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Statistical Analysis Plan for Prospective, Randomized Controlled, Double-Blind, Multicenter Registered Clinical Studies of Nimotuzumab (Taixinsheng®) Plus Gemcitabine versus Placebo Plus Gemcitabine in K-RAS Wild-Type Locally Advanced or Metastatic Pancreatic Cancer

(TFLs Template)

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Statistical analysis plan version update record

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1.0	2021-12-10	Initial version	NA

catalog

List of abbreviations

abbreviation	notes
AE	Adverse event
ATC	Systematic anatomy and chemotherapeutics
CBR	Clinical benefit rate
CI	Confidence interval
CR	Complete response
CRF	Case report form
CS	Clinical significance with abnormality
CTCAE	Terminology of adverse events
DAS	Data analysis system
DCR	Disease control rate
eCRF	Electronic case report form
FAS	Full analysis set
G-CSF	Granulocyte colony stimulating factor
HR	Hazard risk ratio
IWRS	Interactive network response system
MedDRA	Medical Dictionary of regulatory activities
NCI	National Cancer Research Center
NCS	No clinical significance with abnormality
NMPA	State Drug Administration
ORR	Objective response rate
OS	Overall survival
PD	Disease progression
PFS	Disease progression free survival
PPS	Compliance set
PR	Partial response
PT	Preferred term
RECIST	Criteria for evaluating the efficacy of solid tumors
SD	Stable disease
SOC	Systematic organ classification
SS	Security set
TEAE	Adverse events during treatment
TTP	Time of disease progression
WHO	World health organization

The combination therapy of nimotuzumab (taixinsheng®)and gemcitabine was compared with placebo and gemcitabine: A prospective, randomized, double-blind, multicenter registered clinical study of K-RAS wild-type locally advanced or metastatic pancreatic cancer

Statistical Analysis Plan

This statistical analysis plan is based on the prospective, randomized controlled, double-blind, multicenter registered clinical study of nimotuzumab (taixinsheng®)combined with gemcitabine versus placebo and gemcitabine in the treatment of K-ras wild-type locally advanced or metastatic pancreatic cancer (protocol No.: BPL-nim-pc-1, version date: June 16, 2014, protocol version number: 1.1)and electronic case report form (eCRF version date: 2019. eCRF version No.: 1.6) was formulated on July 25, 2005.The statistical analysis plan will be finalized before the database is locked.

1 Title

A prospective, randomized, double-blind, multicenter, registered clinical trial of nimotuzumab (taixinsheng®)combined with gemcitabine versus placebo plus gemcitabine in the treatment of locally advanced or metastatic pancreatic cancer of K-ras wild type.

2 Objective

2.1 Primary endpoint

Objective to evaluate and compare the overall survival (OS) of nimotuzumab combined with gemcitabine versus placebo plus gemcitabine in the treatment of K-ras wild-type locally advanced or metastatic pancreatic cancer.

2.2 Secondary endpoint

（1） Time to progression (TTP), progression free survival (PFS).

（2） Objective response rate (ORR), disease control rate (DCR).

（3） Clinical benefit rate (CBR).

（4） Objective to evaluate the safety of nimotuzumab combined with gemcitabine (according to NCI-CTCAE v4.03).

3 Study design

3.1 Overall design

In order to closely observe and scientifically evaluate the efficacy and safety of nimotuzumab combined with gemcitabine in the treatment of K-ras wild-type locally advanced or metastatic pancreatic cancer, a prospective, randomized, parallel controlled, double-blind, multicenter registered clinical trial will be initiated.

3.2 Multicenter

A number of qualified cancer centers in China will be selected at the same time.

3.3 Central randomization

Taking into account the following factors, DAS for IWRS will be used to assign random numbers and dispense drugs.

Four stratification factors and factor levels will set up

- Tumor location
  - Head of pancreas

- Body and tail of pancreas
- Have you had surgery
  - yes
  - no
- Have biliary obstruction been treated
  - yes
  - no
- Have you received adjuvant chemotherapy
  - yes
  - no

3.4 Control drug selection

In this study, placebo combined with gemcitabine will be used as the parallel control group.

3.5 Blind method

In this study, a double-blind and single simulation method will be used. The package, shape and smell of nimotuzumab simulator will be consistent with those of the trial drug (nimotuzumab) to ensure that the subjects and researchers in a blind state during the trial.

3.6 Sample size

In this study, 276 subjects will be enrolled, 138 in the experimental group and 138 in the control group. After communication with CDE(Center for drug evaluation of China), CDE agreed to re-estimate the sample size based on the survival data of KRAS wild type pancreatic cancer in pcs07 study in Germany. the median OS was assumed to be 5.67 months in gemcitabine group (control group), and the median OS will be extended to 11.62 months after treatment with nimotuzumab (trial or experimental group). The median OS will be up to 24 months and following up for 12 months, α=0.05,1-β=80%. Two groups at the ratio of 1:1, and the required sample size is 79 cases, there are 39 cases in the control group and 40 cases in the trial group. The total number of events is 64, and the final analysis can be carried out. There were 36 events in the control group and 28 events in the experimental group).

4 Investigational drug and administration method

4.1 Investigational drug

Nimotuzumab injection (taixinsheng®, produced by Baitai biopharmaceutical Co., Ltd., is a colorless and clear solution with the specification of 50mg/ 10ml / piece (packed in a Xilin bottle).Each vial (capacity 13.5ml) contains 10ml of nimotuzumab solution, the concentration of mAb is 5 mg/ ml, and the purity is not less than 95%.The composition of each component in the vial is shown in the table below.

Table 4-1 composition and content of nimotuzumab injection

Components	Content / ml	Content / 10.0 ml
Monoclonal antibody against h-R3	5 mg	50 mg
Sodium dihydrogen phosphate	0.45 mg	4.5 mg
Sodium phosphate	1.8 mg	18.0 mg
Sodium chloride	8.69 mg	86.9 mg
Polysorbate 80	0.2 mg	2.0 mg

Note: except that h-R3 monoclonal antibody is not included in placebo, other ingredients, appearance and specifications are the same as those of nimotuzumab injection.

The product should be stored at 2-8 ℃, and freezing is strictly prohibited. After dilution in normal saline, it can keep stable for 12h at 2-8 ℃ and 8h at room temperature. If the diluted solution is stored for more than the above time, it should not be used.

The trial drugs nimotuzumab injection / placebo and gemcitabine are provided by Baitai biopharmaceutical Co., Ltd. for free, including labels and packages for clinical trials.

4.2 Grouping and administration method

The trial will be divided into two groups: the experimental group received nimotuzumab + gemcitabine treatment, while the control group received placebo (nimotuzumab simulator) + gemcitabine.

（1） Nimotuzumab injection / placebo: 400mg / week, intravenous drip, infusion time 60 minutes or more, Once a week, to until the disease progressed or intolerable toxicity occurrs, or the subject asks to withdraw from the trial.

Usage: 400 mg (8 pieces) of nimotuzumab injection / placebo will be added into 250 ml sterile normal saline for dilution, and the intravenous drip time is not less than 60 min. the patient's condition should be closely monitored during the course of administration and within 1 hour after the end of administration. In addition to sterile normal saline, nimotuzumab solution should not be mixed with any intravenous infusion drugs.

（2） Gemcitabine: 1000mg / m^2, intravenous drip for no less than 30 minutes, continuous use for 3 weeks, rest for 1 week (D1, 8, 15. Q28 days), every 4 weeks as a cycle, until the disease progression or intolerable toxic reaction, or the subject asks to withdraw from the trial.

Usage: each bottle (containing gemcitabine 200mg or 1000mg) should be injected with 5ml or 25ml sterile normal saline at least (containing gemcitabine concentration ≤ 40mg / ml), shaking to dissolve. The required dosage can be further diluted with sterile normal saline. The prepared gemcitabine solution should be stored at room temperature and used within 24 hours. Gemcitabine solution should not be refrigerated to prevent crystallization. According to the solubility of the drug, the concentration of the diluted drug should not exceed 40mg / ml. if the concentration is greater than 40mg / ml, it may lead to incomplete dissolution of the drug, which should be avoided.

At the first treatment, nimotuzumab / placebo should be given on the same day as gemcitabine, and then gemcitabine should be given 1 hour after the end of nimotuzumab / placebo infusion. Since then, nimotuzumab / placebo and gemcitabine will be treated on the same day in the same order as before.

4.3 Combination therapy

During the study period, the drugs that can be used together according to the needs are as follows:

Adjuvant therapy, including prophylactic drugs, such as blood component transfusion, granulocyte colony-stimulating factor (G-CSF), antidiarrheal, antiemetic and analgesic drugs, are allowed and can be operated according to the clinical routine of each center.

When the adverse events caused by the trial drug need to be treated, the drugs for symptomatic treatment can be given.

Symptomatic treatment of skin toxicity, including softeners or other topical drugs, analgesics and vitamins B6, etc.

When the patient has other symptoms, it can be treated with drugs.

5 Efficacy and safety evaluation

5.1 Evaluation of efficacy

5.1.1 Primary endpoint

Overall survival time (OS).

5.1.2 Secondary endpoint

1) Time to progression (TTP).
2) Progression free survival (PFS).
3) Objective response rate (ORR).
4) Disease control rate (DCR).
5) Clinical benefit rate (CBR).

5.2 Efficacy evaluation criteria

According to RECIST 1.1 standard, the patients will be divided into complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD).The response evaluation will be conducted every 8 weeks. If the patient achieved CR or PR, the efficacy should be confirmed 4 weeks after the first evaluation.

Partial or incomplete tumor evaluation will not be included in TTP, PFS, ORR, DCR unless the observable lesions have been evaluated as progression (according to RECIST1.1).

5.3 Definition of efficacy evaluation criteria

- Overall survival (OS) refers to the time from randomization to death due to any cause.
  For patients who are still alive as of the date of analysis or those who have lost follow-up for which there is no evidence to prove that they have died, the date of last contact with them (the last confirmed survival date) or the analysis cutoff date (whichever occurs first) shall be taken as the censor date.

- Time to disease progression (TTP): defined as the time (days) between the date of randomization and the first observation of disease progression (imaging or clinical progress, whichever is earlier).The actual date of tumor evaluation will be used for calculation. The time to progression for patients who will not progress at the time of analysis or death will be calculated as the date of the last tumor evaluation.

- Progression free survival (PFS): defined as the time from the beginning of randomization to progression or all-cause death. Progression free survival defined as the time from randomization to death in patients who will die of any other cause before disease progression. Patients without progression or death (i.e., progression free survival) at the time of the last tumor assessment will be used as the end point.

- Objective response rate (ORR): calculated from the day of the first administration, including the percentage of CR and PR subjects in all enrolled subjects (data will be calculated according to the best response in the whole study period).For patients with complete or partial response for the first time, the efficacy should be confirmed after 4 weeks.

  The imaging results will be evaluated according to RECIST Standard Version 1.1.
  Complete response (CR): all target lesions will be disappeared, and the short diameter of all pathological lymph nodes (including target and non-target nodules) must be reduced to < 10 mm.
  Partial response (PR): the sum of the target lesion diameters will be reduced by at least 30% from baseline.
  Disease progression (PD): Taking the minimum value of the sum of all measured target lesion diameters during the whole study period as reference, the relative increase of diameter sum will be at least 20% (if the baseline measurement value is the minimum, the baseline value is used as reference).In addition, an increase of at least 5 mm in the absolute value of diameter sum must be satisfied (the presence of one or more new lesions is also considered as disease progression).

- Disease control rate (DCR): the best overall assessment is the proportion of patients with confirmed complete and partial response and stable disease. For patients with stable disease, at least one lesion evaluation should meet the SD criteria at least 6 weeks after medication.

- Clinical benefit rate(CBR): Only symptomatic patients will be evaluated in the study, including pain (intensity of pain and consumption of analgesics), PS (performance status, evaluated according to KPS), and weight change.

  Symptomatic pancreatic cancer is defined as having at least one of the following manifestations at baseline:

  1) KPS 60 or 70.
  2) They shall receive morphine / opioid analgesia.
  3) The pain score is more than 20 points on MPAC pain visual analog scale.

  If the patients are in asymptomatic at the time of admission, and having the above symptoms during the treatment, the evaluation of CBR will be started when the symptoms occurs .

Clinical benefit assessment classification

Main evaluation criteria:
Pain
① Pain intensity (assessed daily with MPAC 0-100 visual analogue scale)
Positive: improvement ≥ 50% compared with baseline and lasting for ≥ 4 weeks (assuming minimum pain score ≥ 20)
Negative: any deterioration compared with baseline lasted for 4 weeks
Stable: any other results
② Consumption of analgesics (evaluated according to the consumption of equivalent dose of morphine, once a week)
Positive: improvement ≥ 50% compared with baseline and lasting for ≥ 4 weeks (assuming minimum analgesic consumption ≥ 10)
Negative: any deterioration compared with baseline lasted for 4 weeks
Stable: any other results
KPS physical status score: once a week
Positive: KPS 50, 60, 70 patients, compared with the baseline, the improvement was more than 20 points, and lasted for more than 4 weeks
Negative: any deterioration ≥ 20 points compared with baseline and lasting for more than 4 weeks
Stable: any other results
Secondary evaluation criteria: Weekly evaluation
Weight
Positive: weight gain > 7% (non-fluid retention) compared with baseline and lasting for more than 4 weeks
Non positive: any other results

According to the standards developed by Burris et al

1) There is at least one positive index of body weight.
2) Stable: pain, physical condition or weight change are rated as stable.
3) Invalid: one of the three indicators is aggravated.

5.4 Safety evaluation

1) Adverse events (AE) include TEAE / ADR, SAE / SADR, TEAE / ADR leading to drug reduction, TEAE / ADR leading to drug withdrawal, TEAE / ADR leading to drug increment, TEAE / ADR leading to death and TEAE / ADR leading to withdrawal.

2) Routine safety parameters (including vital signs, physical examination, laboratory examination (including blood routine examination, physical examination, laboratory examination, etc

Electrolytes, blood biochemistry, Serum CA19-9, urine routine test) and electrocardiogram (ECG).

6 Statistical analysis

6.1 Statistical content / method change of the protocol

- Sample size: after consulting CDE and obtaining approval, the sample size is adjusted according to external literature data.
- Handling of missing value: in the protocol, when the primary efficacy variables are missing, last observation carried forward (LOCF) cannot be implemented, and it is adjusted to section 6.5.2.2 of SAP.

6.2 Hypothesis test

H_0(invalid hypothesis):$H_1=H_2$,
H_1(alternative hypothesis):
$H_1 \neq H_2$,
H_1 is the hazard ratio of the experimental group, H_2 is the hazard ratio of the control group.

6.3 Sample size estimation

After communication with CDE, CDE agreed to re-estimate the sample size based on the survival data of K-RAS wild type pancreatic cancer in pcs07 study in Germany: the median OS is assumed to be 5.67 months in gemcitabine group (control group), and the median OS will be extended to 11.62 months after treatment with nimotuzumab (trial Group). The median OS is 24 months and following up for 12 months, α=0.05,1-β=80%, trial group and control group are divided into two groups at the ratio of 1:1, and the required sample size is 79 cases, There are 39 cases in the control group and 40 cases in the study group. The total number of events is 64, and the final analysis can be carried out
There are 36 events in the control group and 28 events in the experimental group).

6.4 Statistical analysis data set

- Full analysis set (FAS): all the cases that are randomized into groups, using the study drug at least once, and having the efficacy evaluation data of post medication at least once.
  Those that do not meet the key inclusion criteria (items 3 and 6) will be excluded from FAS.

- Compliance protocol set (PPS): refers to the set of cases that meeting the inclusion criteria, do not meet the exclusion criteria, and complete the treatment, i.e. analyze the cases that meets the trial protocol, has good compliance, and completes the contents specified in CRF (PP analysis).PP analysis will be mainly used for the primary efficacy endpoint.

- Safety data set (SS): all patients who receive at least one dose of the study drug. This analysis set will be used for the safety analyses..

6.5 Contents and methods of statistical analysis

6.5.1 General considerations

- All analyses will be conducted using SAS version 9.4 version.
- The default significance level will be two-sided 5%. Two-sided 95% confidence intervals will be presented and all tests will be two-sided, unless otherwise specified in the description of the analyses..
- Since there are more than 20 centers involved in this study, it is anticipated that subject accrual will be sparse across centers and hence it is not necessary to include center effect in statistical modelling.
- The continuous variables will be described by number of subjects (n), means, standard deviation, median, 25th and 75th percentiles (Q1, Q3), minimum and maximum value, while the count data will be described by count(s) and percentages (%)..
- Unless otherwise specified, the decimal places of the minimum and maximum values shall be consistent with the original data recorded in the database, if the raw value has x decimal places, then the mean and the median and quartiles will have x+1 decimal places, the standard deviation will have x+2 decimal places.

