SSG XXI: Pazopanib in advanced GISTs refractory to imatinib and sunitib
A Non-comparative Phase II Multicenter Study by the Scandinavian Sarcoma Group **Form 1**

REGISTRATION & BASELINE
Complete this form and fax it to the SSG secretariat:
Fax: +46-46-18 81 43

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 form to the SSG secretariat. Save a copy!

Patient's initials |___|___|___|	Date of birth |___|___|___| |___|___| |___|___| (Year / Month / Day)	Patient's ID No. |___|___|___|___|
Responsible Clinician	Institution	*To be completed at the SSG secretariat*

Check (not to be entered into database):
Have all the mandatory investigations* for SSG XXI been performed? ☐ Yes**
Are all eligibility criteria* for SSG XXI fulfilled? ☐ Yes**
***See the SSG XXI protocol
** **If not**, please **DO NOT INCLUDE** the patient in the SSG XXI study. **All eligibility criteria will be closely monitored!**

\|___\|___\|___\|___\| \|___\|___\| \|___\|___\| **Date of written informed consent**

\|___\|___\|___\|___\| \|___\|___\| \|___\|___\| **Date of last CT showing disease progression**
Year Month Day

Sum of longest diameters (SLD) for the target lesions measured at Baseline CT \|___\|___\|___\| mm

\|___\| **Sex**
1 = Male
2 = Female

\|___\| **WHO 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 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

\|___\|___\|___\|___\| \|___\|___\| \|___\|___\| **Date of GIST diagnosis**
Year Month Day

\|___\| **Primary mutation**
1 = c-kit, Exon 9
2 = c-kit , Exon 11
3 = c-kit , Exon 13
4 = c-kit , Exon 17
5 = PDGFR-α, Exon 12
6 = PDGFR-α, Exon 14
7 = PDGFR-α, Exon 18
8 = Wildtype
9 = Not available

Do not forget to register the study drug treatment start date in the Pazopanib treatment log (form 3)

Previous treatment with TKIs

Start date	Stop Date	
|___|___|___|___| |___|___| |___|___|	|___|___|___|___| |___|___| |___|___|	**imatinib**
|___|___|___|___| |___|___| |___|___|	|___|___|___|___| |___|___| |___|___|	**sunitinib**
|___|___|___|___| |___|___| |___|___| (Year / Month / Day)	|___|___|___|___| |___|___| |___|___| (Year / Month / Day)	**nilotinib** |___| **NA**

To be completed at the SSG secretariat:

Registered by ..... *Date for registration* \|___\|___\|___\|___\| \|___\|___\| \|___\|___\| (Year / Month / Day)

SSG XXI: Pazopanib in advanced GISTs refractory to imatinib and sunitib
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FOLLOW-UP FORM

Complete the Follow-up forms (form 2:1-2:3) at each follow-up visit and send them to:
SSG secretariat, Regional Tumor Registry, Skåne University Hospital, SE-221 85 LUND, Sweden
Save a copy of each form!

Follow-up visit number |___|___| Patient's initials |___|___|___| Patient's ID No. |___|___|___|___|

Visit date
|___|___|___|___| |___|___| |___|___|
Year Month Day

|___| **CT**
0 = No
1=Yes*

*If CT performed, please report

SLD for the target lesions |___|___|___| mm

|___| **Disease status**
1 = Complete remission
2 = Partial remission
3 = Stable disease
4 = Progressive disease, *discontinue study drug and complete the Pazopanib treatment log (Form 3) and the End of study form (Form 4)*

NCI/NIH Common Toxicity Criteria. All listed AEs should be evaluated at each follow-up visit. Please circle the correct alternative. If not evaluated, please report "ND" on the concerned row.

