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PROPRIETARY DRUG NAME® / GENERIC DRUG NAME: Sutent® / Sunitinib malate

PROTOCOL NO.: A6181030

PROTOCOL TITLE: A Treatment Protocol for Patients Continuing From a Prior SU-011248 Protocol

Study Centers: Forty-three centers took part in the study and randomized subjects; 26 in the United States (US), 4 in the United Kingdom (UK), 3 in Australia, 2 in Italy and Sweden and 1 each in Canada, France, Greece, Netherlands, Singapore, and Switzerland.

Study Initiation Date and Final Completion Date: 17 March 2004 to 13 December 2011

The study was terminated prematurely.

Phase of Development: Not applicable

Study Objective: The study objective was to provide access to SU011248 treatment for subjects who have participated in a SU011248.

METHODS

Study Design: This was an open-label treatment protocol for subjects who had participated in other sunitinib protocols to completion and were believed to have the potential to derive clinical benefit from sunitinib treatment.

Sunitinib was administered in the 4/2 schedule; subjects received cycles of daily dosing for 4 consecutive weeks followed by a 2 week rest period. The typical starting dose was 50 mg daily. If a subject entered this study using a different regimen than the 4/2 schedule, the regimen and dose to be used in this study were decided after discussion between the Investigator and Sponsor. Subjects experiencing adverse events (AEs) that required dose reductions in the previous study began this study at the reduced dose. Intrasubject dose-modification prior to the start of each cycle was permitted.

Disease assessments for tumor response and progression were performed for data collection on selected subjects; specifically, subjects who previously participated in a study for which objective disease response or time-to-progression was a study endpoint (eg, Phase 2 or 3 studies) and when the subject had not yet experienced progression while in the previous study, or was assigned to placebo, or received limited duration of treatment in the previous study (eg, short-treatment Phase 1 studies). Subjects had accessed sunitinib on this protocol

as long as there was reasonable evidence of benefit. Survival beyond study participation in this study was monitored only in individual subjects previously participating in protocols with an overall survival endpoint.

Number of Subjects (Planned and Analyzed): A total of 314 subjects were planned and enrolled in this protocol, from which 313 subjects were randomized (280 in United States (US), 7 in United Kingdom (UK), 6 in Australia, 4 each in France and Netherlands, 3 each in Greece and Switzerland, 2 each in Italy and Sweden and 1 each in Canada and Singapore). A total of 311 subjects were treated and received at least 1 dose of sunitinib. All 311 subjects discontinued from the study, most commonly due to lack of efficacy (68.5%).

Diagnosis and Main Criteria for Inclusion: Subjects included in this study were subjects who participated in a previous sunitinib protocol and were judged to have the potential to derive clinical benefit from sunitinib treatment by the treating physician. Subjects assigned to placebo in a previous study who did not qualify for crossover within the original protocol due to declining health status (eg, performance status lower than crossover eligibility criterion) were included in this study.

Study Treatment: Administration of the study drug was performed on an outpatient basis. A typical starting dose for the 4/2 schedule was 50 mg daily. If a subject entered the study using other than the 4/2 schedule (eg, 2/2, 2/1, or continuous dosing), the regimen and dose to use in this study were decided after discussion between the Investigator and Sponsor. Subjects experiencing AEs requiring dose reduction in the previous study participation began this study at the reduced dose. The dose should have been taken orally once daily at approximately the same time of day with a glass of water. Subjects receiving the 4/2 regimen were required to be off study drug for 2 weeks after each 28 day dosing period. The study Investigator may have implemented dose suspension or reduction in order to ensure subject safety.

Modifications to the sunitinib dose were permitted. The dosing period, however, was not to be extended to compensate for interruptions in sunitinib treatment due to any cause. The start of the next cycle may have been delayed beyond the scheduled Day 1 of the next cycle, if additional time was required for the subject to recover from sunitinib-associated toxicity experienced during the previous cycle.

A typical treatment cycle included 28 dosing days plus 2 weeks off, although subjects may have continued to receive treatment using other regimens begun in the previous study.

