Instructions for completion of SSG XVIII CRF

General instructions

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).

Important! The original of each CRF should be sent to the SSG secretariat by mail (except from the Registration form that should be sent by fax; see below). Remember to take a copy of each CRF and file it at the clinic before sending the original.

Data Query Forms (DQFs)

Information given on a DQF is superior to the corresponding information given in the CRF. Take a copy of the DQF and file it together with the rest of the patients' CRFs before sending the original DQF to the SSG secretariat.

Correction of data

Corrections in 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.

New CRF version from April 2008

From April 2008, the CRF version dated March 2008 should be used to collect data for all patients that are treated or followed in the SSG XVIII study. The new CRF version can be downloaded from the SSG website: www.ssg-org.net under the link Treatment protocols and recommendations – Ongoing – SSGXVIII. Some data will be re-collected according to the new protocol amendment.

CRF-specific instructions

The following CRFs (version 2) should be completed for all patients included in the SSGXVIII-study:

- Form 1: Registration
- Form 2: Screening at baseline
- Form 3A: Screening at baseline
- Form 3B: Screening at baseline
- Form 4A: Follow-up, Month 1, week 4 (except for patients that withdraw their consent before this follow-up visit)
- Form 4B1-2: Adverse Event, Follow-up, Month 1, week 4 (except for patients that withdraw their consent before this follow-up visit)

- Form 29: End of treatment
- Form 30: Complication log
- Form 31: End of study
- Form 33: Investigator confirmation

For patients with recurrent GIST should:

- Form 32: GIST recurrence

be completed as well.

SAE (Serious Adverse Event) Report Form

Information about all SAEs and assessment of its relationship to Novartis treatment must be recorded in English by the investigator on the SAE Report Form. Each SAE must be reported to the SSG secretariat fax +46 46 18 81 43 and to the local Novartis Clinical Safety & Epidemiology (CS&E) Department within 24 hours of learning of its occurrence even if it is not felt to be related to treatment.
The original copy of the SAE form and the fax confirmation sheet must be kept with the CRF documentation at the study site.

Form 1: Registration/Randomization

All patients must sign the informed consent form before registration in SSG XVIII. Note that the latest version of the patient information and informed consent form must be used. The Registration form (Form 1) can be downloaded from the SSG website: www.ssg-org.net under the link Treatment protocols and recommendations – Ongoing – SSGXVIII. Complete all fields on the Registration form, except from the section at the bottom of the page, and fax it to the SSG secretariat. Note that all **Inclusion criteria** must be answered **Yes** and that all **Exclusion criteria** must be answered **No** to randomize the patient into the SSGXVIII study. The Registration form will be returned to the clinic by fax as soon as the Patient randomization number, Treatment arm and Randomization date in the section at the bottom of the page have been filled in at the SSG secretariat. **A complete CRF set with the patient randomization number and initials filled in will also be sent to the clinic as soon as the randomization process is complete.**

Form 2: Screening at baseline

Main presenting symptoms or signs of GIST
It is only the main presenting symptoms/signs of GIST that should be reported in this section, not other concomitant diseases.

Surgery
Date of surgery: Must be before Screening visit date on Form 1.
Type of open surgery: GIST must be removed by open surgery, meaning that laparoscopic or endoscopic surgery is not accepted as the sole surgical procedure.

Form 3B: Screening at baseline

Concomitant medications
It is only the concomitant medications reported at the Screening visit that should be registered on the CRF.

Arm 1: Form 4A-8A / Arm 2: Form 4A-16A: Follow-up

If a planned follow-up visit was not performed but the patient still is included in the study, the concerned Follow-up page should be stroke and ND (Not done) should be written on it.

Current status

- Alive, no recurrence: No recurrence during the study.
- Alive, GIST recurred: GIST recurred during the study, i.e. this box should be ticked at each follow-up visit after the first recurrence (except for if the patient dies, then "Dead" should be ticked instead). In case of GIST recurrence, imatinib treatment should be discontinued and the End of treatment form should be filled in. Details regarding GIST recurrence and progression should be registered on the GIST recurrence form.
- Dead: Fill in the End of treatment form, the End of study form, the Complication log and the Investigator confirmation form.

Study medication

This section should be completed at each follow-up visit during the first 12 months (arm 1) respective 36 months (arm 2) or until the end of treatment if premature discontinuation of study treatment.

If imatinib treatment within the study was interrupted or reduced between two follow-up visits the dates and reason(s) for interruption or reduction must be specified.

Arm 1: Form 4B1-2 – 8B1-2 / Arm 2: Form 4B1-2 – 16B1-2: Adverse Event

Adverse events that occur during study treatment or within two weeks after end of treatment should be reported on these CRFs at each follow-up visit during the first 12 months (arm 1) respective 36 months (arm 2) or until end of treatment if premature discontinuation of study treatment.