AE	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Trombocytopenia	None	<LLN - 75,000/mm3; <LLN - 75.0 x 10e9 /L	<75,000 - 50,000/mm3; <75.0 - 50.0 x 10e9 /L	<50,000 - 25,000/mm3; <50.0 - 25.0 x 10e9 /L	<25,000/mm3; <25.0 x 10e9 /L
Neutropenia	None	<LLN - 3000/mm3; <LLN - 3.0 x10e9 /L	<3000 - 2000/mm3; <3.0 - 2.0 x10e9 /L	<2000 - 1000/mm3; <2.0 - 1.0 x10e9 /L	<1000/mm3; <1.0 x10e9 /L
Hypothyroidism	None	Asymptomatic; clinical or diagnostic observations only; Intervention not indicated	Symptomatic; thyroid replacement indicated; limiting instrumental ADL	Severe symptoms; limiting self care ADL; hospitalization indicated	Life-threatening consequences; urgent intervention indicated
Myalgia	None	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self care ADL	–
Headache	None	Mild	Moderate; limiting instrumental ADL	Severe; limiting self care ADL	-
Dizziness	None	Mild unsteadiness or sensation of movement	Moderate unsteadiness or sensation of movement; limiting instrumental ADL	Severe unsteadiness or sensation of movement; limiting self care ADL	-
Hypertension	None	Prehypertension (systolic BP 120 - 139 mm Hg or diastolic BP 80 - 89 mm Hg)	Stage 1 hypertension (systolic BP 140 - 159 mm Hg or diastolic BP 90 - 99 mm Hg); medical intervention indicated; recurrent or persistent (>=24 hrs); symptomatic increase by >20 mm Hg (diastolic) or to >140/90 mm Hg if previously WNL; monotherapy indicated	Stage 2 hypertension (systolic BP >=160 mm Hg or diastolic BP >=100 mm Hg); medical intervention indicated; more than one drug or more intensive therapy than previously used indicated	Life-threatening consequences (e.g., malignant hypertension, transient or permanent neurologic deficit, hypertensive crisis); urgent intervention indicated
Epistaxis	None	Mild symptoms; intervention not indicated	Moderate symptoms; medical intervention indicated (e.g.,nasal packing, cauterization; topical vasoconstrictors)	Transfusion, radiologic, endoscopic, or operative intervention indicated (e.g., hemostasis of bleeding site)	Life-threatening consequences; urgent intervention indicated
Hoarseness	None	Mild or intermittent voice change; fully understandable; self-resolves	Moderate or persistent voice changes; may require occasional repetition but understandable on telephone; medical evaluation indicated	Severe voice changes including predominantly whispered speech	-
Stomatitis (mucositis)	None	Asymptomatic or mild symptoms; intervention not indicated	Moderate pain; not interfering with oral intake; modified diet indicated	Severe pain; interfering with oral intake	Life-threatening consequences; urgent intervention indicated

Investigator signature ..... Date of signature |___|___|___|___| |___|___| |___|___|
Year Month Day

SSG XXI: Pazopanib in advanced GISTs refractory to imatinib and sunitib
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FOLLOW-UP FORM

Complete the form and send it to:
SSG secretariat, Regional Tumor Registry, Skåne University Hospital, SE-221 85 LUND, Sweden
Save a copy!

Follow-up visit number |___|___| Patient's initials |___|___|___| Patient's ID No. |___|___|___|___|

NCI/NIH Common Toxicity Criteria. All listed AEs should be evaluated at each follow-up visit. Please circle the correct alternative. If not evaluated, please report "ND" on the concerned row.

AE	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Abdominal pain	None	Mild	Moderate; limiting instrumental ADL	Severe; limiting self care ADL	-
Nausea	None	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated	-
Vomiting	None	1 - 2 episodes (separated by 5 minutes) in 24 hrs	3 - 5 episodes (separated by 5 minutes) in 24 hrs	>=6 episodes (separated by 5 minutes) in 24 hrs; tube feeding, TPN or hospitalization indicated	Life-threatening consequences; urgent intervention indicated
Dyspepsia	None	Mild; intervention not indicated	Moderate; medical intervention indicated	Severe; surgical intervention indicated	-
Diarrhea	None	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline	Increase of >=7 stools per day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self care ADL	Life-threatening consequences; urgent intervention indicated
Flatulence	None	Mild; intervention not indicated	Moderate; persistent; psychosocial sequelae	-	-
Abdominal distension	None	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; limiting instrumental ADL	Severe discomfort; limiting self care ADL	-
Anorexia	None	Loss of appetite without alteration in eating habits	Oral intake altered without significant weight loss or malnutrition; oral nutritional supplements indicated	Associated with significant weight loss or malnutrition (e.g. inadequate oral caloric and/or fluid intake); tube feeding or TPN indicated	Life-threatening consequences; urgent intervention indicated
Dysgeusia	None	Altered taste but no change in diet	Altered taste with change in diet (e.g., oral supplements); noxious or unpleasant taste; loss of taste	-	–
Increased ALT	None	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Increased AST	None	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Increased ALP	None	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Hyperbilirubinemia	None	>ULN - 1.5 x ULN	>1.5 - 3.0 x ULN	>3.0 - 10.0 x ULN	>10.0 x ULN
Alopecia	None	Hair loss of <50% of normal for that individual that is not obvious from a distance but only on close inspection; a different hair style may be required to cover the hair loss but it does not require a wig or hair piece to camouflage	Hair loss of >=50% normal for that individual that is readily apparent to others; a wig or hair piece is necessary if the patient desires to completely camouflage the hair loss; associated with psychosocial impact	-	-
Hair colour change	None	Mild	Pronounced	-	-
Fatigue	None	Fatigue relieved by rest	Fatigue not relieved by rest; limiting instrumental ADL	Fatigue not relieved by rest, limiting self care ADL	-