Subjects may have continued to receive treatment for as long as the study was open at the site, provided they did not fulfill criteria for withdrawal from the study.

Efficacy Endpoints: The determination of objective disease response was made according to the Response Evaluation Criteria in Solid Tumors (RECIST) system of one-dimensional evaluation. Tumor imaging was conducted at least every 3 months only in subjects who previously participated in a study for which objective disease response or time-to-progression was a study endpoint (eg, Phase 2 or 3 studies), when the subject had not yet experienced progression while on the previous study, or was previously assigned to placebo, or received

limited duration of treatment in the previous study (eg, short-treatment Phase 1 study). All partial or complete objective responses were to be confirmed no sooner than 4 weeks after the initial documentation of response.

Safety Evaluations: Safety evaluations included clinical monitoring that included assessment of AEs and clinical laboratory measurements, as well as physical examinations and electrocardiograms (if not done in the same subjects the prior study).

Statistical Methods: The analysis sets analyzed for the study are

Intent-to-Treat Population: Intent-To-Treat population included all subjects enrolled in the study that received at least 1 dose of study medication. This population was the study population for all analyses.

All continuous data were summarized using descriptive statistics (mean, standard deviation, median, minimum, and maximum values). All categorical data were summarized using frequencies and percentages.

All AEs reported after initiation of treatment were considered as treatment-emergent AEs (TEAEs). A pre-existing condition that worsened during the treatment period was also considered as a TEAE. All AEs were coded by system organ class and preferred term using National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE).

RESULTS

Subject Disposition and Demography: A summary of subject disposition is provided in Table 1.

Table 1. Subject Disposition

Number (%) of Subjects	Sunitinib
Enrolled subjects	314
Intent-to-treat population[a]	311
Completed[b]	0
Discontinued	311 (100.0)
Adverse event	53 (17.0)
Protocol violation	2 (0.6)
Consent withdrawn	31 (10.0)
Lost to follow-up	1 (0.3)
Lack of efficacy	213 (68.5)
Decision of sponsor	11 (3.5)

a. The intent-to-treat population included all subjects who enrolled in the study that received at least 1 dose of study medication.
b. Per the study protocol, there was no definition of subjects completing treatment/study.

A summary of demographic characteristics is provided in Table 2.

Table 2. Demographic Characteristics (Intent-to-Treat Population)

	Sunitinib (N=311)
Male, n (%)	198 (63.7)
Female, n (%)	113 (36.3)
Age (years), n (%)	
<18	0
18-44	40 (12.9)
45-64	179 (57.6)
≥65	92 (29.6)
Mean (SD)	58.5 (11.62)
Median	59.0
Range	20.0, 88.0
Race, n (%)	
White	272 (87.5)
Black	13 (4.2)
Not allowed to ask	4 (1.3)
Asian	12 (3.9)
Not listed	10 (3.2)

N = number of subjects; n = number of subjects in the specified category; SD = standard deviation.

Efficacy Results*:* No statistical evaluations were performed for efficacy.

Safety Results:

Duration of Treatment: The duration of treatment is provided in Table 3.

Table 3. Duration of Treatment (Intent-to-Treat Population)

	Sunitinib (N=311)
Duration category (days), n (%)	
≤1	0 (0.0)
2-7	2 (0.6)
8-14	6 (1.9)
15-28	33 (10.6)
29-60	18 (5.8)
61-90	40 (12.9)
≥91	212 (68.2)
Median duration	190
Range	3, 2289

Duration was defined as the total number of days from the first to the last dose of study treatment.
N = number of subjects in treatment population; n = number of subjects in each duration category (days).

Overall Summary of Adverse Event: An overall summary of AEs is provided in Table 4.

Table 4. Overall Summary of Adverse Events (Intent-to-Treat Population)

	Sunitinib (N=311)
Number of AEs[a]	9899
Number (%) subjects with ≥1 AE	307 (98.7)
Number (%) subjects with ≥1 SAE	118 (37.9)
Number (%) subjects with ≥1 treatment-related AE	282 (90.7)
Number (%) subjects with ≥1 treatment-related SAE	39 (12.5)
Number (%) subjects who discontinued due to AE	53 (17.0)
Number (%) subjects who died	159 (51.1)
Number (%) subjects with dose delayed/changed due to AE	158 (50.8)

AEs and SAEs are not separated out.
AE = adverse event; N = number of subjects; SAE = serious adverse event.
a. Includes all reported AEs.

