  11. PNH test done: ............................................................................................................. 7
      11.1. Date of PNH test: ................................................................................................. 7
      11.2. PNH diagnostics by flow cytometry: ................................................................. 7
      11.3. Flow cytometry assessment done on: ............................................................... 7
      11.4. Clinical manifestation of PNH: ......................................................................... 7
      11.5. Date of clinical manifestation of PNH .............................................................. 7
      11.6. Anti-complement treatment given? .................................................................. 8

Cause of Death (if patient died) ............................................................................................ 8

  12. Main cause of death: .................................................................................................... 8
      12.1. Select treatment related cause: ........................................................................ 9
Immunosuppressive treatment day 100 follow-up

IST Day 100 form must be submitted to the EBMT Registry database 100 days after an IST episode or at time of patient death, whichever occurs first.

1. Date of follow-up:

Report the follow-up date which is the closest to the Day 100 follow-up assessment post-IST. If the patient died or was lost to follow-up, enter the date the patient was last seen alive.

2. Survival status:

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

3. Date of the last IST for this patient:

Report the start date of the immunosuppressive treatment episode that this follow-up is reported for.

Best response

4. Best response after this IST:

Report the best response achieved since the immunosuppressive treatment, even if the patient got worse again afterwards. The definitions of the best responses for severe aplastic anaemia can be found in table 1. For congenital bone marrow failures, no formal response criteria are available.

<table>
<thead>
<tr>
<th>Response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Severe aplastic anaemia</strong></td>
</tr>
<tr>
<td>Stable disease/no change/no</td>
<td>Not meeting any of the response criteria defined below</td>
</tr>
<tr>
<td>response</td>
<td></td>
</tr>
<tr>
<td>Complete Remission (CR)</td>
<td>All of the following:</td>
</tr>
<tr>
<td></td>
<td>• No evidence of clonal evolution, by marrow cytogenetic and flow cytometry</td>
</tr>
<tr>
<td></td>
<td>• Peripheral blood counts: hemoglobin &gt;10 gr/dL, absolute neutrophils &gt;1.0</td>
</tr>
<tr>
<td></td>
<td>x 10^9/L, platelets &gt;100 x 10^9/L</td>
</tr>
</tbody>
</table>
| Partial Remission (PR) | All of the following:  
|-----------------------|-----------------------------------------------------------|
|                       | • No longer meeting criteria for diagnosis of SAA  
|                       | • Transfusion independence (defined as no need of any PRBC or platelet transfusion)  
|                       | • Peripheral blood counts: hemoglobin >8 gr/dL, absolute neutrophils >0.5 x 10^9/L, platelets >20 x 10^9/L  
|                       | At least one of the following:  
|                       | • transfusion independence (if previously required) doubling or normalization of at least one cell line  
|                       | • increase above baseline* by:  
|                       | 3 g/dl hemoglobin and 0.5x10^9/L neutrophils and 20x10^9/L platelets  
| Hematological improvement (HI) (NIH Partial Response) | No longer meeting criteria for diagnosis of SAA  
| Relapse/progression | Any of the following events after a hematological response (CR or PR):  
|                     | • Meeting again the criteria for SAA  
|                     | • Requirement of transfusion support (if not due to independent medical conditions)  
|                     | • Decrease in any of the peripheral blood counts as follows:  
|                     | • Decrease to less than 50% of the medium sustained count during remission if: absolute neutrophils < 1.0 x 10^9/L, platelets <50 x 10^9/L; or  
|                     | • Or in any case if: absolute neutrophils < 0.5 x 10^9/L, platelets <20 x 10^9/L  
|                     | • The peripheral blood count decrease must be:  
|                     | • not due to any independent concomitant medical condition  
|                     | • demonstrated in at least 3 tests over a period of 2 weeks  
|                     | • not responding to re-introduction of low dose cyclosporin A  

Table 1, definitions of best responses

5. Date best response first observed:

Report the date the best response was first observed. The response date is the date that the sample or image was taken for assessing the response. If the patient is in CR, enter the date CR was achieved or assessed. If the date is unknown, select the Unknown checkbox.
6. RBC

Count and indicate the total number of red blood cells (RBC) units transfused since last IST episode by ticking an appropriate checkbox:

- < 20 units;
- 20 - 50 units;
- > 50 units.