Investigator signature ..... Date of signature |___|___|___|___| |___|___| |___|___|
Year Month Day

SSG XXI: Pazopanib in advanced GISTs refractory to imatinib and sunitib
A Non-comparative Phase II Multicenter Study by the Scandinavian Sarcoma Group **Form 2:3**

FOLLOW-UP FORM

Complete the form and send it to:
SSG secretariat, Regional Tumor Registry, Skåne University Hospital, SE-221 85 LUND, Sweden
Save a copy!

Follow-up visit number |___|___| Patient's initials |___|___|___| Patient's ID No. |___|___|___|___|

NCI/NIH Common Toxicity Criteria. All listed AEs should be evaluated at each follow-up visit. Please circle the correct alternative. If not evaluated, please report "ND" on the concerned row.

AE	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Skin hypopigmentation	None	Hypopigmentation or depigmentation covering <10% BSA; no psychosocial impact	Hypopigmentation or depigmentation covering >10% BSA; associated psychosocial impact	-	-
Rash maculo-papular	None	Macules/papules covering <10% BSA with or without symptoms (e.g., pruritus, burning, tightness)	Macules/papules covering 10 - 30% BSA with or without symptoms (e.g., pruritus, burning, tightness); limiting instrumental ADL	Macules/papules covering >30% BSA with or without associated symptoms; limiting self care ADL	-
Hand-foot syndrome	None	Minimal skin changes or dermatitis (e.g., erythema, edema, or hyperkeratosis) without pain	Skin changes (e.g., peeling, blisters, bleeding, edema, or hyperkeratosis) with pain; limiting instrumental ADL	Severe skin changes (e.g., peeling, blisters, bleeding, edema, or hyperkeratosis) with pain; limiting self care ADL	-
Erythema	None	Mild	Pronounced	-	-
Proteinuria	None	1+ proteinuria; urinary protein <1.0 g/24 hrs	2+ proteinuria; urinary protein 1.0 - 3.4 g/24 hrs	Urinary protein >=3.5 g/24 hrs	-
Edema face	None	Limited localized facial edema	Moderate localized facial edema; limiting instrumental ADL	Severe swelling; limiting self care ADL	-
Edema limbs	None	5 -10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection	>10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour; limiting instrumental ADL	>30% inter-limb discrepancy in volume; gross deviation from normal anatomic contour; limiting self care ADL	-
Edema trunk	None	Swelling or obscuration of anatomic architecture on close inspection	Readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour; limiting instrumental ADL	Gross deviation from normal anatomic contour; limiting self care ADL	-
Other, specify: …… ……	None				
Other, specify: …… ……	None				

To remember at each visit:
- **All investigations and lab samples must be performed**
- **Any changes in pazopanib treatment must be registered in the Pazopanib treatment log (form 3)**

To remember at the week 12 visit:
- **Plasma sampling for later PK analysis, see protocol appendix 2**

Investigator signature ..... Date of signature |___|___|___|___| |___|___| |___|___|
Year Month Day

SSG XXI: Pazopanib in advanced GISTs refractory to imatinib and sunitib
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Form 3

PAZOPANIB TREATMENT LOG

Report pazopanib start- & final discontinuation date AND any interruptions/reductions during the study

When the form is complete, please send it to (*save a copy!*):

SSG secretariat, Regional Tumor Registry, Skåne University Hospital, SE-221 85 LUND, Sweden