Incidence of Adverse Events: An overview of all-causality TEAEs experienced by ≥5% of subjects is provided in Table 5.

Table 5. Summary of Non-serious Adverse Events Experienced by ≥5% of Subjects by MedDRA System Organ Class and Preferred Term (Intent-to-Treat Population)

System Organ Class and Preferred Term	Number (%) of Subjects (N=311)	Number of Events (N=311)
Any Non-Serious Adverse Events ≥5%	**299 (96.1)**	**6953**
Blood and lymphatic system disorders	130 (41.8)	561
Anaemia	71 (22.8)	180
Leukopenia	32 (10.3)	71
Neutropenia	54 (17.4)	212
Thrombocytopenia	48 (15.4)	98
Endocrine disorders	39 (12.5)	46
Hypothyroidism	39 (12.5)	46
Eye disorders	23 (7.4)	43
Periorbital oedema	23 (7.4)	43
Gastrointestinal disorders	255 (82.0)	2261
Abdominal discomfort	18 (5.8)	23
Abdominal distension	29 (9.3)	49
Abdominal pain	73 (23.5)	141
Abdominal pain upper	41 (13.2)	58
Constipation	66 (21.2)	107
Diarrhoea	179 (57.6)	817
Dry mouth	25 (8.0)	38
Dyspepsia	56 (18.0)	146
Flatulence	31 (10.0)	57
Gastrooesophageal reflux disease	36 (11.6)	50
Haemorrhoids	22 (7.1)	28
Nausea	141 (45.3)	344
Oral pain	34 (10.9)	74
Stomatitis	45 (14.5)	104
Vomiting	93 (29.9)	225
General disorders and administration site conditions	250 (80.4)	1280
Asthenia	23 (7.4)	36
Chest pain	29 (9.3)	36
Chills	30 (9.6)	45
Fatigue	206 (66.2)	753
Mucosal inflammation	58 (18.6)	97
Oedema	24 (7.7)	34
Oedema peripheral	68 (21.9)	166
Pain	25 (8.0)	34
Pyrexia	60 (19.3)	79
Infections and infestations	47 (15.1)	68
Sinusitis	18 (5.8)	23
Upper respiratory tract infection	33 (10.6)	45
Investigations	68 (21.9)	172
Aspartate aminotransferase increased	16 (5.1)	20
Blood creatinine increased	20 (6.4)	60
Haemoglobin decreased	20 (6.4)	58
Weight decreased	28 (9.0)	34
Metabolism and nutrition disorders	118 (37.9)	266
Decreased appetite	103 (33.1)	194
Dehydration	25 (8.0)	39
Hyperglycaemia	16 (5.1)	33
Musculoskeletal and connective tissue disorders	151 (48.6)	547
Arthralgia	55 (17.7)	110
Back pain	65 (20.9)	91

Table 5. Summary of Non-serious Adverse Events Experienced by ≥5% of Subjects by MedDRA System Organ Class and Preferred Term (Intent-to-Treat Population)