The number of decimal places of all statistical data shall not exceed three.

- Percentage (%) : retain 1 decimal place, the second digit is rounded, for example, 52.34% is recorded as 52.3%, 0% is directly recorded as 0.

6.5.2 Data definition and processing

6.5.2.1 Date missing

Missing date of first diagnosis of pancreatic cancer

The imputation of partial dates will follow the following rules:

- If year, month and the data are all missing, do not impute.
- If only year of the date is known, month and day would be imputed as July 1st.
- If year and month of are known but the day of date is unknown, day will be imputed as 15.
-

Previous / concomitant medication, concomitant treatment date missing, start date missing:

- If year, month and the data are all missing, do not impute.
- If only year of the date is known, month and day would be imputed as July 1st.
- If year and month of are known but the day of date is unknown, day will be imputed as 15.
-

AE date missing

AE start date missing:

- If the start date is completely missing, and the year (year only) or year / month (year / month only) is the same as the first treatment date, fill in with the minimum value of the first treatment date and AE end date.
- Otherwise, fill in the missing date and month with 1 day and 1 month.

AE end date missing:

- If only the date is missing, if the patient's death and death month are the same as AE month and the date of death is missing, the last day of the month shall be filled in. otherwise, the date of death shall be used.
- If the date and month are missing, when the year and the last visit year are the same, the date of the last visit shall be used to fill in, and when the year is different, it shall be filled with December 31.
- Other cases are not filled in.

Date of death missing

If the subject is determined to have died, but the date of death is missing, it can be filled according to the following filling rules:

- If the date, year, and day are missing, they are filled with (last confirmed survival date + 1)
- If the day is missing, or the month and day are missing, fill in with the latest of the following dates
  （1） Last confirmed survival date + 1
  （2） If only the day is missing, the first day of the year is used. If both the month and day are missing or only the month is missing, the January 1 of the year in which the month is not missing is used

New anti-tumor treatment date missing

Judgment criteria of anti-tumor treatment: the reasons of combined drug use are: anti-tumor treatment, anti-tumor, anti-tumor of traditional Chinese medicine, pancreatic cancer, tumor chemotherapy.

Missing start date of new anti-tumor therapy

For patients with progression, the relationship between the start date of new anti-tumor treatment and the date of progression should be collected as far as possible, and then filled in according to the following methods:

- If the start date of new anti-tumor treatment is after the progress, fill in with the latest of the following dates:
  （1） Progress date + 1
  （2） If only the day is missing, the first day of the year is used. If both the month and day are missing or only the month is missing, the January 1 of the year in which the month is not missing is used
- If the start date of the new anti-tumor treatment is before the progress, fill in with the earliest of the following dates:
  （1） Progress date-1
  （2） If only the day is missing, the first day of the year is used. If both the month and day are missing or only the month is missing, the January 1 of the year in which the month is not missing is used
- If the relationship between the start date of new anti-tumor treatment and the date of progression cannot be judged, the latest of the following dates shall be used for filling:
  （1） Progress date + 1
  （2） If only the day is missing, the first day of the year is used. If both the month and the day are missing or only the month is missing, the January 1 of the year without missing is used

For subjects who will do not make progress,

- If the start date of the new anti-tumor treatment is after the date of the last imaging examination, fill in with the latest of the following dates:
  （3） Date of last imaging examination + 1
  （4） If only the day is missing, the first day of the year is used. If both the month and day are missing or only the month is missing, the January 1 of the year in which the month is not missing is used
- If the start date of the new anti-tumor treatment is before the date of the last imaging examination, fill in with the earliest of the following dates:
  （3） Date of last imaging examination - 1
  （4） If only the day is missing, the first day of the year is used. If both the month and day are missing or only the month is missing, the January 1 of the year in which the month is not missing is used
- If the relationship between the start date of the new anti-tumor treatment and the date of the last imaging examination cannot be judged, the earliest of the following dates should be filled in:
  （3） Date of last imaging examination + 1
  （4） If only the day is missing, the first day of the year is used. If both the month and the day are missing or only the month is missing, the January 1 of the year without missing is used

For the cases of monthly and daily missing or only monthly missing, special care should be taken. Before filling with the 1st January of the year not missing, all relevant information (including remarks) that can be collected should be consulted to see if there are other more accurate dates that may be used for filling.

New treatment end date missing

The missing end date of new anti-tumor therapy will be not filled in.

The dates in the data list are listed according to what is written on the CRF.

6.5.2.2 Missing value procession

The missing data is not filled, and the actual data obtained is used for analysis. See 6.5.2.4 for censored rules.

6.5.2.3 Baseline definition

Unless otherwise specified, the baseline assessment refers to the last non- missing assessment before the first administration of the study drug.

6.5.2.4 Data derivation and conversion

- The duration of pancreatic cancer (month) = (signing date of informed consent - date of first diagnosis of pancreatic cancer + 1) / 30.4375, rounding up or down to one decimal place.
- Age (yr) = int(date of signing informed consent - date of birth + 1) / 365.25, rounding down.
- The overall survival time (OS) (month) = (all cause death date /censor date - random date + 1) / 30.4375, rounding up or down to one decimal place. For the lost subjects who will do not observe the death outcome, the date of the last recorded contact with the subjects will be taken as the censor date. For the subjects who will still survive at the time point of the final analysis, the last contact date will be used as the censor date.
- Progression free survival (PFS) (month) = (progression date / all cause death date / censor date - random date)
  +1) / 30.4375, rounding up or down to one decimal place. The censor rules are as follows:

Table 6-1 PFS censored data rule list

Data situation	**Censor date**
There is no baseline imaging assessment	Randomization date
There is no imaging assessment after baseline (the first planned imaging review. No death before assessment)	Randomization date
No disease progression or death occurs during the trial	Date of last imaging assessment
After two or more consecutive imaging evaluations, data are missing, disease progression or death	Date of last imaging assessment (disease progression or Before death)
New anti-tumor treatment is given before the disease progression	Last image before new anti-tumor treatment Assessment date

Note:

1. The absence of two consecutive imaging assessments is defined as no imaging evaluation with an interval of more than 126 days (i.e. [2 * (8 weeks + 7 days time window)]).
2. The progression / censored date of PFS is the date of imaging examination, not the date of tumor evaluation or visit. The overall efficacy evaluation of a visit may be based on the results of imaging examinations will be conducted on different dates. In this case, the progression / censor date of PFS is derived according to the following rules: first, determine the corresponding progress date of target lesion, non-target lesion and new lesion, and then select a date from the progress date of target, non-target and new lesion as the overall efficacy progress date of the visit.

（1） Target lesion: if the target lesion is evaluated as progression and the imaging examination of different target lesions is not on the same day, the earliest date is selected as the target lesion progression date.

（2） Non-target lesions: if the efficacy evaluation of non-target lesions is progressive, and the imaging examination of different non-target lesions is not on the same day, the earliest date is selected as the non-target disease progress date.

（3） New lesions: if there are multiple new lesions and the imaging examination of different new lesions is not on the same day, the earliest date is selected as the date of new lesions.

（4） If the overall efficacy evaluation is progression, if the target lesion progression date, non-target lesion progression date and new lesion occurrence date are not on the same day, the earliest date is selected as the overall efficacy progression date of the visit.

（5） If the overall efficacy evaluation is not progressive, if the imaging examination date of target lesion and non-target lesion are not on the same day, the latest date is selected as the overall efficacy evaluation date of the visit.

- Time to disease progression (TTP) (month) = (first observe disease progression (imaging or clinical progress, whichever is earlier) date / censor date - random date + 1) / 30.4375, rounding up or down to one decimal place. For all subjects, the date of tumor progression at or before the last assessment of the disease will be taken as the date of tumor progression.
- Objective response rate (ORR) = (CR + PR cases) / total cases×100%
- Disease control rate (DCR) = (CR + PR + SD cases) / total cases×100%
- Exposure time of test drug (d) = last application date of test drug - date of first application of test drug
  +1
- Test drug exposure (mg) = ∑ test drug dose
- Gemcitabine exposure time (d) = gemcitabine last medication date - gemcitabine first use date +1
- Gemcitabine exposure (mg) = ∑ gemcitabine dose

6.5.3 Subject distribution analysis

- The number of subjects screening, randomly to enroll and complete the trial in the population and each center are listed, and three analysis data sets (FAS, PPS, SS) are determined.
- The number of screening cases, the number of screening failure subjects and the number and percentage of subjects with reasons are listed.
- The number and percentage of subjects who will be randomly enrolled, completed the trial, withdrawals and their reasons are calculated.
- The number and percentage of subjects with primary and secondary deviant protocol are summarized according to the type of deviation.
- The reasons for excluding PPS are classified and analyzed, and the number and percentage of subjects in different categories are calculated.
- A detailed list of subjects divided by population will be listed, including the reasons why they are not enrolled in PPS / FAS/ SS.
- The flow chart of subjects distribution will be drawn.

6.5.4 Demographic data and baseline analysis

Based on the actual data in FAS.

Descriptive demographic data and other baseline eigenvalues:

- Continuous variables will be used to calculate the number of cases, mean, standard deviation, quartiles, minimum and maximum values: age, height, weight, body surface area, course of disease, vital signs (body temperature, pulse rate, respiration, systolic blood pressure, diastolic pressure), pain intensity, KPS score, number of target lesions, sum of target lesion diameters, and number of non-target lesions.

- Calculation count(s) and percentages (%) of qualitative variables:
  - Age (< 65 years old, ≥ 65 years old)
  - Gender (male, female)
  - Ethnicity
  - Occupation (manual, non-manual)
  - History of surgery (with or without)
  - Course of disease (< 1 year, ≥ 1 year)
  - Diagnosis types of pancreatic cancer (locally advanced pancreatic adenocarcinoma, metastatic pancreatic adenocarcinoma, others)
  - Tumor location (head, body and tail of pancreas)
  - Have you received chemotherapy (yes, no)
  - No, radiotherapy or not

- Management of intestinal obstruction (yes, no)
- Drug allergy (with or without)
- Concomitant diseases (with or without)
- Concomitant treatment (with or without)
- Physical examination (normal, abnormal, not checked)
- K-RAS gene mutation detection (wild type, mutant type)
- Target lesion (with or without)
- Non-target lesions (with or without)
- KPS score (60-80, 90-100)

- Inferential statistical results (P values) are listed as descriptive results.

6.5.5 Analysis of medication compliance and concomitant medications

- Based on the actual data of FAS and SS.

6.5.5.1 Analysis of medication compliance

- Cumulative dose (mg) of nimotuzumab or simulant will be compared by t-test.
- Cumulative dose (mg) of gemcitabine will be compared by t-test.
- Total duration of exposure (days) of nimotuzumab or simulant will be compared by t-test.
- The time of gemcitabine exposure (d) will be compared by t-test.
- T test is used to compare the difference between the two groups.
- The medication situation of the subjects is described in the list.

6.5.5.2 Analysis of concomitant medications

- Previous medication refers to the start date of the non-study drug used before the date of the first use of the study drug.
- Concomitant medication refers to the non-study drug that meets one of the following conditions:
  - On or after the date of first use of study drugs.
  - All non-study drug start dates are prior to the first study drug use date and continued on or after the first study drug administration date.
- If the end date of the non-study drug is missing or partially missing, if the content that is not missing (including the non-missing part of the start date and the end date of the study drug) can be used to judge whether it belongs to the medication before or during the treatment, it shall be judged. If it is impossible to judge, it is considered that the drug will be started before the date of the first use of the study drug and continued to be used during the treatment.
- WHO-ATC will be used to code the combined drugs. The number of cases and percentage will be calculated according to the first level classification and the second level classification of ATC.
- Make a list of concomitant medications.

6.5.6 Efficacy analysis

Primary efficacy variable:

Primary analysis:

- The FAS data set is used, and all participants with K-ras wild-type locally advanced or metastatic pancreatic cancer are selected as the primary analysis population.
- Kaplan Meier method is used to analyze the overall survival time (OS). The number of events, censored number and percentage, median survival time, 25%, 75% survival time and 95% confidence interval will be listed respectively (Brookmeyer-Crowley method).

- The method of comparison between groups is as follows
  - Primary analysis: The primary analysis of OS will be based on FAS set. The primary comparison of OS between the two groups is to be performed using log-rank test stratified by stratified factors collected by EDC.
  - Sensitivity analysis 1: log rank test stratified by stratified factors collected by IWRS using to compare the differences between groups.
  - Sensitivity analysis 2: using un-stratified log rank test to compare the differences between groups.

- The 6,12,18,24,36,48,60,72 and 84 months survival rates and 95% CI of the two groups will be calculated
  The confidence interval (log-log conversion) is used, and Kaplan Meier curve of survival rate is drawn.
- Taking stratified factors as covariates, Cox proportional hazard model (TIES = Efron) is used to calculate HR and its 95% confidence interval (Wald method).
- The OS and related variables are listed (random date, calculated OS date, censored status OS, date of death, last confirmed survival date, censored reason).
- At the same time, in order to evaluate the robustness of OS results, the above analysis will be repeated with PPS.

Supporting analysis

- At the same time, subjects with K-ras wild-type locally advanced or metastatic pancreatic cancer who having not received biliary obstruction treatment are selected as the supporting analysis population. The same as the primary analysis method and population.

Analysis of secondary efficacy indicators:

- The analysis will be based on FAS and supportive analysis will be conducted based on the population who having not received biliary obstruction treatment.
- Disease progression free survival (PFS) will be analyzed by Kaplan Meier method. The number of events, censored number and percentage, median progression free survival time, 25%, 75% progression free survival time and 95% confidence interval are listed respectively (Brookmeyer-Crowley method).
- The method of comparison between groups is as follows
  - Primary analysis: log rank test will be used to compare the differences between groups.
  - Sensitivity analysis 1: log rank test will be used to compare the differences between groups.
  - Sensitivity analysis 2: log rank test will be used to compare the differences between groups.
- The progression free survival (PFS) rate and 95% confidence interval (CI) at 3, 6, 9, 12, 18, 24, 30 and 36 months are calculated and the Kaplan Meier curve of the two groups is drawn.
- Taking dynamic random influencing factors as covariates, Cox proportional hazard model (TIES = Efron) using to calculate HR and its 95% confidence interval (Wald method).
- PFS and related variables were listed (random date, PFS calculation date, censored status, PFS, progression date, death date, last effective imaging examination date, new anti-tumor treatment start date, censored reason).

- The time to disease progression (TTP) is analyzed by Kaplan Meier method. The number of events, censored number and percentage, median time to disease progression, 25%, 75% time to disease progression and their 95% confidence interval are listed respectively (Brookmeyer-Crowley method).
- The method of comparison between groups is as follows

- Primary analysis: log rank test using to compare the differences between groups.
- Sensitivity analysis 1: log rank test using to compare the differences between group by the adjusted IWRS gathered data
- Sensitivity analysis 2: log rank test using to compare the differences between groups without the adjusted stratifications

- The disease progression rate and its 95% confidence interval at 3, 6, 9, 12, 18, 24, 30 and 36 months in the two groups are calculated (using log-log conversion), and the Kaplan Meier curve of disease progression rate is drawn.
- Taking dynamic random influencing factors as covariates, Cox proportional hazard model (TIES = Efron) using to calculate HR and its 95% confidence interval (Wald method).
- TTP and related variables are listed (random date, TTP calculation date, censored status, TTP, progression date, disease progression date, last effective imaging examination date, start date of new anti-tumor treatment, and reasons for censored data).

- Subgroup analysis
  - OS, PFS and TTP are analyzed according to the following factors and HR forest map was drawn.
    i. Location of tumor (head of pancreas vs. body and tail of pancreas)
    ii. Have you ever had surgery (yes vs. no)
    iii. Whether biliary obstruction has been treated (yes vs. no)
    iv. Have you received adjuvant chemotherapy (yes vs. no)
    v. Diagnosis types of pancreatic cancer (locally advanced pancreatic adenocarcinoma vs. metastatic pancreatic adenocarcinoma)
    vi. KPS score (60-80 vs. 90-100)
    vii. Gender (male vs. female)
    viii. Age (< 65 years vs. ≥ 65 years)
    ix. Duration of disease (< 1 year vs. ≥ 1 year)
  - In each subgroup, HR and 95 %CI are calculated by non-stratified Cox regression and Wald method,, and median PFS is calculated by non-stratified log rank method.