Patient's initials |___|___|___| Patient's ID No. |___|___|___|___|

	Dose	Start date	Stop date	
1st row must be completed →	|8|0|0| mg/day	|___|___|___|___| |___|___| |___|___| Year Month Day	|___|___|___|___| |___|___| |___|___| Year Month Day	|___| **Final stop date** 0 = No* 1 = Yes**

Dose modifications NB! Any modifications in the pazopanib treatment should be performed in accordance with the protocol

	Dose	Start date	Stop date	
|___| **Reason for dose change** 1 = AE, report on form 2:1-2:3 3 = Other*** Please specify:	|___|___|___| mg/day	|___|___|___|___| |___|___| |___|___| Year Month Day	|___|___|___|___| |___|___| |___|___| Year Month Day	|___| **Final stop date** 0 = No* 1 = Yes**

	Dose	Start date	Stop date	
|___| **Reason for dose change** 1 = AE, report on form 2:1-2:3 2 = Adjustment due to previous change 3 = Other*** Please specify:	|___|___|___| mg/day	|___|___|___|___| |___|___| |___|___| Year Month Day	|___|___|___|___| |___|___| |___|___| Year Month Day	|___| **Final stop date** 0 = No* 1 = Yes**

*Please, report new dose. In case of temporary interruption in the pazopanib treatment, report 0 mg/day.
**Please, complete the End of study form (form 4)
***The alternative'Other' thus represents some protocol violation, e.g., a non-approved change made by the patient

Check (not to be entered into database):
Plasma sample for PK analysis collected and frozen according to protocol appendix 2? ☐ Yes

Investigator signature…….....

Date of signature |___|___|___|___| |___|___| |___|___|

SSG XXI: Pazopanib in advanced GISTs refractory to imatinib and sunitib
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Extra Form 3

PAZOPANIB TREATMENT LOG

Report interruptions/reductions in the pazopanib treatment during the study

When the log is complete, please send it to (save a copy!):
SSG secretariat, Regional Tumor Registry, Skåne University Hospital, SE-221 85 LUND, Sweden

Patient's initials |___|___|___| Patient's ID No. |___|___|___|___|

Dose modifications NB! Any modifications in the pazopanib treatment should be performed in accordance with the protocol

|___| **Reason for dose change**	**Dose**	**Start date**	**Stop date**	|___| **Final stop date**
1 = AE, report on form 2:1-2:3 2 = Adjustment due to previous change 3 = Other***	|___|___|___| mg/day	|___|___|___|___| |___|___| |___|___| (Year / Month / Day)	|___|___|___|___| |___|___| |___|___| (Year / Month / Day)	0 = No* 1 = Yes**

Please specify:

.....

|___| **Reason for dose change**	**Dose**	**Start date**	**Stop date**	|___| **Final stop date**
1 = AE, report on form 2:1-2:3 2 = Adjustment due to previous change 3 = Other***	|___|___|___| mg/day	|___|___|___|___| |___|___| |___|___| (Year / Month / Day)	|___|___|___|___| |___|___| |___|___| (Year / Month / Day)	0 = No* 1 = Yes**

Please specify:

.....

*Please, report new dose. In case of temporary interruption in the pazopanib treatment, report 0 mg/day.
**Please, complete the End of study form (form 4)
***The alternative'Other' thus represents some protocol violation, e.g., a non-approved change made by the patient

Investigator signature……..... Date of signature |___|___|___|___| |___|___| |___|___|

SSG XXI: Pazopanib in advanced GISTs refractory to imatinib and sunitib
A Non-comparative Phase II Multicenter Study by the Scandinavian Sarcoma Group **Form 4**

END OF STUDY FORM

When the form is complete, please send it to (save a copy!):
SSG secretariat, Regional Tumor Registry, Skåne University Hospital, SE-221 85 LUND, Sweden

Patient's initials |___|___|___| Patient's ID No. |___|___|___|___|

|___|___|___|___| |___|___| |___|___|
Year Month Day

Date when the reason for study discontinuation occurred, eg. date for CT scan. Please note that the discontinuation date for the pazopanib treatment should be reported on form 3.

|___| **Reason for study discontinuation**

1 = Disease progression
2 = Unacceptable toxicity, please report on form 2:1-2:3
3 = Intercurrent condition contradicting pazopanib, please specify……