System Organ Class and Preferred Term	Number (%) of Subjects (N=311)	Number of Events (N=311)
Muscle spasms	28 (9.0)	58
Musculoskeletal pain	22 (7.1)	28
Myalgia	23 (7.4)	42
Pain in extremity	64 (20.6)	218
Nervous system disorders	132 (42.4)	366
Dizziness	39 (12.5)	52
Dysgeusia	48 (15.4)	114
Headache	73 (23.5)	129
Neuropathy peripheral	25 (8.0)	49
Peripheral sensory neuropathy	16 (5.1)	22
Psychiatric disorders	68 (21.9)	157
Anxiety	24 (7.7)	45
Depression	21 (6.8)	36
Insomnia	49 (15.8)	76
Respiratory, thoracic and mediastinal disorders	140 (45.0)	446
Cough	73 (23.5)	115
Dyspnoea	79 (25.4)	144
Dyspnoea exertional	19 (6.1)	23
Epistaxis	36 (11.6)	124
Oropharyngeal pain	25 (8.0)	40
Skin and subcutaneous tissue disorders	166 (53.4)	609
Dry skin	35 (11.3)	57
Erythema	19 (6.1)	29
Palmar—plantar erythrodysaesthesia syndrome	81 (26.0)	251
Pruritus	19 (6.1)	24
Rash	55 (17.7)	114
Skin discolouration	58 (18.6)	90
Skin exfoliation	18 (5.8)	44
Vascular disorders	67 (21.5)	131
Flushing	21 (6.8)	33
Hypertension	54 (17.4)	98

All non-serious AEs are summarized, even if a subject had a serious event of the same preferred term.
% = (n/N)*100
AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities; N = number of subjects; n = number of subjects in the specified category.

Treatment-Related Adverse Events: An overview of treatment-related TEAEs experienced by ≥5% of subjects is provided in Table 6. The most common treatment-related, TEAEs were fatigue (58.2%), diarrhea (49.5%), nausea (31.5%), and palmar-plantar erythrodysesthesia syndrome (23.8%).

Table 6. Summary of Treatment-Related Treatment-Emergent Adverse Events Experienced by ≥5% of Subjects (Intent-to-Treat Population)

MedDRA (v14.1) Preferred Term	Treatment Related Sunitinib (N=311) n (%)
Any treatment-related AE	282 (90.7)
Fatigue	181 (58.2)
Diarrhoea	154 (49.5)
Nausea	98 (31.5)
Palmar-plantar erythrodysaesthesia syndrome	74 (23.8)
Decreased appetite	61 (19.6)
Skin discolouration	58 (18.6)
Vomiting	54 (17.4)
Mucosal inflammation	53 (17.0)
Anaemia	51 (16.4)
Neutropenia	50 (16.1)
Dysgeusia	45 (14.5)
Thrombocytopenia	44 (14.1)
Hypertension	43 (13.8)
Stomatitis	41 (13.2)
Rash	41 (13.2)
Pain in extremity	39 (12.5)
Dyspepsia	39 (12.5)
Hypothyroidism	32 (10.3)
Oral pain	31 (10.0)
Oedema peripheral	29 (9.3)
Headache	29 (9.3)
Dry skin	27 (8.7)
Leukopenia	26 (8.4)
Gastrooesophageal reflux disease	26 (8.4)
Epistaxis	25 (8.0)
Flatulence	22 (7.1)
Dyspnoea	22 (7.1)
Abdominal distension	21 (6.8)
Constipation	20 (6.4)
Dry mouth	20 (6.4)
Abdominal pain	19 (6.1)
Haemoglobin decreased	17 (5.5)
Periorbital oedema	17 (5.5)
Muscle spasms	16 (5.1)

AEs and SAEs are not separated out
AEs= adverse events; MedDRA = Medical Dictionary for Regulatory Activities; N = number of subjects; n = number of subjects in the specified category; SAEs = serious adverse events; v = version.

Grade 3, 4, and 5 Adverse Events: An overview of all-causality and treatment-related Grade 3, 4, and 5 TEAEs occurring in at least 2% of subjects is provided in Table 7.

Table 7. Summary of Grades 3, 4, and 5 Treatment-Emergent Adverse Events Occurring in at Least 2% of Subjects (All Causality and Treatment Related) (Intent-to-Treat Population)