- Objective response rate (ORR) is used χ^2 test between the two groups are compared. Logistic regression model using to calculate ORs and 95% CI.
- Disease control rate (DCR) is used χ^2 test between the two groups are compared.
- Clinical benefit rate (CBR) using to calculate the effective rate of the two groups. At the end, using the χ^2 to test the differences between groups.

6.5.7 Safety analysis

- Based on the actual data in SS.

6.5.7.1 Adverse event

- Adverse events are coded according to the ICH Medical Dictionary of regulatory activities (MedDRA 24.0).
- Pre-treatment AE is defined as an adverse event occurring between the signing of informed consent form and the first dose of study drug.
- Treatment emergent adverse event (TEAE) is defined as an adverse event that occurs or aggravates after the first dose of the study drug.
- Adverse reactions: adverse events related to the study drug as "definitely related, likely to be related and possibly related".

- TEAEs are summarized according to the following categories:
  - TEAE/ADR
  - SAE/SADR
  - TEAE / ADR leading to drug interruption or dose reduction
  - TEAE / ADR leading to permanent discontinuation of study medication
  - TEAE / ADR causing death
  - TEAE / ADR leading to withdrawal
- According to SOC and PT, all kinds of adverse events are summarized, and the number, number and incidence of adverse events are calculated.
- According to the different severity of SOC and PT (Grade 1, Grade 2, Grade 3, Grade 4, Grade 5), the number of cases, number of events and incidence rate are calculated. Each subject is counted at most once in the same severity level of the same term (SOC or PT).
- According to SOC and PT, the adverse events with incidence > 10% (PT incidence in either group of test group or control group) are summarized.
- A detailed list of various adverse events is listed.

6.5.7.2 Laboratory examination

- The laboratory and blood biochemical indexes are summarized (Blood routine, electrolytes, blood biochemistry, serum CA19-9) measured value and change value are diachronic.
- Shift table of laboratory examination results (blood routine, electrolyte, blood biochemistry, Serum CA19-9, urine routine) from baseline to worst post-baseline value according to abnormality which will be assessed by investigator, including the unplanned visit after medication.
- List the subjects with normal baseline and abnormal after medication, including the results of examination value and clinical significance.
- A list of subjects whose baseline abnormality is not clinically significant and whose abnormality after medication has clinical significance is listed, including the results of examination value and clinical significance judgment.
- List the measured values of laboratory inspection.

6.5.7.3 ECG examination

- Descriptive summary of ECG indicators (Heart rate, RR interval, PR interval, QRS duration QT interval and QTC) are measured and changed in a diachronic manner.
- The number and proportion of subjects with absolute prolongation of QTc after administration will be analyzed according to the following criteria:
  - 450ms< QTc≤480ms
  - 480ms< QTc≤500ms
  - QTc>500ms
- The number and proportion of subjects with QTc prolongation relative to baseline will be analyzed according to the following criteria:
  - 30ms<ΔQTc≤60ms
  - ΔQTc>60ms
- Shift table from baseline to worst post-baseline value according to abnormality assessed by investigator, including the unplanned visit after medication.
- The subjects with normal baseline and abnormal ECG after medication are listed, including the results of examination value and clinical significance.
- List the subjects whose ECG baseline abnormality has no clinical significance and whose abnormality after medication has clinical significance, including the results of examination value and clinical significance judgment.
- List the measured values of ECG.

6.5.7.4 Vital signs

The changes and measured values of vital signs compared with baseline are analyzed by descriptive statistics.

List the measured values of vital signs.

6.5.7.5 Physical examination

Shift table from baseline to worst post-baseline value according to abnormality that will be assessed by investigator, including the unplanned visit after medication.

A list of subjects with normal baseline, abnormal after medication and subjects with clinically significant baseline abnormality and post medication abnormality are listed.

List the measured values of physical examination.

6.5.8 Supplementary analysis

Subgroup analysis of OS is performed, the subgroup is the frequency of Drug Administration.

The RMSTREG algorithm is used to analyze OS and PFS, and stratification factors are considered in the model.

6.6 Interim analysis

No formal interim analysis will be performed.

Appendix 1: EY140810_Clinical study of nimotuzumab combined with gemcitabine in the treatment of pancreatic cancer TFLS for SAP_1.0_20211210

NMPA clinical trial approval No. 2011L01239 **Project No. EY140810**

Statistical Analysis Plan for Prospective, Randomized Controlled, Double-Blind, Multicenter Registered Clinical Studies of Nimotuzumab (Taixinsheng®) Plus Gemcitabine versus Placebo Plus Gemcitabine in K-RAS Wild-Type Locally Advanced or Metastatic Pancreatic Cancer

(TFLs Template)

Sponsor: Baitai biopharmaceutical Co., Ltd

Beijing biovoice Technology Co., Ltd
Tel: (86) 10-6758 7407, 6753 8432
Address: room 2-2209, Shidai Fengfan building, No.15, Majiapu West Road, Fengtai District, Beijing
Version: 2021-12-10

Catalog

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List of abbreviations

abbreviation	notes
ADR	Adverse reactions
AE	Adverse event
ATC	Anatomical therapeutics and chemical classification system
CBR	Clinical benefit rate
CI	Confidence interval
CIL	Lower limit of confidence interval
CIU	Upper limit of confidence interval
CR	Complete response
CS	Clinically Significant
CTCAE	Common Terminology Criteria for Adverse Events
DAS	Data analysis system
DCR	Disease control rate
DF	Degree of freedom
eCRF	Electronic case report form
FAS	Full analysis set
HR	Hazard ratio
HR	Heart rate
IWRS	Interactive Web Response System
Max	Maximum
MedDRA	Medical Dictionary of regulatory activities
Min	Minimum
NCI	National Cancer Research Center
NCS	Not Clinically Significant
ND	Not Detected
NE	Not evaluable
NMPA	National Medical Products Administration
OR	Odds ratio
ORR	Objective response rate
OS	Overall survival
PD	Disease progression
PFS	Disease progression free survival
PPS	Per protocol set
PR	Partialresponse
PT	Preferred term
Q1	Lower quartile
Q3	Upper quartile
RECIST	Criteria for evaluating the efficacy of solid tumors
SADR	Serious adverse reactions
SAE	Serious adverse events
SD	Standard deviation
SD	Stable disease
SE	Standard error
SOC	Systematic organ classification
SS	Safety set
TEAE	Treatment-Emergent Adverse Event

TTP	Time to disease progression

Statistical Analysis Plan for Prospective, Randomized Controlled, Double-Blind, Multicenter Registered Clinical Studies of Nimotuzumab (Taixinsheng®) Plus Gemcitabine versus Placebo Plus Gemcitabine in K-RAS Wild-Type Locally Advanced or Metastatic Pancreatic Cancer (TFLs Template)

1. Distribution of subjects

Table 1-1 Screening failure (Screening subjects)

index	Statistical results
Summary	
Screen	XXX
Screen failure n%	XX(XX.X)
Screen failure reason	
Not meeting the inclusion criteria n%	XX(XX.X)
Meeting the exclusion criteria n%	XX(XX.X)
Subjects withdraw n%	XX(XX.X)
Other n%	XX(XX.X)
Center 1	
Screen	XXX
Screen failure n%	XX(XX.X)
Screen failure reason	
Not meeting the inclusion criteria n%	XX(XX.X)
Meeting the exclusion criteria n%	XX(XX.X)
Subjects asked to withdraw n%	XX(XX.X)
Other n%	XX(XX.X)
….	
Center XX	
Screen	XXX
Screen failure n%	XX(XX.X)
Screen failure reason	
Not meeting the inclusion criteria n%	XX(XX.X)
Meeting the exclusion criteria n%	XX(XX.X)
Subjects asked to withdraw n%	XX(XX.X)
Other n%	XX(XX.X)

%Subjects were screened based on summary / center.

Table 1-2 distribution of subjects in each center (enrolled subjects)

index	Experimental group	Control group	Total
Summary			
Screen			XXX
Randomly enrolled	XX	XX	XX
Complete	XX	XX	XX
FAS	XX	XX	XX
PPS	XX	XX	XX
SS	XX	XX	XX
Center 1			
Screen			XX
Randomly enrolled	XX	XX	XX
Complete	XX	XX	XX

FAS	XX	XX	XX
PPS	XX	XX	XX
SS	XX	XX	XX
…			
Screen			XX
Randomly enrolled	XX	XX	XX
Complete	XX	XX	XX
FAS	XX	XX	XX
PPS	XX	XX	XX
SS	XX	XX	XX
Center XX			
Screen			XX
Randomly enrolled	XX	XX	XX
Complete	XX	XX	XX
FAS	XX	XX	XX
PPS	XX	XX	XX
SS	XX	XX	XX

Table 1-3 classification of subjects' completion (enrolled subjects)

Table 1-4 classification of subjects' completion (without treatment of biliary obstruction)

index	Experimental group	Control group	Total
Randomization (n)	XX	XX	XX
Completed n%	XX(XX.X)	XX(XX.X)	XX(XX.X)
Withdrawn n%	XX(XX.X)	XX(XX.X)	XX(XX.X)
Reasons for withdrawn			
Subjects ask to withdraw from the trial actively (%)	XX(XX.X)	XX(XX.X)	XX(XX.X)
Loss of follow-up n (%)	XX(XX.X)	XX(XX.X)	XX(XX.X)
In the course of treatment, the disease progressed or deteriorated, and the researchers considered that who is not suitable to continue trial n%	XX(XX.X)	XX(XX.X)	XX(XX.X)
The patient is pregnant or not using enough contraceptive measures	XX(XX.X)	XX(XX.X)	XX(XX.X)
The researchers believe that the compliance is poor and the medication can not be carried out on time	XX(XX.X)	XX(XX.X)	XX(XX.X)
Use of drugs or foods prohibited in the protocol n%	XX(XX.X)	XX(XX.X)	XX(XX.X)
Occurrence of adverse events n%	XX(XX.X)	XX(XX.X)	XX(XX.X)
Other reasons n%	XX(XX.X)	XX(XX.X)	XX(XX.X)

%Based on randomized subjects.

Table 1-5 subjects who deviated from the protocol during the trial (enrolled subjects)

index	Experimental group	Control group	Total
Randomization (n)	XX	XX	XX
At least 1 PD n%	XX(XX.X)	XX(XX.X)	XX(XX.X)
Primary PD n%	XX(XX.X)	XX(XX.X)	XX(XX.X)
Primary PD 1 N%	XX(XX.X)	XX(XX.X)	XX(XX.X)
Primary PD 2 n%	XX(XX.X)	XX(XX.X)	XX(XX.X)
…… n(%)*	XX(XX.X)	XX(XX.X)	XX(XX.X)
Secondary PD n%	XX(XX.X)	XX(XX.X)	XX(XX.X)
Secondary PD 1 N%	XX(XX.X)	XX(XX.X)	XX(XX.X)

Secondary PD 2 N%	XX(XX.X)	XX(XX.X)	XX(XX.X)
…… n(%)	XX(XX.X)	XX(XX.X)	XX(XX.X)

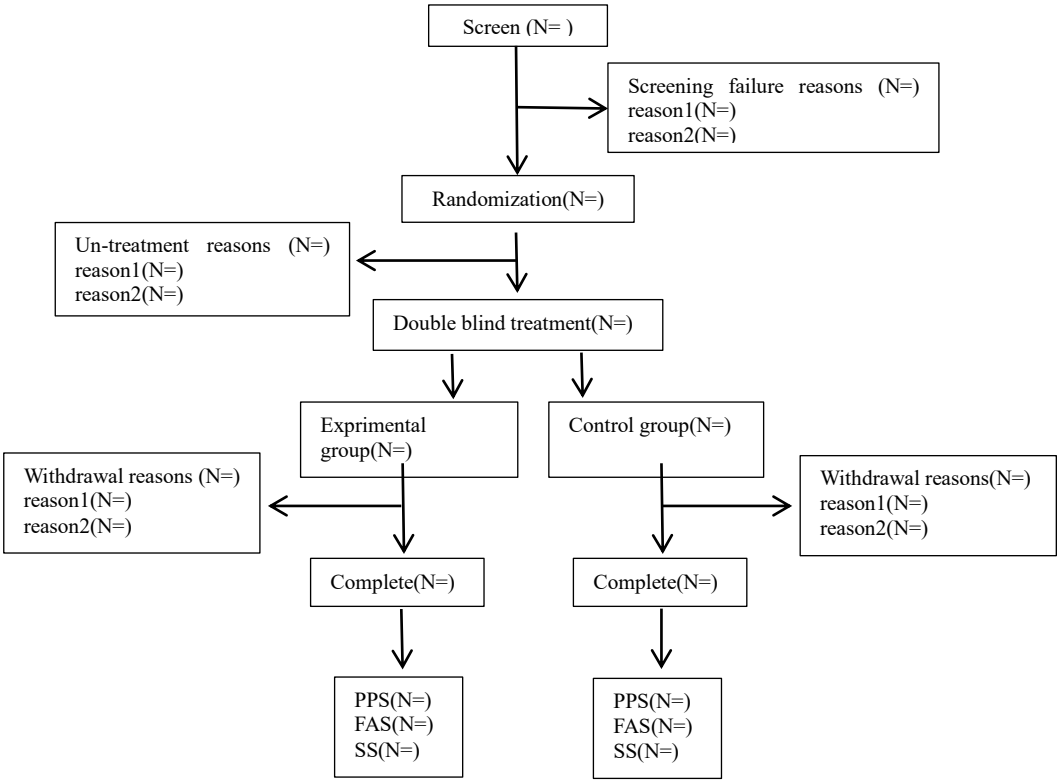
PD: Protocol deviation.% Based on randomized subjects.

Table 1-6 classification analysis of reasons for non PPS subjects (enrolled subjects)

index	Experimental group	Control group	Total
Randomization (n)	XXX	XXX	XXX
Never received study drug n%	XX(XX.X)	XX(XX.X)	XXX(XX.X)
Combined forbidden drugs n%	XX(XX.X)	XX(XX.X)	XXX(XX.X)
…… n(%)	XX(XX.X)	XX(XX.X)	XXX(XX.X)

%Based on randomized subjects.

Figure 1-1 Flow chart of subjects distribution (enrolled subjects)



2. Baseline analysis

Table 2-1 analysis of demographic data and baseline characteristics (FAS)

	Experimental group	Control group	Total	Statistics	P value	method
Age (yr)*						
N	XX	XX	XX	X.XXX	X.XXX	T-test
Mean±SD	XX.X±XX.XX	XX.X±XX.XX	XX.X±XX.XX			
Median	XX.X	XX.X	XX.X			
Q1~Q3	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
Min~Max	XX ~XX	XX ~XX	XX ~XX			
Age						
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
< 65 years old, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
≥65 years old, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Height (cm)						
N	XX	XX	XX	X.XXX	X.XXX	T-test
Mean±SD	XX.XX±XX.XXX	XX.XX±XX.XXX	XX.XX±XX.XXX			
Median	XX.XX	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX	XX.XX~XX.XX			
Min~Max	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
Weight (kg)						
N	XX	XX	XX	X.XXX	X.XXX	T-test

Mean±SD	XX.XX±XX.XXX	XX.XX±XX.XXX	XX.XX±XX.XXX			
Median	XX.XX	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX	XX.XX~XX.XX			
Min~Max	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
Body surface area (m^2)						
N	XX	XX	XX	X.XXX	X.XXX	T-test
Mean±SD	XX.XX±XX.XXX	XX.XX±XX.XXX	XX.XX±XX.XXX			
Median	XX.XX	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX	XX.XX~XX.XX			
Min~Max	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
Gender						
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
Male, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Female, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Nation						
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
Han nationality, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Other, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Occupation						
N	XXX	XXX	XXX	X.XXX	X.XXX	Chisq/Fisher
Physical labor, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Non manual labor, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			

*: age = (date of signing informed consent - date of birth +1) / 365.25, rounded down.

