When to fill out the HOVON Serious Adverse Event Report

Please fill out the report if a patient included in a HOVON trial experiences a Serious Adverse Event (SAE) during the trial. Report all SAEs that occur from the first trial related procedure or treatment at least until as specified in the protocol. For definitions and trial specific conditions please refer to the trial protocol. Every SAE should be reported to HOVON within 24 hours.

Who should fill out the HOVON Serious Adverse Event Report

Any authorized member of the site trial staff may fill out the report; this can be a (sub-) investigator, research nurse, data manager or other qualified person. However, the investigator (or sub-investigator) is responsible for the SAE report and should review the medical content of the form and sign the final report.

How to complete the HOVON Serious Adverse Event Report

Please fill out all applicable items, detailed instructions are listed below. Please fill out a separate form for each Serious Adverse Event. Please note that the SAE can be completed either on a paper report or by use of the fillable PDF. Always send in all pages of the form. Please complete the form in English.
Please also see document 'required items on SAE report' for more information.
Each SAE report is identified by a set of items that must always be filled out for each report and repeated on every page of the report:

- *Patient study number*: number that was assigned by HOVON to the patient at registration/randomization;
- *Date of report:* as reported on the first page of the form;
- *Type of report*: initial, follow up or final report; mark the applicable box.

Corrections and new information

Corrections can be made by crossing out the incorrect answer once (do not obscure the original entry) and writing the new answer next to it, dated, initial, and (if necessary) explained. Do not use correction tape or fluid. When sending in a corrected copy of a report that was sent earlier, please make sure that it is clearly marked as a revision.

New information can be added when sending in a follow up or final report (see below). Use the existing SAE form and simply add the new information to the form or make corrections as described above.

Please avoid using a new blank form to send in corrections or new information on a previously sent in SAE. However, there may be a reason why this is necessary, for example no more space to add information. If you are using a new blank form, copy all items needed for identification; patient study number, sex, date of birth, adverse event term, date onset AE and date AE became Serious from the previous report (initial or follow up) to the new report (follow up or final). If you use a new form for the follow up or final report, make sure that the information does not contradict the information on the previous report.

Initial report

Please send the initial report to HOVON within 24 hours after the event was known to the investigator/site, using the SAE report form provided. The report should preferably contain all information that is known at the time of completion but should always contain at least the following:

- *Patient information*
- *Report information*
- *Serious Adverse Event information*
- *Trial medication, IMP(s), Trial treatment and relationship to SAE*
- *Signature*

If not all information (except for the mandatory items) regarding the SAE could be completed in the initial report, a complete report must be sent to HOVON as a follow up report within 2 working days after the initial report was sent. The complete report should contain all information regarding the SAE as available at that time.

Follow up report

Please send in follow up reports at least once every month until a final report could be completed. Update the information as applicable in each follow up report.

Please make sure that a new date of follow up report is filled out for each new follow up report. Please see the paragraph “Corrections and new information” if you need to complete a new blank SAE form.

Final report

Please send a final report to HOVON as soon as the outcome of the SAE is known. Please note that every SAE must have a final report. The final report should contain all information regarding the SAE. Please note that a SAE cannot be final when the outcome is ‘ongoing’.
The final report should always be signed by the (sub) investigator.

Instructions for completion of specific items:

Patient information

Patient study number: number that was assigned by HOVON to the patient at registration/randomization;

Sex: the gender of the patient.

Report information

Site name: name of the hospital that is reporting the SAE;

Investigator: name of local investigator for that hospital;

Type of report: mark the applicable box. Every SAE must have at least an initial report and a final report. The initial report may already contain all the information required for the final report - mark the boxes for "initial report" and "final report" with identical date of initial report and date of final report;

Date of report: the date the report (initial, follow up or final) was filled out. Please make sure that a new date of follow up report is filled out for each new follow up report.