Each NCI/NIH Common Toxicity Criteria must be evaluated at each occasion. The correct alternative should be circled; if no toxicity this should be reported by putting a circle in the Grade 0-column. If, for some reason, a toxicity was not evaluated that row should be marked ND (Not Done).

Arm 1: Form 9-28 / Arm 2: Form 17-28: Follow-up

These forms should be completed until month 132 or the end of study.

Form 29: End of treatment

This CRF should be completed for all patients included in the study.

Reason for discontinuation

- Completed assigned therapy: Patient completed the imatinib treatment in accordance with the study protocol, i.e. 12 months for patients in arm 1 and 36 months for patients in arm 2. Patient should be asked to come to the follow-up visits in accordance with the study protocol.

- GIST recurrence: Patient discontinued study treatment due to GIST recurrence. Details regarding the recurrence should be reported on the GIST recurrence form. Patient should be asked to come to the follow-up visits in accordance with the study protocol.
- Adverse effects/lab values: Patient discontinued study treatment due to adverse effects/lab values. NB! Must be reported on the Adverse Event forms (4B1-2 – 8/16B1-2) and specified on form 29. Patient should be asked to come to the follow-up visits in accordance with the study protocol.
- Patient wished to discontinue adjuvant imatinib: Patient doesn't want to continue study treatment but should be asked to come to the follow-up visits in accordance with the study protocol.
- Patient withdrew consent: Patient withdraws consent. Further follow-up visits must not be performed and further study data must not be collected for the patient. Complete the End of study form (Date for last follow-up contact=Date for withdrawal of consent), the Complication log and the Investigator confirmation form.
- Death: Complete the End of study form (Date for last follow-up contact=Date of death), the Complication log and the Investigator confirmation form (and the GIST recurrence form if GIST recurred).
- Other: If any other reason for discontinuation of study treatment this must be specified.

Form 30: Complication log

This CRF should be completed for all patients. All cardiac events and/or second cancers diagnosed during or after study treatment should be reported.

The CRF will be collected for all patients before the final analysis of RFS, i.e. when all randomized patients have completed their first visit following one year of adjuvant therapy and at least 110 events have been recorded. If no complications at the time of the first report, then tick the first "No complications"-box. For all patients that didn't reach the end of study at the time for the final analysis for RFS, the CRF will be completed again when the patient reached the end of study. If no further complications were registered since the first report, then tick the second "No complications"-box.

Form 31: End of study

This CRF should be completed for all patients.

Status at End of study
More than one alternative may be ticked. For example; if the patient withdraws his/her consent but has a known GIST recurrence then the alternatives "Patient withdrew consent" and "Alive, GIST recurrence" should be ticked.

- Alive, no GIST recurrence: Patient is alive at end of study and GIST did not recur during the SSG XVIII study
- Alive, GIST recurrence: Patient is alive at end of study and GIST did recur during the SSG XVIII study. The GIST recurrence form should be completed.
- Alive with cancer other than GIST: Patient is alive at end of study and has been diagnosed with a cancer other than GIST (however, this alternative does not exclude GIST recurrence that may be ticked as well). Details regarding the other cancer should be registered in the Complication log.

- Lost to follow-up: Patient is lost to follow-up. Date for last follow-up contact should be the date when the last attempt to contact the patient was made.
- Patient withdrew consent: Patient withdraws consent. Date for last follow-up contact should be the date when patient withdrew consent. No further study data can be collected for the patient (however, the Complication log, the Investigator confirmation form and the GIST recurrence form (if applicable) should be completed).
- Dead: Date for last follow-up contact should be equal to date of death. Information regarding cause of death and autopsy should be registered.

Form 32: GIST recurrence

This CRF should be completed for all patients with recurred GIST *and be sent to SSG secretariat at end of study*. As a minimum the following fields must be completed:

- Date of GIST recurrence
- Recurrence site(s): More than one alternative may be ticked
- Serum sample taken at tumor recurrence
- Tumor tissue sample taken
- Type of systemic therapy given for first GIST recurrence
- Surgery for GIST recurrence
- Radiotherapy for GIST recurrence

If imatinib or other systemic therapy was given for first GIST recurrence then information regarding this treatment and second-line systemic therapy should be filled in. Information regarding third-line systemic therapy should be filled in if second-line systemic therapy was given; information regarding fourth-line systemic therapy should be filled in if third-line systemic therapy was given etc.

Form 33: Investigator confirmation

This CRF should be completed for all patients. All CRFs should be accounted for at the end of study.