Table 2-2 surgery history (FAS)

	Experimental group	Control group	Total	statistic	P value	method
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
N/A	XX(XX.X)	XX(XX.X)	XX(XX.X)			
YES n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			

Table 2-3 current history of pancreatic cancer (FAS)

index	Experimental group	Control group	Total	Statistics	P value	method
Course of disease (month)*						
N	XX	XX	XX	X.XXX	X.XXX	Wilcoxon
Mean±SD	XX.XX±XX.XXX	XX.XX±XX.XX	XX.XX±XX.XX			
Median	XX.XX	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX	XX.XX~XX.X X			
Min~Max	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
Course of disease						
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
< 1 year, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
≥ 1 year, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Diagnosis type						
N	XX	XX	XX	X.XXX	X.XXX	R*C
Locally advanced pancreas Adenocarcinoma, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Metastatic pancreas Adenocarcinoma, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Other, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Tumor site						
N	XX	XX	XX	X.XXX	X.XXX	R*C
Pancreatic head, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Pancreatic body, n (%)	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Tail of pancreas, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			

index	Experimental group	Control group	Total	Statistics	P value	method
Have you received chemotherapy						
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
Yes, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
No, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Have you received radiotherapy						
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
Yes, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
No, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Have biliary tract occurred management of obstruction						
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
Yes, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
No, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			

*: course of disease (month) = (date of informed consent signing - date of first diagnosis of pancreatic cancer + 1) / 30.4375, rounded to one decimal place.

Table 2-4 target lesions (FAS)

index	Experimental group	Control group	Total	Statistics	P value	method
Target lesion						
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
YES n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
N / A	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Number of target lesions						
N	XX	XX	XX	X.XXX	X.XXX	T-test
Mean±SD	XX.XX±XX.XXX	XX.XX±XX.XXX	XX.XX±XX.XXX			
Median	XX.XX	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX	XX.XX~XX.XX			
Min~Max	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
Sum of target lesion diameters (mm)						
N	XX	XX	XX	X.XXX	X.XXX	T-test
Mean±SD	XX.XX±XX.XXX	XX.XX±XX.XXX	XX.XX±XX.XXX			
Median	XX.XX	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX	XX.XX~XX.XX			

Min~Max	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			

Table 2-5 non target lesions (FAS)

index	Experimental group	Control group	Total	Statistics	P value	method
Non-target lesions						
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
YES n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
N / A	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Number of non-target lesions						
N	XX	XX	XX	X.XXX	X.XXX	T-test
Mean±SD	XX.XX±XX.XXX	XX.XX±XX.XX	XX.XX±XX.XX			
Median	XX.XX	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX	XX.XX~XX.XX			
Min~Max	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			

Table 2-6 drug allergy (FAS)

	Experimental group	Control group	Total	statistic	P value	method
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
N / A	XX(XX.X)	XX(XX.X)	XX(XX.X)			
YES n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			

Table 2-7 Medical history (FAS)

	Experimental group	Control group	Total	statistic	P value	method
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
N / A	XX(XX.X)	XX(XX.X)	XX(XX.X)			
YES n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			

Table 2-8 Previous treatment (FAS)

	Experimental group	Control group	Total	statistic	P value	method
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
N / A	XX(XX.X)	XX(XX.X)	XX(XX.X)			
YES n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			

Table 2-9 vital signs (FAS)

index	Experimental group	Control group	Total	Statistics	P value	method
Body temperature (℃)						
N	XX	XX	XX	X.XXX	X.XXX	T-test

Mean±SD	XX.XX±XX.XXX	XX.XX±XX.XXX	XX.XX±XX.XXX			
Median	XX.XX	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX	XX.XX~XX.XX			
Min~Max	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
Pulse rate (times / min)						
N	XX	XX	XX	X.XXX	X.XXX	T-test
Mean±SD	XX.X±XX.X X	XX.X±XX.X X	XX.X±XX. X			
Median	XX.X	XX.X	XX.X			
Q1~Q3	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
Min~Max	XX ~XX	XX ~XX	XX ~XX			
Breathing (times / min)						
N	XX	XX	XX	X.XXX	X.XX	T-test
Mean±SD	XX.X±XX.X X	XX.X±XX.X X	XX.X±XX.XX			
Median	XX.X	XX.X	XX.X			
Q1~Q3	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
Min~Max	XX ~XX	XX ~XX	XX ~XX			
Systolic blood pressure (mmHg)						
N	XX	XX	XX	X.XXX	X.XX	T-test
Mean±SD	XX.X±XX.XX	XX.X±XX.XX	XX.X±XX.XX			
Median	XX.X	XX.X	XX.X			
Q1~Q3	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
Min~Max	XX ~XX	XX ~XX	XX ~XX			
Diastolic blood pressure (mmHg)						
N	XX	XX	XX	X.XXX	X.XX	T-test
Mean±SD	XX.X±XX.X X	XX.X±XX.X X	XX.X±XX.XX			
Median	XX.X	XX.X	XX.X			
Q1~Q3	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
Min~Max	XX ~XX	XX ~XX	XX ~XX			

Table 2-10 physical examination (FAS)

	Experimental group	Control group	Total	Statistic	P value	method
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
Normal, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Abnormal, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Not checked, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			

Table 2-11 clinical benefit rate (FAS)

TFLs for Statistical Analysis Plan

index	Experimental group	Control group	Total	Statistics	P value	method
Pain intensity (mm)						
N	XX	XX	XX	X.XX X		T-test
Mean±SD	XX.XX±XX.XXX	XX.XX±XX.XX	XX.XX±XX.XX			
Median	XX.XX	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.X X	XX.X X			
Min~Max	XX.X~XX.X	XX.X~XX.X	XX.X~XX.X			
KPS score						
N	XX	XX	XX	X.XX	X.XX	T-test
Mean±SD	XX.X±XX. XX	XX.X±XX .XX	XX.X±XX.XX			
Median	XX.X	XX.X	XX.X			
Q1~Q3	XX.X~XX. X	XX.X~XX.X	XX.X~XX.X			
Min~Max	XX ~XX	XX ~XX	XX ~XX			
KPS score						
N	XX	XX	XX	X.XX X	XX X	Chisq/Fisher
60-80 n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
90-100 n(%)	XX(XX.X)	XX(XX.X)	XX(XX.X)			

Table 2-12 KRAS gene mutation detection (FAS)

	Experimental group	Control group	Total	statistic	P value	method
N	XX	XX	XX	X.XXX	X.XXX	Chisq/Fisher
Wild type, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			
Mutant, n%	XX(XX.X)	XX(XX.X)	XX(XX.X)			

3. Analysis of medication compliance and concomitant medications

Table 3-1 analysis of exposure and time of trial drug (FAS)
Table 3-2 exposure and time analysis (SS)
Table 3-3 exposure and time analysis (FAS)
Table 3-4 exposure and time analysis of gemcitabine(SS)

index	Experimental group	Control group	statistic	P value	method
Drug exposure (mg)					
N	XXX	XXX	X.XXX	X.XXX	T-test
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX			
Median	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX			
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX			
Drug exposure time (d)					
N	XXX	XXX	X.XXX	X.XXX	T-test
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX			
Median	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX			
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX			

Table 3-5 treatment cycle (week) analysis (FAS)
Table 3-6 treatment cycle (week) analysis (SS)

	Experimental group	Control group	statistic	P value	method
N	XXX	XXX	X.XXX	X.XXX	T-test
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX			
Median	XX.XX	XX.XX			
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX			
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX			

Table 3-7 ATC classification analysis of prior concomitant medications (FAS)
Table 3-8 ATC classification analysis of prior concomitant medications (SS)
Table 3-9 ATC classification analysis of concomitant medications (FAS)
Table 3-10 ATC classification analysis of concomitant medications(SS)

ATC level 1 Classification ATC secondary classification Preferred term	Experimental group	Control group
N	XXX	XXX
Total N%	XX(XX.X)	XX(XX.X)
ATC1 n(%)	XX(XX.X)	XX(XX.X)
ATC2 n(%)	XX(XX.X)	XX(XX.X)
PT n(%)	XX(XX.X)	XX(XX.X)
…	XX(XX.X)	XX(XX.X)
…	XX(XX.X)	XX(XX.X)

4. Efficacy analysis

4.1 Overall survival (OS)

Table 4-1 overall survival (OS) (month) analysis (FAS)

index	Experimental group	Control group
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

Table 4-2 overall survival (OS) (month) between group comparison results (FAS)

method	Statistical results
Primary analysis	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 1	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 2	
Statistics (P value)	X.XXX(X.XXX)

Note:
Primary analysis: log rank test using to correct the stratified factors collected by EDC.
Sensitivity analysis 1: log rank test using to correct stratification factors collected by IWRS.
Sensitivity analysis 2: log rank test without correction of stratification factors is used.

Table 4-3 overall survival rate (%)at different time (month) (FAS)

time (month)	Experimental group					Control group				
	Number of deaths (n)	censored Number (n)	Exposure to Risk (n)	survival rate (%)	The survival rate 95% CI	Number of deaths (n)	censored number (n)	Exposure to Risk (n)	survival rate (%)	The survival rate 95% CI
3	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
6	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
9	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
12	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
18	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X

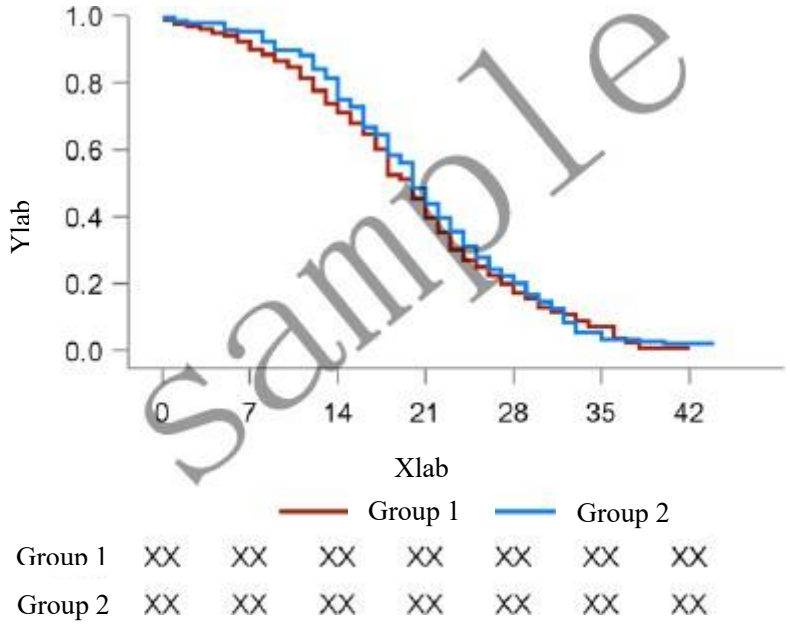


Figure 4-1 Kaplan Meier curve of survival rate at each time point (FAS)

Table 4-4 overall survival (OS) (month) subgroup analysis (FAS)

index	Experimental group	Control group
Tumor location		
Head of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Body and tail of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you had surgery		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you biliary obstruction been treated		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you received adjuvant chemotherapy		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Diagnostic types of pancreatic cancer		
Locally advanced pancreatic adenocarcinoma		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		

25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Metastatic adenocarcinoma of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
KPS score		
60-80		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
90-100		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Gender		
male		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
female		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Age		
< 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

≥ 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Course of disease		
< 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	X.X (XX.X~XX.X)	X.X (XX.X~XX.X)
50%(95%CI)	X.X (XX.X~XX.X)	X.X (XX.X~XX.X)
75%(95%CI)	X.X (XX.X~XX.X)	X.X (XX.X~XX.X)
≥ 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	X.X (XX.X~XX.X)	X.X (XX.X~XX.X)
50%(95%CI)	X.X (XX.X~XX.X)	X.X (XX.X~XX.X)
75%(95%CI)	X.X (XX.X~XX.X)	X.X(XX.X~XX.X)

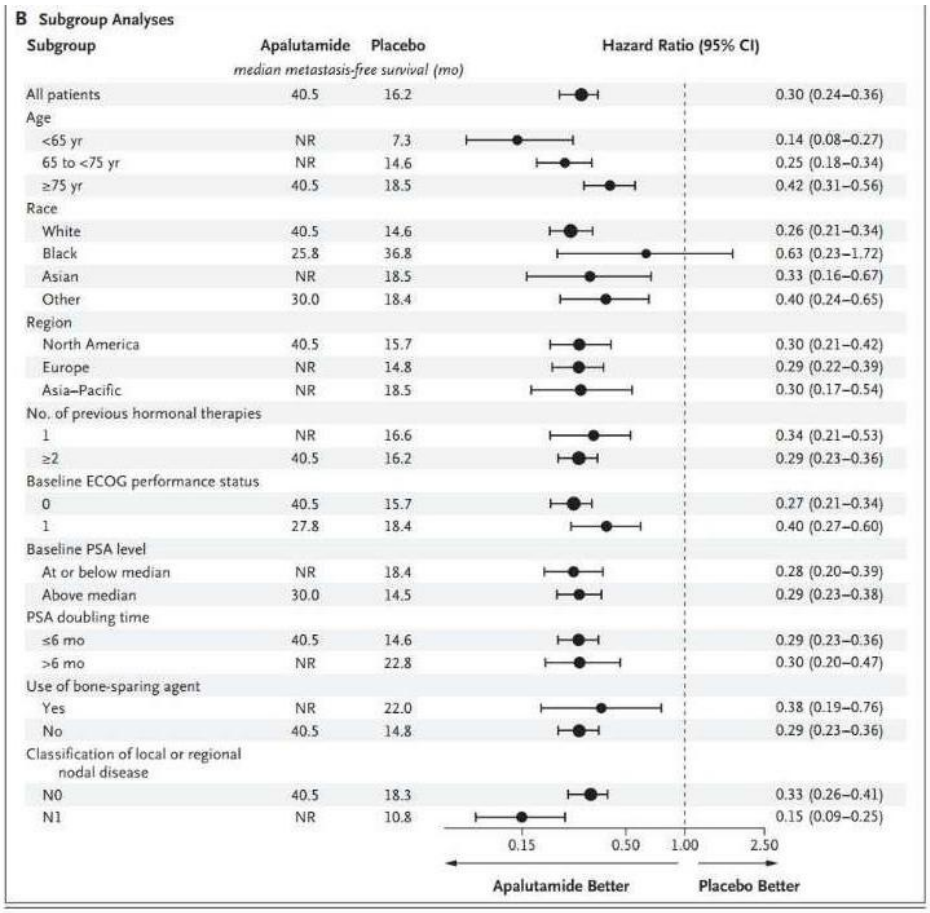


Fig. 4-2 survival forest figure (sample figure) (FAS)

Note: All subjects are stratified by Cox regression to calculate Hazard ratio. Stratified factors are randomized factors from EDC, and Wald method using to calculate HR 95% CI.
In the other subgroups, HR is calculated by non-stratified Cox regression, HR 95% CI is calculated by Wald method, and median OS is calculated by non-stratified log rank method.

Table 4-5 overall survival (OS) (month) analysis (PPS)

index	Experimental group	Control group
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

Table 4-6 overall survival (OS) (month) inter-group comparison results (PPS)

method	Statistical results
Principal analysis	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 1	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 2	
Statistics (P value)	X.XXX(X.XXX)

Note:
Main analysis: log rank test using to correct the stratified factors collected by EDC.
Sensitivity analysis 1: log rank test using to correct stratification factors collected by IWRS.
Sensitivity analysis 2: log rank test without correction of stratification factors.