MedDRA (v14.1) Preferred Term	All Causality Sunitinib (N=311) n (%)	Treatment Related Sunitinib (N=311) n (%)
Any Grade 3, 4, or 5 AE	195 (62.7)	106 (34.1)
Abdominal pain	21 (6.8)	1 (0.3)
Anemia	15 (4.8)	9 (2.9)
Dehydration	15 (4.8)	2 (0.6)
Diarrhea	19 (6.1)	11 (3.5)
Disease progression	10 (3.2)	0
Dyspnea	14 (4.5)	3 (1.0)
Fatigue	36 (11.6)	26 (8.4)
Hypertension	12 (3.9)	12 (3.9)
Leukopenia	7 (2.3)	6 (1.9)
Nausea	14 (4.5)	5 (1.6)
Neutropenia	28 (9.0)	25 (8.0)
Palmar-plantar erythrodysesthesia syndrome	12 (3.9)	12 (3.9)
Pneumonia	7 (2.3)	1 (0.3)
Thrombocytopenia	10 (3.2)	9 (2.9)
Vomiting	19 (6.1)	5 (1.6)

AEs and SAEs are not separated out.
AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities; N = number of subjects in treatment population; n = number of subjects in each duration category (days); SAE = serious adverse events; v = version.

Serious Adverse Events: An overview of all-causality and treatment-related treatment-emergent SAEs occurring in subjects is provided in Table 8.

Table 8. Summary of Serious Adverse Events Occurring in Subjects (All Causality and Treatment Related) (Intent-to-Treat Population)

MedDRA (v14.1) Preferred Term	All Causality Sunitinib (N=311) n (%)	Treatment Related Sunitinib (N=311) n (%)
Any SAE	118 (37.9)	39 (12.5)
Abdominal abscess	1 (0.3)	-
Abdominal pain	14 (4.5)	1 (0.3)
Abdominal pain lower	1 (0.3)	-
Abdominal pain upper	2 (0.6)	-
Acetabulum fracture	1 (0.3)	-
Acute pulmonary oedema	1 (0.3)	-
Adverse drug reaction	1 (0.3)	1 (0.3)
Anaemia	8 (2.6)	5 (1.6)
Angioedema	1 (0.3)	1 (0.3)
Arrhythmia	2 (0.6)	-
Arrhythmia supraventricular	1 (0.3)	-
Arthralgia	2 (0.6)	-
Aspartate aminotransferase increased	1 (0.3)	-
Asthenia	2 (0.6)	-
Atrial fibrillation	1 (0.3)	-
Atrioventricular block first degree	1 (0.3)	-
Back pain	2 (0.6)	-
Bile duct stone	1 (0.3)	-
Biliary fistula	1 (0.3)	-
Blood bilirubin increased	1 (0.3)	-
Bronchitis	1 (0.3)	-
Bursitis	1 (0.3)	1 (0.3)
Caecitis	1 (0.3)	1 (0.3)
Cardiac failure	1 (0.3)	1 (0.3)
Cardiac failure congestive	2 (0.6)	2 (0.6)
Cardio respiratory arrest	1 (0.3)	-
Cellulitis	2 (0.6)	1 (0.3)
Cerebral haemorrhage	1 (0.3)	-
Chest discomfort	1 (0.3)	-
Chest pain	4 (1.3)	1 (0.3)
Cholangitis	2 (0.6)	-
Cholecystitis	4 (1.3)	-
Cholecystitis acute	1 (0.3)	-
Cholelithiasis	1 (0.3)	-
Chronic obstructive pulmonary disease	1 (0.3)	-
Clostridial infection	1 (0.3)	-
Cognitive disorder	1 (0.3)	1 (0.3)
Concussion	1 (0.3)	-
Confusional state	2 (0.6)	-
Convulsion	2 (0.6)	-
Cough	1 (0.3)	-
Cyclic vomiting syndrome	1 (0.3)	1 (0.3)
Deep vein thrombosis	2 (0.6)	2 (0.6)
Dehydration	13 (4.2)	1 (0.3)
Depressed level of consciousness	1 (0.3)	-
Depression	1 (0.3)	-
Diarrhoea	7 (2.3)	2 (0.6)
Disease progression	9 (2.9)	-
Disseminated intravascular coagulation	1 (0.3)	-
Dizziness	1 (0.3)	-
Dyspnoea	8 (2.6)	2 (0.6)
Empyema	1 (0.3)	-
Enterocolitis infectious	1 (0.3)	-

Table 8. Summary of Serious Adverse Events Occurring in Subjects (All Causality and Treatment Related) (Intent-to-Treat Population)

