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PROPRIETARY DRUG NAME®/GENERIC DRUG NAME: Inlyta® / Axitinib

PROTOCOL NO.: A4061016

PROTOCOL TITLE: A Randomized Phase 2 Study of the Anti-Angiogenesis Agent AG-013736 in Combination with Gemcitabine in Patients with Chemotherapy-Naïve Advanced Pancreatic Cancer Preceded by a Phase 1 Portion

Study Center: There were 30 centers who took part in the study and enrolled subjects which included 1 in Belgium, 5 in Canada, 4 in France, 1 in Germany, 2 in Italy, 3 in Spain, 4 in United Kingdom, and 10 in United States.

Study Initiation and Final Completion Dates: 05 July 2005 to 14 March 2008

Phase of Development: Phase 2

Study Objectives:

Primary Objective:

Determine whether the overall survival (OS) of the combination of axitinib and gemcitabine was superior to that of gemcitabine alone in subjects who had advanced pancreatic cancer that had not been previously treated with systemic therapy.

Secondary Objectives:

- Determine the doses of axitinib and gemcitabine that could be safely given together (Phase 1 portion);
- Determine the adverse event (AE) profile and dose-limiting toxicities for the combination;
- Assess gemcitabine and axitinib pharmacokinetic (PK) parameters in the Part 1 portion of the study, and evaluate population PK of axitinib in the Phase 2 portion of the study;
- Document response (Phase 1 portion) and determine the response rate and duration of response (Phase 2 portion) in subjects who had measurable disease at baseline; and
- Determine progression-free survival (PFS) and 1-year survival (Phase 2 portion); and
- Assess patient-reported outcomes (PROs) of health-related quality of life (HRQoL) and pancreatic cancer-specific symptoms (Phase 2 portion).

METHODS

Study Design:

This was a randomized, open-label Phase 2 , multicenter study of the angiogenesis inhibitor axitinib given in combination with gemcitabine versus gemcitabine alone for subjects who had not received prior chemotherapy for locally advanced, surgically unresectable, or metastatic pancreatic cancer. A lead-in Phase 1 portion of the study was designed to identify the doses of gemcitabine and axitinib in the combination arm and determine the PK of each of the drugs. Table 1 shows the schedule of tests and procedures during the Phase 1 portion of the study. Once the lead-in Phase 1 portion of the study was completed, the randomized Phase 2 portion began. Subjects were randomized in a 2:1 manner between the combination of gemcitabine plus axitinib and gemcitabine alone. Randomization was stratified by Eastern Cooperative Oncology Group (ECOG) performance status (≤1 versus 2) and extent of disease (locally advanced versus metastatic). Overall survival was the primary endpoint. Subjects with measurable disease had assessments for tumor response approximately every 8 weeks. Crossover of subjects receiving gemcitabine alone to axitinib was not permitted. Table 2 shows the schedule of tests and procedures during the Phase 2 portion.

Table 1. Schedule of Tests and Procedures During the Phase 1 Portion

Observation	Screening Days –14 to Day 0	Day 1 (Predose) of Each Cycle[a]	Days 8 and 15 (Predose) of Each Cycle	Follow-Up 28 Days After Last Dose
Informed consent	X			
Medical history[b]	X			
Physical examination[c]	X	X		X
Weight, temperature, BP[d], pulse	X	X		X
ECOG performance status	X	X		X
Chest x-ray[e]	X			
ECG[f]	X			X
Hematology[g]	X	X	X	X
Chemistry[g]	X	X	X[f]	X
Urinalysis[g]	X	X		X
Safety assessment (adverse events)		Monitored throughout the study		
Concomitant treatment	X	Monitored throughout the study		
Tumor measurements[h]	Days –28 to 0	Every 2 cycles		
Pharmacokinetic plasma samples		X[i]		
Pregnancy test	Days –3 to 0			
Gemcitabine treatment		X	X	
Axitinib treatment		Continuous twice daily dosing starting Cycle 1 Day 3		

BP = blood pressure; CR = Complete Response; CT = computed tomography ECG = electrocardiogram; ECOG = eastern cooperative oncology group; MRI = magnetic resonance imaging; PR = Partial Response.

a. Cycle length was 4 weeks. Tests and procedures were performed on schedule, but occasional changes by ± 4 days were allowable for holidays, vacations, and other administrative reasons.
b. Medical history including history of prior treatments for pancreatic cancer and use of nicotine products.
c. Including height on initial examination. After the initial complete examination, targeted examinations based on signs and symptoms could have been performed.
d. Blood pressure was taken in the seated position after the subject had been sitting quietly for 5 minutes. The subject was to take BP measurements at least once daily and record results in the Subject Diary.
e. Additional chest x-rays if clinically necessary. If a CT scan or MRI scan of the chest was performed as part of tumor assessment at baseline, a chest x-ray was not required.
f. Additional ECG if clinically indicated.
g. If baseline values were obtained within 4 days prior to Cycle 1 Day 1, repeat hematology, chemistry and urinalysis were not necessary.
h. Tumor assessments were done every 2 cycles (ie, at the end of the second cycle and the end of every other cycle thereafter). Response (CR/PR) required confirmation at least 4 weeks after the response was noted.
i. Samples collected Cycle 1 Day 1 and Cycle 1 Days 14 and 15.

Table 2. Schedule of Tests and Procedures During the Phase 2 Portion

Observation	Screening Days –14 to Day 0	Day 1 (Predose) of Each Cycle[a]	Days 8 and 15 (Predose) of Each Cycle	Follow-Up 28 Days After Last Dose
Informed consent	X			
Medical history	X			
Physical examination[b]	X	X		X
Weight, temperature, BP[c], pulse	X	X	X[c]	X
ECOG performance status	X	X		X
Chest x-ray[d]	X			
ECG[e]	X			X
Hematology[f]	X	X	X	X
Chemistry[f]	X	X	X[f]	X
Urinalysis[f]	X	X		X
Safety assessment (AEs)	X	Monitored throughout the study		
Concomitant treatment	X	Monitored throughout the study		
Tumor measurements[g]	Day –28 to 0	Every 2 cycles		
Serum or Plasma CA 19-9	X	X		
Health-related Quality of Life (QLQ-C30 and QLQ-PAN26)		X		X
Pharmacokinetic plasma samples[h]		See footnote (h)		
Pregnancy test	Day –3 to 0			
Gemcitabine treatment		X	X	
Axitinib treatment		Continuous twice daily dosing starting Cycle 1 Day 1		
Survival		Until at least 1 year after the randomization of the last subject		

AE = adverse event; BP = blood pressure; CA 19-9 = carbohydrate antigen 19-9; CT = computed tomography; ECG = electrocardiogram; ECOG = eastern cooperative oncology group; QLQ = quality of life questionnaire; MRI = magnetic resonance imaging.

a. Cycle length was 4 weeks. Tests and procedures were done on schedule, but occasional changes by ± 4 days were allowable for holidays, vacations, and other administrative reasons.
b. Including height on initial examination. After the initial complete examination, targeted examinations based on signs and symptoms could have been performed.
c. BP was taken in the seated position after the subject had been sitting quietly for 5 minutes. The subject was to take BP measurements at least once daily and record results in the Subject Diary.
d. Additional chest x-rays if clinically necessary. If a CT scan or MRI scan of the chest was performed as part of tumor assessment at baseline, a chest X-ray was not required.
e. Additional electrocardiograms if clinically indicated.
f. If baseline values were obtained within 4 days prior to Cycle 1 Day 1, repeat hematology, chemistry and urinalysis were not necessary.
g. Baseline assessment of disease was to be done within 28 days before randomization. Tumor assessments were to be done every 2 cycles (ie, at the end of the second cycle and end of every other cycle thereafter). Response (Complete Response/Partial Response) required confirmation at least 4 weeks after the response was noted. For subjects who had not progressed after discontinuing study drug, additional tumor assessments was to be performed approximately every 8 weeks until subject met criteria for progression or alternate therapy started.
h. Required only for subjects randomized to receive gemcitabine plus axitinib.

Number of Subjects (Planned and Analyzed): For Part 1 of the study, 8 subjects were enrolled and treated in the Phase 1 portion of the study; of these, 6 were analyzed for safety and

pharmacokinetics. For Phase 2 portion of the study, 120 subjects were planned for enrollment, 103 were actually enrolled, and 99 subjects received study treatment (20 in Canada, 38 in United States, 15 in Spain, 3 in Belgium, 1 in Germany, 13 in Italy, 14 in France and 13 in United Kingdom).

Diagnosis and Main Criteria for Inclusion:

Inclusion Criteria: Subjects with advanced (localized but surgically unrespectable or metastatic) histologically/cytologically proven epithelial cancer of the exocrine pancreas and with no prior therapy for metastatic disease were included in the study.

Exclusion Criteria: Subjects with locally advanced disease who were candidates for radiation therapy and with uncontrolled brain metastases (a controlled brain metastasis must be previously treated, asymptomatic, and without growth for 4 month were excluded from the study.

Study Treatment: The initial cohort of the lead-in Phase 1 portion was planned to include 6 subjects. Subjects in this cohort had the initial gemcitabine infusion prior to beginning axitinib. The Phase 1 cohort received gemcitabine 1000 mg/m^2 by 30-minute infusion once weekly on Days 1, 8, and 15 (or until toxicity necessitated decreasing or holding a dose) followed by a week off treatment. Subsequent cycles consisted of infusions once weekly for 3 consecutive weeks in 4-week cycles.

The dose of axitinib in the initial Phase 1 cohort was 5 mg given orally twice daily (BID) (at approximately 12-hour intervals) in the fasted state (no food or drink except water for 2 hours before or after dosing). Dosing with axitinib began approximately 48 hours (Day 3) after the first gemcitabine infusion to allow baseline gemcitabine PK to be determined.

Subjects experiencing a drug-related dose-limiting toxicity (DLT) had axitinib, gemcitabine, or both agents held until the toxicity reduced to Grade 1 or lower. Treatment was restarted at approximately 75% of the previous dose of gemcitabine or 80% of the previous dose of axitinib. The agent to be dose reduced was dependent upon the toxicity observed. The dose of axitinib was adjusted for toxicities such as hypertension or proteinuria. The dose of gemcitabine was adjusted for toxicities such as neutropenia or thrombocytopenia. In cases where it was not obvious as to which drug was the major contributor to the AE), both drugs were held and/or reduced. Decisions on individual subject dose reductions were decided jointly by the Phase 1 investigators and the sponsor.

If none or 1 of the 6 subjects in the initial Phase 1 cohort had a drug-related dose-limiting toxicity during the first 4 weeks, the Phase 2 randomized portion of the study was to begin. AEs that required dose reductions after 4 weeks were not considered DLT for the purpose of determining the starting dose of the 2 agents in combination, unless a specific toxicity related to cumulative dosing was identified. In such a case, a course of action was to be determined jointly by the Phase 1 investigators and the sponsor.

If 2 or more of the 6 subjects in the initial Phase 1 cohort had a drug-related dose-limiting toxicity during the first 4 weeks, the starting dose was to be decreased and evaluated in an additional cohort of 6 subjects. Either gemcitabine was to be given at approximately 75% of the previous dose or axitinib at 80% of the previous dose. The agent to be dose-reduced was to be

dependent upon the toxicity observed. The dose of axitinib was adjusted for toxicities such as hypertension or proteinuria. The dose of gemcitabine was adjusted for toxicities such as neutropenia and thrombocytopenia. In cases where it was not obvious as to which drug was the major contributor to the AE(s), both drugs were reduced. Decisions on dose reductions were made by consensus of the Phase 1 investigators and the sponsor.

If none or 1 of the 6 subjects in the second Phase 1 cohort had a DLT during the first 4 weeks, the Phase 2 randomized study began using the drug doses from Cohort 2.

If 2 or more of the 6 subjects in the second cohort had a DLT during the first 4 weeks, decisions regarding dose adjustments were to be dependent upon the toxicity observed, the dose of the individual drugs in the cohort, and whether the PK profile of 1 or both drugs was changed in the combination. Decisions on further dose reductions were to be made by consensus of the Phase 1 investigators and the sponsor. However, the study was not to proceed if gemcitabine was reduced to <750 mg/m^2 or axitinib to <3 mg BID.

Efficacy Pharmacokinetic and Safety Endpoints:

Primary Endpoint:

The primary endpoint was OS (Phase 2 portion). All deaths from any cause were included in the analysis.

Secondary Endpoint:

- Dose confirmation of each drug in the combination, based on the number of dose-limiting toxicities occurring within 6 subject cohort(s) (Phase 1 portion).
- Safety profile of treatments based on physical examinations, laboratory tests, and assessment of adverse events.
- Pharmacokinetic parameters of axitinib and gemcitabine when given in combination during the Phase 1 portion. Population PK modeling with data from subjects enrolled in the Phase 2 portion of the study; this is to be provided in a separate report.
- For subjects with measurable disease at baseline, response was determined according to Response Evaluation Criteria in Solid Tumors (RECIST). Response rate (including complete and partial responses) and duration of response was determined in the Phase 2 portion of the study.
- Progression-free survival, based on progression or death from any cause, and 1-year survival, based on the proportion of subjects still alive 1 year after randomization (Phase 2 portion).
- Patient-reported outcomes of health-related quality of life and pancreatic cancer-specific symptoms, as measured by the EORTC QLQ-C30 and QLQ-PAN26 (Phase 2 portion).

Safety Evaluations: Adverse events, clinical laboratory measurement, electrocardiogram (ECG), and vital signs were assessed throughout the study.

Statistical Methods: Analysis sets includes Intent-To Treat (ITT) Population and Safety Population.

Intent-To Treat (ITT) Population (Full Analysis Set): This population included all subjects who were randomized, with study drug assignment designated according to initial randomization, regardless of whether subjects received study drug or received a different drug from that to which they were randomized. This was the primary population for evaluating all efficacy endpoints as well as patient characteristics.

Safety Population: The safety population consists of all patients who received at least 1 dose of study medication with treatment assignments designated according to actual study treatment received. This population was the primary population for evaluating treatment Administration / compliance and safety.

The number of subjects that were to be enrolled in the Phase 1 portion of the study depended upon the observed safety profile, which determined the number of dose levels.

The sample size for the randomized portion of this study was calculated based on the primary endpoint of survival and the following assumptions:

- Median survival for the gemcitabine arm of 6 months and 10 months for the combination arm;
- Uniform subject accrual over 12 months;
- A 12-month follow-up period after randomization of the last subject; and
- No loss to follow-up

The randomized Phase 2 portion of the study was designed to determine if there was sufficient activity of the combination of axitinib plus gemcitabine to warrant larger scale, comparative studies, in subjects with advanced pancreatic cancer. A 1-sided log rank test comparing the 2 treatment arms with an overall target sample size of 102 subjects (68 subjects in the combination arm and 34 subjects in the gemcitabine arm) achieved 80% power at a 10% significance level to detect a hazard ratio of 1.67 (gemcitabine: gemcitabine + axitinib) under the alternative hypothesis. The required number of events was 68.

Analysis of Efficacy Parameters:

In the Phase 1 portion of the study, if gemcitabine could not have been administered at $\geq$750 mg/m^2 per scheduled dose or axitinib could not have been administered at $\geq$3 mg BID in the combination, the study was to stop.

Primary Efficacy Analysis:

Subjects in the Phase 1 cohort to confirm the safety of the combination were analyzed separately from those subjects in the randomized portion of the study. Only descriptive statistics such as means, medians, standard errors, and ranges for continuous data and frequencies and percentages

for categorical data were presented. For subjects with measurable disease at baseline, tumor responses were tabulated by dose level(s), if any responses are observed; however no efficacy analyses were performed for this part of the study.

The final analysis was conducted when 68 deaths had occurred in the Phase 2 cohort.

Survival:

All randomized subjects were eligible for this analysis. All subjects were followed for survival at least every 3 months after discontinuation of study treatment until at least 1 year after randomization of the last subject. Survival time was the difference in days between the date of death and the date of randomization. Since the day of randomization and the day of death were each counted as a full day, 1 day was be added to each calculation. Subjects who did not expire had their survival times censored on the last date of known contact that the subject was documented to be alive. Subjects lacking data beyond the day of randomization had their survival times censored at 1 day.

Differences in survival between treatment arms were analyzed by the stratified log-rank test where the stratification factors were performance status (≤1 or 2) and extent of disease (locally advanced or metastatic). If the stratified log rank test was significant at the 1-sided 0.1 level in favor of the gemcitabine plus axitinib arm, this was considered a positive study for the primary endpoint. Estimates of the survival curves from the Kaplan-Meier method were presented. Median event time and a 2-sided 95% confidence interval for the median for each arm were provided using a normal approximation. As a secondary sensitivity check, the unstratified log-rank analysis was performed in an identical fashion to the primary analysis to verify that both approaches led to similar result. Also, the survival probability at 1 year was estimated using the Kaplan-Meier method and the 2-sided 95% confidence interval for the log (-log[1-year survival probability]) was calculated using a normal approximation and then back transformed to give the confidence interval for the 1-year survival rate itself. As a supportive analysis, the unstratified and stratified Cox proportional hazards models were fitted, using the same stratification variables as in the primary analysis. The estimated hazard ratio and 2-sided 95% confidence interval from each model was provided. Additionally for each treatment arm, the median survival and a 2-sided 95% confidence interval were provided for each stratum. After discontinuing the study medication, subjects could have been treated with subsequent therapy. Data collected after subjects had been treated with subsequent therapy were not used for efficacy analyses except survival.

Secondary Efficacy Analyses:

Estimation was emphasized for the summaries of the secondary endpoints. For the secondary endpoints, there was no adjustment for multiplicity. For PFS, response rate, and duration of response, the investigator's response assessments were considered the primary data. Additionally, the primary analyses for these endpoints was based on the data collected from the disease assessment method(s) used starting at baseline to follow a subject's lesions. If positron emission tomography scans or ultrasound was used on some subject's during study who were believed to have central tumor necrosis or bleeding, these data and any subsequently collected

lesion assessment data were not used in the primary analyses but could have been used in additional exploratory analyses of PFS, response rate, and duration of response.

Progression-Free Survival: All randomized subjects were included in the analysis. Subjects who were inadvertently randomized (eg, subjects who were categorized with the incorrect histological cancer type, based on histology performed prior to randomization) were excluded from analyses. PFS was defined as the difference in days between the first date that criteria for progression were met or the subject died due to any cause and the date of randomization. Since the day of randomization and the day criteria for progression were met (or the subject died) were each counted as a full day, 1 day was added to each calculation. Subjects lacking an evaluation of tumor response after randomization had their event time censored at 1 day. Subjects not experiencing disease progression during the treatment and follow-up periods and who did not die during the treatment period had their event time censored on the last study date that objective tumor assessments verified lack of disease progression. Differences in PFS between treatment arms were analyzed by the stratified and un-stratified log-rank tests, using the same stratification variables as in the primary analysis for survival. Estimates of the PFS curves from the Kaplan-Meier method were presented. Median event time and a 2-sided 95% confidence interval for the median for each arm was provided using a normal approximation. Additionally, the un-stratified and stratified Cox proportional hazards models were fitted. The estimated hazard ratio and 2-sided 95% confidence interval from each model were provided. Additionally for each treatment arm, the median PFS and a 2-sided 95% confidence interval were provided for each stratum.

Overall Objective Response:

All randomized subjects with measurable disease and a baseline assessment of disease were included in the analysis. Subjects who were inadvertently randomized (eg, subjects who were categorized with the incorrect histological cancer type, based on histology performed prior to randomization) were excluded from analyses. ORR was defined as the percentage of subjects with a complete response (CR) or partial response (PR). Subjects who died, progressed, or dropped out for any reason after randomization prior to responding were included in the analysis as non-responders. The ORR (CR or PR) for the 2 treatment arms were compared using the Cochran-Mantel-Haenzsel method stratified by baseline stratification factors described in the primary analysis for survival. The relative risk ratio estimator was used to contrast the treatment effects on response rates. Both a point estimate and a 2-sided 95% confidence interval were calculated using a normal approximation. Also, the response rate for each treatment arm were provided with an exact 2-sided 95% confidence interval using a method based on the F distribution. Additionally, the response rate for each treatment arm was provided with an exact 2-sided 95% confidence interval using a method based on the F distribution for each stratum.

Duration of Overall Objective Response:

Analyses on duration of overall objective response were performed for all responding subjects. Duration of overall objective response was defined as the difference in days between the first date criteria for progression occurred or the subject died due to any cause and the first date that criteria for a PR or CR were met. Since the day the criteria for PR or CR were met and the first day criteria for progression occurred (or the subject died) were each counted as a full day, 1 day

was added to each calculation. Subjects who achieved a PR or CR and who did not experience disease progression during the treatment and follow-up periods and who did not die during the treatment period had their event times censored on the last study date that objective tumor assessments verified lack of disease progression. Subjects who achieved a PR and then a CR had times calculated using the date of the PR as the first day. Estimates of duration of overall objective response from the Kaplan-Meier method were presented. Median event time (if appropriate) and a 2 sided 95% confidence interval for the median for each arm were provided using a normal approximation. If the number of CR and PR subjects was small, descriptive statistics or listings were to be provided.

Analysis of Subject-Reported Outcomes Parameters:

On both the QLQ-C30 and Pan26, the proportion of subjects in each arm with a missing subscale score was noted, as were the reasons for not completing a questionnaire. Scoring of the EORTC QLQ-C30 was done consistently with the scoring manual and for the Pan26 on the scoring guidelines. Missing data was not imputed. Scales were prorated if more than 50% of the items were answered for a specific scale. For all subjects in the Phase 2 portion of the study, PROs on multi-item subscale and single-item subscale scores were summarized by the mean and median change from baseline for each treatment group and plotted by time. Differences in the mean and median changes from baseline to each time point, along with standard errors and sample sizes, were examined within and between treatments on Day 1 of every cycle and at end of study. For each subscale, a summary measures analysis was conducted based on mean change from baseline across time for each individual. For each subscale on the EORTC QLQ-C30 and Pan26, the proportion of subjects in each arm that changed by 0 to 4 points, 5 to 9 points and by at least 10 points from baseline was obtained at each time point and across time (based on the summary measures analysis). The same type of assessment was provided for improvement (proportions that improved by 5 to 9 points and by 10+ points) and, separately, for worsening (proportions that deteriorated by 5 to 9 points and by 10+ points). All descriptive analyses, highlighted in the preceding paragraph, were accompanied by within-group and between-group 95% confidence intervals using *t* tests for the mean change from baseline.