Table 4-7 overall survival rate (%) (PPS) at different time (month)

time (month)	Experimental group					Control group				
	Number of deaths (n)	censored Number (n)	Exposure to Risk (n)	survival rate (%)	The survival rate is 95% CI	Number of deaths (n)	Number of omissions (n)	Exposure to Risk (n)	survival rate (%)	The survival rate is 95% CI
3	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
6	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
9	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
12	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
18	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X

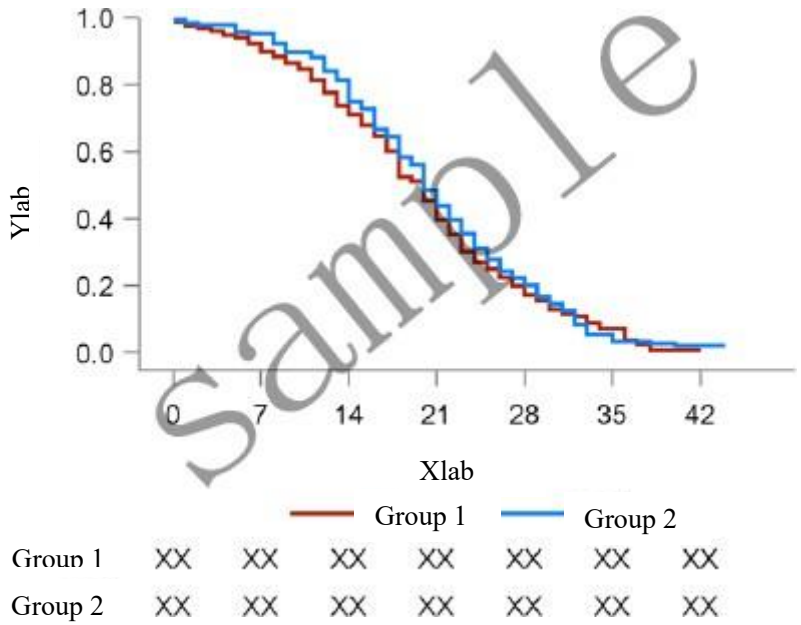


Figure 4-3 Kaplan Meier curve of survival rate at each time point (PPS)

Table 4-8 overall survival (OS) (month) subgroup analysis (PPS)

index	Experimental group	Control group
Tumor location		
Head of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Body and tail of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you had surgery		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation		

(month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have biliary obstruction been treated		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you received adjuvant chemotherapy		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Diagnostic types of pancreatic cancer		
Locally advanced pancreatic adenocarcinoma		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Metastatic adenocarcinoma of pancreas		

N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
KPS score		
60-80		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
90-100		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Gender		
male		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
female		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Age		
< 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
≥ 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)

Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Course of disease		
< 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾ 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

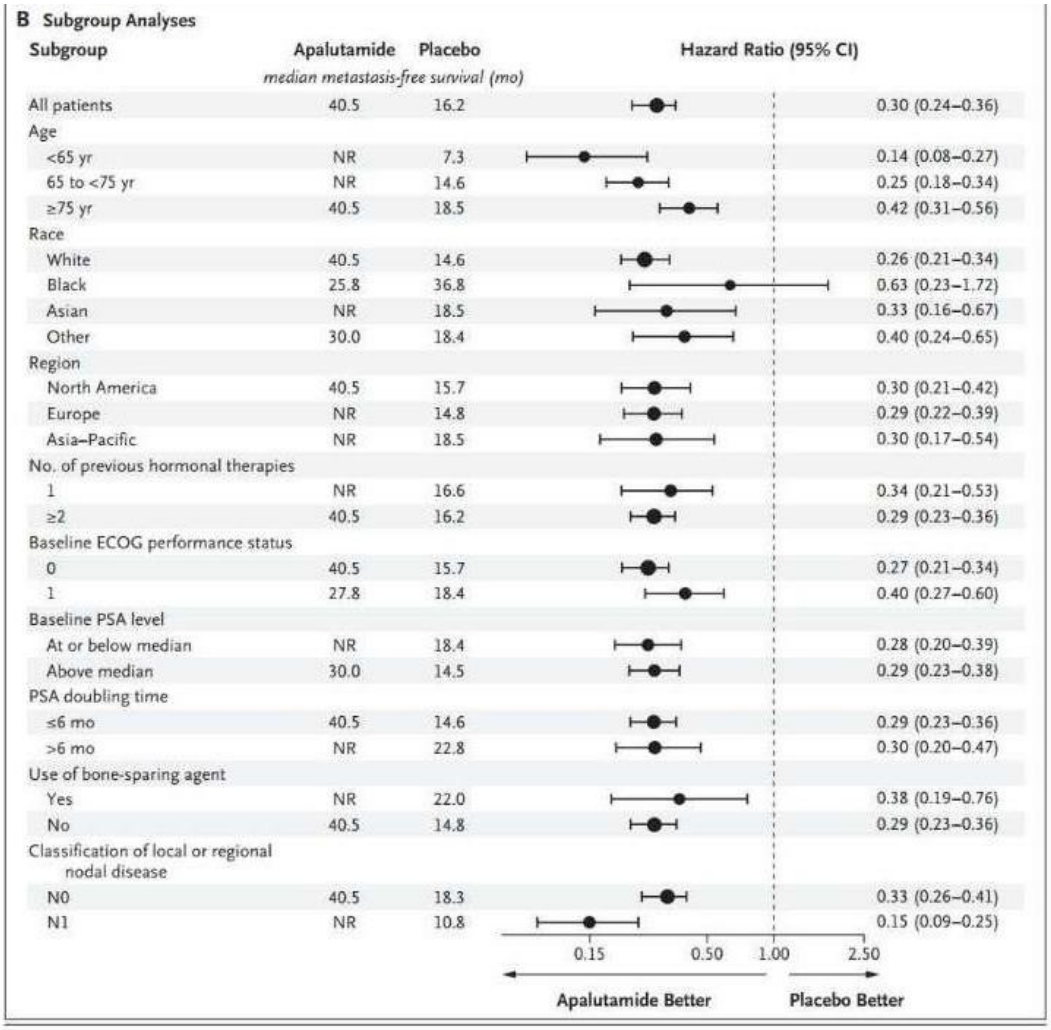


Figure 4-4 survival forest figure (PPS) (sample)

Note:

All subjects are stratified by Cox regression to calculate hazard ratio. Stratified factors are randomized factors from EDC, and Wald method using to calculate HR 95% CI；
In the other subgroups, HR is calculated by non-stratified Cox regression, HR 95% CI is calculated by Wald method, and median OS is calculated by non-stratified log rank method.

4.2 Overall survival (OS) (without treatment for biliary obstruction)

Table 4-9 analysis of overall survival (OS) (month) (FAS)

index	Experimental group	Control group
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

Table 4-10 overall survival (OS) (month) between groups (without biliary obstruction treatment) (FAS)

Method	Statistical results
Principal analysis	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 1	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 2	
Statistics (P value)	X.XXX(X.XXX)

Note:
Main analysis: the patients are divided into three groups: tumor location, whether received surgery, whether received adjuvant chemotherapy or not Log rank test.
Sensitivity analysis 1: log rank test using to adjust the stratification factors (tumor location, whether received surgery, whether received adjuvant chemotherapy) collected by IWRS.
Sensitivity analysis 2: log rank test without correction of stratification factors.

Table 4-11 overall survival rate (%) (without biliary obstruction treatment) (FAS)

time (month)	Experimental group					Control group				
	Number of deaths (n)	censored Number (n)	Exposure to Risk (n)	survival rate (%)	The survival rate is 95% CI	Number of deaths (n)	Number of omissions (n)	Exposure to Risk (n)	survival rate (%)	The survival rate is 95% CI
3	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
6	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
9	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
12	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
18	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X

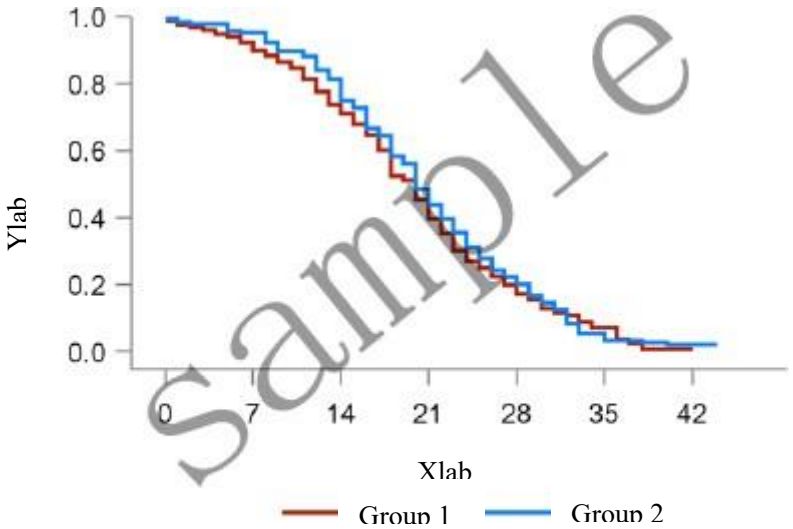


Figure 4-5 Kaplan Meier curve of survival rate at each time point (FAS)

Table 4-12 subgroup analysis of overall survival (OS) (month) (FAS)

index	Experimental group	Control group
Tumor location		
Head of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Body and tail of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you had surgery		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX

Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you received adjuvant chemotherapy		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Diagnostic types of pancreatic cancer		
Locally advanced pancreatic adenocarcinoma		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Metastatic adenocarcinoma of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
KPS score		
60-80		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
90-100		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Gender		
male		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
female		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Age		
< 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾ 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Course of disease		
< 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾ 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

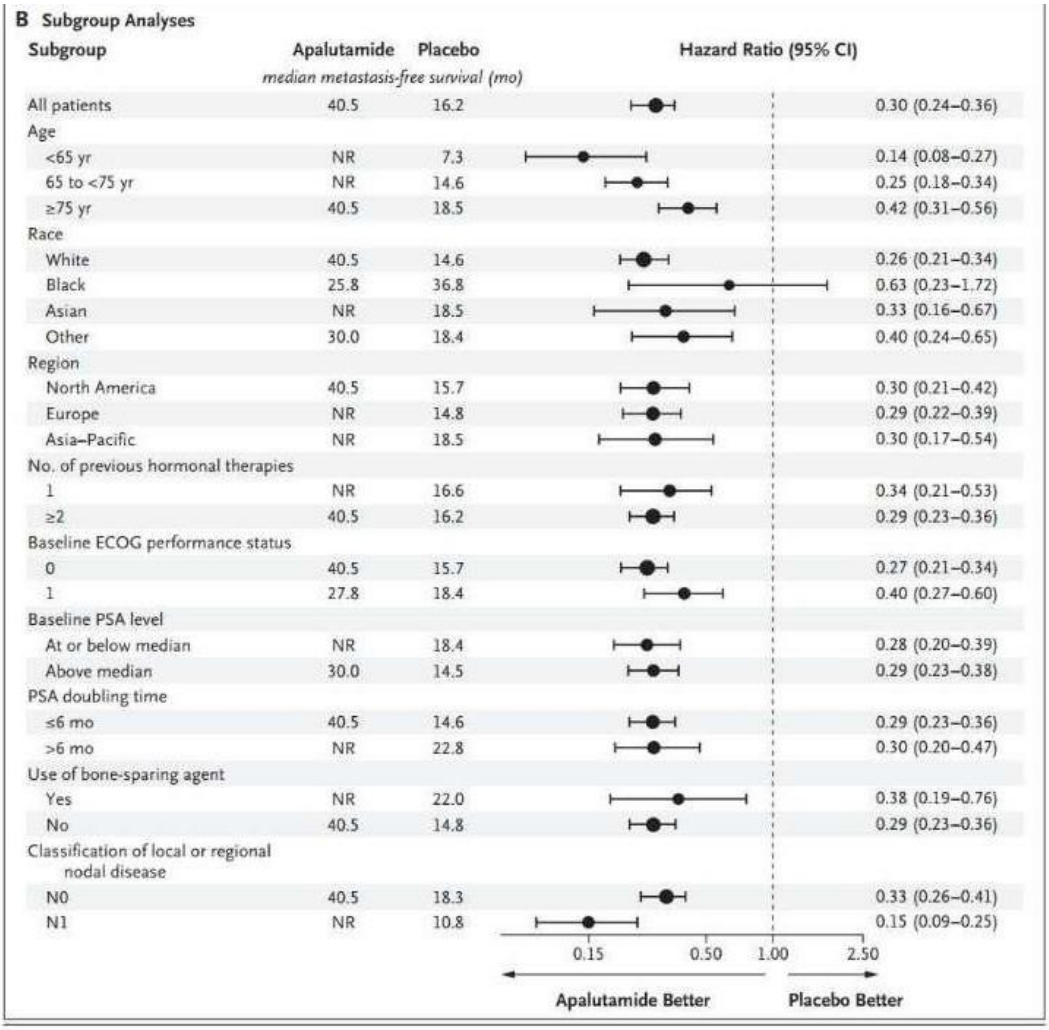


Image of untreated biliary tract obstruction (FAS-6)

Note:
Stratified Cox regression using to calculate HR. Random factors are tumor location, surgery, adjuvant chemotherapy. Wald method is used to calculate HR 95% CI.
In the other subgroups, HR is calculated by non-stratified Cox regression, HR 95% CI is calculated by Wald method, and median OS is calculated by non-stratified log rank method.

Table 4-13 analysis of overall survival (OS) (month) (PPS)

index	Experimental group	Control group
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

Table 4-14 comparison results of overall survival (OS) (month) between groups (without biliary obstruction treatment) (PPS)

method	Statistical results
Principal analysis	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 1	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 2	
Statistics (P value)	X.XXX(X.XXX)

Note:
Main analysis: the patients are divided into groups on randomized stratification factor (tumor location, whether received surgery, whether received adjuvant chemotherapy or not) to do log rank test.
Sensitivity analysis 1: log rank test is used to adjust the stratification factors (tumor location, whether received surgery, whether received adjuvant chemotherapy) collected by IWRS.
Sensitivity analysis 2: log -rank test without correction of stratification factors is used.

Table 4-15 overall survival rate (%) at different time (month) (without biliary obstruction treatment) (PPS)

time (month)	Experimental group					Control group				
	Number of deaths (n)	censored Number (n)	Exposure to Risk (n)	survival rate (%)	The survival rate is 95% CI	Number of deaths (n)	Number of omissions (n)	Exposure to Risk (n)	survival rate (%)	The survival rate is 95% CI
3	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
6	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
9	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
12	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
18	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X

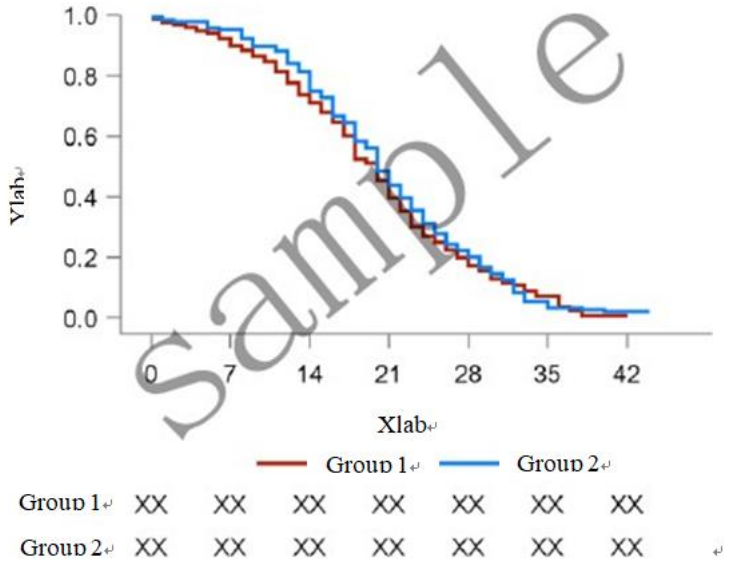


Figure 4-7 Kaplan Meier curve of survival rate at each time point (PPS)

Table 4-16 subgroup analysis of overall survival (OS) (month) (PPS)

index	Experimental group	Control group
Tumor location		
Head of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Body and tail of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you had surgery		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you received adjuvant chemotherapy		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Diagnostic types of pancreatic cancer		
Locally advanced pancreatic adenocarcinoma		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Metastatic adenocarcinoma of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
KPS score		
60-80		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
90-100		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Gender		
male		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
female		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

Age		
< 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾ 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Course of disease		
< 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾ 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

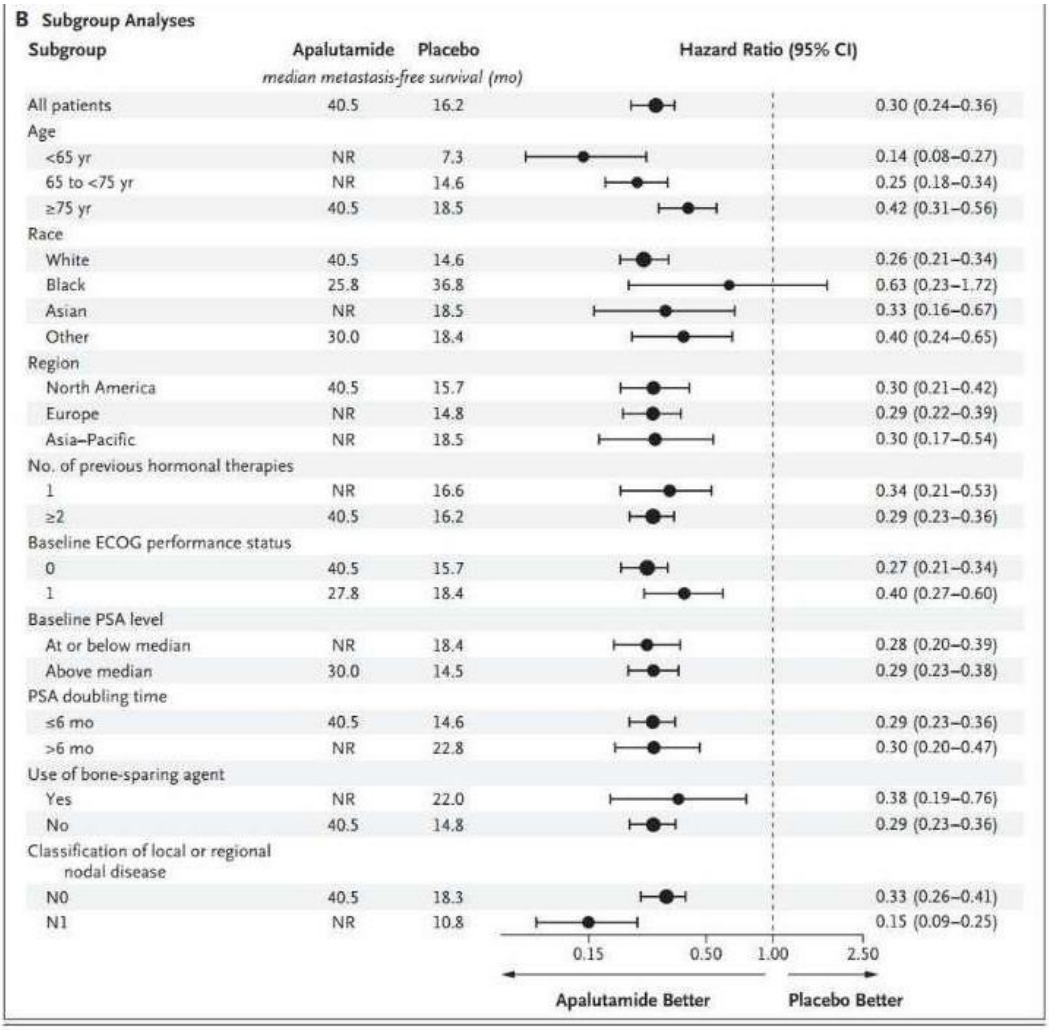


Figure 4-8 survival forest figure (without biliary obstruction treatment) (PPS) (sample)

Note:

Stratified Cox regression is used to calculate HR. Random factors are tumor location, surgery, adjuvant chemotherapy. Wald method using to calculate HR 95% CI.