Serious Adverse Event information

Adverse Event term: the most precise diagnosis available for the event as assessed by the investigator or treating physician; this should be a single term (for example "sepsis" or "pulmonary embolism") and not an elaborate description. Please provide the most relevant sign or symptom (for example "fever" or "dyspnea"), if no diagnosis is available (yet). Once a diagnosis is available, adverse event term on the SAE report should be adjusted accordingly.
If the SAE is a complex case with multiple related Adverse Events or symptoms occurring simultaneously, please report the most relevant AE term (as assessed by the investigator, e.g. the AE term cited in medical records as the primary reason for hospital admission). The other related AEs or symptoms should be reported in the *SAE description and comments* as concomitant AEs. Please indicate that these AEs are related to the SAE. All other Adverse Events that occur at the same time and are not related should be reported as separate AE. If these Adverse Events are qualified as serious, please send in a separate SAE report for each Event.

Date onset AE: date the Adverse Event started, regardless whether it was already serious at that time;

Date AE became Serious: date that the AE first met the criteria for being an SAE, this can be the same date as *Date onset AE* or later;

Date site became aware: date that the site became aware of the SAE. Please note that an SAE must be reported within 24 hours after becoming aware of the SAE. In case of late reporting (more than 24 hours), a reason must be provided under SAE description and comments;

Reason AE is Serious: if the AE meets more than one of the listed criteria, please choose the most relevant;

Severity of AE: the highest CTCAE grade that was observed during the course of the Adverse Event; for AEs that increase in severity after the initial SAE report was sent, this item will have to be updated in the follow up or final report. Please adjust CTCAE grade into 5 when SAE is or becomes fatal.

SAE description and comments

Use this box to describe the course of events from onset AE until end of the SAE. Please include dates and results of any relevant tests or procedures that were used to diagnose the SAE and actions taken to treat the SAE. For a final report also describe outcome of adverse events and all test results. Please also include concomitant AEs and symptoms if applicable (see *Adverse Event term instructions).*

Trial medication/Trial Treatment

Report the medication that is part of the protocol treatment schedule and that the patient was receiving in the protocol phase or cycle during or after which the Adverse Event started.

Please always report the IMP(s) treatment that the patient has received, even if not given during this protocol phase or cycle and if not (possibly) related.
When other trial treatment is not given during this protocol phase, but relationship seems to be (possibly) related, this information should also be provided (e.g. when possibly related to allo-SCT, this information should also be provided in treatment section).

Drugs that are used for supportive care or prophylaxis as recommended by the protocol (for example antibiotics), are not to be regarded as trial medication but as concomitant medication (see below).

Treatment arm: for randomized trials, enter the treatment arm the patient is treated in. Should this for some reason be different from the arm the patient was assigned to at randomization, explain the discrepancy in the SAE description;

Protocol phase: enter the protocol phase during or after which the Adverse Event started;

IMP(s)/Trial treatment(s); enter all details of the IMP(s) and/or trial treatment(s) that the patient has received, even if not given during the protocol phase in which the SAE occurred. If IMP(s) are not given during this

protocol phase, please report last time received. The relationship to SAE on an initial report must always be reported;

Other trial medication: enter all other trial medications that the patient received during the protocol phase in which the SAE occurred, choose from the listed trial medications. In addition, when treatment is not given during this protocol phase, but relationship seems to be (possibly) related, this information should also be provided (e.g. when possibly related to allo-SCT, this information should also be provided in treatment section).
Please fill out items below for both the IMPs, trial treatments and other trial medication:

Total daily Dose or Total amount of treatments: Total daily dose accompanied by unit– for example if the patient received 200 mg twice a day, the total daily dose is 400 mg. Total amount of treatments received;

Date first dose: date the patient received the first dose of the trial medication as part of the associated protocol phase (unless it concerns an IMP only given during previous cycles) - so if the SAE started during cycle 2 and the patient already received this drug in cycle 1, use the start date from cycle 2;

Date last dose: date the patient received the last dose of this trial medication prior to the date the SAE started. . If the drug was continued after the SAE started, date last dose should be marked as the same date as *date AE became Serious*;

**Batch no/lot no + expiry date:* the batch number/lot number of the IMP given during the period the SAE occurred. Please also add the expiry date of the IMP given during the period the SAE occurred. Please request batch no/lot no at your pharmacy department.