Analysis of Pharmacokinetic Parameters:

Subjects in the Phase 1 portion of the study had blood samples taken for PK analysis of axitinib and gemcitabine. Standard plasma PK parameters (maximal plasma concentration [C_{max}], time of maximal plasma concentration [T_{max}], area under the plasma concentration-time profile from time zero to the time of the last quantifiable concentration [AUC_{last}], area under the plasma concentration-time profile from time zero extrapolated to infinite time [AUC_{inf}], plasma terminal elimination half-life [$t_{1/2}$]) for axitinib and gemcitabine were estimated using non-compartmental methods. Changes in PK parameters of gemcitabine were evaluated using the first and third infusions (Cycle 1 Day 1 and Cycle 1 Day 15) and of axitinib using Day 14 and Day 15 doses. The Phase 1 portion of the study was not powered to detect differences in gemcitabine or axitinib PK. As an exploratory analysis, the PK data for the 2 drugs alone and in combination was summarized and reported. For subjects receiving gemcitabine plus axitinib in the randomized Phase 2 portion of the study, population PK analysis was performed for axitinib. Population PK analysis of samples collected in this study was performed in accordance with the Food and drug administration guidance on Population Pharmacokinetics The plasma concentration data set

from this study was pooled with data sets from additional axitinib Phase 2 studies in other oncology subject populations. Population PK analysis involved mixed effects modeling performed using appropriate software (eg, NONMEM). The population PK analysis will be published in a separate report.

Safety: Safety evaluations were summarized descriptively.

RESULTS

Subject Disposition and Demography: Eight subjects were screened and treated in the Phase 1 portion of the study. Table 3 shows a summary of subject disposition. Six subjects completed at least 1 cycle of therapy and were assessable for the safety of the dose level. Two subjects withdrew from treatment for reasons other than treatment-related toxicity prior to completing 4 weeks of dosing, they were considered not evaluable and consequently replaced. Of the 103 screened subjects, 99 (68 in the axitinib + gemcitabine and 31 in the gemcitabine arm) received the study treatment in the Phase 2 portion of the study. A summary of disposition for these subjects is provided in Table 4.

Table 3. Phase 1 Portion: Subject Disposition for Analysis

Number of Subjects, N=8	Axitinib + Gemcitabine
Discontinuation from axitinib	
Insufficient clinical response	3 (37.5%)
Adverse event	2 (25.0%)
Other[a]	1 (12.5%)
Subject no longer willing to participate in study	1 (12.5%)
Discontinuation from gemcitabine	
Insufficient clinical response	4 (50.0%)
Adverse event	1 (12.5%)
Subject no longer willing to participate in study	2 (25.0%)
Completed study (as indicated on CRF)	1 (12.5%)

CRF = case report form; N = number of treated subjects.
a. Started chemotherapy at different institution.

Table 4. Phase 2 Portion: Subject Disposition for Analysis

Treatment Group	Axitinib +Gemcitabine	Gemcitabine
Number of Subjects (%)	**N=69**	**N=34**
Never received axitinib	1 (1.4)	
At least 1 axitinib dose reduction	20 (29.0)	
Discontinuation from axitinib		
Insufficient clinical response	21 (30.4)	
Adverse event	22 (31.9)	
Subject died	8 (11.6)	
Other	8 (11.6)	
Subject no longer willing to participate in study	9 (13.0)	
Never received gemcitabine	1 (1.4)	3 (8.8)
Discontinuation from gemcitabine		
Insufficient clinical response	23 (33.3)	15 (44.1)
Adverse event	23 (33.3)	2 (5.9)
Subject died	6 (8.7)	2 (5.9)
Other	8 (11.6)	6 (17.6)
Subject no longer willing to participate in study	8 (11.6)	5 (14.7)
Completed (as indicated on CRF)	0	1 (2.9)

CRF = case report form; N = number of subjects per treatment group.

Table 5 and Table 6 show subject demographics for the Phase 1 and Phase 2 portion of the study respectively.

Table 5. Phase 1 Portion: Subject Demographics

	Axitinib + Gemcitabine N=8
Male/female	7/1
Mean age (range) years	64.1 (56-77)
Race: white/asian/other/unspecified	2/1/4/1
Weight (range) kg	69.6 (40.0-93.7)
Height (range) cm	165.5 (153.0-192.0)

N= total number of subjects in treatment group.

Table 6. Phase 2 Portion: Subject Demographics

	Axitinib + Gemcitabine N=69	Gemcitabine N=34
Male/female	35/34	16/18
Mean age (SD) years	63.6 (9.2)	59.8 (11.2)
Race: White/black/asian/other/unspecified	61/0/2/6/0	31/1/0/1/1
Weight (SD) kg	66.1 (14.6)	70.5 (18.2)
Height (SD) cm	166.0 (10.9)	169.0 (9.1)

N = number of subjects per treatment group; SD = standard deviation.

Efficacy Results:

Primary Results: Overall Survival

Figure 1 shows the Kaplan-Meier curve estimate for OS for the ITT population. The median OS for the axitinib + gemcitabine and gemcitabine treated arms was 210 days (95% CI: 162, 308) and 171 days (95% CI: 125, 267), respectively (Table 7). Figure 2 and Figure 3 show the Kaplan-Meier curve estimates for OS for all randomized subjects with locally advanced disease and metastatic disease, respectively. For the locally advanced subjects, the median OS for the axitinib + gemcitabine and gemcitabine treated arms was 379 days (95% CI: 208, 502) and 197 days (95% CI: 125, 352), respectively (Table 8). For the metastatic subjects, the median OS for the axitinib + gemcitabine and gemcitabine treated arms was 170 days (95% CI: 112, 220) and 156 days (95% CI: 91, 267), respectively. Figure 4 shows the Kaplan-Meier curve estimates for OS for all randomized subjects with ECOG performance status ≤1. For the subjects with ECOG performance status ≤1, the median OS for the axitinib + gemcitabine and gemcitabine treated arms was 220 days (95% CI: 170, 379) and 173 days (95% CI: 125, 267), respectively (Table 9). Overall survival by treatment and stratification factors is shown in Table 10. There were only 9 subjects with ECOG performance status 2 and it was not possible to determine the efficacy outcome of this group.

Figure 1. Kaplan-Meier Curve Estimate for Overall Survival (ITT Population)

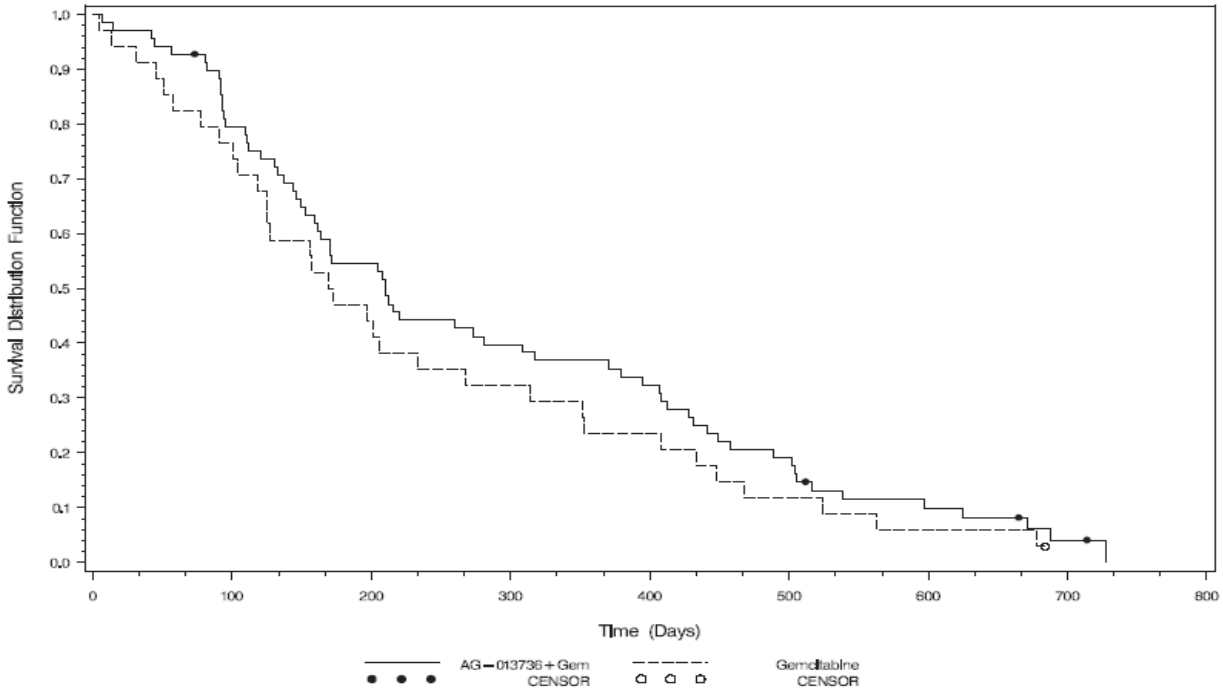

Figure 2. Kaplan-Meier Curve Estimate for Overall Survival: All Randomized Subjects With Locally Advanced Disease

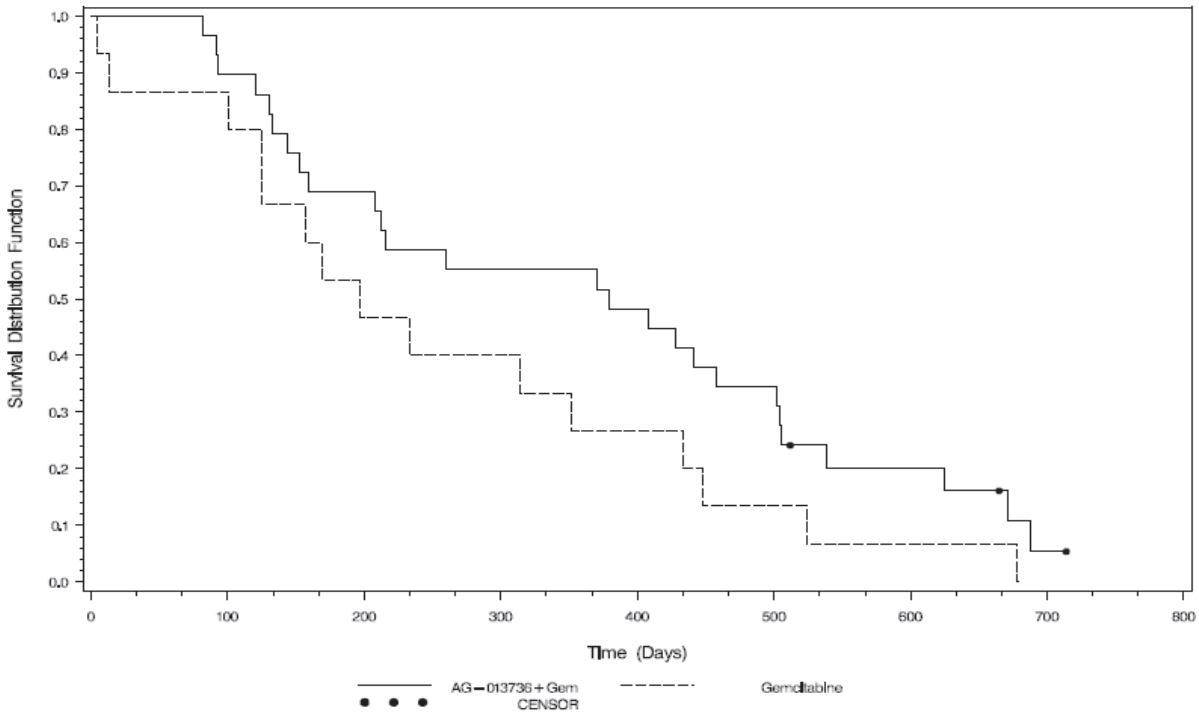

Figure 3. Kaplan-Meier Curve Estimate for Overall Survival: All Randomized Subjects with Metastatic Disease

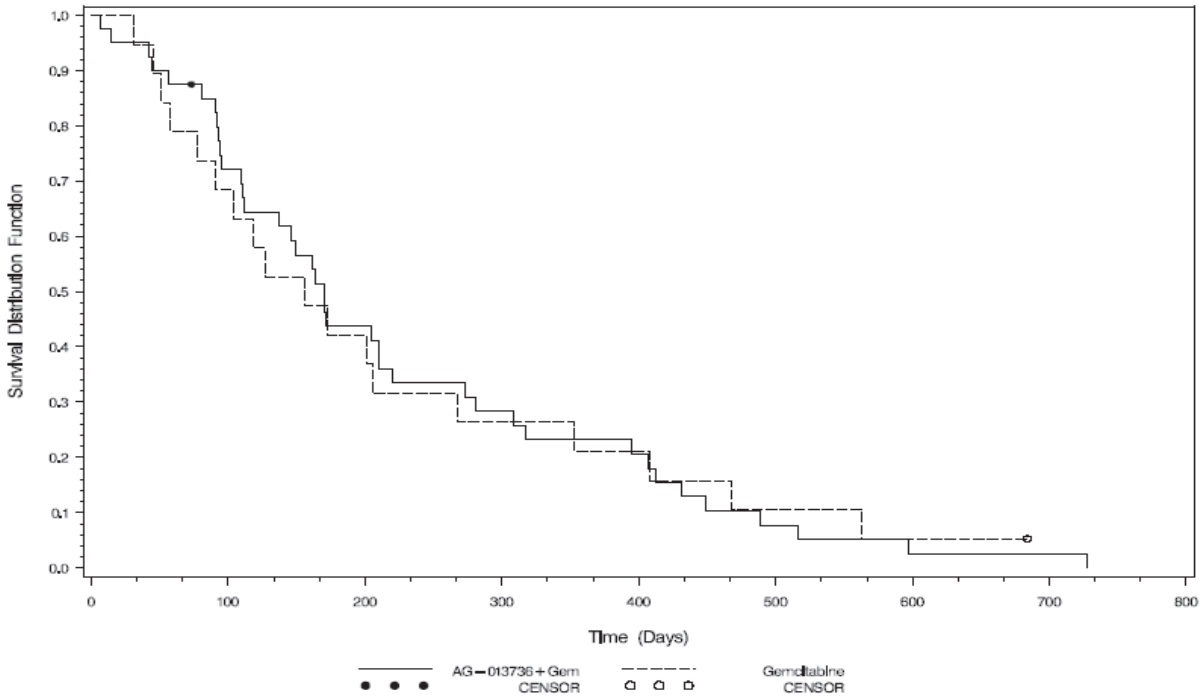

Figure 4. Kaplan-Meier Curve Estimate for Overall Survival: All Randomized Subjects with ECOG Performance Status ≤1

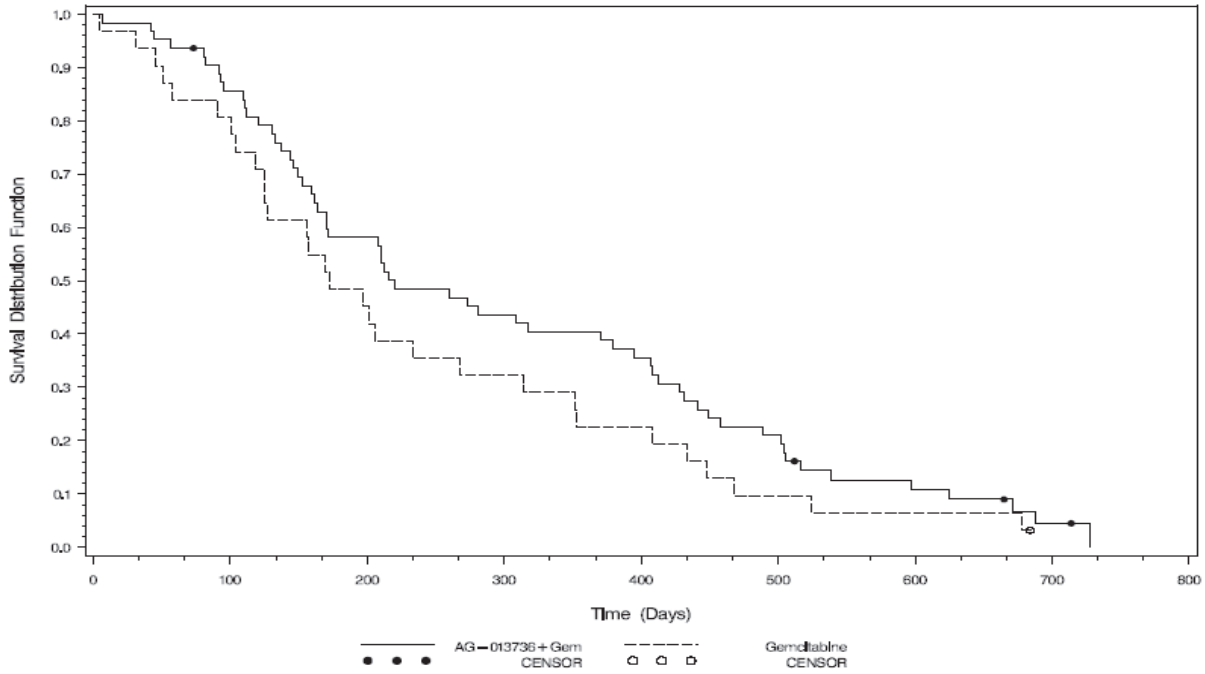

Table 7. Phase 2 Portion: Overall Survival

	Axitinib + Gemcitabine N=69	Gemcitabine N=34
Subject status		
Dead	65 (94.20%)	33 (97.06%)
Alive	4 (5.80%)	1 (2.94%)
Median survival (days)[a]	210	171
95% CI[b]	(162.00, 308.00)	(125.00, 267.00)
1-year survival (%)[a]	36.807	23.529
95% CI[c]	(25.71, 47.93)	(11.48, 38.01)
Hazard ratio (Axitinib + gemcitabine:gemcitabine)[d]	0.758	
95% CI[d]	(0.49, 1.17)	
p-value[e]	0.1026	

CI = confidence interval; CRF = case report form; ECOG = eastern cooperative oncology group; N = number of subjects per treatment group.

a. Estimated from the Kaplan-Meier curve.
b. Based on the Brookmeyer and Crowley method.
c. Calculated from the log [-log (1-year survival probability)] using a normal approximation and back transformation.
d. Based on the Cox Proportional hazards model stratified by extent of disease and ECOG performance status.
e. 1-sided p-value from the log-rank test stratified by extent of disease and ECOG performance status.

Table 8. Phase 2 Portion: Overall Survival: All Randomized Subjects With Locally Advanced and Metastatic Disease

	Axitinib + Gemcitabine N=69		Gemcitabine N=34
Locally advanced	29		15
Number of subjects who died	26 (89.66%)		15 (100%)
Median survival (days)[a]	379		197
95% CI[b]	(208.0, 502.0)		(125.0, 352.0)
1-year survival (%)[a]	55.17		26.67
95% CI[c]	(36.10, 70.67)		(9.33, 47.88)
Hazard ratio (AG+gem:gem)[d]		0.575	
95% CI[d]		(0.299, 1.106)	
p-value[e]		0.0475	
Metastatic	40		19
Number of subjects who Died	39 (97.50%)		18 (94.74%)
Median survival (days)[a]	170		156
95% CI[b]	(112.0, 220.0)		(91.0, 267.0)
1-year survival (%)[a]	23.16		21.05
95% CI[c]	(11.87, 36.64)		(7.30, 39.55)
Hazard ratio (AG+gem:gem)[d]		0.925	
95% CI[d]		(0.521, 1.643)	
p-value[e]		0.3919	

If a subject had no record on the CRF survival page, then the last visit date from the other CRF pages was used as the last date of known contact that the subjects was documented to be alive. Survival time was 1+ number of days between date of randomization and the date of death.
CI = confidence interval; CRF = case report form; gem = gemcitabine; ECOG = eastern cooperative oncology group; N = number of subjects per treatment group.

a. Estimated from the Kaplan-Meier curve.
b. Based on the Brookmeyer and Crowley method.
c. Calculated from the log[-log(1-year survival probability)] using a normal approximation and back transformation.
d. Based on the Cox Proportional hazards model stratified by ECOG performance status.
e. One-sided p-value from the log-rank test stratified by ECOG performance status.

Table 9. Phase 2 Portion: Overall Survival: All Randomized Subjects With ECOG Performance Status ≤1

	Axitinib + Gemcitabine N=69	Gemcitabine N=34
Number of subjects	63	31
Number of subjects who died	59 (93.65%)	30 (96.77%)
Median survival (days)[a]	220	173
95% CI[b]	(170.00, 379.00)	(125.00, 267.00)
1-year survival (%)[a]	40.367	22.581
95% CI[c]	(28.37, 52.03)	(10.41, 37.58)
Hazard ratio (AG+gem:gem)[d]	0.726	
95% CI[d]	(0.47, 1.13)	
p-value[e]	0.0782	

If a subject had no record on the CRF survival page, then the last visit date from the other CRF pages was used as the last date of known contact that the subjects was documented to be alive. Survival time was 1 + number of days between date of randomization and the date of death.
CI = confidence interval; CRF = case report form; gem = gemcitabine; ECOG = eastern cooperative oncology group; N = number of subjects in each treatment group.

a. Estimated from the Kaplan-Meier curve.
b. Based on the Brookmeyer and Crowley method.
c. Calculated from the log[-log(1-year survival probability)] using a normal approximation and back transformation.
d. Based on the Cox Proportional hazards model stratified by extent of disease.
e. One-sided p-value from the log-rank test stratified by extent of disease.

Table 10. Phase 2 Portion: Overall Survival by Treatment and Stratification Factors

	Axitinib + Gemcitabine N=69		Gemcitabine N=34
Locally advanced, ECOG ≤1	28		14
Number of subjects who died	25 (89.29%)		14 (100.00%)
Median survival (days)[a]	393.5		215
95% CI[b]	(212.00, 502.00)		(125.00, 433.00)
1-year survival (%)[a]	57.143		28.571
95% CI[c]	(37.57, 72.62)		(10.01, 50.56)
Hazard ratio (AG+gem:gem)[d]		0.5997	
95% CI[d]		(0.308, 1.167)	
Locally advanced, ECOG=2	1		1
Number of subjects who died	1 (100.00%)		1 (100.00%)
Median survival (days)[a]	92		13
Metastatic, ECOG ≤1	35		17
Number of subjects who died	34 (97.14%)		16 (94.12%)
Median survival (days)[a]	171		156
95% CI[b]	(146.00, 281.00)		(91.00, 267.00)
1-year survival (%)[a]	26.571		17.647
95% CI[c]	(13.70, 41.32)		(5.13, 36.32)
Hazard ratio (AG+gem:gem)[d]		0.8409	
95% CI[d]		(0.462, 1.530)	
Metastatic, ECOG=2	5		2
Number of subjects who died	5 (100.00%)		2 (100.00%)
Median survival (days)[a]	93		320
95% CI[b]	(14.00, 204.00)		(77.00, 563.00)
1-year survival (%)[a]	0		50
95% CI[c]	-		(5.78, 84.49)

If a subject had no record on the CRF survival page, then the last visit date from the other CRF pages was used as the last date of known contact that the subjects was documented to be alive. Survival time was 1+ number of days between date of randomization and the date of death.
CI = confidence interval; CRF = case report form; gem = gemcitabine; ECOG = eastern cooperative oncology group; N = number of subjects in each treatment group.
a. Estimated from the Kaplan-Meier curve.
b. Based on the Brookmeyer and Crowley method.
c. Calculated from the log[-log(1-year Survival Probability)] using a normal approximation and transformation.
d. Based on the unstratified Cox Proportional hazards model.

