Completion and management of the SSGXXI CRFs

General

SSGXXI study data should be collected on the SSGXXI Case Report Forms (CRF) that are stored in the CRF binder at the clinic. It is also possible to download the CRFs, study protocol, patient information, newsletters and contact information from www.ssg-org.net.

CRF completion and data management

Data will be read from the CRFs and entered into a database by personnel at the SSG secretariat in Lund, Sweden. The personnel at the SSG secretariat are not allowed to make their own interpretations of data, meaning that it is of great importance to complete all boxes and fields in the CRFs where required by logic. If a requested value is missing this should be confirmed by writing NA (Not applicable), NK (Not known) or ND (Not Done) in the concerned box/field. Any missing, ambiguous or unclear value will be requested on a Data Query Form (DQF). Please also remember that each CRF page should be signed and dated by the investigator.

Correction of data in CRF

Corrections of data in the CRF may only be performed by the investigator or another authorized person (should be documented in the Delegation log in the site file at the clinic). When correcting data, the incorrect value should be stroked, the correct value should be written next to it and the correction should be signed and dated**. Tipp-ex or other correction fluids are not allowed.** A DQF will be issued if a correction is not performed in accordance with these instructions.

Data Query Forms (DQF)

If CRF data are incorrect, ambiguous or missing a Data Query Form (DQF) will be issued at the SSG secretariat and sent to the clinic. Information given on a DQF is superior to the corresponding information given in the CRF. If a DQF is received at the clinic: provide the requested information on the form, sign and date it. Finally, take a copy of the DQF and file it with the rest of the patients' CRFs before sending the original to the SSG secretariat.

Note that DQFs must be resolved by the investigator or another authorized person (should be documented in the Delegation log in the site file at the clinic).

CRF flow

The CRFs should be sent to the SSG secretariat by ordinary mail or fax in accordance with the instructions below.

Important! Remember to take a copy of each CRF and file it at the clinic before sending the originals to the SSG secretariat by ordinary mail.

SSG fax number: +46 46-188143

SSG Address: Regional tumor registry
Att: SSG secretariat
Skåne University Hospital
SE-221 85 LUND

Registration & Baseline form (Form 1): Fax the form to the SSG secretariat as soon as the baseline visit has been performed. The SSG secretariat will provide an unique study identification id for the patient (Patient ID No.) and return the Registration & Baseline form to the clinic by fax. File the returned Registration & Baseline form together with the other CRFs for the concerned patient.
Note! If the SLD from the Baseline CT is not available at the time of registration, please complete this information as soon as available and send the updated Registration form to the SSG secretariat.

Follow-up visit forms (Form 2:1-2:3) before the first monitoring visit: Save all CRF originals at the clinic until the first monitoring visit. The study monitor will monitor and collect the CRFs.

Follow-up visit forms (Form 2:1-2:3) after the first monitoring visit: Send the CRF originals to the SSG secretariat by ordinary mail every second month.

Pazopanib treatment log (Form 3): Send the CRF original to the SSG secretariat when the patient has discontinued the pazopanib treatment OR when all the rows on the Pazopanib treatment log (form 3) have been completed. If the patient still is treated with pazopanib after completion of all rows on the Pazopanib treamtent log further changes in the pazopanib treatment should be reported on the Extra form 3.

End of study form (Form 4): Send the CRF original to the SSG secretariat after the last study related contact, i.e. follow-up visit or telephone contact, with the patient.

Serious Adverse Event Report (Form 5): Complete a SAE report and fax it to the SSG secretariat **+46 46-188143** within one working day each time a serious adverse event (SAE)/serious adverse reaction (SAR) is reported in the study. Send the original form to the SSG secretariat as soon as possible. SAE Follow-up reports should be sent as originals to the SSG secretariat after completion.

Eligibility criteria violation form (Form 6): Send the CRF original to the SSG secretariat after the first monitoring visit.

CRF specific instructions

Registration & Baseline (Form 1)
The patient must sign the Informed consent form before study registration and pazopanib treatment start. This means that the"Date of written informed consent" must be before or equal to the "Date for registration" and before or equal to the pazopanib 800 mg Start date (reported on form 3).

Note that the following fields should be completed at the SSG secretariat: ”Patient’s ID No.”, ”Registered by” och ”Date of Registration”.

Please assure that all eligibility criteria for the SSGXXI (see the study protocol) are fulfilled before a patient is registered in the study. If it’s later found out that a registered patient, i.e. a patient that received a unique patient id number within the SSGXXI study, didn’t fulfilled the eligibility criteria at the time of registration this should be reported on the Eligibility criteria violation form (form 6).

The Sum of Longest Diameters (SLD) for the pre-defined target lesions must be reported on the Registration & Baseline form. Previous treatment with imatinib and sunitinib is mandatory for study inclusion, meaning that start and stop dates for these TKI treatments must be reported on the Registration & Baseline CRF. However, previous treatment with nilotinib is allowed but not mandatory for study inclusion. Report treatment start and stop date if the patient was previously treated with nilotinib but tick the NA box if the patient didn’t receive previous treatment with nilotinib.

Follow-up forms (Form 2:1-2:3)
The Follow-up forms (form 2:1-2:3) must be completed at each follow-up visit up and until the patient discontinues the pazopanib treatment. Information obtained at the mandatory telephone contact 30 days after discontinuation of the pazopanib treatment should also be reported on the Follow-up forms.

Note that the Follow-up visit number must be completed on each Follow-up form.

There are just two Follow-up form sets (form 2:1-2:3x2) per CRF set. Thus, it’s recommended to make copies of these forms but it’s also possible to download the forms from www.ssg-org.net.