MedDRA (v14.1) Preferred Term	All Causality Sunitinib (N=311) n (%)	Treatment Related Sunitinib (N=311) n (%)
Enterocutaneous fistula	1 (0.3)	-
Epistaxis	3 (1.0)	2 (0.6)
Failure to thrive	1 (0.3)	-
Fall	1 (0.3)	-
Fatigue	2 (0.6)	-
Febrile neutropenia	1 (0.3)	-
Femur fracture	1 (0.3)	-
Flank pain	1 (0.3)	-
Gastric haemorrhage	1 (0.3)	1 (0.3)
Gastroenteritis	1 (0.3)	-
Gastroenteritis viral	1 (0.3)	-
Gastrointestinal fistula	1 (0.3)	1 (0.3)
Gastrointestinal haemorrhage	4 (1.3)	-
Gastrointestinal obstruction	1 (0.3)	-
Gastrointestinal stromal tumour	1 (0.3)	-
Grand mal convulsion	1 (0.3)	-
Haematemesis	1 (0.3)	-
Haematochezia	1 (0.3)	-
Haemoglobin decreased	1 (0.3)	1 (0.3)
Haemothorax	1 (0.3)	1 (0.3)
Headache	1 (0.3)	1 (0.3)
Hepatic encephalopathy	2 (0.6)	-
Hepatic failure	4 (1.3)	-
Hepatic haemorrhage	1 (0.3)	-
Hepatitis	1 (0.3)	1 (0.3)
Humerus fracture	1 (0.3)	-
Hydronephrosis	1 (0.3)	-
Hyperbilirubinaemia	1 (0.3)	-
Hypercalcaemia	1 (0.3)	-
Hyperkalaemia	1 (0.3)	-
Hypernatraemia	1 (0.3)	5 (1.6)
Hypertension	5 (1.6)	5 (1.6)
Ileus	1 (0.3)	-
Incontinence	1 (0.3)	-
Infection	3 (1.0)	-
Infectious peritonitis	1 (0.3)	-
Intestinal perforation	1 (0.3)	-
Intra abdominal haemorrhage	1 (0.3)	-
Ischaemic stroke	1 (0.3)	-
Klebsiella bacteraemia	1 (0.3)	-
Large intestine perforation	1 (0.3)	-
Limb injury	1 (0.3)	-
Liver abscess	2 (0.6)	-
Lower respiratory tract infection	1 (0.3)	1 (0.3)
Melaena	1 (0.3)	-
Menorrhagia	1 (0.3)	-
Mental status changes	3 (1.0)	-
Muscle abscess	1 (0.3)	-
Myocardial infarction	2 (0.6)	2 (0.6)
Nausea	10 (3.2)	3 (1.0)
Neck pain	1 (0.3)	1 (0.3)
Neutropenia	1 (0.3)	1 (0.3)
Pain	1 (0.3)	-
Pain in extremity	1 (0.3)	1 (0.3)

Table 8. Summary of Serious Adverse Events Occurring in Subjects (All Causality and Treatment Related) (Intent-to-Treat Population)