Secondary Results:

Phase 1 Portion: Documentation of Response:

No analysis for survival was performed for the Phase 1 portion of the study. Six of 8 subjects were considered evaluable for response (all 6 with at least 1 post-baseline scan). There were 3 subjects with a confirmed PR resulting in an ORR 50% for the Phase 1 portion of the study.

Phase 2 Portion: Overall Response Rate and Duration of Response:

No subjects had a CR. Five subjects had a confirmed PR in the axitinib + gemcitabine arm and 1 subject had a confirmed PR in the gemcitabine arm (Table 11). ORR by treatment and stratification factors is shown in Table 12. Four subjects in the axitinib + gemcitabine arm and 1

subject in the gemcitabine with a PR had locally advanced disease at screening (Table 13). All subjects with a PR in both arms had ECOG performance status ≤1 (Table 13). Controlling for baseline stratification factors, ECOG performance status (≤1 versus 2) and extent of disease (locally advanced versus metastatic), the relative risk ratio (axitinib + gemcitabine:gemcitabine) was 1.83 (95% CI: 0.32, 10.48; p-value: 0.37). The median duration of objective response of the subjects with a PR was 379 days (95% CI: 136, 379) and 155 days (1 subject) in the axitinib + gemcitabine and gemcitabine arms, respectively (Table 14). Duration of response among responders by treatment and stratification factors is shown in Table 15.

Table 11. Phase 2 Portion: Overall Response Rate and Duration of Response

	Axitinib + Gemcitabine N=69	**Gemcitabine N=34**
Complete response (CR)	0	0
Partial response (PR)	5 (7.2%)	1 (2.9%)
Stable disease (SD)[a]	20 (29.0%)	10 (29.4%)
Progressive disease (PD)[b]	25 (36.2%)	9 (26.5%)
Indeterminate (IND)	7 (10.1%)	4 (11.8%)
Missing[c]	12 (17.4%)	10 (29.4%)
Overall response rate (ORR)[d]	5 (7.2%)	1 (2.9%)
95% CI[e]	(2.4, 16.1)	(0.1, 15.3)
Difference in response rates (95% CI)[f]	4.3 (-4, 12.7)	
p-value[g]	0.661	
Duration of OR Among Responders	**N=5**	**N=1**
Subjects with PR progressed or died	3 (60.00%)	1 (100.00%)
Subjects did not progress or die	2 (40.00%)	
Median duration of response (days)[h]	379	155
95% CI[i]	(136.00, 379.00)	

Population included all randomized subjects who had a baseline assessment of disease and had the correct histological cancer type.
CI = confidence interval; OR = objective response; RECIST = response evaluation criteria in systemic tumors; N = number of subjects.
a. Protocol defined SD as measurements demonstrating neither sufficient shrinkage to qualify for PR, nor sufficient increase to qualify as PD during the first 12 weeks after the start of treatment.
b. Subjects with SD for less than 12 weeks were categorized as PD.
c. Because of early treatment discontinuation only baseline CT scans were available.
d. ORR = CR + PR according to RECIST.
e. Exact CI for the ORR based on the F-distribution.
f. Asymptotic CI for difference in response rates based on a normal distribution.
g. p-value from Fisher's exact test (2-sided) comparing treatment group response rates.
h. Estimated from the Kaplan-Meier curve.
i. Based on the Brookmeyer and Crowley method.

Table 12. Objective Response Rate by Treatment and Stratification Factors

Stratification Factor	Axitinib + Gemcitabine N=69	Gemcitabine N=34
Locally advanced, ECOG<=1	28	14
Complete response (CR)		
Partial response (PR)	4 (14.3 %)	1 (7.1 %)
Stable disease (SD)	13 (46.4 %)	6 (42.9 %)
Progressive disease (PD)	7 (25.0 %)	5 (35.7 %)
Indeterminate (IND)	2 (7.1 %)	
Missing	2 (7.1 %)	2 (14.3 %)
Overall response rate[a]	4 (14.3 %)	1 (7.1 %)
95% CI[b]	(4.0, 32.7)	(0.2, 33.9)
Locally advanced, ECOG=2	1	1
Complete response (CR)		
Partial response (PR)		
Stable disease (SD)		
Progressive disease (PD)		
Indeterminate (IND)		
Missing	1 (100 %)	1 (100 %)
Metastatic, ECOG<=1	35	17
Complete response (CR)		
Partial response (PR)	1 (2.9 %)	
Stable disease (SD)	7 (20.0 %)	4 (23.5 %)
Progressive disease (PD)	16 (45.7 %)	4 (23.5 %)
Indeterminate (IND)	3 (8.6 %)	4 (23.5 %)
Missing	8 (22.9 %)	5 (29.4 %)
Overall response Rate[a]	1 (2.9 %)	
95% CI[b]	(0.1, 14.9)	(0, 19.5)
Metastatic, ECOG=2	5	2
Complete response (CR)		
Partial response (PR)		
Stable disease (SD)		
Progressive disease (PD)	2 (40.0 %)	
Indeterminate (IND)	2 (40.0 %)	
Missing	1 (20.0 %)	2 (100 %)

CI = confidence interval; ECOG = Eastern Cooperative Oncology Group; N = number of the subjects.

a. Overall Response Rate = Complete Responders (CR) + Partial Responders (PR) according to RECIST.

b. Exact confidence interval for the overall response rate based on the F-distribution.

Table 13. Treatment Comparison of Objective Response Rate

	Axitinib + Gemcitabine		Gemcitabine		Treatment Comparison		
	N[a]	n (%)[b]	N[a]	n (%)[b]	p-value[c]	Risk Ratio[d]	95% CI of Risk Ratio
Extent of disease							
Locally advanced	29	4 (13.8)	15	1 (6.7)			
Metastatic	40	1 (2.5)	19				
Screening ECOG performance status							
0 or 1	63	5 (7.9)	31	1 (3.2)			
2	6		3				
Total					0.369	1.831	(0.32, 10. 481)

Population includes all randomized subjects who had a baseline assessment of disease and have the correct histological cancer type.

a. N = number of subjects in stratification factor.
b. n = number of responders.
c. P-value from Cochran-Mantel-Haenszel test stratified by extent of disease and screening ECOG performance status.
d. Axitinib + Gemcitabine is in the numerator and Gemcitabine is in the denominator of the risk ratio.

Table 14. Duration of Objective Response Among Responders by Treatment

	Axitinib + Gemcitabine (N=5)	Gemcitabine (N=1)
	n (%)	n (%)
Status		
Subjects progressed or died	3 (60.0)	1 (100)
Subjects did not progress or die	2 (40.0)	
Median duration of response (Days)[a]	379	155
95% CI of duration of response (Days)[b]	(136.00, 379.00)	

Duration of Response = First date that criteria for progression was met or the subject died due to any cause-First date that criteria for PR or CR met +1. Subjects who achieved a PR or CR and who did not experience disease progression during the treatment and follow-up periods and who did not die during the treatment period will have their event times censored on the last study date that objective tumor assessments verified lack of disease progression.

CI = confidence interval; N = number of subjects per treatment group; (n = number of subjects per response group)

a. Estimated from the Kaplan-Meier curve.
b. Based on the Brookmeyer and Crowley method.

Table 15. Duration of Response among Responders by Treatment and Stratification Factors

	Axitinib + Gemcitabine (N=5)	Gemcitabine (N=1)
	n (%)	n (%)
Locally advanced, ECOG <=1	4	1
Subjects progressed or died	2 (50.0)	1 (100)
Subjects did not progress or die	2 (50.0)	0
Median duration of response (Days)[a]	379	155
25th and 75th Percentile of duration of response (Days)[b]	(222.0, 379.0)	(155.0, 155.0)
Locally advanced, ECOG=2	0	0
Subjects Progressed or Died	0	0
Subjects did not progress or Die	0	0
Metastatic, ECOG <= 1	1	0
Subjects progressed or died	1 (100)	0
Subjects did not progress or die	0	0
Median duration of Response (Days)[a]	136	
25th and 75th percentile of duration of response (Days)	(136.0, 136.0)	
Metastatic, ECOG=2	0	0
Subjects progressed or died	0	0
Subjects did not progress or die	0	0

Note: Duration of Response=First date that criteria for progression was met or the subjects died due to any cause-First date that criteria for PR or CR met+1. Subjects who achieved a PR or CR and who did not experience disease progression during the treatment and follow-up periods and who did not die during the treatment period will have their event times censored on the last study date that objective tumor assessments verified lack of disease progression.
ECOG = Eastern Cooperative Oncology Group; N = number of the subjects per treatment group; n = number of subjects in specific category.
a. Estimated from the Kaplan-Meier curve.
b. Based on the Brookmeyer and Crowley method.

Phase 2 Portion: Progression-Free Survival:

Figure 5 shows the Kaplan-Meier curve for PFS. The median PFS was 116 days (95% CI: 109, 160) and 113 days (95% CI: 68, 205) for the axitinib + gemcitabine and gemcitabine arms, respectively. Controlling for baseline stratification factors, ECOG performance status (≤1 versus 2) and extent of disease (locally advanced versus metastatic), the hazard ratio (axitinib + gemcitabine:gemcitabine) was 0.96 (95% CI: 0.54, 1.73, 1-sided p-value: 0.45, Table 16).

Subjects with locally advanced disease and with an ECOG performance status ≤1 in the axitinib + gemcitabine arm had median PFS of 343 days (95% CI: 130, 441) and subjects treated with gemcitabine had median PFS of 125 days (95% CI: 53, 205) with a hazard ratio of 0.39 (axitinib + gemcitabine:gemcitabine, 95% CI: 0.15, 0.98) (Table 17). Subjects with

metastatic disease and with an ECOG performance status ≤1 in the axitinib + gemcitabine arm had median PFS of 110 days (95% CI: 70, 126) and subjects treated with gemcitabine had median PFS of 77 days (95% CI: 68, 317) with a hazard ratio of 1.69 (axitinib + gemcitabine:gemcitabine, 95% CI: 0.76, 3.76).

Figure 5. Kaplan-Meier Curve for Progression-Free Survival

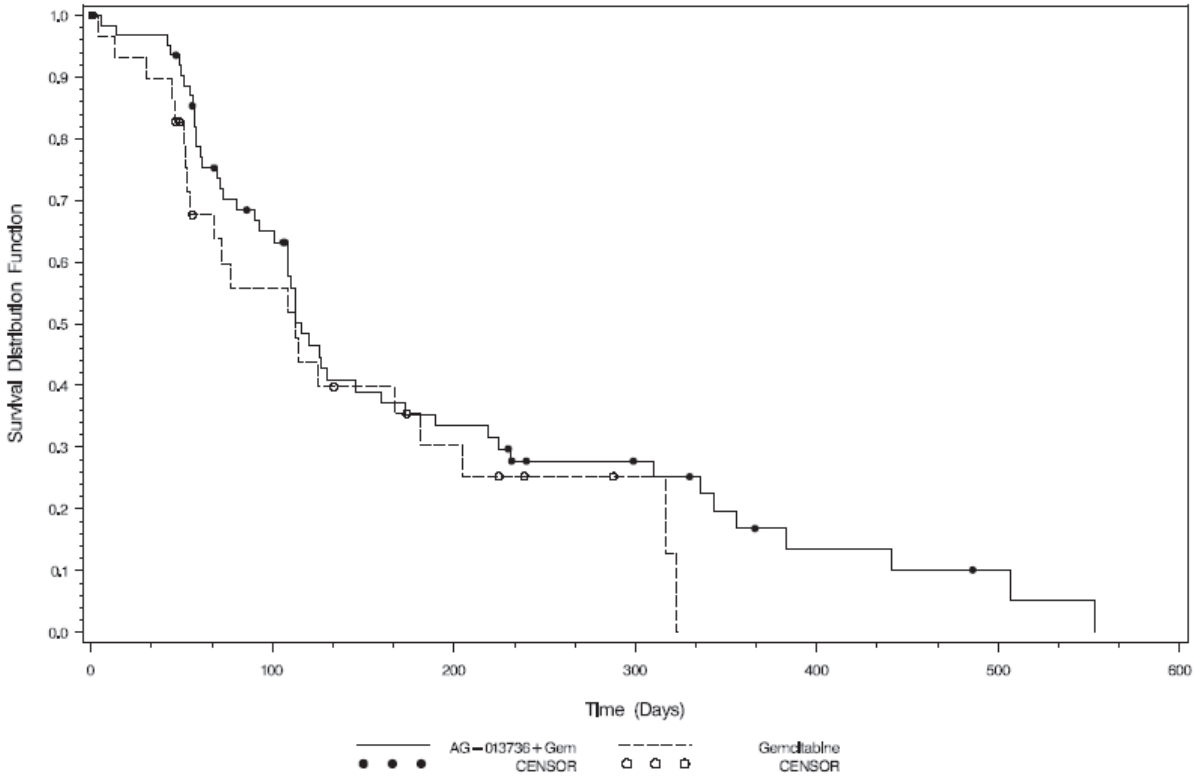

Table 16. Phase 2 Portion: Progression-Free Survival

	Axitinib +gemcitabine N=69	Gemcitabine N=34
Status		
Subject Progressed or Died	49 (71.0%)	20 (58.8%)
Subject did not Progress or Die	20 (29.0%)	14 (41.2%)
Median PFS (days)[a]	116	113
95% CI[b]	(109.00, 160.00)	(68.00, 205.00)
Hazard Ratio (AG+gem:gem)[c]	0.9648	
95% CI[c]	(0.54, 1.73)	
p-value[d]	0.4466	

Population included all randomized subjects who had a baseline assessment of disease and had the correct histological cancer type. PFS = (First date that criteria for progression was met or the subject died due to any cause) – (date of randomization) +1.
Subjects lacking an evaluation of tumor response after randomization had their event times censored at 1 day.
Subjects who did not experience disease progression during the treatment and follow-up periods and who did not die during the treatment period had their event time censored on the last study date that objective tumor assessments verified lack of disease progression.
CI = confidence interval; gem = gemcitabine; PFS = progression free survival; ECOG = eastern cooperative oncology group; N = number of subjects per treatment group.

a. Estimated from the Kaplan-Meier curve.
b. Based on the Brookmeyer and Crowley method.
c. Based on the Cox proportional hazards model stratified by extent of disease and screening ECOG performance status.
d. One-sided p-value form the log-rank test stratified by extent of disease and screening ECOG performance.

Table 17. Phase 2 Portion: Progression-Free Survival by Treatment and Stratification Factors

	Axitinib + Gemcitabine N=69		Gemcitabine N=34
Locally advanced, ECOG ≤1	28		14
Subject progressed or died	16 (57.1%)		9 (64.3%)
Median PFS (days)[a]	343		125
95% CI[b]	(130.00, 441.00)		(53.00, 205.00)
Hazard ratio (AG+gem:gem)[c]		0.3854	
95% CI[c]		(0.152, 0.975)	
Metastatic, ECOG ≤1	35		17
Subject progressed or died	28 (80.0%)		10 (58.8%)
Median PFS (days)[a]	110		77
95% CI[b]	(70.00, 126.00)		(68.00, 317.00)
Hazard ratio (AG+gem:gem)[c]		1.6886	
95% CI[c]		(0.759, 3.758)	

Population included all randomized subjects who had a baseline assessment of disease and had the correct histological cancer type. PFS = (First date that criteria for progression was met or the subject died due to any cause) – (date of randomization) + 1.
Subjects lacking an evaluation of tumor response after randomization had their event times censored at 1 day.
Subjects who did not experience disease progression during the treatment and follow-up periods and who did not die during the treatment period had their event time censored on the last study date that objective tumor assessments verified lack of disease progression.
CI = confidence interval; gem = gemcitabine; PFS = progression free survival; ECOG = eastern cooperative oncology group; N = number of subjects per treatment group.

a. Estimated from the Kaplan-Meier curve.
b. Based on the Brookmeyer and Crowley method.
c. Based on the unstratified Cox proportional hazards model.

Patient-Reported Outcomes Evaluations:

Baseline values for various parameters of 30-item quality of life questionnaire (QLQ-C30) and 26-item pancreatic cancer-specific quality of life questionnaire (Pan26) in presented in Table 18 and change from baseline for QLQ-C30 and Pan26 is given in Table 19 and Table 20 respectively.

Table 18. Baseline Values for Both Treatment Arms on the QLQ-C30 and Pan26

Scale	Axitinib + Gemcitabine (N=65)[a]	Gemcitabine (N=27)[b]
	Mean (SD)	Mean (SD)
QLQ-C30		
Global health status/QOL	55.60 (27.18)	54.32 (21.10)
Functioning Scales		
Physical functioning	76.90 (24.73)	82.22 (14.44)
Role functioningb	62.56 (33.21)	60.26 (35.30)
Emotional functioning	67.22 (26.17)	66.98 (23.96)
Cognitive functioning	82.82 (23.93)	82.10 (19.57)
Social functioningb	67.44 (33.00)	70.51 (29.56)
Symptoms		
Fatigue	43.50 (29.78)	42.80 (25.73)
Nausea & vomiting	19.74 (28.24)	13.58 (20.17)
Pain	40.00 (33.31)	37.04 (31.80)
Dyspneaa	12.50 (21.82)	16.05 (26.75)
Insomnia	31.28 (31.66)	39.51 (39.26)
Appetite loss	41.03 (40.30)	33.33 (34.59)
Constipation	34.87 (37.93)	38.27 (38.90)
Diarrhea	20.00 (27.51)	16.05 (28.30)
Financial difficultiesa	10.42 (19.59)	28.40 (41.04)
Pan26	**(N=59)[c]**	**(N=27)[d]**
Pancreatic pain	37.52 (27.88)	38.89 (21.18)
Eating related items	40.40 (35.18)	33.95 (27.92)
Altered bowel habits	22.32 (26.19)	25.31 (28.26)
Jaundice	9.89 (18.34)	15.38 (23.06)
Body image	31.64 (29.80)	26.54 (25.84)
Health care satisfaction	79.38 (27.57)	69.75 (25.33)
Sexual functioning	44.35 (34.42)	57.97 (37.56)
Ascites	37.29 (31.00)	25.93 (25.04)
Indigestion	24.86 (28.09)	30.86 (34.50)
Flatulence	35.59 (32.67)	39.51 (29.29)
Cachexia	33.62 (25.43)	31.48 (23.72)
Side effects	27.78 (24.80)	27.35 (21.77)
Fear of future health	63.22 (31.03)	59.26 (33.76)
Ability to plan future	39.55 (35.27)	41.98 (36.51)

Gem = gemcitabine, N = number of subjects per treatment group QLQ=quality of life questionnaire, SD=standard deviation.

a. n was 64 for dyspnea and financial difficulties in the axitinib + Gem arm.
b. n was 26 for role functioning and social functioning in the Gem arm.
c. n was 58 for fear of future health and n was 56 for sexual functioning in the axitinib + Gem arm.
d. n was 26 for jaundice and side effects, n was 23 for sexual functioning in the Gem arm.