Relationship to SAE: assessment by the (sub) investigator for the causal relationship between the Adverse Event and the trial medications; The relationship to SAE on an initial report must always be reported;

Action taken as a result of this SAE: action taken regarding the trial medication as a consequence of the Adverse Event. Please use “drug withdrawn (temporarily or permanently)” if the treatment was stopped before completion of the protocol phase during which the SAE occurred. “Not applicable” can be used in circumstances such as death of the patient or if the treatment had been completed prior to the onset of the event.

Possible Causes of SAE other than Trial medication(s)

Use this section to describe any circumstances other than trial medication that may have contributed to the occurrence of the SAE.

Disease under study (including progression): The disease under study may have contributed to the occurrence of the SAE. Progression itself should not be reported as SAE. For example, the SAE term is infection and the patient has pancytopenia due to (the progression of) the disease under study and is therefore prone to infections. The disease under study has contributed to the SAE in this case;

Medical condition(s): Any relevant past or current medical disorders, allergies, surgeries that could help explain the SAE. Use the box *Specification* to describe these medical condition(s);

Concomitant medication(s): Any relevant concomitant medication(s) that could help explain the SAE or may have caused the SAE. Use the box *Specification* to give the name of all concomitant medication(s) that could help explain the SAE or may have caused the SAE;

Trial related procedure(s): Any trial related procedure (for example placing IV line, stem cell transplantation or bone marrow biopsy) that may have contributed to the SAE or may have caused the SAE- for example the SAE term is pneumothorax and this was caused by placing a central venous catheter. Use the box *Specification* to describe these trial related procedure(s);

Other: Any possible cause of SAE other than trial medication(s) and other than the causes listed here above that could help explain the SAE. Use the box *Specification* to describe these other cause(s).

Outcome of the SAE

Outcome of SAE:

• resolved	the Adverse Event is no longer present
• ongoing	the Adverse Event is still present – regardless of changes in severity
• death	the Adverse Event is the (suspected) cause of death
• ongoing at death	the Adverse Event was not yet resolved when the patient died from another cause: the Adverse Event is definitely not the cause of death
• ongoing closed (because stable situation reached)"	the Adverse Event is still ongoing but no longer a Serious Adverse Event and it is not likely that the Adverse event will resolve. For example, patient was hospitalized for GvHD. The GvHD is still present but a stable situation has been reached and patient no longer needs to be hospitalized.

Date SAE resolved: date the Adverse Event ended (only in case of outcome "resolved ");

If patient died: please note that when patient died, outcome might be “death” or “ongoing at death”. For both outcomes, “date of death” and “cause of death” are required to be filled out. Please note that if the patient died from another cause (“ongoing at death”), the cause of death may be an SAE in itself and may have to be reported as such. Please refer to the trial protocol.

Signatures

The reporter responsible for the content of the SAE report should sign each report. The (sub) investigator should always sign the final report.

Instructions for sending and filing the form:

After completing the report, send it to HOVON, saereports@erasmusmc.nl
Please keep the original report at the site in a safe place where it can be easily accessed for further processing and monitoring (for example in the Investigator Trial File or a specific SAE Report File, with a copy stored in the patient file for reference by the treating physician and data manager).

The Pharmacovigilance department from HOVON will assess every SAE report. In case there are any questions regarding the SAE report, the site will receive queries via e-mail or in exceptional cases via phone. These queries require an urgent- or non-urgent answer, according to seriousness of the questions. Answers to the queries should be provided by sending in an updated SAE report or by e-mail.

Questions:

For questions regarding the SAE report please contact the HOVON Pharmacovigilance department.
Telephone: +31 (0)10 70 41 560
E-mail: HOVONpv@erasmusmc.nl (please do not use e-mail for urgent questions)