MedDRA (v14.1) Preferred Term	All Causality Sunitinib (N=311) n (%)	Treatment Related Sunitinib (N=311) n (%)
Pancreatic abscess	1 (0.3)	-
Pancreatitis	5 (1.6)	2 (0.6)
Paraplegia	1 (0.3)	-
Pathological fracture	1 (0.3)	-
Pelvic fracture	1 (0.3)	-
Peripheral vascular disorder	1 (0.3)	-
Perirectal abscess	1 (0.3)	-
Pleural effusion	3 (1.0)	-
Pneumonia	5 (1.6)	1 (0.3)
Pneumothorax	1 (0.3)	-
Portal vein thrombosis	1 (0.3)	-
Presyncope	1 (0.3)	-
Proctalgia	1 (0.3)	-
Pubis fracture	1 (0.3)	-
Pulmonary embolism	1 (0.3)	1 (0.3)
Pyelonephritis	1 (0.3)	-
Pyrexia	6 (1.9)	-
Rectal haemorrhage	1 (0.3)	-
Rectal obstruction	1 (0.3)	-
Renal failure	3 (1.0)	-
Renal failure acute	2 (0.6)	2 (0.6)
Renal impairment	1 (0.3)	-
Respiratory failure	1 (0.3)	-
Retching	1 (0.3)	1 (0.3)
Sepsis	4 (1.3)	-
Septic shock	1 (0.3)	-
Shock haemorrhagic	1 (0.3)	-
Sinus bradycardia	1 (0.3)	-
Small intestinal obstruction	1 (0.3)	-
Spinal cord compression	2 (0.6)	-
Squamous cell carcinoma of skin	1 (0.3)	-
Sudden death	1 (0.3)	1 (0.3)
Syncope	2 (0.6)	-
Thrombosis	2 (0.6)	1 (0.3)
Transfusion reaction	1 (0.3)	-
Transient ischaemic attack	1 (0.3)	-
Tumour haemorrhage	2 (0.6)	2 (0.6)
Upper gastrointestinal haemorrhage	2 (0.6)	1 (0.3)
Urinary retention	1 (0.3)	-
Urinary tract infection	3 (1.0)	-
Vaginal haemorrhage	1 (0.3)	-
Vomiting	11 (3.5)	2 (0.6)
Weight decreased	1 (0.3)	-
Wound complication	1 (0.3)	-
Wound infection	2 (0.6)	-

MedDRA = Medical Dictionary for Regulatory Activities; N = number of subjects; n = number of subjects in the specified category; SAE = serious adverse event; v = version.

Deaths: A summary of deaths is provided in Table 9. The most common reason for deaths during follow-up was progressive disease (36.3%).

Table 9. Summary of Deaths (Intent-to-Treat Population)

	Sunitinib (N=311) n (%)
Subjects who died	159 (51.1)
Subject who died on study[a]	27 (8.7)
Arrhythmia	1 (0.3)
Cardiopulmonary arrest	1 (0.3)
Disease progression (includes progressive disease)	11 (3.5)
Dyspnea	1 (0.3)
GI stromal tumor	1 (0.3)
GI bleed	1 (0.3)
Intercerebral bleed	1 (0.3)
Liver failure	4 (1.3)
Pneumonia	1 (0.3)
Recurring renal failure	1 (0.3)
Respiratory failure	1 (0.3)
Septic shock/Septic shock	1 (0.3)
Sudden death	1 (0.3)
Tumor hemorrhage	1 (0.3)
Subjects who died during follow-up[b]	132 (42.4)
2 episodes of hematemesis after upper GI endoscopy	1 (0.3)
Cardiopulmonary arrest	1 (0.3)
Date of death only found on SSDI. No data on cause of death available.	1 (0.3)
Date of death reported in database	1 (0.3)
Multiple leptomeningeal metastasis	1 (0.3)
Progressive disease	113 (36.3)
Renal failure	1 (0.3)
Respiratory failure, COPD	1 (0.3)
Stroke	1 (0.3)
Unknown	11 (3.5)

COPD = chronic obstructive pulmonary disease; GI = gastrointestinal; N = number of subjects in treatment population; n = number of subjects in each duration category (days); SSDI = Security Death Index Database.

a. On-study deaths were those that occurred after the first dose of study drug and within 28 days of the last dose of study drug.

b. Follow-up deaths were those that occurred > 28 days after the last dose of study drug.

Discontinuations due to Adverse Events: A total of 53 subjects discontinued due to AEs.

Laboratory Results: A summary of hematological laboratory results by maximum CTCAE grade is provided in Table 10.