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Change from Baseline Score at Cycle 2 Day 1												
Global health status / QoL:												
Global QoL	49	-5.1	0	21.17	(-11.18, 0.98)	20	3.33	0	16.97	(-4.61, 11.28)	-8.44	(-19.06, 2.19)
Functioning Scales:												
Physical Functioning	51	-5.07	0	18.85	(-10.37, 0.24)	21	0.95	0	16.23	(-6.44, 8.34)	-6.02	(-15.4, 3.36)
Role Functioning	51	0.33	0	25.93	(-6.96, 7.62)	19	9.65	0	29.56	(-4.6, 23.9)	-9.32	(-23.77, 5.12)
Emotional Functioning	52	3.21	0	21.34	(-2.74, 9.15)	21	7.94	8.33	17.77	(-0.15, 16.03)	-4.73	(-15.25, 5.79)
Cognitive Functioning	52	-3.53	0	21.48	(-9.5, 2.45)	21	1.59	0	18.93	(-7.03, 10.21)	-5.11	(-15.83, 5.61)
Social Functioning	52	-4.17	0	29.5	(-12.38, 4.05)	20	-0.83	0	28.85	(-14.34, 12.67)	-3.33	(-18.72, 12.06)
Symptoms:												
Fatigue	51	1.42	0	21.74	(-4.7, 7.53)	21	-8.99	0	26.67	(-21.14, 3.15)	10.41	(-1.62, 22.44)
Nausea and Vomiting	51	-5.88	0	26.84	(-13.43, 1.67)	21	-1.59	0	12.81	(-7.42, 4.24)	-4.3	(-16.55, 7.96)
Pain	52	-9.29	0	27.89	(-17.06, -1.53)	21	-16.67	-16.67	31.62	(-31.06, -2.27)	7.37	(-7.57, 22.32)
Dyspnea	50	9.33	0	26.97	(1.67, 17)	21	-3.17	0	25.61	(-14.83, 8.48)	12.51	(-1.28, 26.3)
Insomnia	51	-9.15	0	28.35	(-17.12, -1.18)	21	-19.05	0	34.27	(-34.65, -3.45)	9.9	(-5.7, 25.49)
Appetite loss	51	-0.65	0	35.58	(-10.66, 9.35)	21	-14.29	0	35.86	(-30.61, 2.04)	13.63	(-4.81, 32.07)
Constipation	52	-9.62	0	32.56	(-18.68, -0.55)	21	-14.29	0	29	(-27.49, -1.08)	4.67	(-11.62, 20.96)
Diarrhea	52	-1.28	0	29.49	(-9.49, 6.93)	21	0	0	18.26	(-8.31, 8.31)	-1.28	(-15.1, 12.54)
Financial Difficulties	50	0.67	0	19.62	(-4.91, 6.24)	21	-4.76	0	19.11	(-13.46, 3.94)	5.43	(-4.67, 15.53)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Change From Baseline Score at Cycle 3 Day 1												
Global health status / QoL:												
Global QoL	40	-9.17	-8.33	30.36	(-18.88, 0.54)	15	6.67	8.33	15.17	(-1.73, 15.07)	-15.83	(-32.34, 0.67)
Functioning Scales:												
Physical Functioning	42	-8.13	-6.67	21.46	(-14.82, -1.45)	15	3.44	0	18.73	(-6.93, 13.82)	-11.58	(-24.12, 0.96)
Role Functioning	42	-5.56	0	27.71	(-14.19, 3.08)	14	13.1	0	25.47	(-1.61, 27.8)	-18.65	(-35.47, -1.83)
Emotional Functioning	41	-1.69	0	26.8	(-10.15, 6.77)	15	12.22	8.33	19.89	(1.21, 23.24)	-13.92	(-29.16, 1.32)
Cognitive Functioning	41	-4.88	0	24.79	(-12.7, 2.95)	15	2.22	0	16.51	(-6.92, 11.36)	-7.1	(-20.97, 6.77)
Social Functioning	41	-4.07	0	32.66	(-14.37, 6.24)	15	5.56	0	24.93	(-8.25, 19.36)	-9.62	(-28.28, 9.04)
Symptoms:												
Fatigue	42	7.41	11.11	28.61	(-1.51, 16.32)	14	-8.73	-5.56	26.57	(-24.07, 6.61)	16.14	(-1.27, 33.54)
Nausea and Vomiting	42	-4.37	0	29	(-13.4, 4.67)	13	-2.56	0	16.45	(-12.51, 7.38)	-1.8	(-18.78, 15.18)
Pain	42	-6.75	0	33.75	(-17.26, 3.77)	15	-23.33	-16.67	30.08	(-39.99, -6.68)	16.59	(-3.22, 36.39)
Dyspnea	41	3.25	0	27.69	(-5.49, 11.99)	14	-7.14	0	19.3	(-18.29, 4)	10.39	(-5.68, 26.47)
Insomnia	42	-10.32	0	34.13	(-20.95, 0.32)	14	-11.9	-16.67	38.36	(-34.05, 10.24)	1.59	(-20.19, 23.36)
Appetite loss	42	11.11	16.67	39.42	(-1.17, 23.39)	13	-5.13	0	29.96	(-23.23, 12.97)	16.24	(-7.62, 40.1)
Constipation	41	-10.57	0	32.86	(-20.94, -0.2)	15	-13.33	0	35.19	(-32.82, 6.15)	2.76	(-17.49, 23.02)
Diarrhea	41	7.32	0	32.07	(-2.81, 17.44)	15	4.44	0	30.52	(-12.45, 21.34)	2.87	(-16.29, 22.03)
Financial Difficulties	40	3.33	0	24.81	(-4.6, 11.27)	15	-2.22	0	26.63	(-16.97, 12.52)	5.56	(-9.81, 20.92)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Change From Baseline Score at Cycle 4 Day 1												
Global health status / QoL:												
Global QoL	30	-6.67	-4.17	21.04	(-14.52, 1.19)	12	-0.69	0	15.27	(-10.39, 9.01)	-5.97	(-19.52, 7.57)
Functioning Scales:												
Physical Functioning	32	-6.67	-5.83	23.15	(-15.01, 1.68)	13	-1.03	0	15.36	(-10.31, 8.26)	-5.64	(-19.75, 8.46)
Role Functioning	32	-7.81	0	29.63	(-18.49, 2.87)	12	9.72	0	36.56	(-13.5, 32.95)	-17.53	(-39.11, 4.05)
Emotional Functioning	31	-3.23	0	22.64	(-11.53, 5.08)	12	9.03	12.5	14.42	(-0.13, 18.19)	-12.25	(-26.5, 2)
Cognitive Functioning	31	-6.99	0	25.74	(-16.43, 2.45)	12	0	0	15.89	(-10.1, 10.1)	-6.99	(-23.13, 9.15)
Social Functioning	31	-8.6	0	35.45	(-21.61, 4.4)	11	-1.52	0	24.1	(-17.71, 14.68)	-7.09	(-30.48, 16.31)
Symptoms:												
Fatigue	32	7.47	0	25.19	(-1.62, 16.55)	13	-3.42	0	25.41	(-18.78, 11.94)	10.88	(-5.86, 27.63)
Nausea and Vomiting	32	-4.69	0	19.96	(-11.88, 2.51)	13	6.41	0	18.68	(-4.88, 17.7)	-11.1	(-24.11, 1.91)
Pain	32	16.67	-16.67	29.02	(-27.13, -6.2)	13	-11.54	-16.67	28.37	(-28.68, 5.61)	-5.13	(-24.26, 14)
Dyspnea	31	0	0	28.54	(-10.47, 10.47)	13	-5.13	0	29.96	(-23.23, 12.97)	5.13	(-14.18, 24.44)
Insomnia	32	-11.46	0	28.85	(-21.86, -1.06)	13	-5.13	0	32.9	(-25.01, 14.76)	-6.33	(-26.25, 13.59)
Appetite loss	32	6.25	0	36.35	(-6.86, 19.36)	12	-2.78	0	33.21	(-23.88, 18.32)	9.03	(-15.26, 33.32)
Constipation	30	-24.44	0	37.07	(-38.29, -10.6)	12	-25	0	40.51	(-50.74, 0.74)	0.56	(-25.71, 26.82)
Diarrhea	31	7.53	0	39.17	(-6.84, 21.89)	12	5.56	0	34.33	(-16.26, 27.37)	1.97	(-24.07, 28.01)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Financial Difficulties	29	1.15	0	22.68	(-7.48, 9.78)	12	-8.33	0	20.72	(-21.5, 4.83)	9.48	(-5.89, 24.86)
Change From Baseline Score at Cycle 5 Day 1												
Global health status / QoL:												
Global QoL	26	-9.29	-12.5	27.82	(-20.53, 1.94)	7	10.71	16.67	21.36	(-9.04, 30.47)	-20.01	(-43.19, 3.17)
Functioning Scales:												
Physical Functioning	28	-8.57	-6.67	23.08	(-17.52, 0.38)	8	0	-3.33	22.25	(-18.6, 18.6)	-8.57	(-27.24, 10.1)
Role Functioning	28	-8.93	0	29.22	(-20.26, 2.4)	7	7.14	0	28.64	(-19.34, 33.63)	-16.07	(-41.1, 8.96)
Emotional Functioning	28	-3.87	-4.17	22.96	(-12.77, 5.03)	7	20.24	16.67	14.32	(7, 33.48)	-24.11	(-42.72, -5.5)
Cognitive Functioning	28	-2.38	0	24.73	(-11.97, 7.21)	7	7.14	0	16.27	(-7.9, 22.19)	-9.52	(-29.66, 10.61)
Social Functioning	28	-15.48	0	33.92	(-28.63, -2.32)	7	4.76	0	23	(-16.51, 26.04)	-20.24	(-47.93, 7.46)
Symptoms:												
Fatigue	28	9.72	11.11	28.59	(-1.37, 20.81)	8	-15.28	-16.67	17.76	(-30.12, -0.43)	25	(3.23, 46.77)
Nausea and Vomiting	28	0	0	26.06	(-10.1, 10.1)	8	-6.25	0	15.27	(-19.01, 6.51)	6.25	(-13.49, 25.99)
Pain	28	-5.36	0	34.26	(-18.64, 7.93)	8	-25	-25	26.73	(-47.34, -2.66)	19.64	(-7.12, 46.41)
Dyspnea	28	9.52	0	27	(-0.95, 19.99)	8	-12.5	0	24.8	(-33.23, 8.23)	22.02	(0.38, 43.66)
Insomnia	28	-19.05	-33.33	35.63	(-32.87, -5.23)	8	-29.17	-16.67	33.03	(-56.78, -1.55)	10.12	(-18.49, 38.73)
Appetite loss	28	0	0	42.55	(-16.5, 16.5)	8	-20.83	0	43.42	(-57.13, 15.46)	20.83	(-13.98, 55.65)
Constipation	28	-21.43	0	35.39	(-35.15, -7.71)	7	-33.33	-33.33	38.49	(-68.93, 2.26)	11.9	(-19.02, 42.83)
Diarrhea	28	7.14	0	33.16	(-5.71, 20)	7	-4.76	0	29.99	(-32.5, 22.98)	11.9	(-16.13, 39.94)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Financial Difficulties	27	0	0	22.65	(-8.96, 8.96)	6	0	0	36.51	(-38.32, 38.32)	0	(-23.38, 23.38)
Change From Baseline Score at Cycle 6 Day 1												
Global health status / QoL:												
Global QoL	17	-14.22	-16.67	20.36	(-24.69, -3.75)	3	-5.56	-8.33	12.73	(-37.18, 26.07)	-8.66	(-34.53, 17.21)
Functioning Scales:												
Physical Functioning	19	-6.32	0	25.38	(-18.55, 5.92)	2	6.67	6.67	18.86	(-162.75, 176.08	-12.98	(-52.01, 26.04)
Role Functioning	19	-9.65	0	27.95	(-23.12, 3.82)	2	16.67	16.67	47.14	(-406.87, 440.21	-26.32	(-71.87, 19.24)
Emotional Functioning	19	2.19	0	15.92	(-5.48, 9.87)	3	8.33	0	14.43	(-27.52, 44.19)	-6.14	(-26.59, 14.31)
Cognitive Functioning	19	-0.88	0	18.82	(-9.95, 8.19)	3	11.11	16.67	9.62	(-12.79, 35.01)	-11.99	(-35.46, 11.48)
Social Functioning	19	-2.63	0	27.92	(-16.09, 10.83)	3	-16.67	-16.67	16.67	(-58.07, 24.74)	14.04	(-20.97, 49.04)
Symptoms:												
Fatigue	19	6.73	0	24.19	(-4.93, 18.38)	2	-16.67	-16.67	39.28	(-369.62, 336.28	23.39	(-15.83, 62.61)
Nausea and Vomiting	19	-4.39	0	22.8	(-15.37, 6.6)	2	-8.33	-8.33	11.79	(-114.22, 97.55)	3.95	(-30.84, 38.73)
Pain	19	-8.77	0	30.11	(-23.28, 5.74)	3	-33.33	-33.33	16.67	(-74.74, 8.07)	24.56	(-13.08, 62.2)
Dyspnea	18	-1.85	0	21.3	(-12.45, 8.74)	2	0	0	47.14	(-423.54, 423.54	-1.85	(-38.65, 34.94)
Insomnia	19	-7.02	0	30.59	(-21.76,7.73)	2	-16.67	-16.67	23.57	(-228.44, 195.1)	9.65	(-37.43, 56.73)
Appetite loss	19	-3.51	0	53.16	(-29.13, 22.12)	2	-16.67	-16.67	70.71	(-651.98, 618.64	13.16	(-71.22, 97.54)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Constipation	19	-10.53	0	35.23	(-27.51, 6.45)	3	-33.33	-33.33	33.33	(-116.14, 49.47)	22.81	(-22.61, 68.22)
Diarrhea	19	-1.75	0	28.27	(-15.38, 11.87)	3	0	0	33.33	(-82.8, 82.8)	-1.75	(-39.1, 35.59)
Financial Difficulties	19	1.75	0	13.49	(-4.75, 8.26)	3	-22.22	0	38.49	(-117.84, 73.39)	23.98	(1.09, 46.86)
Change From Baseline Score at Cycle 7 Day 1												
Global health status / QoL:												
Global QoL	9	-4.63	0	37.76	(-33.65, 24.39)	3	-16.67	-8.33	14.43	(-52.52, 19.19)	12.04	(-39.03, 63.11)
Functioning Scales:												
Physical Functioning	10	-3.33	-6.67	24.8	(-21.07, 14.4)	3	-22.22	-20	36.72	(-113.43, 68.99)	18.89	(-20.74, 58.52)
Role Functioning	10	-15	0	30.88	(-37.09, 7.09)	2	33.33	33.33	70.71	(-601.98, 668.64	-48.33	(-111.94, 15.28)
Emotional Functioning	10	-8.33	-8.33	13.03	(-17.65, 0.99)	3	-7.41	-13.89	21.58	(-61.01, 46.19)	-0.93	(-22.59, 20.74)
Cognitive Functioning	10	1.67	0	24.15	(-15.61, 18.94)	3	-5.56	0	9.62	(-29.46, 18.35)	7.22	(-24.98, 39.43)
Social Functioning	10	-15	0	41.16	(-44.45, 14.45)	2	-25	-25	11.79	(-130.89, 80.89)	10	(-57.71, 77.71)
Symptoms:												
Fatigue	10	-2.22	-5.56	25.01	(-20.11, 15.67)	3	14.81	33.33	42.07	(-89.68, 119.31)	-17.04	(-58.87, 24.79)
Nausea and Vomiting	10	1.67	0	21.44	(-13.67, 17.01)	3	16.67	16.67	0		-15	(-43.1, 13.1)
Pain	10	-3.33	0	32.2	(-26.37, 19.7)	3	-11.11	-16.67	41.94	(-115.3, 93.08)	7.78	(-41.75, 57.3)
Dyspnea	10	16.67	0	23.57	(-0.19, 33.53)	3	33.33	33.33	33.33	(-49.47, 116.14)	-16.67	(-53.79, 20.46)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Insomnia	10	-10	-16.67	35.31	(-35.26, 15.26)	3	11.11	33.33	38.49	(-84.5, 106.73)	-21.11	(-73.14, 30.92)
Appetite loss	10	-10	0	58.9	(-52.13, 32.13)	3	22.22	33.33	50.92	(-104.26, 148.71	-32.22	(-115.58, 51.13)
Constipation	10	-13.33	0	47.66	(-47.43, 20.76)	3	-66.67	-100	57.74	(-210.09, 76.76)	53.33	(-18.6, 125.26)
Diarrhea	10	3.33	0	29.19	(-17.55, 24.21)	3	0	0	0		3.33	(-34.92, 41.58)
Financial Difficulties	10	-6.67	0	21.08	(-21.75, 8.41)	3	0	0	0		-6.67	(-34.3, 20.96)
Change From Baseline Score at Cycle 8 Day 1												
Global health status / QoL:												
Global QoL	10	-12.5	-8.33	33.62	(-36.55, 11.55)	1	-33.33	-33.33			20.83	(-58.94, 100.6)
Functioning Scales:												
Physical Functioning	10	-10.67	-6.67	22.71	(-26.91, 5.58)	1	-20	-20			9.33	(-44.54, 63.2)
Role Functioning	10	-13.33	-16.67	23.31	(-30.01, 3.34)	1	-33.33	-33.33			20	(-35.3, 75.3)
Emotional Functioning	10	-7.5	-16.67	18.61	(-20.82, 5.82)	1	0	0			-7.5	(-51.66, 36.66)
Cognitive Functioning	10	0	0	22.22	(-15.9, 15.9)	1	-16.67	-16.67			16.67	(-36.06, 69.39)
Social Functioning	10	-11.67	0	34.29	(-36.2, 12.86)	1	-16.67	-16.67			5	(-76.36, 86.36)
Symptoms:												
Fatigue	10	4.44	0	25.23	(-13.6, 22.49)	1	22.22	22.22			-17.78	(-77.63, 42.08)
Nausea and Vomiting	10	0	0	19.25	(-13.77, 13.77)	1	16.67	16.67			-16.67	(-62.33, 28.99)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Pain	10	-8.33	0	37.06	(-34.84, 18.18)	1	-16.67	-16.67			8.33	(-79.59, 96.26)
Dyspnea	9	14.81	0	29.4	(-7.78, 37.41)	1	33.33	33.33			-18.52	(-89.98, 52.94)
Insomnia	10	-20	-33.33	47.66	(-54.09, 14.09)	1	0	0			-20	(-133.08, 93.08)
Appetite loss	10	-3.33	0	48.3	(-37.89, 31.22)	1	33.33	33.33			-36.67	(-151.27, 77.94)
Constipation	10	-3.33	0	29.19	(-24.21, 17.55)	1	0	0			-3.33	(-72.58, 65.91)
Diarrhea	10	6.67	0	37.84	(-20.4, 33.74)	1	-66.67	-66.67			73.33	(-16.45, 163.12)
Financial Difficulties	10	-3.33	0	18.92	(-16.87, 10.2)	1	0	0			-3.33	(-48.23, 41.56)
Change From Baseline Score at Cycle 9 Day 1												
Global health status / QoL:												
Global QoL	8	-17.71	-4.17	36.03	(-47.83, 12.42)	1	-33.33	-33.33			15.62	(-74.75, 106)
Functioning Scales:												
Physical Functioning	8	-6.67	-6.67	20.16	(-23.52, 10.19)	1	-40	-40			33.33	(-17.22, 83.89)
Role Functioning	8	-29.17	-25	24.8	(-49.9, -8.43)	1	-33.33	-33.33			4.17	(-58.04, 66.37)
Emotional Functioning	8	-3.13	0	13.32	(-14.26, 8.01)	1	-8.33	-8.33			5.21	(-28.19, 38.61)
Cognitive Functioning	8	-2.08	0	28.78	(-26.15, 21.98)	1	-33.33	-33.33			31.25	(-40.94, 103.44)
Social Functioning	8	-6.25	0	47.09	(-45. 62, 33.12)	1	-33.33	-33.33			27.08	(-91.02, 145.18)
Symptoms:												
Fatigue	8	18.06	11.11	33.56	(-10, 46.12)	1	33.33	33.33			-15.28	(-99.46, 68.9)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Nausea and Vomiting	8	-8.33	0	17.82	(-23.23, 6.56)	1	16.67	16.67			-25	(-69.69, 19.69)
Pain	8	0	0	30.86	(-25.8, 25.8)	1	0	0			0	(-77.4, 77.4)
Dyspnea	7	19.05	33.33	26.23	(-5.21, 43.3)	1	33.33	33.33			-14.29	(-82.89, 54.32)
Insomnia	8	-4.17	0	33.03	(-31.78, 23.45)	1	0	0			-4.17	(-87.02, 78.69)
Appetite loss	8	8.33	33.33	63.62	(-44.86, 61.52)	1	33.33	33.33			-25	(-184.57, 134.57)
Constipation	8	-8.33	0	38.83	(-40.8, 24.13)	1	0	0			-8.33	(-105.73, 89.06)
Diarrhea	8	12.5	33.33	43.42	(-23.8, 48.8)	1	-66.67	-66.67			79.17	(-29.72, 188.06)
Financial Difficulties	8	-4.17	0	21.36	(-22.03, 13.69)	1	0	0			-4.17	(-57.74, 49.41)
Change From Baseline Score at Cycle 10 Day 1												
Global health status / QoL:												
Global QoL	7	-16.67	-25	21.52	(-36.57, 3.23)	1	-33.33	-33.33			16.67	(-39.62, 72.95)
Functioning Scales:												
Physical Functioning	7	-19.05	-13.33	13.01	(-31.08, -7.01)	1	-46.67	-46.67			27.62	(-6.42, 61.66)
Role Functioning	7	-23.81	-16.67	21.21	(-43.42, -4.2)	1	-50	-50			26.19	(-29.28, 81.66)
Emotional Functioning	7	-20.24	-16.67	23	(-41.51, 1.04)	1	-16.67	-16.67			-3.57	(-63.74, 56.6)
Cognitive Functioning	7	-9.52	0	21.21	(-29.14, 10.09)	1	-33.33	-33.33			23.81	(-31.66, 79.28)
Social Functioning	7	-21.43	0	31.5	(-50.56, 7.7)	1	-50	-50			28.57	(-53.82, 110.96)
Symptoms:												
Fatigue	7	25.4	22.22	24.61	(2.64, 48.15)	1	55.56	55.56			-30.16	(-94.53, 34.21)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Nausea and Vomiting	7	0	0	25.46	(-23.55, 23.55)	1	16.67	16.67			-16.67	(-83.26, 49.93)
Pain	7	11.9	16.67	35.63	(-21.05, 44.86)	1	16.67	16.67			-4.76	(-97.98, 88.45)
Dyspnea	6	22.22	16.67	27.22	(-6.34, 50.78)	1	33.33	33.33			-11.11	(-86.68, 64.46)
Insomnia	7	4.76	0	23	(-16.51, 26.04)	1	0	0			4.76	(-55.41, 64.93)
Appetite loss	7	23.81	33.33	46	(-18.74, 66.36)	1	33.33	33.33			-9.52	(-129.86, 110.82)
Constipation	7	-19.05	0	37.8	(-54, 15.91)	1	0	0			-19.05	(-117.92, 79.82)
Diarrhea	7	9.52	33.33	31.71	(-19.8, 38.85)	1	-66.67	-66.67			76.19	(-6.75, 159.13)
Financial Difficulties	7	-4.76	0	23	(-26.04, 16.51)	1	0	0			-4.76	(-64.93, 55.41)
Change From Baseline Score at Cycle 11 Day 1												
Global health status / QoL:												
Global QoL	3	-38.89	-16.67	53.58	(-171.98, 94.2)	1	-33.33	-33.33			-5.56	(-271.74, 260.62)
Functioning Scales:												
Physical Functioning	3	-24.44	-6.67	36.72	(-115.65, 66.77)	1	-40	-40			15.56	(-166.87, 197.98)
Role Functioning	3	-38.89	-16.67	53.58	(-171.98, 94.2)	1	-66.67	-66.67			27.78	(-238.4, 293.96)
Emotional Functioning	3	-25	-8.33	52.04	(-154.28, 104.28	1	-8.33	-8.33			-16.67	(-275.22, 241.89)
Cognitive Functioning	3	-27.78	0	63.1	(-184.52, 128.97	1	-33.33	-33.33			5.56	(-307.94, 319.05)
Social Functioning	3	-38.89	-16.67	53.58	(-171.98, 94.2)	1	-66.67	-66.67			27.78	(-238.4, 293.96)
Symptoms:												

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Fatigue	3	37.04	22.22	46.26	(-77.88, 151.95)	1	22.22	22.22			14.81	(-215.01, 244.64)
Nausea and Vomiting	3	27.78	0	63.1	(-128.97, 184.52	1	16.67	16.67			11.11	(-302.38, 324.6)
Pain	3	22.22	0	69.39	(-150.15, 194.59	1	-16.67	-16.67			38.89	(-305.85, 383.63)
Dyspnea	3	22.22	0	69.39	(-150.15, 194.59	1	33.33	33.33			-11.11	(-355.85, 333.63)
Insomnia	3	22.22	0	69.39	(-150.15, 194.59	1	0	0			22.22	(-322.52, 366.97)
Appetite loss	3	44.44	33.33	50.92	(-82.04, 170.93)	1	0	0			44.44	(-208.53, 297.42)
Constipation	3	0	0	33.33	(-82.8, 82.8)	1	0	0			0	(-165.61, 165.61)
Diarrhea	3	11.11	0	19.25	(-36.7, 58.92)	1	-66.67	-66.67			77.78	(-17.84, 173.39)
Financial Difficulties	3	-11.11	0	19.25	(-58.92, 36.7)	1	0	0			-11.11	(-106.73, 84.5)
Change From Baseline Score at Cycle 12 Day 1												
Global health status / QoL:												
Global QoL	3	-11.11	-16.67	17.35	(-54.2, 31.98)							
Functioning Scales:												
Physical Functioning	3	-6.67	-6.67	6.67	(-23.23, 9.89)							
Role Functioning	3	-11.11	0	19.25	(-58.92, 36.7)							
Emotional Functioning	3	-2.78	0	20.97	(-54.87, 49.32)							
Cognitive Functioning	3	0	0	16.67	(-41.4, 41.4)							