In the other subgroups, HR is calculated by non-stratified Cox regression, HR 95% CI is calculated by Wald method, and median OS is calculated by non-stratified log rank method.

4.3 Progression free survival (PFS)

Table 4-17 progression free survival (PFS) (month) analysis (FAS)

index	Experimental group	Control group
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

Table 4-18 progression free survival (PFS) (month) results are compared

Method	Statistical results
Principal analysis	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 1	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 2	
Statistics (P value)	X.XXX(X.XXX)

Note:
Main analysis: log rank test is used to correct the stratified factors collected by EDC.
Sensitivity analysis 1: log rank test is used to correct stratification factors collected by IWRS.
Sensitivity analysis 2: log rank test without correction of stratification factors is used.

Table 4-19 progression free survival rate (%) (FAS) at different time (month)

	Experimental group						Control group					
time (month)	Number of new lesions (n)	Number of deaths (n)	Censored(n)	Exposure to risk (n)	Disease progression free rate (%)	Progression free survival 95%CI	Number of new lesions (n)	Number of deaths (n)	Censored (n)	Exposure to risk (n)	Disease progression free rate (%)	Progression free survival 95% CI
3	XX	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX	XX.X	XX.X～XX.X
6	XX	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX	XX.X	XX.X～XX.X
9	XX	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX	XX.X	XX.X～XX.X
12	XX	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX	XX.X	XX.X～XX.X
18	XX	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX	XX.X	XX.X～XX.X

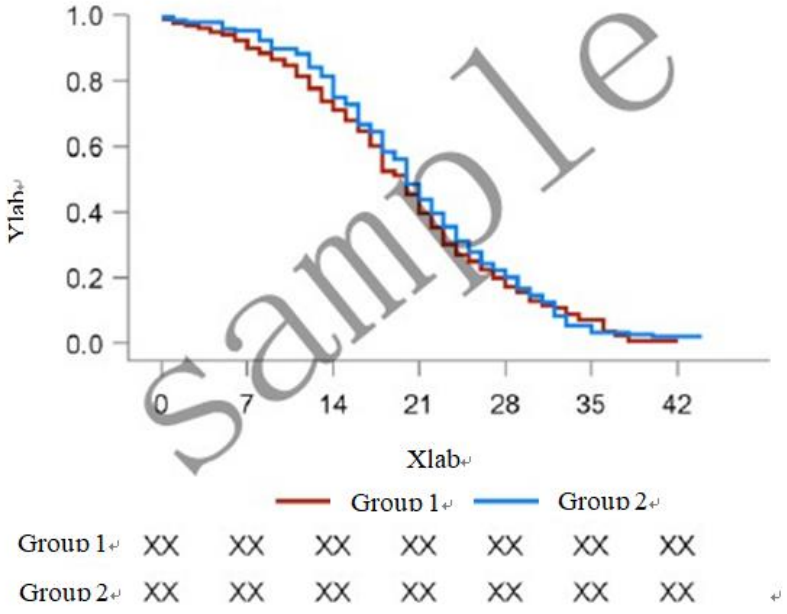


Figure 4-9 Kaplan Meier curve of progression free survival at each time point (FAS)

Table 4-20 progression free survival (PFS) (month) subgroup analysis (FAS)

index	Experimental group	Control group
Tumor location		
Head of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Body and tail of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you had surgery		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have biliary obstruction been treated		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		

25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you received adjuvant chemotherapy		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Diagnostic types of pancreatic cancer		
Locally advanced pancreatic adenocarcinoma		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Metastatic adenocarcinoma of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
KPS score		
60-80		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
90-100		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Gender		
male		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
female		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Age		
< 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾ 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Course of disease		
< 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾ 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

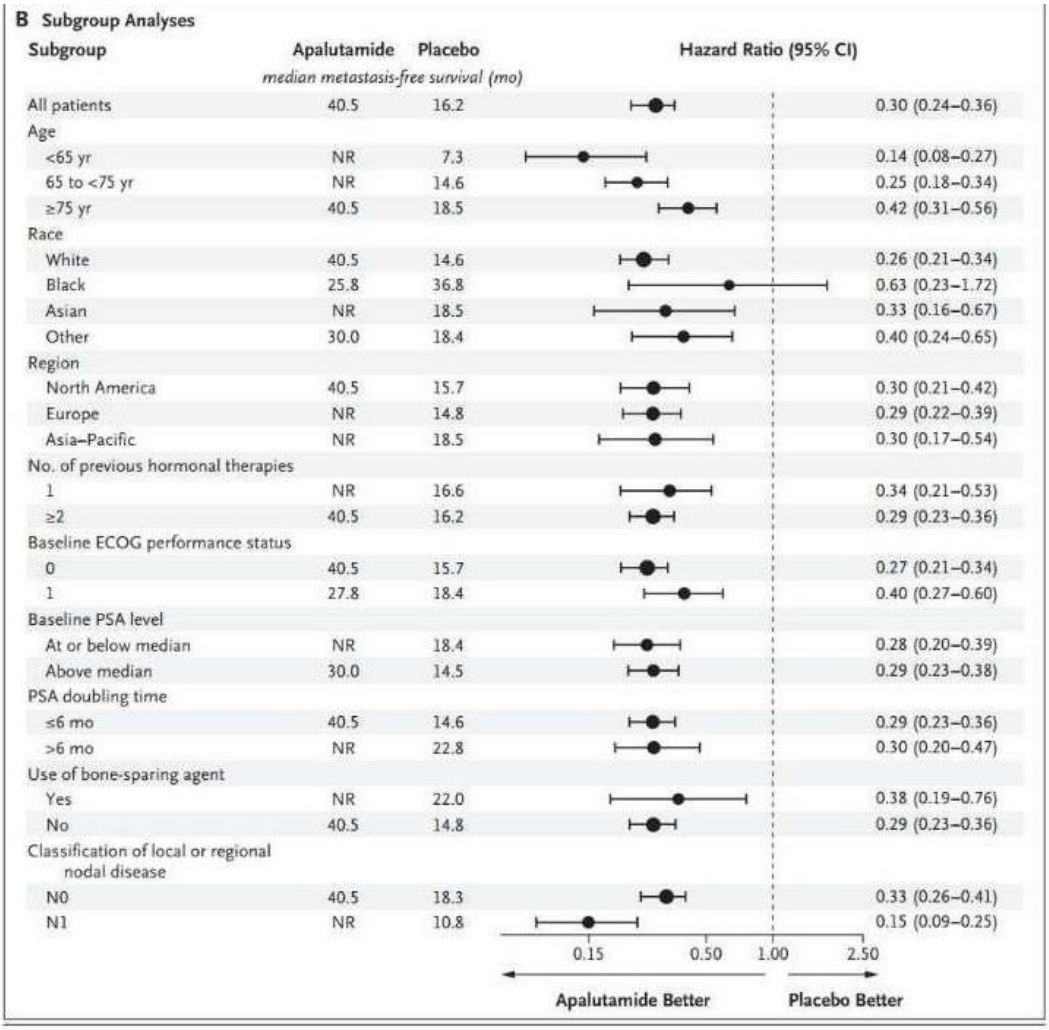


Figure 4-10 forest figure of progression free survival (FAS) (sample)

Note:
All subjects use stratified Cox regression to calculate HR. Stratified factors are random factors from EDC, and Wald method is used to calculate HR 95% CI.
In the other subgroups, HR is calculated by non-stratified Cox regression, HR 95% CI is calculated by Wald method, and median PFS is calculated by non-stratified log rank method.

Table 4-21 analysis of progression free survival (PFS) (Not treated for biliary obstruction)(month) (FAS)

index	Experimental group	Control group
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

Table 4-22 comparison results of progression free survival (PFS)(Not treated for biliary obstruction) (month) (FAS)

method	Statistical results
Principal analysis	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 1	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 2	
Statistics (P value)	X.XXX(X.XXX)

Note:
Main analysis: the patients are divided into three groups: tumor location, whether received surgery, whether received adjuvant chemotherapy or not (log rank test).
Sensitivity analysis 1: log rank test is used to adjust the stratification factors (tumor location, whether received surgery, whether received adjuvant chemotherapy) collected by IWRS.
Sensitivity analysis 2: log rank test without correction of stratification factors is used.

Table 4-23 progression free survival rate (%) at different time (month) (without treatment of biliary obstruction) (FAS)

time (month)	Experimental group						Control group					
	Number of new lesions (n)	Number of deaths (n)	Censored (n)	Exposure to risk (n)	Disease progression free rate (%)	Progression free survival 95%CI	Number of new lesions (n)	Number of deaths (n)	Censored (n)	Exposure to risk (n)	Disease progression free rate (%)	Progression free survival 95% CI
3	XX	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX	XX.X	XX.X～XX.X
6	XX	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX	XX.X	XX.X～XX.X
9	XX	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX	XX.X	XX.X～XX.X
12	XX	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX	XX.X	XX.X～XX.X
18	XX	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX	XX.X	XX.X～XX.X

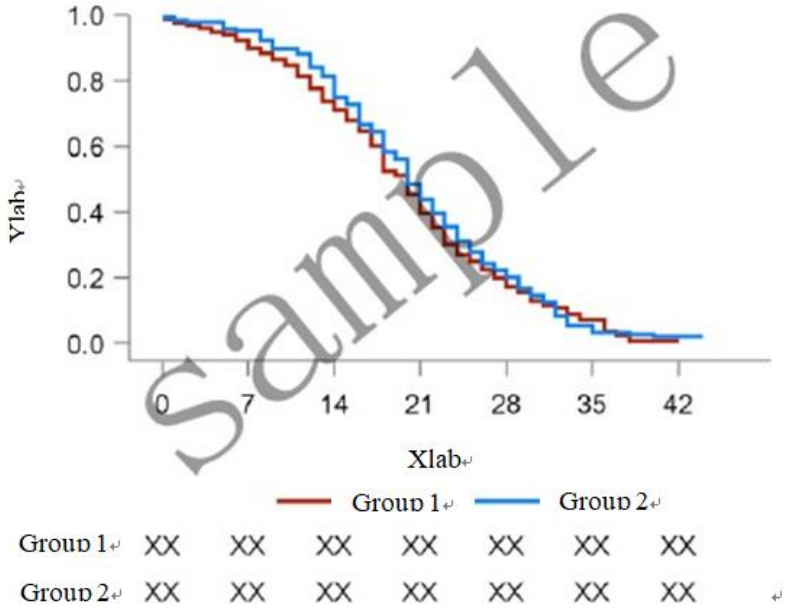


Figure 4-11 Kaplan Meier curve of progression free survival at each time point (FAS)

Table 4-24 subgroup analysis of progression free survival (PFS) (Not treated for biliary obstruction)(month) (FAS)

index	Experimental group	Control group
Tumor location		
Head of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Body and tail of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you had surgery		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you received adjuvant chemotherapy		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Diagnostic types of pancreatic cancer		
Locally advanced pancreatic adenocarcinoma		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Metastatic adenocarcinoma of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
KPS score		
60-80		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
90-100		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Gender		
male		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
female		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Age		
< 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾ 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Course of disease		
< 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾ 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Total events	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

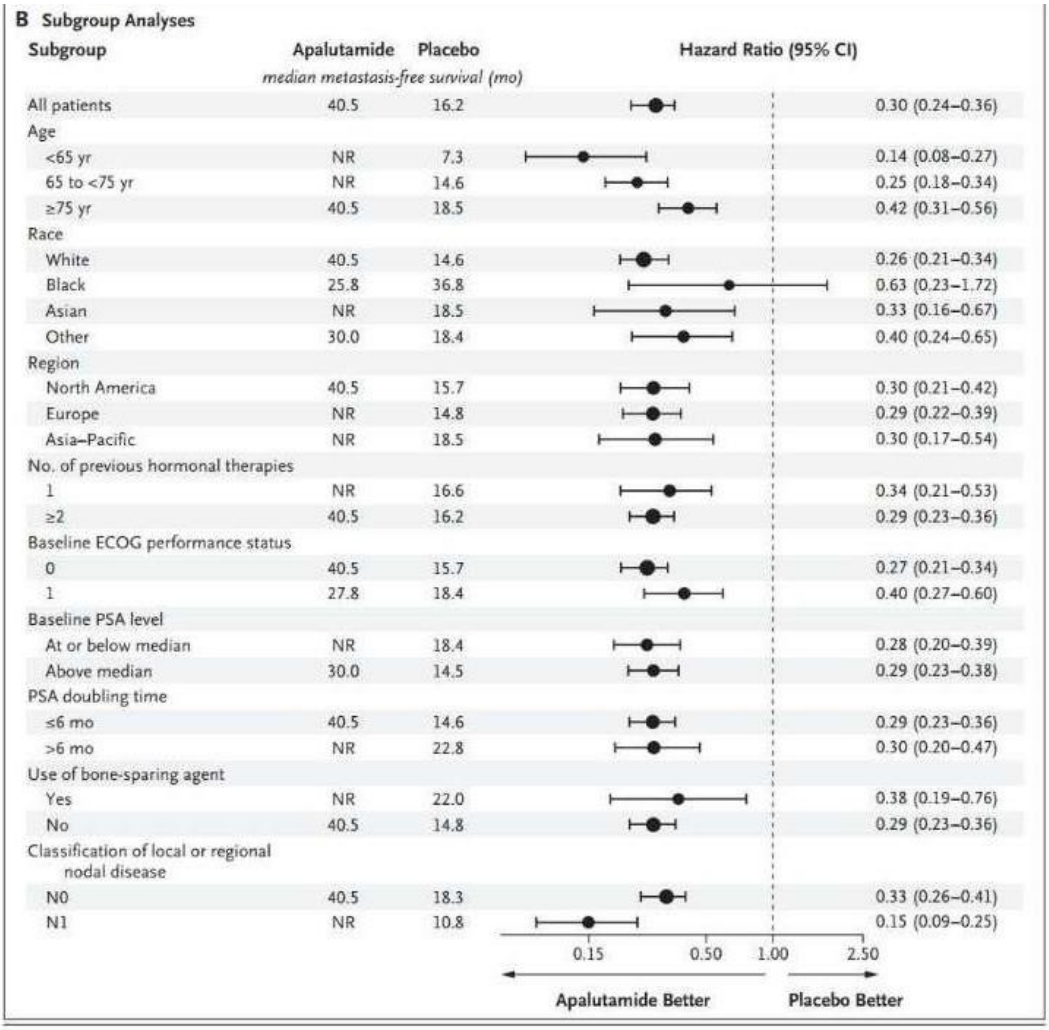


Figure 4-12 Forest figure of progression free survival (Not treated for biliary obstruction) (sample) (FAS)

Note:
Stratified Cox regression is used to calculate HR. Random factors (tumor location, surgery, adjuvant chemotherapy) are used to calculate HR. Wald method is used to calculate HR 95% CI.
In the other subgroups, HR is calculated by non -stratified Cox regression, HR 95% CI is calculated by Wald method, and median PFS is calculated by non -stratified log rank method.