Table 10. Summary of Hematological Laboratory Results by Maximum CTCAE Grade (Intent-to-Treat Population)

Parameter	Sunitinib (N=311) Maximum CTCAE Grade					
	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Absolute neutrophil count	102 (32.8)	28 (9.0)	81 (26.0)	33 (10.6)	50 (16.1)	294 (94.5)
Hemoglobin	38 (12.2)	173 (55.6)	78 (25.1)	14 (4.5)	1 (0.3)	304 (97.7)
Lymphocytes	140 (45.0)	31 (10.0)	57 (18.3)	36 (11.6)	30 (9.6)	294 (94.5)
Platelets	123 (39.5)	137 (44.1)	26 (8.4)	14 (4.5)	4 (1.3)	304 (97.7)
White blood cells	74 (23.8)	109 (35.0)	99 (31.8)	20 (6.4)	2 (0.6)	304 (97.7)

NCI CTCAE version 3.0 was used for grading laboratory results.
CTCAE = Common Terminology Criteria for Adverse Events; N = number of subjects in treatment population; n = number of subjects in each duration category (days); NCI = National Cancer Institute.

A summary of serum biochemistry laboratory results by maximum CTCAE grade is provided in Table 11.

Table 11. Summary of Serum Biochemistry Laboratory Results by Maximum CTCAE Grade (Intent-to-Treat Population)

Parameter	Sunitinib (N=311) Maximum CTCAE Grade					
	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Alanine aminotransferase	198 (63.7)	81 (26.0)	12 (3.9)	9 (2.9)	0	300 (96.5)
Aspartate aminotransferase	148 (47.6)	130 (41.8)	16 (5.1)	8 (2.6)	0	302 (97.1)
Albumin	8 (2.6)	3 (1.0)	0	0	0	11 (3.5)
Alkaline phosphatase	169 (54.3)	97 (31.2)	24 (7.7)	12 (3.9)	0	302 (97.1)
Amylase	134 (43.1)	19 (6.1)	2 (0.6)	0	0	155 (49.8)
Calcium (hypercalcemia)	280 (90.0)	19 (6.1)	2 (0.6)	0	2 (0.6)	303 (97.4)
Calcium (hypocalcemia)	196 (63.0)	72 (23.2)	28 (9.0)	4 (1.3)	3 (1.0)	303 (97.4)
Creatinine	184 (59.2)	82 (26.4)	34 (10.9)	1 (0.3)	1 (0.3)	302 (97.1)
Glucose (hyperglycemia)	87 (28.0)	141 (45.3)	57 (18.3)	17 (5.5)	0	302 (97.1)
Glucose (hypoglycemia)	262 (84.2)	34 (10.9)	4 (1.3)	0	2 (0.6)	302 (97.1)
Lipase	113 (36.3)	15 (4.8)	9 (2.9)	10 (3.2)	0	147 (47.3)
Phosphorus (hypophosphatemia)	209 (67.2)	8 (2.6)	53 (17.0)	8 (2.6)	0	278 (89.4)
Potassium (hyperkalemia)	243 (78.1)	49 (15.8)	8 (2.6)	3 (1.0)	0	303 (97.4)
Potassium (hypokalemia)	241 (77.5)	58 (18.6)	0	4 (1.3)	0	303 (97.4)
Sodium (hypernatremia)	266 (85.5)	37 (11.9)	0	0	0	303 (97.4)
Sodium (hyponatremia)	203 (65.3)	84 (27.0)	0	16 (5.1)	0	303 (97.4)
Total bilirubin	236 (75.9)	28 (9.0)	22 (7.1)	15 (4.8)	0	301 (96.8)
Uric acid (hyperuricemia)	207 (66.6)	59 (19.0)	0	0	16 (5.1)	282 (90.7)

NCI CTCAE version 3.0 was used for grading laboratory results.
CTCAE = Common Terminology Criteria for Adverse Events; N = number of subjects in treatment population; n = number of subjects in each duration category (days); NCI = National Cancer Institute.

CONCLUSIONS:

- Sunitinib treatment was provided to subjects who participated in a previous sunitinib protocol.

- Sunitinib was generally well tolerated; 53 (17.0%) of the subjects discontinued the study due to an AE. The types, frequencies, and seriousness of reported events were similar to the known safety profile of sunitinib.

- A total of 159 (51.1%) subjects died including 27 (8.7%) subjects who died within 28 days of the last dose of study drug and 132 (42.4%) subjects who died >28 days after the last dose of study drug. The most common reason for deaths was progressive disease.