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Social Functioning	3	-5.56	0	9.62	(-29.46, 18.35)							
Symptoms:												
Fatigue	3	7.41	0	12.83	(-24.46, 39.28)							
Nausea and Vomiting	3	16.67	0	60.09	(-132.61, 165.94)							
Pain	3	-5.56	0	9.62	(-29.46, 18.35)							
Dyspnea	2	0	0	0								
Insomnia	3	-11.11	0	19.25	(-58.92, 36.7)							
Appetite loss	3	22.22	33.33	19.25	(-25.59, 70.03)							
Constipation	3	-22.22	0	38.49	(-117.84, 73.39)							
Diarrhea	3	22.22	33.33	19.25	(-25.59, 70.03)							
Financial Difficulties	3	-11.11	0	19.25	(-58.92, 36.7)							
Change From Baseline Score at Cycle 13 Day 1												
Global health status / QoL:												
Global QoL	2	-50	-50	35.36	(-367.66, 267.66)							
Functioning Scales:												
Physical Functioning	2	-23.33	-23.33	33	(-319.81, 273.14)							
Role Functioning	2	-41.67	-41.67	35.36	(-359.32, 275.99)							
Emotional Functioning	2	-8.33	-8.33	11.79	(-114.22, 97.55)							

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Cognitive Functioning	2	0	0	0								
Social Functioning	2	-8.33	-8.33	35.36	(-325.99, 309.32)							
Symptoms:												
Fatigue	2	33.33	33.33	47.14	(-390.21, 456.87)							
Nausea and Vomiting	2	-8.33	-8.33	35.36	(-325.99, 309.32)							
Pain	2	41.67	41.67	58.93	(-487.76, 571.09)							
Dyspnea	1	0	0									
Insomnia	2	0	0	0								
Appetite loss	2	33.33	33.33	47.14	(-390.21, 456.87)							
Constipation	2	-16.67	-16.67	23.57	(-228.44, 195.1)							
Diarrhea	2	16.67	16.67	23.57	(-195.1, 228.44)							
Financial Difficulties	2	-16.67	-16.67	23.57	(-228.44, 195.1)							
Change From Baseline Score at Cycle 14 Day 1												
Global health status / QoL:												
Global QoL	1	-16.67	-16.67									
Functioning Scales:												
Physical Functioning	1	-6.67	-6.67									
Role Functioning	1	-33.33	-33.33									

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Emotional Functioning	1	-8.33	-8.33									
Cognitive Functioning	1	16.67	16.67									
Social Functioning	1	0.00	0.00									
Symptoms:												
Fatigue	1	22.22	22.22									
Nausea and Vomiting	1	0.00	0.00									
Pain	1	16.67	16.67									
Dyspnea	1	33.33	33.33									
Insomnia	1	-33.33	-33.33									
Appetite loss	1	0.00	0.00									
Constipation	1	0.00	0.00									
Diarrhea	1	33.33	33.33									
Financial Difficulties	1	-33.33	-33.33									
Change From Baseline Score at Follow-Up												
Global health status / QoL:												
Global QoL	3	-11.11	-16.67	9.62	(-35.01, 12.79)	5	8.33	8.33	10.21	(-4.34, 21.01)	-19.44	(-37.34, -1.55)
Functioning Scales:												
Physical Functioning	3	-17.22	0	29.83	(-91.32, 56.88)	5	-6.67	-6.67	6.67	(-14.94, 1.61)	-10.56	(-42.83, 21.72)
Role Functioning	3	-16.67	-16.67	16.67	(-58.07, 24.74)	5	10	0	25.28	(-21.38, 41.38)	-26.67	(-67.36, 14.02)
Emotional Functioning	3	16.67	16.67	8.33	(-4.03, 37.37)	5	8.33	0	15.59	(-11.02, 27.69)	8.33	(-15.98, 32.65)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Cognitive Functioning	3	-22.22	0	38.49	(-117.84, 73.39)	5	3.33	0	21.73	(-23.65, 30.32)	-25.56	(-76.37, 25.26)
Social Functioning	3	-5.56	0	9.62	(-29.46, 18.35)	5	-6.67	0	36.51	(-52.01, 38.67)	1.11	(-53.08, 55.31)
Symptoms:												
Fatigue	3	22.22	0	38.49	(-73.39, 117.84)	5	-4.44	-11.11	16.85	(-25.37, 16.48)	26.67	(-20.04, 73.37)
Nausea and Vomiting	3	0	0	16.67	(-41.4, 41.4)	5	10	0	25.28	(-21.38, 41.38)	-10	(-50.69, 30.69)
Pain	3	5.56	0	9.62	(-18.35, 29.46)	5	-10	0	25.28	(-41.38, 21.38)	15.56	(-22.64, 53.75)
Dyspnea	3	33.33	33.33	33.33	(-49.47, 116.14)	5	6.67	0	27.89	(-27.96, 41.3)	26.67	(-26.61, 79.94)
Insomnia	3	0	0	33.33	(-82.8, 82.8)	5	-26.67	-33.33	43.46	(-80.63, 27.3)	26.67	(-45.47, 98.8)
Appetite loss	3	33.33	33.33	0		5	0	0	23.57	(-29.27, 29.27)	33.33	(-1.06, 67.72)
Constipation	3	11.11	0	50.92	(-115.37, 137.6)	5	0	0	47.14	(-58.53, 58.53)	11.11	(-75.44, 97.66)
Diarrhea	3	0	0	0		5	6.67	0	36.51	(-38.67, 52.01)	-6.67	(-59.94, 46.61)
Financial Difficulties	3	22.22	33.33	19.25	(-25.59, 70.03)	5	-6.67	0	14.91	(-25.18, 11.84)	28.89	(-0.56, 58.34)
Change From Baseline Score at End of Study												
Global health status / QoL:												
Global QoL	2	-54.17	-54.17	29.46	(-318.88, 210.55	1	0	0			-54.17	(-512.66, 404.33)
Functioning Scales:												
Physical Functioning	2	-70	-70	4.71	(-112.35, -27.65	1	0	0			-70	(-143.36, 3.36)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Role Functioning	2	-33.33	-33.33	23.57	(-245.1, 178.44)	1	0	0			-33.33	(-400.13, 333.46)
Emotional Functioning	2	-66.67	-66.67	35.36	(-384.32, 250.99	1	-25	-25			-41.67	(-591.86, 508.53)
Cognitive Functioning	2	-66.67	-66.67	0	(-66.67, -66.67)	1	0	0			-66.67	(-66.67, -66.67)
Social Functioning	2	-83.33	-83.33	23.57	(-295.1, 128.44)	1	0	0			-83.33	(-450.13, 283.46)
Symptoms:												
Fatigue	2	55.56	55.56	15.71	(-85.62, 196.74)	1	-11.11	-11.11			66.67	(-177.86, 311.2)
Nausea and Vomiting	2	33.33	33.33	23.57	(-178.44, 245.1)	1	0	0			33.33	(-333.46, 400.13)
Pain	2	41.67	41.67	82.5	(-699.53, 782.86	1	16.67	16.67			25	(-1258.79, 1308.79
Dyspnea	2	83.33	83.33	23.57	(-128.44, 295.1)	1	0	0			83.33	(-283.46, 450.13)
Insomnia	2	66.67	66.67	47.14	(-356.87, 490.21	1	33.33	33.33			33.33	(-700.26, 766.93)
Appetite loss	2	50	50	70.71	(-585.31, 685.31	1	0	0			50	(-1050.39, 1150.39
Constipation	2	-16.67	-16.67	117.85	(-1075.52, 1042.	1	0	0			-16.67	(-1850.65, 1817.32
Diarrhea	2	33.33	33.33	47.14	(-390.21, 456.87	1	0	0			33.33	(-700.26, 766.93)
Financial Difficulties	2	-16.67	-16.67	23.57	(-228.44, 195.1)	1	0	0			-16.67	(-383.46, 350.13
Change From Baseline Score at Unplanned												
Global health status / QoL: Global QoL	4	-12.5	-4.17	32.27	(-63.86, 38.86)	1	-8.33	-8.33			-4.17	(-119, 110.67)

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Functioning Scales:												
Physical Functioning	3	-8.89	6.67	26.94	(-75.82, 58.04)	1	-20	-20			11.11	(-122.75, 144.97)
Role Functioning	3	5.56	0	9.62	(-18.35, 29.46)	1	0	0			5.56	(-42.25, 53.36)
Emotional Functioning	4	-8.33	-8.33	6.8	(-19.16, 2.49)	1	-8.33	-8.33			0	(-24.21, 24.21)
Cognitive Functioning	4	12.5	8.33	28.46	(-32.79, 57.79)	1	0	0			12.5	(-88.78, 113.78)
Social Functioning	4	0	8.33	36	(-57.29, 57.29)	1	-50	-50			50	(-78.11, 178.11)
Symptoms:												
Fatigue	3	3.70	0	16.97	(-38.46, 45.87)	1	22.22	22.22			-18.52	(-102.84, 65.81)
Nausea and Vomiting	3	5.56	0	25.46	(-57.69, 68.8)	1	-33.33	-33.33			38.89	(-87.6, 165.37)
Pain	4	-41.67	-50	61.61	(-139.71, 56.38)	1	16.67	16.67			-58.33	(-277.56, 160.89)
Dyspnea	3	22.22	0	38.49	(-73.39, 117.84)	1	0	0			22.22	(-169.01, 213.45)
Insomnia	3	-55.56	-66.67	50.92	(-182.04, 70.93)	1	66.67	66.67			-122.2	(-375.19, 130.75)
Appetite loss	3	22.22	0	69.39	(-150.15, 194.59	1	33.33	33.33			-11.11	(-355.85, 333.63)
Constipation	4	-33.33	-33.33	27.22	(-76.64, 9.97)	1	66.67	66.67			-100	(-196.84, -3.16)
Diarrhea	4	-8.33	-16.67	31.91	(-59.12, 42.45)	1	0	0			-8.33	(-121.89, 105.22)
Financial Difficulties	4	0	0	27.22	(-43.31, 43.31)	1	33.33	33.33			-33.33	(-130.17, 63.51)
Change From Baseline Score at Cycle 7 Day 8												

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Global health status / QoL:												
Global QoL	0											
Functioning Scales:												
Physical Functioning	1	-6.67	-6.67									
Role Functioning	1	0.00	0.00									
Emotional Functioning	1	0.00	0.00									
Cognitive Functioning	1	0.00	0.00									
Social Functioning	1	16.67	16.67									
Symptoms:												
Fatigue	1	11.11	11.11									
Nausea and Vomiting	1	-50.00	-50.00									
Pain	1	0.00	0.00									
Dyspnea	1	0.00	0.00									
Insomnia	1	0.00	0.00									
Appetite loss	1	0.00	0.00									
Constipation	1	0.00	0.00									
Diarrhea	1	33.33	33.33									
Financial Difficulties	1	33.33	33.33									

Table 19. Descriptive Summary of EORTC QLQ-C30: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change

Sample size is the number of subjects who has qol data at baseline and the corresponding assessment.
Change score = Cycle X, Day 1-Baseline.
Positive scores on the function and global scales equal higher functioning. Negative scores on the function and global scales equal poorer functioning.
Positive change scores on the symptom scales equal higher levels of symptoms. Negative scores on the symptom scales equal a reduction in symptoms.
The difference between the treatment groups = AG + gem - gem.
Positive difference scores on the functioning scales mean that the AG + gem arm was better, whereas negative scores mean that the gem arm was better.
Positive difference scores on the symptom scales mean that the gem arm was better, whereas negative scores mean that the AG + gem arm was better.
AG = axitinib; CI = confidence interval; EORTC = European organization for research and treatment of cancer; gem = gemcitabine; SD = standard deviation; QLQ = quality of life questionnaire; QoL = quality of life.

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Change From Baseline Score at Cycle 2 Day 1												
QLQ PAN-26												
Pancreatic pain	44	-11.05	-8.33	25.39	(-18.77, -3.33)	22	-13.64	-12.5	22.05	(-23.41, -3.86)	2.59	(-10.11, 15.29)
Eating related items	44	-0.38	0	34.19	(-10.77, 10.02)	22	-3.79	0	27.67	(-16.05, 8.48)	3.41	(-13.39, 20.2)
Altered bowel habits	44	8.33	0	28.19	(-0.24, 16.9)	22	-11.36	-8.33	22.05	(-21.14, -1.59)	19.7	(5.96, 33.43)
Jaundice	44	0	0	20.65	(-6.28, 6.28)	21	-12.7	0	25.22	(-24.18, -1.22)	12.7	(0.93, 24.47)
Body image	44	7.95	0	26.53	(-0.11, 16.02)	21	-7.14	0	25.04	(-18.54, 4.26)	15.1	(1.28, 28.91)
Health care satisfaction	43	0.39	0	34.6	(-10.26, 11.03)	21	-3.97	0	37.6	(-21.09, 13.15)	4.36	(-14.59, 23.3)
Sexual functioning	39	-2.56	0	22.14	(-9.74, 4.61)	17	18.63	0	38.59	(-1.21, 38.47)	-21.19	(-37.53, -4.85)
Ascitis	43	-10.85	0	36.89	(-22.21, 0.5)	22	-3.03	0	22.79	(-13.14, 7.08)	-7.82	(-25.04, 9.4)
Indigestion	43	-4.65	0	24.75	(-12.27, 2.97)	22	-10.61	0	37.64	(-27.29, 6.08)	5.95	(-9.59, 21.5)
Flatulence	44	5.3	0	34.43	(-5.17, 15.77)	22	-9.09	0	21.04	(-18.42, 0.24)	14.39	(-1.61, 30.4)
Cachexia	44	9.47	0	19.15	(3.65, 15.29)	22	-3.03	0	17.55	(-10.81, 4.75)	12.5	(2.78, 22.22)
Side effects	44	7.7	11.11	16.39	(2.72, 12.69)	21	-3.17	0	20.9	(-12.69, 6.34)	10.88	(1.36, 20.39)
Fear of future health	43	-2.33	0	23.45	(-9.54, 4.89)	21	0	0	31.62	(-14.39, 14.39)	-2.33	(-16.36, 11.71)
Ability to plan future	44	4.55	0	35.65	(-6.29, 15.38)	20	-1.67	0	27.52	(-14.55, 11.21)	6.21	(-11.78, 24.2)
Change From Baseline Score at Cycle 3 Day 1												
QLQ PAN-26												
Pancreatic pain	38	-8.92	-4.17	24.62	(-17.01, -0.83)	16	-23.78	-19.44	20.61	(-34.77, -12.8)	14.87	(0.79, 28.94)
Eating related items	38	3.07	0	37.34	(-9.2, 15.34)	16	-10.42	0	28.46	(-25.58, 4.75)	13.49	(-7.45, 34.42)

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Altered bowel habits	38	10.53	0	31.34	(0.22, 20.83)	16	-8.33	-8.33	31.03	(-24.87, 8.2)	18.86	(0.17, 37.55)
Jaundice	38	2.19	0	13.52	(-2.25, 6.64)	16	-9.38	0	26.51	(-23.5, 4.75)	11.57	(0.66, 22.48)
Body image	37	13.51	0	30.89	(3.21, 23.81)	16	-5.21	0	29.01	(-20.67, 10.25)	18.72	(0.49, 36.95)
Health care satisfaction	37	-5.41	0	40.07	(-18.77, 7.96)	16	5.21	0	24.88	(-8.05, 18.47)	-10.61	(-32.4, 11.17)
Sexual functioning	32	-3.13	0	21.77	(-10.97, 4.72)	15	-4.44	0	31.79	(-22.05, 13.16)	1.32	(-14.63, 17.27)
Ascitis	38	-2.63	0	28.35	(-11.95, 6.69)	16	-4.17	0	23.96	(-16.93, 8.6)	1.54	(-14.7, 17.78)
Indigestion	37	-4.5	0	34.39	(-15.97, 6.96)	15	-15.56	0	37.52	(-36.33, 5.22)	11.05	(-10.65, 32.75)
Flatulence	38	9.65	0	37.09	(-2.54, 21.84)	16	6.25	0	27.81	(-8.57, 21.07)	3.4	(-17.33, 24.13)
Cachexia	38	14.47	16.67	24.56	(6.4, 22.55)	16	5.21	0	17.97	(-4.37, 14.78)	9.27	(-4.4, 22.93)
Side effects	38	11.55	11.11	27.41	(2.54, 20.56)	16	-7.64	-11.11	26.28	(-21.64, 6.37)	19.19	(2.99, 35.39)
Fear of future health	35	-2.86	0	34.65	(-14.76, 9.05)	15	-2.22	0	42.66	(-25.85, 21.4)	-0.63	(-23.7, 22.43)
Ability to plan future	37	9.01	0	43.5	(-5.49, 23.51)	16	-12.5	-33.33	34.16	(-30.7, 5.7)	21.51	(-3.1, 46.12)
Change From Baseline Score at Cycle 4 Day 1												
QLQ PAN-26												
Pancreatic pain	29	-18.3	-16.67	26.9	(-28.53, -8.06)	13	-14.1	-16.67	22.92	(-27.95, -0.25)	-4.19	(-21.57, 13.19)
Eating related items	29	-7.47	0	26.57	(-17.58, 2.64)	13	5.13	0	36.88	(-17.16, 27.42)	-12.6	(-32.86, 7.66)
Altered bowel habits	29	16.09	0	35.21	(2.7, 29.49)	13	3.85	0	28.99	(-13.67, 21.37)	12.25	(-10.33, 34.82)
Jaundice	29	1.72	0	19.59	(-5.73, 9.18)	12	-11.11	0	16.41	(-21.54, -0.68)	12.84	(-0.18, 25.85)
Body image	26	12.82	0	31.02	(0.29, 25.35)	13	8.97	0	26.01	(-6.74, 24.69)	3.85	(-16.45, 24.14)
Health care satisfaction	26	-1.92	0	49.51	(-21.92, 18.08)	13	-8.97	-16.67	29.36	(-26.71, 8.77)	7.05	(-23.23, 37.34)

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Sexual functioning	22	-5.3	0	27.88	(-17.67, 7.06)	12	-2.78	0	40.72	(-28.65, 23.1)	-2.53	(-26.55, 21.5)
Ascitis	29	-6.9	0	25.79	(-16.71, 2.91)	13	2.56	0	28.74	(-14.81, 19.93)	-9.46	(-27.48, 8.56)
Indigestion	28	-9.52	0	33.77	(-22.62, 3.57)	13	-2.56	0	37.17	(-25.03, 19.9)	-6.96	(-30.62, 16.7)
Flatulence	29	1.15	0	39.32	(-13.81, 16.11)	13	-2.56	0	25.32	(-17.86, 12.74)	3.71	(-20.37, 27.8)
Cachexia	29	9.2	0	29.07	(-1.86, 20.25)	13	-3.85	0	24.68	(-18.76, 11.07)	13.04	(-5.73, 31.81)
Side effects	29	11.88	11.11	28.59	(1, 22.75)	12	-3.24	-5.56	19.88	(-15.87, 9.39)	15.12	(-3.23, 33.46)
Fear of future health	24	-2.78	0	41.61	(-20.35, 14.79)	13	5.13	0	38.12	(-17.91, 28.16)	-7.91	(-36.18, 20.37)
Ability to plan future	26	10.26	0	53.97	(-11.54, 32.06)	13	-5.13	-33.33	46.84	(-33.43, 23.18)	15.38	(-20.24, 51.01)
Change From Baseline Score at Cycle 5 Day 1												
QLQ PAN-26												
Pancreatic pain	26	-7.26	0	27.99	(-18.57, 4.04)	9	-18.52	-16.67	24.22	(-37.13, 0.1)	11.25	(-10.09, 32.59)
Eating related items	26	0	0	45.22	(-18.26, 18.26)	9	-7.41	0	26.5	(-27.78, 12.96)	7.41	(-25.22, 40.03)
Altered bowel habits	26	13.46	0	30.92	(0.97, 25.95)	9	-14.81	0	29.4	(-37.41, 7.78)	28.28	(4.23, 52.32)
Jaundice	26	3.85	0	19.04	(-3.84, 11.54)	9	-20.37	0	36.11	(-48.13, 7.39)	24.22	(5.09, 43.34)
Body image	25	14	16.67	28.74	(2.14, 25.86)	9	-11.11	-16.67	39.97	(-41.83, 19.61)	25.11	(-0.16, 50.38)
Health care satisfaction	25	-2.67	0	51.52	(-23.93, 18.6)	9	7.41	0	34.47	(-19.09, 33.9)	-10.07	(-47.95, 27.8)
Sexual functioning	19	-1.75	0	20.71	(-11.74, 8.23)	9	1.85	0	24.22	(-16.76, 20.47)	-3.61	(-21.78, 14.57)
Ascitis	26	-5.13	0	24.39	(-14.98, 4.72)	9	-11.11	0	40.82	(-42.49, 20.27)	5.98	(-17.02, 28.99)

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Indigestion	26	-3.85	0	28.79	(-15.48, 7.78)	9	-25.93	-33.33	49.38	(-63.88, 12.03)	22.08	(-5.39, 49.55)
Flatulence	25	-1.33	0	28.02	(-12.9, 10.23)	9	-11.11	0	40.82	(-42.49, 20.27)	9.78	(-15.33, 34.89)
Cachexia	26	10.26	0	36.84	(-4.62, 25.14)	9	-5.56	0	18.63	(-19.88, 8.77)	15.81	(-10.43, 42.06)
Side effects	26	10.04	11.11	28.55	(-1.49, 21.57)	9	-11.73	-11.11	17.22	(-24.97, 1.51)	21.77	(1.11, 42.43)
Fear of future health	24	0	0	35.44	(-14.97, 14.97)	9	14.81	0	29.4	(-7.78, 37.41)	-14.81	(-41.91, 12.28)
Ability to plan future	25	20	33.33	41.94	(2.69, 37.31)	9	-11.11	0	16.67	(-23.92, 1.7)	31.11	(1.6, 60.62)
Change From Baseline Score at Cycle 6 Day 1												
QLQ PAN-26												
Pancreatic pain	17	-3.76	8.33	24.06	(-16.13, 8.61)	4	-12.5	-16.67	30.81	(-61.52, 36.52)	8.74	(-20.62, 38.1)
Eating related items	17	-4.9	0	50.95	(-31.1, 21.29)	4	8.33	8.33	21.52	(-25.9, 42.57)	-13.24	(-68.52, 42.05)
Altered bowel habits	17	13.73	0	25.16	(0.79, 26.66)	4	-8.33	0	28.87	(-54.27, 37.6)	22.06	(-7.93, 52.05)
Jaundice	17	1.96	0	11.61	(-4.01, 7.93)	4	-16.67	0	45.13	(-88.48, 55.15)	18.63	(-5.64, 42.89)
Body image	16	23.96	16.67	31.6	(7.12, 40.8)	4	0	0	0		23.96	(-9.93, 57.84)
Health care satisfaction	16	-11.46	0	42.04	(-33.86, 10.94)	4	-25	-25	21.52	(-59.24, 9.24)	13.54	(-32.7, 59.78)
Sexual functioning	13	-7.69	0	30.14	(-25.9, 10.52)	4	-20.83	-16.67	49.77	(-100.03, 58.36)	13.14	(-29.46, 55.74)
Ascitis	17	-1.96	0	24.92	(-14.77, 10.85)	4	-8.33	-16.67	31.91	(-59.12, 42.45)	6.37	(-24.04, 36.79)
Indigestion	17	3.92	0	35.12	(-14.14, 21.98)	4	-16.67	-16.67	19.25	(-47.29, 13.96)	20.59	(-17.94, 59.12)
Flatulence	17	1.96	0	27.56	(-12.21, 16.13)	4	-8.33	0	16.67	(-34.85, 18.19)	10.29	(-20.12, 40.71)