If a CT was performed: Report the Sum of Longest Diameters (SLD) for the pre-defined target lesions. If progressive disease, i.e. new lesions or >20 % increase in the SLD compared to the smallest SLD reported since the pazopanib treatment started (nadir) and minimum 5 mm over the nadir, then discontinue the study drug & complete the Treatment log and the End of study form.

Adverse events (AEs) that occur during study treatment or within two weeks after end of pazopanib treatment should be reported on the Follow-up forms at each follow-up visit during the study. For definition of adverse events, see page 15 in the SSGXXI protocol. Each NCI/NIH Common Toxicity Criteria must be evaluated at each occasion. The correct alternative should be circled; if no toxicity has occurred since the last evaluation this should be reported by putting a circle in the Grade 0-column. If, for some reason, a toxicity was not evaluated the concerned row should be marked ND (Not Done) else a DQF will be issued. In case an adverse event that is not predefined on the CRF occurs, this should be reported by specifying the symptoms/diagnose in the field(s) “Other” and mark the applicable grade.

Pazopanib treatment log (Form 3):

The first row on form 3, i.e. Start and Stop date for pazopanib 800 mg treatment and information regarding whether the reported stop date is the final stop date for the pazopanib treatment, must be completed for all patients.

Any dose modifications must be performed in accordance with the study protocol. All dose modifications that lasts ≥72 hours must be reported in the Pazopanib treatment log.

- If the pazopanib dose was decreased due to an adverse event the modified dose should be reported on form 3 and the adverse event should be reported on the concerned Follow-up form.
- If the pazopanib dose was increased after resolution of the adverse event, the increased dose should be reported on a new row on form 3 and the Reason for dose change should be "Adjustment due to previous change".
- In case a temporary interruption in the pazopanib treatment occurred, e.g. if the patient neglected to take the study drug during a period, this should be reported as "Dose"=0 mg/day and the Reason for dose change should be "Other" followed by a short description of the scenario. When the patient starts to take pazopanib again the Stop date for Dose=0 mg/day should be reported and the new Dose and adherent Start date should be reported on the following row.

When the pazopanib treatment is finally discontinued the Stop date should be reported and the question "Final stop date" should be answered "Yes" on the row for the last prescribed dose.

End of study form (Form 4):
The "Date when the reason for study discontinuation occurred" should be reported on the End of study form (form 4) but the "Stop date" for the pazopanib treatment should be reported on the Pazopanib treatment log (Form 3). For each alternative for treatment discontinuation listed in the SSGXXI protocol the following applies for the reporting of the "Date when the reason for study discontinuation occurred":

- **Progressive disease**: The date for the first CT scan that shows disease progression should be reported. May be before the pazopanib stop date.
- **Unacceptable toxicity**: The onset date of the toxicity that leads to the treatment discontinuation should be reported. May be before the pazopanib stop date. The toxicity should be reported on a Follow-up form (form 2:1-2:3) and, if one or several criteria for a serious adverse event (SAE) are fulfilled, on a Serious Adverse Event report (form 5).
- **Intercurrent condition contraindicating pazopanib**: The onset date of the condition that leads to the treatment discontinuation should be reported. May be before the pazopanib stop date. Consider whether the condition should be reported on a Follow-up form (form 2:1-2:3) and, if one or several criteria for a serious adverse event (SAE) are fulfilled, on a Serious Adverse Event report (form 5).
- **Patient´s wish**: The date when the patient decides to stop the pazopanib treatment, i.e. equal to the pazopanib stop date.

If the "Reason for treatment discontinuation" is one of the alternatives listed above then a telephone contact with the patient should be performed approximately 30 days after treatment discontinuation. The date for the telephone contact should be reported as "Date for last study related contact" and the information obtained during the telephone contact should be reported on the Follow-up forms (form 2:1-2:3).

In addition to the reasons listed above the following events are listed as Reasons for study discontinuation on the End of study form:

- **Lost to follow-up**: If the patient doesn't show up to scheduled visits and is impossible to get in touch with despite several attempts. The "Date when the reason for study discontinuation occurred" should be equal to the date when it is decided that no further efforts should be made to contact the patient, i.e. the date when the patient is declared lost to follow-up. The pazopanib stop date on form 3 has to be estimated based upon the number of tablets that was handed out to the patient at the previous follow-up visit, presumed that the patient took all the tablets.
- **Death**: The date of death should be reported as "Date when the reason for study discontinuation occurred" and as the pazopanib stop date on form 3.

For patients that are deceased or declared Lost to follow-up the last contact with the patient (visit or telephone contact) within the study should be reported as "Date for last study related contact".

Serious adverse event report (Form 5):
The definition of serious adverse events (SAEs) and reporting instructions is found on page 16 in the SSGXXI protocol. An initial SAE report should be sent to the SSG secretariat within one working day as soon as the investigator is notified that a SAE has occurred. A Follow-up SAE report should follow if the Outcome of the SAE is not known at the time of the Initial SAE report. If the SAE leads to a reduction/discontinuation of the pazopanib dose then this information should be reported on the Pazopanib treatment log (form 3) and, in case of treatment discontinuation, on the End of study form (form 4).

Eligibility criteria violation form (Form 6):
If it is detected that a patient was incorrectly included in the SSGXXI study, i.e. one or several eligibility criteria was violated, this should be reported on form 6. If no protocol violations regarding eligibility criteria were detected after registration then form 6 should be crossed out, signed and dated.

Questions?

Please contact the SSG secretariat if you have any questions regarding completion of the CRFs or data management within the SSGXXI study:
Phone: +46 46 177555
E-mail: ssg@med.lu.se

Questions regaring study procedures and monitoring will be answered by CROAK:
Phone: +46 730 711118
E-mail: jeanette.ceberg@croak.se

Good luck with the SSG XXI study!