……
4 = Patient's wish
5 = Lost to follow-up
6 = Death

|___|___|___|___| |___|___| |___|___|
Year Month Day

Date for last study related contact (visit or telephone contact 30 days after discontinuation of study treatment). Please report information regarding the last visit/telephone contact performed within the study on the Follow-up forms 2:1-2:3

Please, check that all

- **Follow-up visits and Adverse Events (form 2:1-2:3)**
- **Serious Adverse Events (form 5)**
- **Start and stop date and any changes in the pazopanib treatment (form 3)**

have been reported in accordance with the study protocol and the CRF instructions

Investigator signature ..... Date of signature |___|___|___|___| |___|___| |___|___|
Year Month Day

SSG XXI: Pazopanib in advanced GISTs refractory to imatinib and sunitib **Form 5**
A Non-comparative Phase II Multicenter Study by the Scandinavian Sarcoma Group

SERIOUS ADVERSE EVENT REPORT

Complete one form per SAE within one working day and fax it to the SSG secretariat:
Fax: +46-46-18 81 43

Patient's initials |___|___|___| Patient's ID No. |___|___|___|___|

Type of report

☐ Initial

☐ Follow-up

Description of the SAE

|___|___|___|___| |___|___| |___|___| Onset date (Year / Month / Day)

|___|___|___|___| |___|___| |___|___| Resolved date (Year / Month / Day)

Brief description (if possible include diagnosis):

.....

.....

.....

.....

.....

.....

.....

.....

Study medication

Date of last intake of pazopanib before SAE

|___|___|___|___| |___|___| |___|___| Date (Year / Month / Day)

Dose: ☐ Full ☐ Reduced

Action taken with pazopanib*

☐ None
☐ Reduction*
☐ Stopped*
☐ Other; ……

Outcome of the SAE:

☐ Complete recovery
☐ Recovery with sequele
☐ Not recovered
☐ Unknown
☐ Death, date of death |___|___|___|___| |___|___| |___|___| (Year / Month / Day)

Seriousness

Why was the event classified as serious?

☐ Unexpected hospitalisation
☐ Secondary malignancy
☐ Persistent or significant disability
☐ Life-threatening event
☐ Results in death

Causality assessment by investigator

Is SAE related to pazopanib?

☐ Not related
☐ Unlikely/doubtful
☐ Possible
☐ Probable
☐ Definite/very likely

*Please report any changes in the pazopanib treatment on the Pazopanib treatment log (form 3)

Investigator signature ……..... Date of signature |___|___|___|___| |___|___| |___|___| (Year / Month / Day)

ELIGIBILITY CRITERIA VIOLATION FORM

Only applicable for patients later found to be ineligible at registration.

To be completed by investigator as soon as violation of any eligibility criteria was detected or by monitor if violation was detected at monitoring visit. If no eligibility criteria violations were detected, please cross out and sign the form.

Send the completed form (save a copy) to:

SSG secretariat, Regional Tumor registry, Skåne University Hospital, SE-221 85 LUND, Sweden.

Patient's initials |___|___|___| Patient's ID No. |___|___|___|___|

Eligibility criteria not fulfilled
(registered patients later found to be ineligible at registration)

|___| |___| |___| |___|

a = Metastatic and/or locally advanced GIST, confirmed by histology with positive c-kit and/or DOG-1, or with a GIST-typical mutation in KIT or PDGFRA

b = Measurable disease on CT as defined by RECIST criteria; at least one measurable lesion not given radiotherapy

c = History of progressive disease on CT according to RECIST criteria after both imatinib and sunitinib treatment, and also after nilotinib if this drug has been given

d = No other TKIs given than imatinib, sunitinib and nilotinib

e = Age at least 18 years at the time of diagnosis of GIST

f = WHO performance status 0-2

g = Resolution of all toxic side effects from earlier TKI treatment and any other potential non-TKI treatment to grade 1 or below

h = Sufficient organ functions as defined in the protocol

i = Absence of all the conditions specified in the protocol

j = No pregnancy or lactation; negative serum or urine pregnancy test mandatory in women with childbearing potential

k = Women with childbearing potential must accept the use of adequate contraception throughout the study period

l = Written informed consent

Investigator/Monitor signature ..... Date of signature |___|___|___|___| |___|___| |___|___|
Year Month Day