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Cachexia	17	4.9	0	31.05	(-11.06, 20.87)	4	-20.83	-25	15.96	(-46.22, 4.56)	25.74	(-8.22, 59.69)
Side effects	17	16.34	11.11	30.4	(0.71, 31.97)	4	-22.22	-16.67	15.71	(-47.23, 2.78)	38.56	(5.32, 71.81)
Fear of future health	15	-4.44	0	45.19	(-29.47, 20.58)	4	0	0	0		-4.44	(-53.14, 44.25)
Ability to plan future	16	12.5	0	54.26	(-16.41, 41.41)	4	16.67	0	63.83	(-84.9, 118.23)	-4.17	(-69.9, 61.57)
Change From Baseline Score at Cycle 7 Day 1												
QLQ PAN-26												
Pancreatic pain	9	-3.7	8.33	22.09	(-20.68, 13.28)	2	-16.67	-16.67	11.79	(-122.55, 89.22)	12.96	(-24.52, 50.45)
Eating related items	9	-14.81	0	31.67	(-39.16, 9.53)	2	8.33	8.33	11.79	(-97.55, 114.22)	-23.15	(-76.41, 30.11)
Altered bowel habits	9	5.56	16.67	23.57	(-12.56, 23.67)	2	25	25	58.93	(-504.43, 554.43	-19.44	(-71.89, 33)
Jaundice	9	5.56	0	11.79	(-3.5, 14.61)	2	-41.67	-41.67	58.93	(-571.09, 487.76	47.22	(7.31, 87.13)
Body image	9	16.67	0	41.67	(-15.36, 48.69)	2	-25	-25	58.93	(-554.43, 504.43	41.67	(-36, 119.34)
Health care satisfaction	9	5.56	0	26.35	(-14.7, 25.81)	2	-33.33	-33.33	0		38.89	(-5.05, 82.83)
Sexual functioning	7	-9.52	0	18.9	(-27, 7.95)	2	-41.67	-41.67	11.79	(-147.55, 64.22)	32.14	(-2.09, 66.37)
Ascitis	9	0	0	0		2	0	0	0		0	
Indigestion	9	-7.41	0	22.22	(-24.49, 9.67)	2	0	0	0		-7.41	(-44.46, 29.64)
Flatulence	9	-3.7	0	30.93	(-27.48, 20.07)	2	-16.67	-16.67	23.57	(-228.44, 195.1)	12.96	(-40.45, 66.37)
Cachexia	9	5.56	16.67	25	(-13.66, 24.77)	2	-8.33	-8.33	35.36	(-325.99, 309.32	13.89	(-32.71, 60.49)
Side effects	9	8.64	11.11	25.93	(-11.29, 28.57)	2	-22.22	-22.22	31.43	(-304.58, 260.14	30.86	(-16.16, 77.89)

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Fear of future health	8	4.17	0	27.82	(-19.09, 27.42)	2	-16.67	-16.67	70.71	(-651.98, 618.64	20.83	(-44.95, 86.62)
Ability to plan future	9	14.81	0	55.56	(-27.89, 57.52)	2	33.33	33.33	47.14	(-390.21, 456.87	-18.52	(-115.22, 78.19)
Change From Baseline Score at Cycle 8 Day 1												
QLQ PAN-26												
Pancreatic pain	9	-1.54	0	25.99	(-21.52, 18.43)	1	-25	-25			23.46	(-39.71, 86.63)
Eating related items	9	3.7	0	48.43	(-33.52, 40.93)	1	16.67	16.67			-12.96	(-130.69, 104.76)
Altered bowel habits	9	14.81	0	22.74	(-2.66, 32.29)	1	-33.33	-33.33			48.15	(-7.12, 103.42)
Jaundice	9	9.26	0	12.11	(-0.05, 18.57)	1	-83.33	-83.33			92.59	(63.16, 122.02)
Body image	9	22.22	16.67	37.27	(-6.42, 50.87)	1	16.67	16.67			5.56	(-85.03, 96.14)
Health care satisfaction	9	3.7	0	27.36	(-17.33, 24.73)	1	-33.33	-33.33			37.04	(-29.46, 103.54)
Sexual functioning	7	-7.14	0	13.11	(-19.27, 4.98)	1	0	0			-7.14	(-41.45, 27.16)
Ascitis	9	-3.7	0	26.06	(-23.73, 16.33)	1	0	0			-3.7	(-67.04, 59.64)
Indigestion	9	-7.41	0	40.06	(-38.2, 23.39)	1	0	0			-7.41	(-104.79, 89.97)
Flatulence	9	-11.11	0	33.33	(-36.73, 14.51)	1	-33.33	-33.33			22.22	(-58.8, 103.25)
Cachexia	9	11.11	0	26.35	(-9.15, 31.37)	1	-16.67	-16.67			27.78	(-36.28, 91.83)
Side effects	9	11.11	0	35.14	(-15.9, 38.12)	1	0	0			11.11	(-74.3, 96.52)
Fear of future health	8	4.17	16.67	45.21	(-33.63, 41.96)	1	33.33	33.33			-29.17	(-142.55, 84.21)
Ability to plan future	9	11.11	0	64.55	(-38.51, 60.73)	1	66.67	66.67			-55.56	(-212.46, 101.35)
Change From Baseline Score at Cycle 9 Day 1												

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
QLQ PAN-26												
Pancreatic pain	7	0	0	30.43	(-28.14, 28.14)	1	-16.67	-16.67			16.67	(-62.93, 96.26)
Eating related items	7	14.29	33.33	39	(-21.79, 50.36)	1	0	0			14.29	(-87.74, 116.31)
Altered bowel habits	7	23.81	33.33	25.2	(0.51, 47.11)	1	-50	-50			73.81	(7.9, 139.72)
Jaundice	7	9.52	16.67	16.27	(-5.52, 24.57)	1	-66.67	-66.67			76.19	(33.64, 118.74)
Body image	7	28.57	33.33	35.63	(-4.39, 61.53)	1	0	0			28.57	(-64.64, 121.79)
Health care satisfaction	7	2.38	0	24.4	(-20.18, 24.94)	1	-33.33	-33.33			35.71	(-28.11, 99.53)
Sexual functioning	5	-13.33	0	29.81	(-50.35, 23.69)	1	0	0			-13.33	(-104.01, 77.34)
Ascitis	6	-11.11	0	34.43	(-47.24, 25.02)	1	33.33	33.33			-44.44	(-140.03, 51.14)
Indigestion	7	4.76	0	35.63	(-28.19, 37.72)	1	0	0			4.76	(-88.45, 97.98)
Flatulence	7	14.29	33.33	26.23	(-9.97, 38.54)	1	0	0			14.29	(-54.32, 82.89)
Cachexia	7	23.81	16.67	34.5	(-8.1, 55.72)	1	0	0			23.81	(-66.45, 114.07)
Side effects	7	31.75	44.44	33.6	(0.67, 62.82)	1	0	0			31.75	(-56.14, 119.63)
Fear of future health	6	-16.67	0	40.82	(-59.51, 26.18)	1	33.33	33.33			-50	(-163.35, 63.35)
Ability to plan future	7	19.05	0	42.41	(-20.18, 58.27)	1	33.33	33.33			-14.29	(-125.23, 96.66)
Change from Baseline Score at Cycle 10 Day 1												
QLQ PAN-26												
Pancreatic pain	6	8.33	4.17	25.28	(-18.19, 34.86)	1	-16.67	-16.67			25	(-45.18, 95.18)

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Eating related items	6	25	25	25.28	(-1.53, 51.53)	1	0	0			25	(-45.18, 95.18)
Altered bowel habits	6	27.78	25	22.77	(3.88, 51.67)	1	-50	-50			77.78	(14.55, 141)
Jaundice	6	2.78	0	16.39	(-14.42, 19.97)	1	-83.33	-83.33			86.11	(40.61, 131.61)
Body image	6	25	16.67	29.34	(-5.8, 55.8)	1	0	0			25	(-56.48, 106.48)
Health care satisfaction	6	13.89	0	30.58	(-18.2, 45.98)	1	-33.33	-33.33			47.22	(-37.69, 132.13)
Sexual functioning	5	-13.33	0	29.81	(-50.35, 23.69)	1	-33.33	-33.33			20	(-70.68, 110.68)
Ascitis	6	0	0	21.08	(-22.12, 22.12)	1	33.33	33.33			-33.33	(-91.87, 25.2)
Indigestion	6	27.78	33.33	25.09	(1.44, 54.11)	1	0	0			27.78	(-41.89, 97.45)
Flatulence	6	16.67	16.67	18.26	(-2.49, 35.83)	1	0	0			16.67	(-34.03, 67.36)
Cachexia	6	25	25	39.09	(-16.02, 66.02)	1	16.67	16.67			8.33	(-100.19, 116.86)
Side effects	6	37.04	38.89	28.69	(6.93, 67.14)	1	11.11	11.11			25.93	(-53.73, 105.58)
Fear of future health	5	0	0	0		1	33.33	33.33			-33.33	
Ability to plan future	6	33.33	16.67	42.16	(-10.91, 77.58)	1	33.33	33.33			0	(-117.07, 117.07)
Change From Baseline Score at Cycle 11 Day 1												
QLQ PAN-26												
Pancreatic pain	3	5.56	-8.33	47.39	(-112.16, 123.27	1	-8.33	-8.33			13.89	(-221.53, 249.31)
Eating related items	3	38.89	16.67	53.58	(-94.2, 171.98)	1	33.33	33.33			5.56	(-260.62, 271.74)
Altered bowel habits	3	50	66.67	44.1	(-59.54, 159.54)	1	-16.67	-16.67			66.67	(-152.41, 285.75)

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Jaundice	3	16.67	0	44.1	(-92.87, 126.21)	1	-83.33	-83.33			100	(-119.08, 319.08)
Body image	3	50	33.33	44.1	(-59.54, 159.54)	1	16.67	16.67			33.33	(-185.75, 252.41)
Health care satisfaction	3	27.78	33.33	25.46	(-35.47, 91.02)	1	-16.67	-16.67			44.44	(-82.04, 170.93)
Sexual functioning	2	-33.33	-33.33	47.14	(-456.87, 390.21	1	-33.33	-33.33			0	(-733.59, 733.59)
Ascitis	3	22.22	0	38.49	(-73.39, 117.84)	1	33.33	33.33			-11.11	(-202.34, 180.12)
Indigestion	3	11.11	0	19.25	(-36.7, 58.92)	1	0	0			11.11	(-84.5, 106.73)
Flatulence	3	11.11	0	19.25	(-36.7, 58.92)	1	0	0			11.11	(-84.5, 106.73)
Cachexia	3	55.56	50	25.46	(-7.69, 118.8)	1	16.67	16.67			38.89	(-87.6, 165.37)
Side effects	3	55.56	66.67	50.92	(-70.93, 182.04)	1	11.11	11.11			44.44	(-208.53, 297.42)
Fear of future health	2	0	0	0		1	33.33	33.33			-33.33	
Ability to plan future	3	44.44	33.33	50.92	(-82.04, 170.93)	1	66.67	66.67			-22.22	(-275.19, 230.75)
Change From Baseline Score at Cycle 12 Day 1												
QLQ PAN-26												
Pancreatic pain	3	-5.56	-8.33	20.97	(-57.65, 46.54)							
Eating related items	3	16.67	16.67	16.67	(-24.74, 58.07)							
Altered bowel habits	3	27.78	16.67	34.69	(-58.41, 113.96)							
Jaundice	3	0	0	0								
Body image	3	16.67	16.67	16.67	(-24.74, 58.07)							
Health care satisfaction	3	-5.56	0	41.94	(-109.75, 98.64)							

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Sexual functioning	3	0	0	66.67	(-165.61, 165.61							
Ascitis	3	-22.22	-33.33	19.25	(-70.03, 25.59)							
Indigestion	3	0	0	0								
Flatulence	3	0	0	0								
Cachexia	3	33.33	50	28.87	(-38.38, 105.04)							
Side effects	3	33.33	22.22	40.06	(-66.19, 132.85)							
Fear of future health	3	0	0	0								
Ability to plan future	3	0	0	0								
Change From Baseline Score at Cycle 13 Day 1												
QLQ PAN-26												
Pancreatic pain	2	20.83	20.83	5.89	(-32.11, 73.78)							
Eating related items	2	58.33	58.33	58.93	(-471.09, 587.76							
Altered bowel habits	2	8.33	8.33	11.79	(-97.55, 114.22)							
Jaundice	2	25	25	35.36	(-292.66, 342.66							
Body image	2	41.67	41.67	58.93	(-487.76, 571.09							
Health care satisfaction	2	-16.67	-16.67	23.57	(-228.44, 195.1)							
Sexual functioning	2	-50	-50	23.57	(-261.77, 161.77							
Ascitis	2	16.67	16.67	23.57	(-195.1, 228.44)							

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Indigestion	2	0	0	0								
Flatulence	2	16.67	16.67	23.57	(-195.1, 228.44)							
Cachexia	2	33.33	33.33	47.14	(-390.21, 456.87							
Side effects	2	16.67	16.67	7.86	(-53.92, 87.26)							
Fear of future health	2	0	0	0								
Ability to plan future	2	16.67	16.67	23.57	(-195.1, 228.44)							
Change From Baseline Score at Cycle 14 Day 1												
QLQ PAN-26												
Pancreatic pain	1	-8.33	-8.33									
Eating related items	1	16.67	16.67									
Altered bowel habits	1	33.33	33.33									
Jaundice	1	33.33	33.33									
Body image	1	33.33	33.33									
Health care satisfaction	1	0	0									
Sexual functioning	1	-33.33	-33.33									
Ascitis	1	0	0									
Indigestion	1	0	0									
Flatulence	1	33.33	33.33									
Cachexia	1	50	50									
Side effects	1	0	0									
Fear of future health	1	0	0									

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Ability to plan future	1	0	0									
Change From Baseline Score at Follow-Up												
QLQ PAN-26												
Pancreatic pain	3	-2.78	0	20.97	(-54.87, 49.32)	3	-19.44	0	33.68	(-103.11, 64.22)	16.67	(-46.93, 80.26)
Eating related items	3	16.67	0	28.87	(-55.04, 88.38)	3	-5.56	0	25.46	(-68.8, 57.69)	22.22	(-39.48, 83.92)
Altered bowel habits	3	5.56	0	9.62	(-18.35, 29.46)	3	0	0	0		5.56	(-9.87, 20.98)
Jaundice	3	5.56	0	9.62	(-18.35, 29.46)	3	-5.56	0	9.62	(-29.46, 18.35)	11.11	(-10.7, 32.92)
Body image	3	-11.11	-16.67	25.46	(-74.35, 52.13)	3	-11.11	-16.67	9.62	(-35.01, 12.79)	0	(-43.63, 43.63)
Health care satisfaction	3	5.56	0	9.62	(-18.35, 29.46)	3	-16.67	-16.67	50	(-140.87, 107.54	22.22	(-59.4, 103.84)
Sexual functioning	3	-16.67	-16.67	16.67	(-58.07, 24.74)	2	33.33	33.33	23.57	(-178.44, 245.1)	-50	(-105.91, 5.91)
Ascitis	3	11.11	0	50.92	(-115.37, 137.6)	3	0	0	33.33	(-82.8, 82.8)	11.11	(-86.44, 108.67)
Indigestion	3	-11.11	0	19.25	(-58.92, 36.7)	3	11.11	0	19.25	(-36.7, 58.92)	-22.22	(-65.85, 21.41)
Flatulence	3	-22.22	-33.33	19.25	(-70.03, 25.59)	3	0	0	0		-22.22	(-53.07, 8.63)
Cachexia	3	5.56	0	9.62	(-18.35, 29.46)	3	-11.11	-16.67	9.62	(-35.01, 12.79)	16.67	(-5.15, 38.48)
Side effects	3	11.11	22.22	19.25	(-36.7, 58.92)	3	7.41	11.11	6.42	(-8.53, 23.34)	3.7	(-28.81, 36.22)
Fear of future health	3	0	0	33.33	(-82.8, 82.8)	3	-33.33	-66.67	57.74	(-176.76, 110.09	33.33	(-73.53, 140.2)
Ability to plan future	3	-22.22	0	38.49	(-117.84, 73.39)	3	-11.11	0	19.25	(-58.92, 36.7)	-11.11	(-80.09, 57.87)
Change From Baseline Score at End of Study												

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
QLQ PAN-26												
Pancreatic pain	2	58.33	58.33	35.36	(-259.32, 375.99	1	0	0			58.33	(-491.86, 608.53)
Eating related items	2	25	25	82.5	(-716.2, 766.2)	1	0	0			25	(-1258.79, 1308.79
Altered bowel habits	2	83.33	83.33	23.57	(-128.44, 295.1)	1	0	0			83.33	(-283.46, 450.13)
Jaundice	2	8.33	8.33	11.79	(-97.55, 114.22)	1	0	0			8.33	(-175.06, 191.73)
Body image	2	66.67	66.67	0	(66.67, 66.67)	1	-16.67	-16.67			83.33	
Health care satisfaction	1	0	0			1	33.33	33.33				
Sexual functioning	1	0	0			1	33.33	33.33				
Ascitis	2	33.33	33.33	47.14	(-390.21, 456.87	1	33.33	33.33			0	(-733.59, 733.59)
Indigestion	2	33.33	33.33	47.14	(-390.21, 456.87	1	33.33	33.33			0	(-733.59, 733.59)
Flatulence	2	83.33	83.33	23.57	(-128.44, 295.1)	1	0	0			83.33	(-283.46, 450.13)
Cachexia	2	66.67	66.67	0	(66.67, 66.67)	1	0	0			66.67	
Side effects	2	19.44	19.44	90.35	(-792.34, 831.23	1	-11.11	-11.11			30.56	(-1375.5, 1436.61)
Fear of future health	1	33.33	33.33			1	-33.33	-33.33				
Ability to plan future	1	66.67	66.67			1	33.33	33.33				
Change From Baseline Score at Unplanned												
QLQ PAN-26												
Pancreatic pain	4	-25	-29.17	39.09	(-87.2, 37.2)	1	50	50			-75	(-214.07, 64.07)

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Eating related items	4	12.5	16.67	20.97	(-20.87, 45.87)	1	0	0			12.5	(-62.12, 87.12)
Altered bowel habits	4	12.5	16.67	36.96	(-46.31, 71.31)	1	16.67	16.67			-4.17	(-135.66, 127.33)
Jaundice	4	-16.67	-8.33	23.57	(-54.17, 20.84)	1	-33.33	-33.33			16.67	(-67.2, 100.53)
Body image	3	22.22	0	38.49	(-73.39, 117.84)	1	33.33	33.33			-11.11	(-202.34, 180.12)
Health care satisfaction	3	-16.67	0	44.1	(-126.21, 92.87)	1	50	50			-66.67	(-285.75, 152.41)
Sexual functioning	3	22.22	0	69.39	(-150.15, 194.59	1	-50	-50			72.22	(-272.52, 416.97)
Ascitis	4	-16.67	0	33.33	(-69.71, 36.37)	1	33.33	33.33			-50	(-168.6, 68.6)
Indigestion	4	16.67	16.67	43.03	(-51.81, 85.14)	1	33.33	33.33			-16.67	(-169.78, 136.45)
Flatulence	4	-33.33	-33.33	38.49	(-94.58, 27.91)	1	33.33	33.33			-66.67	(-203.62, 70.28)
Cachexia	4	12.5	8.33	28.46	(-32.79, 57.79)	1	33.33	33.33			-20.83	(-122.11, 80.44)
Side effects	4	13.89	5.56	29.22	(-32.61, 60.39)	1	27.78	27.78			-13.89	(-117.86, 90.08)
Fear of future health	3	0	0	0		1	33.33	33.33			-33.33	
Ability to plan future	3	0	0	33.33	(-82.8, 82.8)	1	0	0			0	(-165.61, 165.61)
Change From Baseline Score at Cycle 7 Day 8												
QLQ PAN-26												
Pancreatic pain	1	-33.33	-33.33									
Eating related items	1	-16.67	-16.67									

Table 20. Descriptive Summary of EORTC QLQ-PAN26: Changes From Baseline

Symptom or Functioning Scale	Axitinib + Gemcitabine					Gemcitabine					Mean Change Difference Between Treatment Groups	
	Sample Size	Mean	Median	SD	95% CI for Mean	Sample Size	Mean	Median	SD	95% CI for Mean	Mean Change	95% CI for Mean Change
Altered bowel habits	1	33.33	33.33									
Jaundice	1	0	0									
Body image	1	0	0									
Health care satisfaction	1	-33.33	-33.33									
Sexual functioning	1	0	0									
Ascitis	1	-33.33	-33.33									
Indigestion	1	0	0									
Flatulence	1	0	0									
Cachexia	1	16.67	16.67									
Side effects	1	-27.78	-27.78									
Fear of future health	1	0	0									
Ability to plan future	1	0	0									

Sample size is the number of subjects who have pan data at baseline and the corresponding assessment.
Change score = Cycle X, Day 1 – Baseline.
Positive change scores on the symptom scales equals higher levels of symptoms with the exception of sexual functioning. Negative change scores on the symptomscales equals a reduction in symptoms with the exception of sexual functioning.
Positive change scores on the sexual functioning scale equals better sexual functioning. Negative change scores on the sexual functioning scale equals poorer sexual functioning.
The difference between the treatment groups = AG + gem - gem.
Positive difference scores on the symptom scales mean that the gem arm was better, whereas negative scores mean that the AG + gem arm was better.
AG = axitinib; CI = confidence interval; EORTC = European organization for research and treatment of cancer; gem = gemcitabine; SD = standard deviation; QLQ = quality of life questionnaire.