Select None to mark that there were no RBC transfusions. Answer Unknown if there is no information on RBC transfusions in the patient's medical records.

7. RBC irradiated

Indicate if RBC were irradiated (answer Yes), not irradiated (answer No) or if it is unknown (answer Unknown).

8. Platelets

Count and indicate the total number of platelets transfused before the start of IST by ticking an appropriate checkbox:

- < 20 units;
- 20 - 50 units;
- > 50 units.

Select None to mark that there were no platelet transfusions. Answer Unknown if there is no information on platelet transfusions in the patient's medical records.

9. Platelets irradiated

Indicate if platelets were irradiated (answer Yes), not irradiated (answer No) or if it is unknown (answer Unknown).

Secondary malignancies

10. Did a secondary malignancy or autoimmune disorder occur?

Answer No if neither secondary malignancy nor autoimmune disorder has been observed after this IST episode. Answer Yes if secondary malignancy or autoimmune disorder occurred and specify:
10.1. Was this disease an indication for a subsequent HCT/CT/IST?

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

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

**PNH Tests at this Follow-Up**

11. PNH test done:

Report if PNH test was done in the follow up period or not. If it is not known if the PNH test was performed please select **Unknown**.

11.1. Date of PNH test:

If the answer to the previous question is **Yes**, indicate the date of the PNH test. In case the date is not known, report **Unknown**.

11.2. PNH diagnostics by flow cytometry:

Indicate if clone was absent or present by selecting the respective check box, or mark it as **Not evaluated** if applicable.

If the **Clone present** option is selected, specify also the **Size of the clone** in % (PNH clone size refers to the proportion of PNH-affected cells versus normal cells within the total cell population). This information can be found in the haematology report.

11.3. Flow cytometry assessment done on:

Check the corresponding check box to indicate if **Granulocytes**, red blood cells (**RBC**) or **Both** were analysed by flow cytometry. If flow cytometry was done on other cells, select **Other** and specify the cell type in English.

11.4. Clinical manifestation of PNH:

If there are any clinical manifestations of PNH, select **Yes**, if not, select **No**.

You can find more details on PNH manifestation in the bone marrow failures completion guidelines.

11.5. Date of clinical manifestation of PNH

If the answer to the previous question is **Yes**, report the date when the clinical manifestation was first reported. In case the date is not known, report **Unknown**.
11.6. Anti-complement treatment given?

Indicate if any anti-complement treatment was given to the patient by selecting either No or Yes. Including compounds that inhibit the complement system, for example: C-5 inhibitors (Eculizumab & Ravulizumab) and C-3 inhibitors (Pegcetacoplan). If the anti-complement treatment that has been given is not listed please select: Other; specify.

If anti-complement treatment was given, provide details.

11.6.1. Drug:

Select the drug name from the list of options or use Other field and report the generic drug/agent name(s) in the textbox in English.

Please consult the List of Chemotherapy Drugs, Agents and Regimens on the EBMT website for drug/agent names. This document provides alternative names for many of the drugs/agents. Once you have found the drug/agent of interest on the list, add its database name to the table.

11.6.2. Start date:

Indicate the date when the treatment was started. In case the date is not known, report Unknown.

11.6.3. Stop date:

Indicate the date when the treatment was stopped. If the treatment is still in progress, select Ongoing. In case the date is not known, report Unknown.

If there were more drugs given during one line of treatment use copies of the page for the paper form. It is also possible to add additional fields in the online EBMT Registry application to report multiple drugs here.

Cause of Death (if patient died)

12. Main cause of death:

Check only one main cause that applies. In case of doubt, consult a physician. If none of the answers in the table match, tick the box Other and specify it. If the cause of death is not known, select Unknown.

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

- Relapse or progression/persistent disease
- Secondary malignancy
- Cellular therapy-related - death caused by complications or infections after cellular therapy (also indicate the treatment related cause)
- HCT-related - death caused by complications or infections after transplant (also indicate the treatment related cause)
• **IST-related** – death caused by complications or infections after an immunosuppressive episode (also indicate the treatment related cause).

12.1. Select treatment related cause:

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

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

12.1.1. *Infectious complication:*

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

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