4.4 Time to progression (TTP)

Table 4-25 time to progression (TTP) (month) analysis (FAS)

index	Experimental group	Control group
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of disease progression events (%)	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

Table 4-26 time to progression (TTP) (month) inter group comparison results (FAS)

method	Statistical results
Principal analysis	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 1	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 2	
Statistics (P value)	X.XXX(X.XXX)

Note:
Main analysis: log rank test is used to correct the stratified factors collected by EDC.
Sensitivity analysis 1: log rank test is used to correct stratification factors collected by IWRS.
Sensitivity analysis 2: log rank test without correction of stratification factors is used.

Table 4-27 time to disease progression rate (%) (FAS)

	Experimental group					Control group				
time (month)	Disease progression (n)	Censored (n)	Exposure to risk (n)	Disease progression rate (%)	Disease progression rate 95%CI	Disease progression (n)	Number of omissions (n)	Exposure to risk (n)	Disease progression rate (%)	Disease progression rate 95%CI
3	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
6	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
9	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
12	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
18	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X

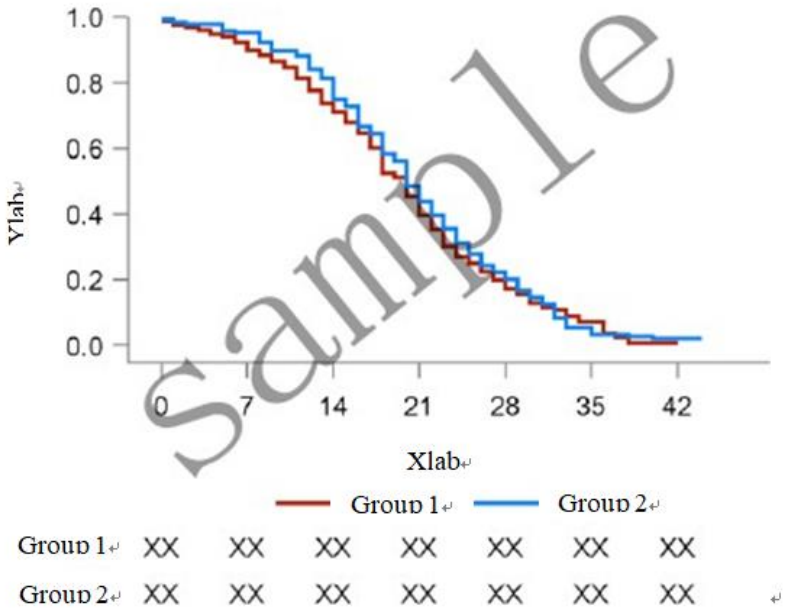


Figure 4-13 Kaplan Meier curve of disease progression rate at each time point (FAS)

Table 4-28 time to progression (TTP) (month) subgroup analysis (FAS)

index	Experimental group	Control group
Tumor location		
Head of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Body and tail of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you had surgery		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)

Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have biliary obstruction been treated		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you received adjuvant chemotherapy		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Diagnostic types of pancreatic cancer		
Locally advanced pancreatic adenocarcinoma		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Metastatic adenocarcinoma of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
KPS score		
60-80		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
90-100		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Gender		
male		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
female		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Age		
< 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
≥ 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Course of disease		
< 1 year		

N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾ 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

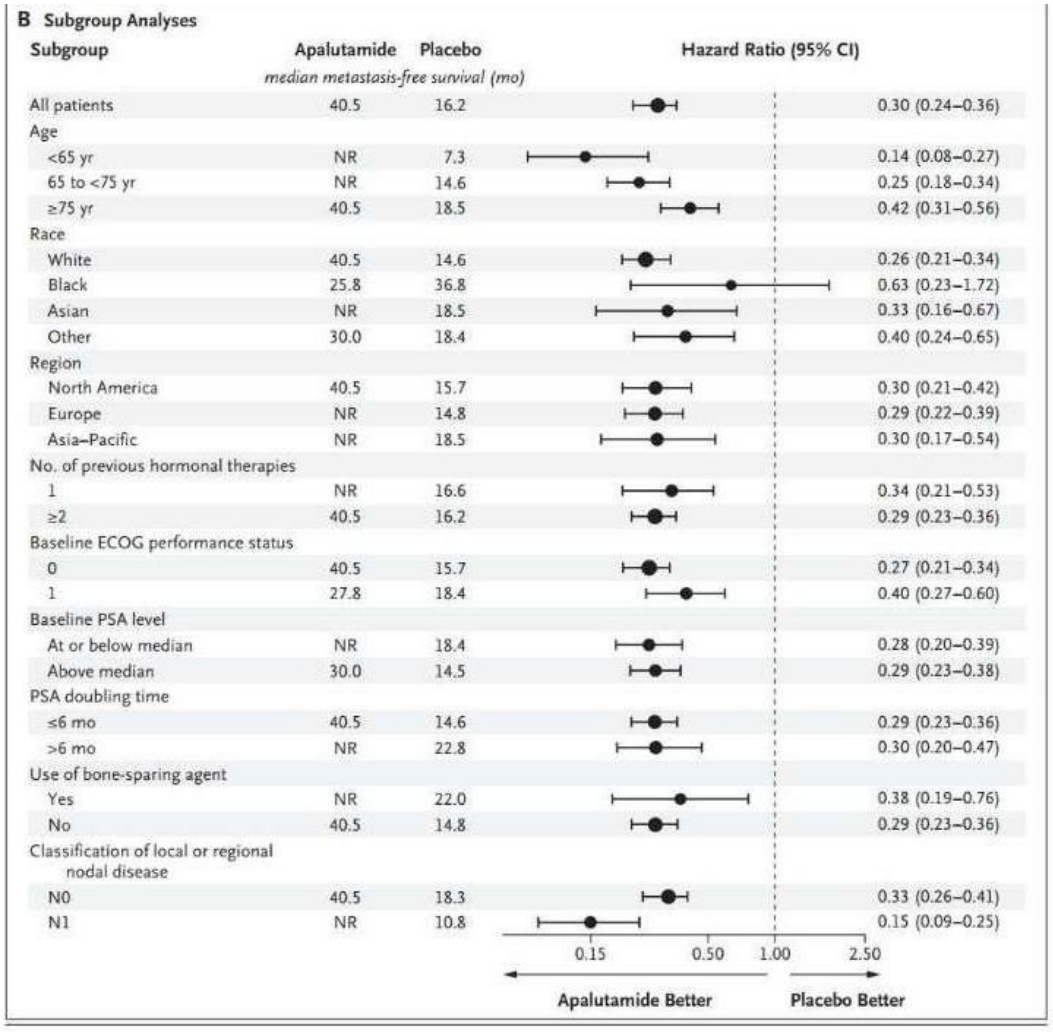


Figure 4-14 forest figure of disease progression time (sample figure) (FAS)

Note:
All subjects are stratified Cox regression to calculate HR. Stratified factors are random factors from EDC, and Wald method is used to calculate HR 95% CI;
In the other subgroups, HR is calculated by non-stratified Cox regression, HR 95% CI is calculated by Wald method, and median TTP is calculated by non -stratified log rank method.

Table 4-29 analysis of time to progression (TTP) (month) (FAS)

index	Experimental group	Control group
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of disease progression events (%)	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

Table 4-30 time to progression (TTP) (month) results between groups (without treatment of biliary obstruction)(FAS)

method	Statistical results
Principal analysis	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 1	
Statistics (P value)	X.XXX(X.XXX)
Sensitivity analysis 2	
Statistics (P value)	X.XXX(X.XXX)

Note:
Main analysis: the patients are divided into three groups: tumor location, whether received surgery, whether received adjuvant chemotherapy or not to do log rank test.
Sensitivity analysis 1: log rank test is used to adjust the stratification factors (tumor location, whether received surgery, whether received adjuvant chemotherapy) collected by IWRS.
Sensitivity analysis 2: log rank test without correction of stratification factors is used.

Table 4-31 disease progression rate (%) at different time (month) (without treatment of biliary obstruction) (FAS)

time (month)	Experimental group					Control group				
	Disease progression (n)	Censored (n)	Exposure to risk (n)	Disease progression rate (%)	Disease progression rate 95%CI	Disease progression (n)	Number of omissions (n)	Exposure to risk (n)	Disease progression rate (%)	Disease progression rate 95%CI
3	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
6	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
9	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
12	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X
18	XX	XX	XX	XX.X	XX.X～XX.X	XX	XX	XX	XX.X	XX.X～XX.X

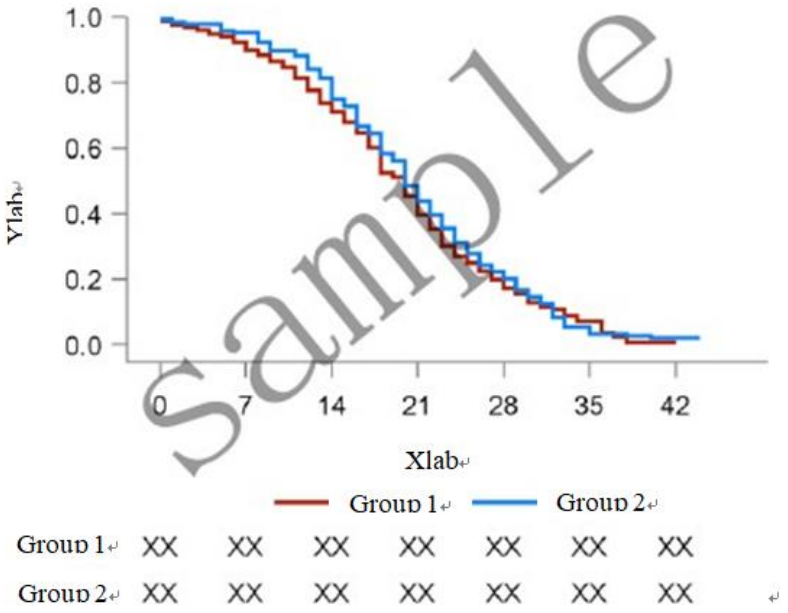


Figure 4-15 Kaplan Meier curve of disease progression rate at each time point (Not treated for biliary obstruction) (FAS)

Table 4-32 time to progression (TTP) (month) subgroup analysis (Not treated for biliary obstruction) (FAS)

index	Experimental group	Control group
Tumor location		
Head of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Body and tail of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you had surgery		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX

Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Have you received adjuvant chemotherapy		
yes		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
no		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Diagnostic types of pancreatic cancer		
Locally advanced pancreatic adenocarcinoma		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Metastatic adenocarcinoma of pancreas		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
KPS score		
60-80		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
90-100		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		

25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Gender		
male		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
female		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Age		
< 65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾65 years old		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
Course of disease		
< 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
⩾ 1 year		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Progressive events	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

index	Experimental group	Control group
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)

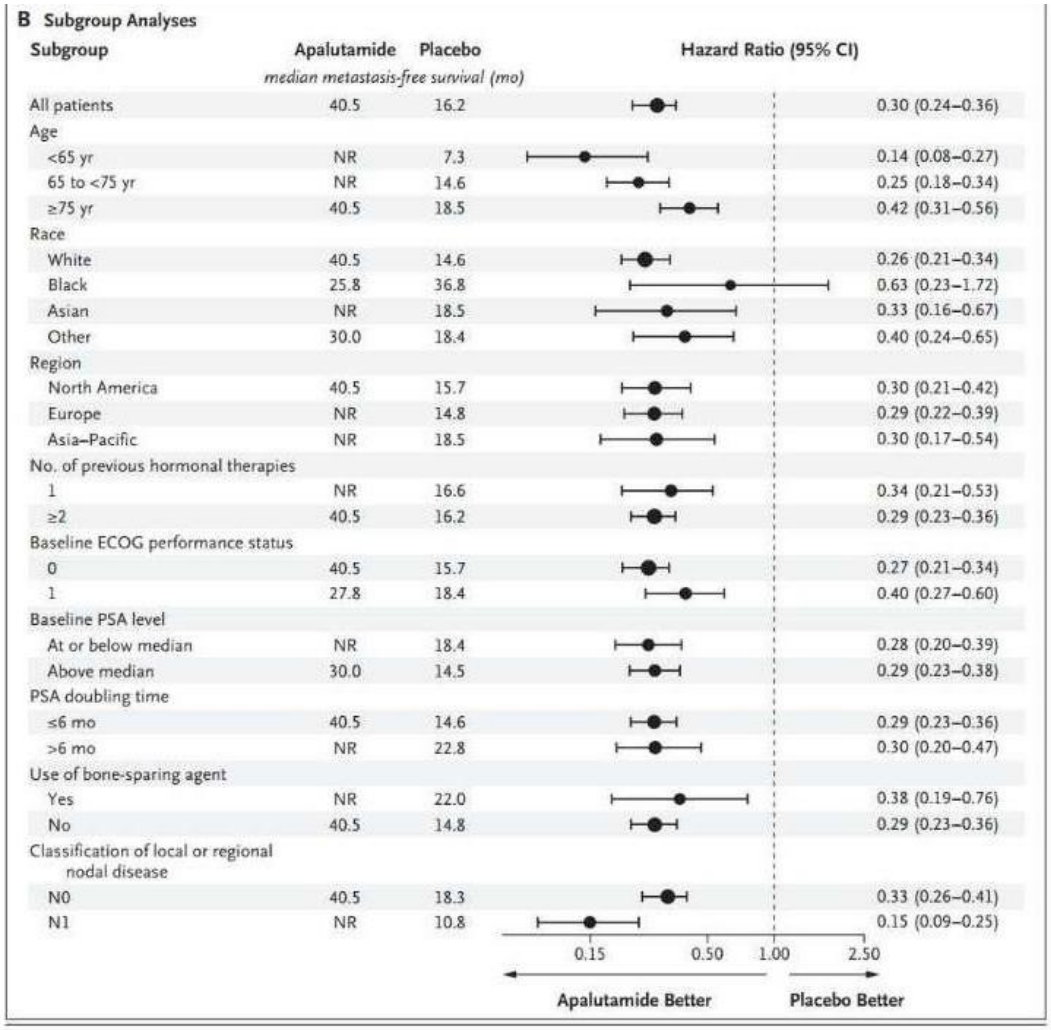


Fig. 4-16 forest chart of disease progression time

(sample figure without biliary obstruction treatment) (FAS)

Note:
Stratified Cox regression is used to calculate HR. Random factors (tumor location, surgery, adjuvant chemotherapy) are used to calculate hr. Wald method is used to calculate HR 95% CI.
In the other subgroups, HR is calculated by non-stratified Cox regression, HR 95% CI is calculated by Wald method, and median TTP is calculated by non-stratified log rank method.

4.5 Objective remission rate analysis

Table 4-33 objective response rate (ORR) analysis (FAS)

	Experimental group	Control group	statistic	P value	method
N	XX	XX			
CR n(%)	XX(XX.X)	XX(XX.X)			
PR n(%)	XX(XX.X)	XX(XX.X)			
SD n(%)	XX(XX.X)	XX(XX.X)			
PD n(%)	XX(XX.X)	XX(XX.X)			
NE n(%)	XX(XX.X)	XX(XX.X)			
ORR	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
ORR 95%CI	XX.X～XX.X	XX.X～XX.X			

Table 4-34 logistic regression (FAS) of related factors of objective response rate (ORR)

variable		parameter estimation	Standard error	Wald χ^2	P value	OR value	ORvalue 95% CI
Intercept term		X.XXX	X.XXX	X.XXX			
group	Experimental group vs Control group	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX~X.XXX
Tumor location	Head of pancreas vs body and tail of pancreas	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX~X.XXX
…		X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX~X.XXX

The correction factors in logistic model are the same as subgroup factors.