Pharmacokinetic Results:

Phase 1:

Seven subjects in the lead-in portion of the Phase 1 study received 1000 mg/m^2 of gemcitabine given as a 30-minute IV infusion once weekly for 3 weeks and 5 mg axitinib administered oral BID without food or drink (other than water) 2 hours before and 2 hours after each axitinib dose. Full PK profiles were collected on Cycle 1 Day 1 (gemcitabine alone), Cycle 1 Day 14 (steady-state axitinib alone), and Cycle 1 Day 15 (gemcitabine plus steady-state axitinib). Final PK parameters for these subjects were estimated using actual collection times and quality-controlled, quality-assured bioanalytical data. Two subjects were excluded from PK parameter summary tables for both gemcitabine and the gemcitabine metabolite, dFdU. Plasma profiles and PK parameters (n=5) of gemcitabine were similar in the presence and absence of axitinib (Table 21). The plasma profiles and PK parameters (n = 5) of the gemcitabine metabolite, dFdU (obtained following the administration of gemcitabine) were similar in the absence and presence of axitinib (Table 22). Axitinib plasma PK parameters could not be reported for 1 subject. Plasma profiles and PK parameters of axitinib (n = 6) were similar in the absence and presence of gemcitabine (Table 23).

For Phase 1 subjects, actual dosing times for axitinib on PK sampling days were not collected on the case report form (CRF). The actual collection times for all PK samples as well as infusion start and stop times for gemcitabine were, however, collected. The axitinib dosing time was imputed from the actual time of the first postdose PK blood draw for axitinib.

For one Phase 1 subject PK parameters could not be reported since the subject discontinued treatment before Cycle 1, Day 15 and hence did not provide data for the combination gemcitabine + axitinib PK evaluation. This subject was excluded from PK parameter summary tables for gemcitabine, dFdU and axitinib.

For another Phase 1 subject, PK parameters were deemed unreliable for gemcitabine and dFdU on Cycle 1, Day 15 due to errors in sample processing; this was related to inadequate protection of gemcitabine in blood from ex vivo conversion by cytidine deaminase during the processing of the samples. This subject was excluded from PK parameter summary tables for gemcitabine and dFdU.

Results for the Phase 2 PK endpoint were to be provided separately from this study.

Table 21. Phase 1 Portion: Plasma Pharmacokinetic Parameters of Gemcitabine

Treatment	C_{max} (ng/mL)	AUC_{inf} (ng.hr/mL)	CL (L/hr)	V_z (L)	$t_{1/2}$ (hr)
Gemcitabine alone, n=5	20801 (9388-46089)	10455 (5162-21175)	174 (84-361)	67 (30-148)	0.27 (0.23-0.31)
Gemcitabine + Axitinib, n=5	25382 (15290-42135)	13196 (9232-18862)	138 (97-196)	61 (46-81)	0.31 (0.27-0.35)

Values reported are geometric least square means with 95% confidence interval for C_{max}, AUC_{inf}, CL, V_z and $t_{1/2}$
Data from 2 subjects excluded.
C_{max} = maximal plasma concentration; AUC_{inf} = area under the plasma concentration versus time curve from 0 to infinity; CL = plasma clearance; V_z = volume of distribution of the drug during the elimination phase; $t_{1/2}$ = plasma terminal elimination half-life.

Table 22. Phase 1 Portion: Plasma Pharmacokinetic Parameters of dFdU

Treatment	C_{max} (ng/mL)	AUC_{inf} (ng.hr/mL)	T_{max} (hr)	$t_{1/2}$ (hr)
Gemcitabine alone, n=5	30959 (25699-37295)	169937 (125070-230899	0.72 (0.50-0.82)	5.01 (4.17-6.01)
Gemcitabine + Axitinib, n=5	29560 (27042-32313)	188864 (131970-270287)	0.75 (0.50-1.00)	5.54 (4.31-7.12)

Values reported are geometric least square mean with 95% confidence interval for C_{max}, AUC_{inf} and $t_{1/2}$ and median with range for T_{max}.
Data from 2 subjects excluded.
C_{max} = maximal plasma concentration; AUC_{inf} = area under the plasma concentration versus time curve from 0 to infinity; Tmax = Time of maximal plasma concentration; t½ = plasma terminal elimination half-life.

Table 23. Phase 1 Portion: Plasma Pharmacokinetic Parameters of Axitinib

Treatment	C_{max} (ng/mL)	$AUC_{(0-24)}$ (ng.hr/mL)	T_{max} (hr)	CL/F (L/hr)	V_z/F (L)	$t_{1/2}$ (hr)
Axitinib alone, n=6	28.2 (13.4-59.3)	230 (173-307)	2.09 (1.50- 4.50)	43.9 (32.5-59.2)	142 (79-258)	2.25 (1.58-3.20)
Axitinib + Gemcitabine, n=6	37.1 (18.6-73.7)	258 (159-418)	1.52 (0.50-2.20)	35.8 (21.6-59.2)	135 (80-228)	2.62 (1.56-4.42)

Geometric least square mean with 95% confidence interval for C_{max}, AUC_{inf}, CL/F, V_z/F and $t_{1/2}$, and median with range for T_{max}.
Data from 1 subject excluded.
C_{max} = maximal plasma concentration; $AUC_{(0-24)}$ = area under the plasma concentration versus time curve from 0 to 24 hour; T_{max} = time of maximal plasma concentration; CL/F = apparent plasma clearance; V_z/F = apparent oral volume of distribution of the drug during the elimination phase; $t_{1/2}$ = plasma terminal elimination half-life.

Safety Results:

Table 24 and Table 25 present treatment emergent and treatment related adverse events respectively in Phase 1 of the study. Table 26 presents treatment emergent adverse events in Phase 2 of the study.

Table 24. Treatment-Emergent Nonserious Adverse Events by System Organ Class and Preferred Term (All Causalities) For Events Having a Frequency Rate Greater Than or Equal to Zero

Number of Subjects	Axitinib+ Gemcitabine n
Subjects evaluable for adverse events	8
Subjects with adverse events	7
Number of Subjects With Adverse Events by System Organ Class MedDRA (v10.1) and Preferred Term:	
Blood and lymphatic system disorders	4
Anaemia	4
Leukopenia	2
Lymphopenia	1
Neutropenia	2
Thrombocytopenia	4
Ear and labyrinth disorders	1
Vertigo	1
Gastrointestinal disorders	6
Abdominal discomfort	1
Abdominal pain	2
Abdominal pain upper	1
Ascites	1
Constipation	2
Diarrhoea	4
Flatulence	1
Gastric ulcer	1
Gastrooesophageal reflux disease	2
Inguinal hernia	1
Nausea	3
Stomatitis	1
Toothache	2
Vomiting	2
General disorders and administration site conditions	7
Asthenia	1
Chest pain	1
Fatigue	7
General physical health deterioration	1
Mucosal inflammation	3
Multi-organ failure	1
Oedema peripheral	1
Pyrexia	1
Hepatobiliary disorders	3
Cholestasis	1
Cytolytic hepatitis	3
Infections and infestations	3
Diverticulitis	1
Folliculitis	1
Gastroenteritis	1
Gingival abscess	1
Influenza	1
Nasopharyngitis	2
Oropharyngeal candidiasis	1
Urinary tract infection	1

Table 24. Treatment-Emergent Nonserious Adverse Events by System Organ Class and Preferred Term (All Causalities) For Events Having a Frequency Rate Greater Than or Equal to Zero

Number of Subjects	Axitinib+ Gemcitabine
	n
Investigations	2
Blood lactate dehydrogenase increased	1
Weight decreased	1
Metabolism and nutrition disorders	5
Anorexia	3
Decreased appetite	1
Dehydration	1
Hypoalbuminaemia	1
Musculoskeletal and connective tissue disorders	3
Arthralgia	1
Back pain	2
Bone pain	1
Muscle spasms	1
Muscular weakness	1
Nervous system disorders	3
Dysgeusia	1
Headache	1
Neuropathy	1
Neuropathy peripheral	1
Paraesthesia	1
Psychiatric disorders	4
Depression	2
Insomnia	2
Reproductive system and breast disorders	1
Erectile dysfunction	1
Respiratory, thoracic and mediastinal disorders	6
Cough	2
Dysphonia	6
Dyspnoea	2
Epistaxis	2
Skin and subcutaneous tissue disorders	3
Alopecia	1
Dry skin	1
Hyperhidrosis	1
Palmar-plantar erythrodysaesthesia syndrome	2
Pruritus	2
Vascular disorders	4
Hypertension	4

Subjects were only counted once per treatment for each row.
Includes data up to 28 days after last dose of study drug.
Medical dictionary of regulatory activities (v10.1) coding dictionary applied.
n = number of subjects with adverse events.

Table 25. Treatment-Emergent Adverse Events Related to Study Treatment by Body System and Preferred Term

Number of Subjects	Axitinib+ Gemcitabine n
Subjects evaluable for adverse events	8
Subjects with adverse events	7
Subjects discontinued due to adverse events	1
Number of Subjects With Adverse Events by Body System and Preferred Term	
Blood and lymphatic system disorders	4
Anaemia	4
Leukopenia	2
Lymphopenia	1
Neutropenia	2
Thrombocytopenia	4
Ear and labyrinth disorders	1
Vertigo	1
Gastrointestinal disorders	5
Abdominal discomfort	1
Abdominal pain upper	1
Constipation	2
Diarrhoea	4
Gastrooesophageal reflux disease	2
Nausea	3
Stomatitis	1
Vomiting	2
General disorders and administration site Conditions	6
Asthenia	1
Chest pain	1
Fatigue	6
Mucosal inflammation	3
Oedema peripheral	1
Pyrexia	1
Hepatobiliary disorders	3
Cholestasis	1
Cytolytic hepatitis	3
Infections and infestations	2
Folliculitis	1
Oropharyngeal candidiasis	1
Urinary tract infection	1
Investigations	1
Platelet count decreased	1
Metabolism and nutrition disorders	3
Anorexia	3
Decreased appetite	1
Musculoskeletal and connective tissue disorders	2
Arthralgia	1
Muscle spasms	1
Muscular weakness	1
Nervous system disorders	3
Dysgeusia	1
Headache	1
Neuropathy	1

Table 25. Treatment-Emergent Adverse Events Related to Study Treatment by Body System and Preferred Term

Number of Subjects	Axitinib+ Gemcitabine n
Neuropathy peripheral	1
Paraesthesia	1
Psychiatric disorders	2
Insomnia	2
Respiratory, thoracic and mediastinal disorders	6
Cough	2
Dysphonia	6
Epistaxis	2
Skin and subcutaneous tissue disorders	3
Alopecia	1
Dry skin	1
Hyperhidrosis	1
Palmar-plantar erythrodysaesthesia syndrome	2
Pruritus	2
Vascular disorders	4
Hypertension	4

Subjects were only counted once per treatment for each row.
Included data up to 28 days after last dose of study drug.
Medical dictionary of regulatory activities (v10.1) coding dictionary applied.
n = number of subjects with adverse events.

Table 26. Treatment-Emergent Nonserious Adverse Events by System Organ Class and Preferred Term (All Causalities)

Number of Subjects	Axitinib + Gemcitabine n (%)	Gemcitabine n (%)
Subjects evaluable for adverse events	68	31
Subjects with adverse events	67 (98.5)	26 (83.9)
Number (%) of Subjects With Adverse Events by System Organ Class MedDRA (v13.1) and Preferred Term:		
Blood and lymphatic system disorders	32 (47.1)	11 (35.5)
Anaemia	16 (23.5)	7 (22.6)
Granulocytopenia	1	0
Iron deficiency anaemia	1	0
Leukopenia	3	0
Neutropenia	15 (22.1)	6 (19.4)
Thrombocytopenia	10 (14.7)	2 (6.5)
Thrombocytosis	1	1
Cardiac disorders	6 (8.8)	3 (9.7)
Atrial fibrillation	1	0
Cardiogenic shock	0	1
Cyanosis	1	0
Pericardial effusion	2	0
Sinus tachycardia	1	0
Tachycardia	1	2 (6.5)
Ear and labyrinth disorders	2	0
Ear pain	1	0
Tinnitus	1	0
Vertigo	1	0
Gastrointestinal disorders	59 (86.8)	22 (71.0)
Abdominal discomfort	0	2 (6.5)
Abdominal distension	4 (5.9)	1
Abdominal hernia	1	0
Abdominal pain	16 (23.5)	8 (25.8)
Abdominal pain upper	11 (16.2)	1
Abdominal tenderness	1	0
Aphthous stomatitis	1	0
Ascites	3	5 (16.1)
Constipation	18 (26.5)	7 (22.6)
Diarrhoea	35 (51.5)	8 (25.8)
Dry mouth	5 (7.4)	1
Duodenal ulcer	1	0
Dyspepsia	9 (13.2)	4 (12.9)
Dysphagia	1	0
Flatulence	5 (7.4)	2 (6.5)
Gastritis	2	1
Gastrointestinal haemorrhage	0	1
Gastrooesophageal reflux disease	1	1
Gingival pain	1	0
Gingival swelling	1	0
Haematochezia	1	0
Haemorrhoids	5 (7.4)	0
Intestinal haemorrhage	1	0
Lip ulceration	1	0
Mesenteric artery stenosis	1	0
Nausea	30 (44.1)	15 (48.4)

Table 26. Treatment-Emergent Nonserious Adverse Events by System Organ Class and Preferred Term (All Causalities)

Number of Subjects	Axitinib + Gemcitabine n (%)	Gemcitabine n (%)
Oral pain	6 (8.8)	0
Peptic ulcer haemorrhage	1	0
Proctalgia	1	0
Rectal haemorrhage	2	1
Sensitivity of teeth	0	1
Small intestinal obstruction	1	0
Steatorrhoea	1	0
Stomatitis	12 (17.6)	2 (6.5)
Tongue coated	1	0
Tongue disorder	1	0
Toothache	2	0
Vomiting	29 (42.6)	12 (38.7)
General disorders and administration site	53 (77.9)	20 (64.5)
conditions	0	0
Adverse drug reaction	1	0
Asthenia	22 (32.4)	4 (12.9)
Catheter site pain	1	0
Chest pain	5 (7.4)	
Chills	5 (7.4)	3 (9.7)
Device occlusion	1	0
Disease progression	1	0
Face oedema	1	0
Fatigue	29 (42.6)	10 (32.3)
Feeling cold	1	0
General physical health deterioration	1	0
Hyperpyrexia	0	1
Influenza like illness	2	0
Infusion related reaction	1	0
Infusion site pain	1	0
Malaise	0	1
Mass	1	0
Mucosal dryness	1	0
Mucosal inflammation	12 (17.6)	2 (6.5)
Oedema	6 (8.8)	0
Oedema peripheral	11 (16.2)	8 (25.8)
Pain	10 (14.7)	2 (6.5)
Performance status decreased	2	0
Pyrexia	12 (17.6)	7 (22.6)
Hepatobiliary disorders	10 (14.7)	4 (12.9)
Bile duct obstruction	1	0
Bile duct stenosis	1	0
Cholangitis	1	0
Cholecystitis	2	0
Cholestasis	1	1
Cytolytic hepatitis	1	1
Hepatotoxicity	2	0
Hyperbilirubinaemia	1	1
Jaundice	2	1
Immune system disorders	1	1
Hypersensitivity	1	1

Table 26. Treatment-Emergent Nonserious Adverse Events by System Organ Class and Preferred Term (All Causalities)

Number of Subjects	Axitinib + Gemcitabine n (%)	Gemcitabine n (%)
Infections and infestations	19 (27.9)	9 (29.0)
Bacteraemia	1	0
Bronchitis	1	0
Candidiasis	2	1
Cellulitis	1	1
Escherichia sepsis	0	1
Herpes ophthalmic	0	1
Hordeolum	1	0
Infected skin ulcer	1	0
Infection	1	1
Localised infection	0	1
Nasopharyngitis	1	0
Oral candidiasis	2	0
Oral herpes	1	0
Periodontal infection	1	0
Pneumonia	1	1
Staphylococcal infection	0	1
Upper respiratory tract infection	1	0
Urinary tract infection	9 (13.2)	3 (9.7)
Vulvovaginal candidiasis	1	0
Wound infection	2	0
Injury, poisoning and procedural complications	8 (11.8)	1
Contusion	1	1
Drug toxicity	1	0
Excoriation	1	0
Fall	1	0
Joint sprain	1	0
Muscle strain	1	0
Periorbital haematoma	1	0
Procedural pain	1	0
Sunburn	1	0
Investigations	34 (50.0)	12 (38.7)
Alanine aminotransferase	1	0
Alanine aminotransferase increased	3	1
Aspartate aminotransferase	1	0
Aspartate aminotransferase increased	2	2 (6.5)
Blood albumin decreased	0	1
Blood albumin increased	1	0
Blood alkaline phosphatase	2	0
Blood alkaline phosphatase increased	2	1
Blood bilirubin increased	0	1
Blood creatinine increased	1	0
Blood glucose	0	1
Blood glucose increased	1	0
Blood lactate dehydrogenase increased	1	0
Blood potassium decreased	1	0
Blood pressure increased	3	0
Blood sodium decreased	1	0
Blood thyroid stimulating hormone increased	1	0
Haemoglobin	0	1

Table 26. Treatment-Emergent Nonserious Adverse Events by System Organ Class and Preferred Term (All Causalities)

Number of Subjects	Axitinib + Gemcitabine n (%)	Gemcitabine n (%)
Haemoglobin decreased	5 (7.4)	2 (6.5)
Heart rate increased	0	1
International normalised ratio	0	1
Neutrophil count	1	0
Neutrophil count decreased	0	1
Platelet count decreased	4 (5.9)	0
Prothrombin time prolonged	1	0
Transaminases increased	2	1
Weight decreased	16 (23.5)	4 (12.9)
Metabolism and nutrition disorders	38 (55.9)	13 (41.9)
Cachexia	1	0
Decreased appetite	29 (42.6)	10 (32.3)
Dehydration	4 (5.9)	0
Diabetes mellitus inadequate control	1	0
Failure to thrive	1	1
Hyperglycaemia	3	0
Hyperkalaemia	2	2 (6.5)
Hypernatraemia	1	0
Hypoalbuminaemia	2	0
Hypocalcaemia	1	0
Hypoglycaemia	1	0
Hypokalaemia	11 (16.2)	4 (12.9)
Hypomagnesaemia	1	1
Musculoskeletal and connective tissue disorders	25 (36.8)	7 (22.6)
Arthralgia	1	0
Back pain	12 (17.6)	2 (6.5)
Bone pain	2	0
Flank pain	1	0
Joint swelling	1	0
Mobility decreased	1	0
Muscle atrophy	1	0
Muscle spasms	1	0
Muscular weakness	3	0
Musculoskeletal chest pain	0	1
Musculoskeletal pain	1	1
Myalgia	3	0
Myositis	1	0
Pain in extremity	6 (8.8)	3 (9.7)
Spinal osteoarthritis	1	0
Trigger finger	1	0
Neoplasms benign, malignant and unspecified (including cysts and polyps)	1	1
Malignant pleural effusion	1	0
Tumour pain	0	1
Nervous system disorders	30 (44.1)	10 (32.3)
Aphasia	1	0
Ataxia	1	0
Balance disorder	1	0
Cerebral ischaemia	1	0
Dizziness	8 (11.8)	3 (9.7)

Table 26. Treatment-Emergent Nonserious Adverse Events by System Organ Class and Preferred Term (All Causalities)

Number of Subjects	Axitinib + Gemcitabine n (%)	Gemcitabine n (%)
Dysarthria	1	0
Dysgeusia	7 (10.3)	2 (6.5)
Dyskinesia	1	0
Facial paresis	1	0
Headache	9 (13.2)	2 (6.5)
Hypoaesthesia	5 (7.4)	0
Lethargy	6 (8.8)	0
Neuropathy peripheral	3	0
Paraesthesia	1	1
Peripheral sensory neuropathy	2	1
Sensory loss	1	0
Somnolence	2	1
Syncope	0	1
Tremor	1	0
Psychiatric disorders	25 (36.8)	5 (16.1)
Agitation	2	1
Anxiety	9 (13.2)	3 (9.7)
Confusional state	2	2 (6.5)
Delirium	0	1
Depressed mood	1	0
Depression	7 (10.3)	2 (6.5)
Insomnia	6 (8.8)	0
Restlessness	1	0
Sleep disorder	1	0
Renal and urinary disorders	11 (16.2)	3 (9.7)
Chromaturia	1	0
Dysuria	1	0
Haematuria	0	1
Haemoglobinuria	1	0
Nocturia	1	1
Oliguria	1	0
Proteinuria	6 (8.8)	0
Renal failure acute	1	1
Urinary incontinence	1	0
Urinary retention	2	0
Urine flow decreased	0	1
Reproductive system and breast disorders	4 (5.9)	1
Metrorrhagia	1	0
Vaginal haemorrhage	2	0
Vulvovaginal dryness	0	1
Vulvovaginal erythema	1	0
Respiratory, thoracic and mediastinal disorders	23 (33.8)	10 (32.3)
Cough	5 (7.4)	3 (9.7)
Dysphonia	11 (16.2)	1
Dyspnoea	15 (22.1)	5 (16.1)
Dyspnoea exertional	0	1
Epistaxis	8 (11.8)	0
Haemoptysis	0	1
Hiccups	1	1
Nasal dryness	1	0

Table 26. Treatment-Emergent Nonserious Adverse Events by System Organ Class and Preferred Term (All Causalities)

Number of Subjects	Axitinib + Gemcitabine n (%)	Gemcitabine n (%)
Orthopnoea	0	1
Pleural effusion	3	1
Pleuritic pain	1	1
Pneumonitis	0	1
Pulmonary oedema	0	1
Respiratory distress	0	1
Rhinorrhoea	1	0
Upper-airway cough syndrome	1	0
Skin and subcutaneous tissue disorders	29 (42.6)	7 (22.6)
Alopecia	10 (14.7)	0
Decubitus ulcer	4 (5.9)	0
Erythema	2	1
Hyperhidrosis	2	3 (9.7)
Livedo reticularis	1	0
Night sweats	0	1
Palmar erythema	1	0
Palmar-plantar erythrodysaesthesia syndrome	1	0
Petechiae	2	0
Photosensitivity reaction	1	0
Pruritus	6 (8.8)	1
Pruritus generalised	1	0
Rash	12 (17.6)	2 (6.5)
Rash generalised	1	0
Skin lesion	1	0
Urticaria	1	0
Surgical and medical procedures	1	0
Pancreaticoduodenectomy	1	0
Vascular disorders	22 (32.4)	3 (9.7)
Deep vein thrombosis	4 (5.9)	2 (6.5)
Haemorrhage	1	0
Hot flush	1	0
Hypertension	16 (23.5)	0
Pallor	1	0
Shock	1	0
Thrombophlebitis	1	0
Thrombosis	0	1

Subjects were only counted once per treatment for each row.
Included data up to 28 days after last dose of study drug.
Medical dictionary of regulatory activities (v13.1) coding dictionary applied.
n = number of subjects with adverse events

Table 27 presents SAEs in phase 1 portion of the study. No events were related to axitinib, but 1 event (platelet count decreased) was attributed to gemcitabine treatment. The infection was related to the disease under study and the prolonged platelet count decreased considered due to sepsis at the time of the event. Table 28 presents summary of all causality SAEs in Phase 2.

In Phase 1, 2 subjects died. Table 29 presents the deaths in Phase 2.

Table 27. Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term (All Causalities) For Events Having a Frequency Rate Greater Than or Equal to Zero

Number of Subjects	Axitinib+ Gemcitabine n
Subjects evaluable for adverse events	8
Subjects with adverse events	3
Number of Subjects With Adverse Events by Body System and Preferred Term	
Blood and lymphatic system disorders	1
Anaemia	1
Ear and labyrinth disorders	1
Tinnitus	1
General disorders and administration site conditions	1
Multi-organ Failure	1
Infections and infestations	1
Infection	1
Investigations	1
Platelet count decreased	1

Subjects were only counted once per treatment for each row.
Included data up to 28 days after last dose of study drug.
Medical dictionary of regulatory activities (v10.1) coding dictionary applied.
n = number of subjects with adverse events.

Table 28. Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term (All Causalities) For Events Having a Frequency Rate Greater Than or Equal to Zero

Number of Subjects	Axitinib + Gemcitabine n (%)	Gemcitabine n (%)
Evaluable for Adverse Events	68	31
Subjects with Adverse Events	35 (51.5)	10 (32.3)
Blood and lymphatic system disorders	4 (5.9)	1
Anaemia	4 (5.9)	1
Disseminated intravascular coagulation	1	0
Thrombocytopenia	1	0
Cardiac disorders	3	3 (9.7)
Atrial fibrillation	2	1
Atrial flutter	1	0
Myocardial infarction	0	1
Pericardial effusion	0	1
Tachycardia	1	0
Gastrointestinal disorders	20 (29.4)	6 (19.4)
Abdominal distension	1	0
Abdominal pain	5 (7.4)	0
Abdominal pain upper	1	0
Abdominal strangulated hernia	2	0
Colitis ischaemic	1	1
Constipation	1	0
Diarrhoea	3	0
Duodenal obstruction	0	1
Gastric haemorrhage	0	1
Gastrointestinal haemorrhage	1	0
Haematemesis	1	0
Intestinal ischaemia	1	0
Intestinal obstruction	2	1
Melaena	1	0
Nausea	2	2 (6.5)
Oral pain	1	0
Peritonitis	1	0
Pneumatosis intestinalis	1	0
Rectal haemorrhage	1	0
Small intestinal haemorrhage	1	0
Small intestinal obstruction	1	0
Vomiting	6 (8.8)	2 (6.5)
General disorders and administration site conditions	11 (16.2)	3 (9.7)
Asthenia	4 (5.9)	0
Chest pain	1	0
Device occlusion	1	0
Disease progression	6 (8.8)	0
Fatigue	1	0
General physical health deterioration	1	0
Pain	1	0
Pyrexia	1	3 (9.7)

Table 28. Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term (All Causalities) For Events Having a Frequency Rate Greater Than or Equal to Zero

Number of Subjects	Axitinib + Gemcitabine n (%)	Gemcitabine n (%)
Hepatobiliary disorders	4 (5.9)	1
Cholangitis	1	1
Cholestasis	1	0
Gallbladder obstruction	1	0
Jaundice cholestatic	1	0
Infections and infestations	8 (11.8)	1
Empyema	1	0
Enterobacter bacteraemia	1	0
Liver abscess	1	0
Lower respiratory tract infection	1	1
Lung abscess	1	0
Lung infection	1	0
Oral candidiasis	1	0
Pneumonia	2	0
Sepsis	2	0
Septic shock	1	0
Investigations	1	0
Blood pressure increased	1	0
Metabolism and nutrition disorders	8 (11.8)	2 (6.5)
Cachexia	1	0
Dehydration	3	2 (6.5)
Failure to thrive	2	0
Hypocalcaemia	1	0
Hypokalaemia	1	0
Hyponatraemia	1	0
Hypophagia	1	0
Lactic acidosis	1	0
Nervous system disorders	4 (5.9)	1
Convulsion	1	0
Headache	1	0
Neuromyopathy	0	1
Syncope	1	0
Transient ischaemic attack	1	0
Psychiatric disorders	2	1
Confusional state	1	0
Mental status changes	1	1
Renal and urinary disorders	0	1
Renal impairment	0	1
Respiratory, thoracic and mediastinal disorders	9 (13.2)	0
Dyspnoea	6 (8.8)	0
Epistaxis	1	0
Hypoxia	1	0
Pneumothorax	1	0
Pulmonary embolism	2	0
Vascular disorders	3	0
Deep vein thrombosis	2	0

Table 28. Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term (All Causalities) For Events Having a Frequency Rate Greater Than or Equal to Zero

Number of Subjects	Axitinib + Gemcitabine n (%)	Gemcitabine n (%)
Post thrombotic syndrome	1	0
Thrombosis	1	0

Subjects were only counted once per treatment for each row.
Included data up to 28 days after last dose of study drug.
Medical dictionary of regulatory activities (v13.1) coding dictionary applied.
n = number of subjects with specified criteria.

Table 29. Phase 2 Portion: Deaths

Serial Number[a]	Day of Last Dose of Study Treatment	Day of Death	Cause of Death
Axitinib + Gemcitabine			
1	Axitinib: 129, gem: 120	130	Unknown
2	Axitinib: 44, gem: 29	52	Peritonitis
3	Axitinib: 81, gem:78	84	Pancytopenia Colitis ischemic (treatment-related) Disseminated intravascular coagulation
4	Axitinib: 56, gem: 64	78	Disease Progression
5	Axitinib G: 64, gem: 58	91	Disease Progression
6	Axitinib: 71, gem: 70	92	Abdominal hematoma
7	Axitinib: 86, gem: 71	91	Cachexia General physical health deterioration
8	Axitinib: 439, gem: 339	441	Septic shock
9	Axitinib: 8, gem: 1	12	Disease progression Pancreatic carcinoma
10	Axitinib: 100, gem: 99	119	Disease progression Pancreatic carcinoma
11	Axitinib: 79, gem: 64	105	Disease progression
12	Axitinib: 34, gem: 8	43	Disease progression Pancreatic carcinoma
13	Axitinib: 197, gem: 177	204	Disease progression Pancreatic carcinoma
14	Axitinib: 449, gem: 312	449	Disease progression Pancreatic carcinoma
15	Axitinib: 395, gem: 286	395	Disease progression Pancreatic carcinoma
16	Axitinib: 143, gem: 113	146	Disease progression Pancreatic carcinoma
17	Axitinib: 140, gem: 127	145	Empyema (treatment-related)
18	Axitinib: 8, gem: 16	39	Disease Progression
Gemcitabine			
19	Gem: 98	120	Acute myocardial infarction
20	Gem: 1	4	Dyspnea Lower respiratory tract infection

a. One subject is in the Part 1 portion of the study. Four Subjects in the axitinib + gemcitabine arm and 2 subjects in the gemcitabine arm died after 28 days following last study treatment.

Two subjects discontinued axitinib treatment (at Cycle 1, Day 6 and Cycle 5, Day 28, respectively) due to AEs not related to treatment (infection with decreased platelet count and anemia, respectively) according to assessment by the Investigator. One subject also discontinued gemcitabine treatment due to an AE of Grade 4 thrombocytopenia (includes Phase 1 subjects). (Subject was considered not evaluable for toxicity and replaced). One subject died 21 days after discontinuation of axitinib treatment. One subject permanently discontinued axitinib treatment at Cycle 24 Day 35 due to symptomatic deterioration that was unrelated to treatment per judgment of the Investigator. Table 30 presents the permanent discontinuations in Phase 2.

Table 30. Phase 2 Portion: Discontinuations from Treatment due to Adverse Events

Serial Number	Cycle and Day of Discontinuation	Reason for Discontinuation (Relationship to Treatment)	
		Axitinib	Gemcitabine
Axitinib + Gemcitabine			
1	Cycle 2, Day 10	Dyspnea (Rel)	Dyspnea (Rel)
2	Cycle 2, Day 21	Hypokalemia (Unr)	Nausea (Unr), Vomiting (Rel)
3	Cycle 2, Day 50	Hyperbilirubinemia (Unr)	Hyperbilirubinemia (Unr)
4	Cycle 2, Day 27	Hepatotoxicity (Rel)	Hepatotoxicity(Rel)
5	Cycle 2, Day 10	Duodenal blood clot (Rel)	
6	Cycle 3, Day 28	Upper Digestive hemorrhage (Rel)	
7	Cycle 10, Day 15	Cachexia (Rel)	Cachexia (Rel)
8	Cycle 3, Day 36		Oral pain (Unr)
9	Cycle 4, Day 7		Cachexia (Unr)
10	Cycle 5, Day 14	Pulmonary embolism (Unr)	Pulmonary embolism (Unr)
11	Cycle 16, Day 21	Septic shock (Unr)	
12	Cycle 10, Day 55	Cerebrovascular ischemia (Rel)	Acute insufficiency renal (Rel)
13	Cycle 24, Day 127	Fatigue (Rel)	Fatigue (Rel)
14	Cycle 2, Day 55	Convulsion (Rel)	Convulsion (Rel)
15	Cycle 6, Day 15	Hypertension (Rel)	
16	Cycle 1, Day 9	Decreased performance status (Unr)	Decreased performance status (Unr)
17	Cycle 3, Day 50	Failure to thrive (Rel)	Failure to thrive (Rel)
18	Cycle 3 Day 36	Failure to thrive (Unr)	
19	Cycle 2, Day 6	Failure to thrive (Unr)	Failure to thrive (Unr)
20	Cycle 9, Day 1 and Cycle 8, Day 126	Clinical disease progression (Unr)	Disease progression (Unr)
21	Cycle 9, Day 1	Clinical disease progression (Unr)	Clinical disease progression (Unr)
22	Cycle 3, Day 28	Fatigue (Unr)	Fatigue (Unr)
23	Cycle 5, Day 34	Weight loss (Unr)	Small bowel obstruction (Unr)
Gemcitabine			
24	Cycle 8, Day 244		Pericardial effusion (Rel)
25	Cycle 2, Day 35		Failure to thrive (Unr)
26	Cycle 1, Day 15		Insufficient clinical response (Unr)
27	Cycle 4, Day 8		Insufficient clinical response (Unr)
28	Cycle 4, Day 14		Acute myocardial infarction (Unr)

ID = identity; gem = gemcitabine; Rel = related; Unr = unrelated.

There were 5 subjects (62.5%) in Phase 1 who had temporary discontinuation of axitinib due to AEs. No subjects had dose reductions in axitinib due to AEs. There were 6 subjects (75.0%) in Phase 1 who had temporary discontinuation of gemcitabine due to AEs. One subject (12.5%) had dose reductions in gemcitabine due to AEs. In Phase 2, there were 6 subjects (8.8%) in the axitinib + gemcitabine arm who had dose reductions of axitinib due to AEs. There were 35 subjects (51.5%) in the axitinib + gemcitabine arm with temporary discontinuations of axitinib due to AEs. Fifteen subjects (22.1%) in the axitinib + gemcitabine arm and 8 subjects (25.8%) in the gemcitabine arm had gemcitabine dose reductions due to AEs. Thirty-eight subjects (55.9%) in the axitinib + gemcitabine arm and 10 subjects (32.3%) in the gemcitabine arm temporarily discontinued gemcitabine treatment due to AEs.

Table 31 and Table 32 summarizes maximum grade for laboratory test results for Phase 1 and Phase 2 respectively.

Table 31. Phase 1 Portion: Maximum CTC Grade on Treatment for Laboratory Test Results

	Axitinib + Gemcitabine Maximum CTC Grade					
Parameter (%)	**Grade 0**	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grades 1 to 4**
Hemoglobin	2 (33.3)	2 (33.3)	1 (16.7)	0	1 (16.7)	4 (66.7)
Platelets	0	3 (50.0)	3 (50.0)	0	0	6 (100.0)
White Blood Cells	1 (16.7)	1 (16.7)	3 (50.0)	1 (16.7)	0	5 (83.3)
Neutrophils (abs)	0	1 (16.7)	3 (50.0)	2 (33.3)	0	6 (100.0)
Lymphocytes (abs)	1 (16.7)	0	2 (33.3)	3 (50.0)	0	5 (83.3)
Total Bilirubin	2 (33.3)	4 (66.7)	0	0	0	4 (66.7)
Hypoalbuminemia	1 (16.7)	4 (66.7)	1 (16.7)	0	-	5 (83.3)
AST	2 (33.3)	3 (50.0)	1 (16.7)	0	0	4 (66.7)
ALT	2 (33.3)	1 (16.7)	3 (50.0)	0	0	4 (66.7)
ALP	3 (50.0)	3 (50.0)	0	0	0	3 (50.0)
Creatinine	4 (66.7)	2 (33.3)	0	0	0	2 (33.3)
Hypernatremia	4 (66.7)	2 (33.3)	0	0	0	2 (33.3)
Hyponatremia	2 (33.3)	4 (66.7)	-	0	0	4 (66.7)
Hyperkalemia	3 (50.0)	3 (50.0)	0	0	0	3 (50.0)
Hypokalemia	4 (66.7)	2 (33.3)	-	0	0	2 (33.3)
Bicarbonate	5 (83.3)	1 (16.7)	0	0	0	1 (16.7)
Hyperglycemia	0	3 (50.0)	3 (50.0)	0	0	6 (100.0)
Hypoglycemia	5 (83.3)	0	0	0	1 (16.7)	1 (16.7)
Urine protein	1 (16.7)	0	0	0	0	0

Abs = absolute; ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CTC = common toxicity criteria.

Table 32. Phase 2 Portion: Maximum CTC Grade on Treatment for Laboratory Test Results

Subjects (%)	Axitinib + Gemcitabine Maximum CTC Grade					
Parameter	**Grade 0**	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grades 1 to 4**
Axitinib + Gem						
Hemoglobin	5 (7.6)	33 (50.0)	23 (34.8)	4 (6.1)	1 (1.5)	61 (92.4)
Platelets	14 (21.2)	33 (50.0)	7 (10.6)	11 (16.7)	0	51 (77.3)
White Blood Cells	21 (31.8)	16 (24.2)	19 (28.8)	10 (15.2)	0	45 (68.2)
Neutrophils (abs)	22 (34.4)	8 (12.5)	18 (28.1)	11 (17.2)	5 (7.8)	42 (65.6)
Lymphocytes (abs)	22 (33.3)	6 (9.1)	25 (37.9)	13 (19.7)	0	44 (66.7)
Total Bilirubin	47 (71.2)	11 (16.7)	3 (4.5)	5 (7.6)	0	19 (28.8)
Hypoalbuminemia	19 (30.2)	20 (31.7)	18 (28.6)	6 (9.5)	0	44 (69.8)
AST	20 (31.3)	26 (40.6)	12 (18.8)	5 (7.8)	0	43 (67.3)
ALT	15 (23.1)	28 (43.1)	16 (24.6)	6 (9.2)	0	50 (76.9)
ALP	13 (20.3)	31 (48.4)	11 (17.2)	9 (14.1)	0	51 (79.7)
Creatinine	56 (84.8)	7 (10.6)	3 (4.5)	0	0	10 (15.2)
Hypernatremia	56 (84.8)	3 (4.5)	1 (1.5)	0	0	4 (6.0)
Hyponatremia	31 (47.0)	25 (37.9)	0	10 (15.2)	0	35 (53.0)
Hyperkalemia	53 (80.3)	9 (13.6)	3 (4.5)	1 (1.5)	0	13 (19.7)
Hypokalemia	31 (47.0)	25 (37.9)	0	7 (10.6)	3 (4.5)	35 (53.0)
Bicarbonate	35 (66.0)	15 (28.3)	2 (3.8)	0	0	17 (32.1)
Hyperglycemia	11 (16.9)	22 (33.8)	24 (36.9)	8 (12.3)	0	54 (83.1)
Hypoglycemia	46 (70.8)	5 (7.7)	2 (3.1)	0	1 (1.5)	8 (12.3)
Urine protein	40 (71.4)	3 (5.4)	1 (1.8)	0	0	4 (7.2)
Gemcitabine						
Hemoglobin	0	18 (60.0)	9 (30.0)	3 (10.0)	0	30 (100.0)
Platelets	7 (23.3)	17 (56.7)	5 (16.7)	1 (3.3)	0	23 (76.7)
White Blood Cells	7 (23.3)	10 (33.3)	8 (26.7)	4 (13.3)	0	22 (73.3)
Neutrophils (abs)	13 (43.3)	4 (13.3)	5 (16.7)	6 (20.0)	2 (6.7)	17 (56.7)
Lymphocytes (abs)	5 (16.7)	4 (13.3)	16 (53.3)	5 (16.7)	0	25 (83.3)
Total Bilirubin	18 (60.0)	7 (23.3)	3 (10.0)	1 (3.3)	1 (3.3)	12 (40.0)
Hypoalbuinemia	6 (20.7)	13 (44.8)	10 (34.5)	0	0	23 (79.3)
AST	7 (23.3)	14 (46.7)	5 (16.7)	4 (13.3)	0	23 (79.3)
ALT	5 (16.7)	15 (50.0)	5 (16.7)	5 (16.7)	0	25 (83.3)
ALP	4 (13.3)	10 (33.3)	14 (46.7)	2 (6.7)	0	26 (86.7)
Creatinine	25 (83.0)	3 (10.0)	1 (3.3)	0	0	4 (13.3)
Hypernatremia	28 (93.3)	1 (3.3)	0	0	0	1 (3.3)
Hyponatremia	13 (43.3)	16 (53.3)	0	1 (3.3)	0	17 (56.7)
Hyperkalemia	21 (70.0)	6 (20.0)	1 (3.3)	0	1 (3.3)	8 (26.3)
Hypokalemia	20 (66.7)	7 (23.3)	0	3 (10.0)	0	10 (33.3)
Bicarbonate	21 (95.5)	0	1 (4.5)	0	0	1 (4.5)
Hyperglycemia	5 (16.7)	13 (43.3)	7 (23.3)	5 (16.7)	0	25 (83.3)
Hypoglycemia	18 (60.0)	1 (3.3)	0	0	1 (3.3)	2 (6.7)
Urine protein	16 (72.7)	1 (4.5)	0	0	0	1 (4.5)

Abs = absolute, ALT = alanine aminotransferase; AST = aspartate aminotransferase, ALP = alkaline phosphatase, gem = gemcitabine; CTC = common toxicity criteria.

In Phase 1, only 1 subject had elevated systolic BP>160 mm Hg during Cycle 23 of treatment. In Phase 2, 3 (4.9%) subjects shifted to diastolic BP>105 mm Hg in the axitinib + gemcitabine arm during the study compared to no subjects in the gemcitabine arm. Ten subjects (16.4%)

shifted to systolic BP >160 mm Hg in the axitinib + gemcitabine arm during the study compared to 2 (7.4%) subjects in the gemcitabine arm.

Conclusions:

- In the randomized Phase 2 portion of the study, the OS of the combination of axitinib + gemcitabine was numerically superior to that of gemcitabine alone as first-line therapy in subjects who had locally advanced, unresectable or metastatic pancreatic cancer. The median OS for the axitinib + gemcitabine and gemcitabine treated arms was 210 days (95% CI: 162, 308) and 171 days (95% CI: 125, 267), respectively. Controlling for baseline stratification factors, ECOG performance status (≤1 versus 2) and extent of disease (locally advanced versus metastatic), the hazard ratio (axitinib + gemcitabine:gemcitabine) was 0.76 (95% CI: 0.49, 1.17; 1-sided p-value: 0.10).

- For the subset of subjects with ECOG performance status ≤1, the median OS for the axitinib + gemcitabine and gemcitabine treated arms was 220 days (95% CI: 170, 379) and 173 days (95% CI: 125, 267), respectively. Controlling for baseline stratification factor, extent of disease (locally advanced versus metastatic), the hazard ratio (axitinib + gemcitabine:gemcitabine) was 0.73 (95% CI: 0.47, 1.13; 1-sided p-value: 0.08).

- There was a numerically larger difference in OS for the subjects with locally advanced compared to metastatic disease. For the locally advanced subjects, the median OS for the axitinib + gemcitabine and gemcitabine treated arms was 379 days (95% CI: 208, 502) and 197 days (95% CI: 125, 352), respectively. Controlling for baseline stratification factor, ECOG performance status (≤1 versus 2), the hazard ratio (axitinib + gemcitabine: gemcitabine) was 0.58 (95% CI: 0.30, 1.11; 1-sided p-value: <0.05).

- The overall objective response rate (Phase 2 portion: CR + PR) was 5/69 (7.2%) and 1/34 (2.9%) in the axitinib + gemcitabine and gemcitabine arms, respectively. The median duration of objective response of the subjects with a PR was 379 days (95% CI: 136, 379) and 155 days (1 subject) in the axitinib + gemcitabine and gemcitabine arms, respectively.

- The median PFS was 116 days (95% CI: 109, 160) and 113 days (95% CI: 68, 205) for the axitinib + gemcitabine and gemcitabine arms, respectively. Controlling for baseline ECOG status and extent of disease, the hazard ratio (axitinib + gemcitabine:gemcitabine) was 0.97 (95% CI: 0.54, 1.73, 1-sided p-value: 0.45).

- Compared to subjects treated with gemcitabine alone, subjects treated with the combination of axitinib + gemcitabine demonstrated minimal disruption in several aspects of HRQoL as measured by the EORTC QLQ-C30 and Pan26. Reductions over time were seen in symptoms of pancreatic cancer (pain and pancreatic pain scales, constipation and diarrhea items) in both arms of subjects. Over half of the subjects in both treatment arms assessed at Cycle 4 Day 1 reported clinically meaningful improvements (>10 points) in the pain and pancreatic pain scales, whereas the largest clinically meaningful deterioration was observed for the effects of treatment-taste, dry mouth, concern about side effects-scale in the axitinib + gemcitabine arm, and the eating related items scale and fear of future item in the gemcitabine arm.

- In comparison to the gemcitabine arm, the axitinib + gemcitabine arm had a higher incidence of ≥5% Grade ≥3 all causality AEs for the following: fatigue, asthenia, dyspnea, thrombocytopenia, anemia, diarrhea, anorexia, hypertension and lethargy.

- The Phase 1 portion of the study confirmed that axitinib + gemcitabine could be safely administered in combination at full dose (ie, axitinib at 5 mg BID and gemcitabine at 1000 mg/m^2 weekly x 3 every 4 weeks).

- The PK of axitinib and gemcitabine (including its metabolite, dFdU) were similar when administered alone or together as combination therapy.