Figure 4-17 forest figure of objective response rate (ORR) logistic regression analysis (FAS)

Table 4-35 objective response rate (ORR) analysis (without treatment for biliary obstruction) (FAS)

	Experimental group	Control group	statistic	P value	method
N	XX	XX			
CR n(%)	XX(XX.X)	XX(XX.X)			
PR n(%)	XX(XX.X)	XX(XX.X)			
SD n(%)	XX(XX.X)	XX(XX.X)			
PD n(%)	XX(XX.X)	XX(XX.X)			
NE n(%)	XX(XX.X)	XX(XX.X)			
ORR	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
ORR 95%CI	XX.X～XX.X	XX.X～XX.X			

Table 4-36 logistic regression of objective response rate (ORR) (FAS)

variable		parameter estimation	Standard error	Wald χ^2	P value	OR value	OR value 95% CI
Intercept term		X.XXX	X.XXX	X.XXX			
group	Experimental group vs Control group	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX~X.XXX
Tumor location	Head of pancreas vs body and tail of pancreas	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX~X.XXX
…		X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX~X.XXX

The correction factors in logistic model are the same as subgroup factors.

Figure 4-18 forest figure of objective response rate (ORR) logistic regression analysis (FAS)

4.6 Analysis of disease control rate

Table 4-37 disease control rate (DCR) analysis (FAS)

	Experimental group	Control group	statistic	P value	method
N	XX	XX			
CR n(%)	XX(XX.X)	XX(XX.X)			
PR n(%)	XX(XX.X)	XX(XX.X)			
SD n(%)	XX(XX.X)	XX(XX.X)			
PD n(%)	XX(XX.X)	XX(XX.X)			
NE n(%)	XX(XX.X)	XX(XX.X)			
DCR	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
DCR 95%CI	XX.X～XX.X	XX.X～XX.X			

DCR: the best overall assessment is the proportion of patients with confirmed complete and partial remission and stable disease. For patients with stable disease, at least one lesion evaluation should meet the SD criteria at least 6 weeks after medication.

Table 4-38 analysis of disease control rate (DCR) (without treatment for biliary obstruction) (FAS)

	Experimental group	Control group	statistic	P value	method
N	XX	XX			
CR n(%)	XX(XX.X)	XX(XX.X)			
PR n(%)	XX(XX.X)	XX(XX.X)			
SD n(%)	XX(XX.X)	XX(XX.X)			
PD n(%)	XX(XX.X)	XX(XX.X)			
NE n(%)	XX(XX.X)	XX(XX.X)			
DCR	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
DCR 95%CI	XX.X～XX.X	XX.X～XX.X			

DCR: the best overall assessment is the proportion of patients with confirmed complete and partial remission and stable disease. For patients with stable disease, at least one lesion evaluation should meet the SD criteria at least 6 weeks after medication.

4.7 Clinical benefit response analysis

Table 4-39 clinical benefit rate (CBR) analysis (FAS)

	Experimental group	Control group	statistic	P value	method
N	XX	XX	X.XXX	X.XXX	Chisq/Fisher
Effective n%	XX(XX.X)	XX(XX.X)			
Stable / ineffective n%	XX(XX.X)	XX(XX.X)			

Table 4-40 analysis of clinical benefit rate (CBR) (without treatment for biliary obstruction) (FAS)

	Experimental group	Control group	statistic	P value	method
N	XX	XX	X.XXX	X.XXX	Chisq/Fisher
Effective n%	XX(XX.X)	XX(XX.X)			
Stable / ineffective n%	XX(XX.X)	XX(XX.X)			

5. Safety analysis

5.1 Analysis of adverse events

Table 5-1 incidence analysis of TEAE (SS)

index	Experimental group	Control group	statistic	P value	method
N	XXX	XXX			
TEAE n(%)	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
ADR n(%)	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
SAE n(%)	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
SADR n(%)	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
Leading to drug reduction or suspension TEAE n%	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
Leading to drug reduction or suspension ADR n%	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
Lead to drug withdrawal TEAE n%	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
Leading to drug withdrawal ADR n%	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
Cause death TEAE n%	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
Cause death ADR n%	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
TEAE leading to withdraw n%	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher
ADR leading to withdraw n%	XX(XX.X)	XX(XX.X)	X.XXX	X.XXX	Chisq/Fisher

Note: the relationship with the study drug is definitely related, likely to be related, and may be related, which are all regarded as drug-related TEAEs.

Table 5-2 TEAE systematic organ classification(SS)
Table 5-3 ADR systematic organ classification(SS)
Table 5-4 SAE systematic organ classification(SS)
Table 5-5 SADR systematic organ classification(SS)
Table 5-6 TEAE subsystem analysis leading to study drug reduction or suspension (SS)
Table 5-7 ADR systematic organ classification leading to study drug reduction or suspension (SS)
Table 5-8 TEAE systematic organ classification leading to study drug withdrawal (SS)
Table 5-9 ADR systematic organ classification leading to study drug discontinuation (SS)
Table 5-10 TEAE systematic organ classification leading to death (SS)
Table 5-11 Analysis of death caused by ADR
Table 5-12 TEAE systematic organ classification leading to withdrawal trial (SS)
Table 5-13 ADR systematic organ classification leading to withdrawal trial (SS)

SOC	Experimental group		Control group	
PT	Number of cases	Frequency	Number of cases	Frequency
N	XX X		XXX	
Total N%	XXX(XX.X)	XXX	XXX(XX.X)	XXX
SOC1 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT1 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT2 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
…				
SOC2	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT1 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT2 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
…				
SOC3	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT1 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT2 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
…				

Note:
MedDRA 24.0 is used for coding. SOC and PT were arranged in descending order according to the Total number of AE cases.

n: patients are counted once within each System Organ Class (SOC) and Preferred Term (PT)..
.Percentages are based on the number of patients in safety population.
N: The Total number of subjects in each group in the safety analysis set..
%The percentage of adverse events in the Total number of subjects in each group..

Table 5-14 TEAE systematic organ classification (SS)
Table 5-15 ADR systematic organ classification (SS)
Table 5-16 SAE systematic organ classification (SS)
Table 5-17 SADR systematic organ classification with different severity (SS)
Table 5-18 TEAE systematic organ classification with different severity leading to study drug reduction or suspension (SS)
Table 5-19 ADR systematic organ classification with different severity leading to study drug reduction or suspension (SS)
Table 5-20 TEAE systematic organ classification with different severity leading to study drug withdrawal (SS)
Table 5-21 ADR systematic organ classification of ADR with different severity leading to study drug withdrawal (SS)
Table 5-22 TEAE systematic organ classification with different severity leading to death (SS)
Table 5-23 ADR systematic organ classification with different severity leading to death (SS)
Table 5-24 TEAE systematic organ classification with different severity leading to withdrawal (SS)
Table 5-25 ADR systematic organ classification leading to withdrawal test with different severity (SS)

Systematic organ classification	Experimental group		Control group	
Preferred term Severity	n(%)	events	n(%)	events
N	XXX		XXX	
Total N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 1 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 2 n%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 3 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 4 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 5 N%	XX(XX.X)	XX	XX(XX.X)	XX
SOC1 n(%)	XX(XX.X)	XX	XX(XX.X)	XX
Grade 1 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 2 n%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 3 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 4 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 5 N%	XX(XX.X)	XX	XX(XX.X)	XX
PT1 n(%)	XX(XX.X)	XX	XX(XX.X)	XX
Grade 1 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 2 n%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 3 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 4 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 5 N%	XX(XX.X)	XX	XX(XX.X)	XX
PT2 n(%)	XX(XX.X)	XX	XX(XX.X)	XX
Grade 1 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 2 n%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 3 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 4 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 5 N%	XX(XX.X)	XX	XX(XX.X)	XX
…				
SOC2 n(%)	XX(XX.X)	XX	XX(XX.X)	XX
Grade 1 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 2 n%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 3 N%	XX(XX.X)	XX	XX(XX.X)	XX

Grade 4 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 5 N%	XX(XX.X)	XX	XX(XX.X)	XX
PT1 n(%)	XX(XX.X)	XX	XX(XX.X)	XX
Grade 1 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 2 n%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 3 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 4 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 5 N%	XX(XX.X)	XX	XX(XX.X)	XX
PT2 n(%)	XX(XX.X)	XX	XX(XX.X)	XX
Grade 1 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 2 n%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 3 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 4 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 5 N%	XX(XX.X)	XX	XX(XX.X)	XX
…				
SOC3 n(%)	XX(XX.X)	XX	XX(XX.X)	XX
Grade 1 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 2 n%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 3 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 4 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 5 N%	XX(XX.X)	XX	XX(XX.X)	XX
PT1 n(%)	XX(XX.X)	XX	XX(XX.X)	XX
Grade 1 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 2 n%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 3 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 4 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 5 N%	XX(XX.X)	XX	XX(XX.X)	XX
PT2 n(%)	XX(XX.X)	XX	XX(XX.X)	XX
Grade 1 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 2 n%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 3 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 4 N%	XX(XX.X)	XX	XX(XX.X)	XX
Grade 5 N%	XX(XX.X)	XX	XX(XX.X)	XX
…				

Note:
MedDRA 24.0 is used for coding. The number of PT and SOC is in descending order.
n: If a patient experienced more than one adverse event, the patient is counted only once within a SOC or PT with the maximum severity. .
Percentages are based on the number of patients in safety population..
N: The Total number of subjects in each group in the safety analysis set.
%The percentage of adverse events in the Total number of subjects in each group.

Table 5-26 analysis of adverse events with incidence > 10% (SS)

SOC	Experimental group		Control group	
PT	Number of cases	Frequency	Number of cases	Frequency
N	XXX		XXX	
SOC1 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT1 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT2 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
…				
SOC2 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT1 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT2 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
…				

SOC3 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT1 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
PT2 n(%)	XXX(XX.X)	XXX	XXX(XX.X)	XXX
…				

Note:
adverse events with PT incidence > 10% in the trial group or Control group will be included.
PT is arranged in descending order according to the number of AE cases.

5.2 Analysis of laboratory criteria

Table 5-27 white blood cell baseline and post medication outcome evaluation shift table (SS)
Table 5-28 neutrophil baseline and post medication outcome evaluation shift table (SS)
Table 5-29 hemoglobin baseline and post medication result evaluation shift table (SS)
Table 5-30 platelet baseline and post medication result evaluation shift table (SS)
Table 5-31 shift table of evaluation of C-reactive protein baseline and post medication results (SS)
Table 5-32 shift table of glutamic pyruvic transaminase baseline and post medication result evaluation (SS)
Table 5-33 shift table of baseline and post-administration evaluation of aspartate aminotransferase
Table 5-34 shift table of alkaline phosphatase baseline and post medication result evaluation (SS)
Table 5-35 shift table of Total bilirubin baseline and post medication result evaluation (SS)
Table 5-36 shift table of direct bilirubin baseline and post medication outcome evaluation (SS)
Table 5-37 shift table of urea nitrogen baseline and post medication result evaluation (SS)
Table 5-38 shift table of creatinine baseline and post medication outcome evaluation (SS)
Table 5-39 potassium baseline and post medication result evaluation cross
Table 5-40 sodium baseline and post medication result evaluation shift table (SS)
Table 5-41 chloride baseline and post medication result evaluation shift table (SS)
Table 5-42 calcium baseline and post medication result evaluation shift table (SS)
Table 5-43 shift table of baseline and post medication evaluation of magnesium (SS)
Table 5-44 CA19-9 shift table of baseline and post medication outcome evaluation (SS)

group	baseline				
Most extreme post-baseline visit value	N	normal	NCS	CS	ND
	n(%)	n(%)	n(%)	n(%)	n(%)
Experimental group					
N n(%)	XX	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
Normal n%	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
NCS n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
CS n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
ND n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
Control group					
N n(%)	XX	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
Normal n%	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
NCS n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
CS n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
ND n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)

Note: the judgment of clinical significance after medication is recorded by the most serious judgment.

Table 5-45 analysis of leukocyte changes (SS)

Visit	Experimental group	Control group
C1D8		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
…		
N	XXX	XXX

Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
CxDx		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX

Table 5-46 analysis of leukocyte changes (SS)

Visit	Experimental group	Control group
baseline		
N	XXX	XXX
Mean±SD	XX.XX±X.XX	XX.XX±X.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
C1D8		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
…		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
CxDx		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX

Repeat the following Table:
Table 5-47 analysis of neutrophil changes (SS)
Table 5-48 analysis of measured neutrophil changes (SS)
Table 5-49 analysis of hemoglobin changes (SS)
Table 5-50 analysis of measured hemoglobin changes (SS)
Table 5-51 analysis of platelet changes (SS)
Table 5-52 analysis of measured platelet changes (SS)
Table 5-53 analysis of C reaction protein changes (SS)
Table 5-54 analysis of measured C reaction protein changes (SS)
Table 5-55 analysis of ALT changes (SS)
Table 5-56 analysis of measured ALT changes (SS)
Table 5-57 analysis of AST changes (SS)
Table 5-58 analysis of measured AST changes (SS)
Table 5-59 analysis of ALP changes (SS)
Table 5-60 analysis of measured ALP changes (SS)
Table 5-61 analysis of total bilirubin changes (SS)
Table 5-62 analysis of measured total bilirubin changes (SS)

5.3 Analysis of electrocardiogram

Table 5-81 analysis of HR by visit(times / min)

Visit	Experimental group	Control group
C1D8		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
…		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
CxDx		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX

Note: visits include: 8 ~ 144wk, once every 8 weeks.

Table 5-82 analysis of measured HR (times / min) (SS)

Visit	Experimental group	Control group
baseline		
N	XXX	XXX
Mean±SD	XX.XX±X.XX	XX.XX±X.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX

Visit	Experimental group	Control group
C1D8		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
…		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
CxDx		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX

Note: visit includes: baseline, 8 ~ 144wk, once every 8 weeks.

Repeat the following Table:
Table 5-83 analysis of RR interval (ms) (SS)
Table 5-84 analysis of measured RR interval (ms) (SS)
Table 5-85 analysis of PR interval (ms)
Table 5-86 analysis of measured PR interval (ms)
Table 5-87 analysis of QRS interval (ms)
Table 5-88 analysis of measured QRS interval (ms)
Table 5-89 analysis of QT interval (ms) (SS)
Table 5-90 analysis of measured QT interval (ms) (SS)
Table 5-91 analysis of QTc (ms) (SS)
Table 5-92 analysis of measured QTc (ms) changes (SS)
Table 5-93 analysis of QTc absolute prolongation after administration (SS)

	Experimental group	Control group	Total
N	XX	XX	XX
450ms<QTc≤480ms	XX(XX.X)	XX(XX.X)	XX(XX.X)
480ms<QTc≤500ms	XX(XX.X)	XX(XX.X)	XX(XX.X)
QTc>500ms	XX(XX.X)	XX(XX.X)	XX(XX.X)

Note: the QTc maximum after baseline is recorded.

Table 5-94 analysis of QTc relative prolongation after administration (SS)

	Experimental group	Control group	Total
N	XX	XX	XX
30ms<ΔQTc≤60ms	XX(XX.X)	XX(XX.X)	XX(XX.X)
ΔQTc>60ms	XX(XX.X)	XX(XX.X)	XX(XX.X)

Table 5-95 shift table of ECG baseline and post medication evaluation (SS)

group	baseline				
After medication	N	normal	NCS	CS	ND
	n(%)	n(%)	n(%)	n(%)	n(%)

group	baseline				
Most extreme post-baseline visit value	N	normal	NCS	CS	ND
	n(%)	n(%)	n(%)	n(%)	n(%)
Experimental group					
N n(%)	XX	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
Normal n%	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
NCS n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
CS n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
ND n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
Control group					
N n(%)	XX	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
Normal n%	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
NCS n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
CS n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
ND n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)

Note: the judgment of clinical significance after medication is recorded by the most serious judgment.

5.4 Vital signs analysis

Table 5-96 analysis of body temperature (℃) change (SS)

Visit	Experimental group	Control group
C1D1		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
…		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
CxDx		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX

Note: the visit includes: 1 ~ 144wk, once a week.

Table 5-97 analysis of measured body temperature (℃)

Visit	Experimental group	Control group
baseline		
N	XXX	XXX
Mean±SD	XX.XX±X.XX	XX.XX±X.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
C1D1		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX

Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
…		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX
CxDx		
N	XXX	XXX
Mean±SD	XX.XX±XX.XX	XX.XX±XX.XX
Median	XX.XX	XX.XX
Q1~Q3	XX.XX~XX.XX	XX.XX~XX.XX
Min~Max	XX.XX~XX.XX	XX.XX~XX.XX

Note: the visit includes: 1 ~ 144wk, once a week.

Repeat the following Table:
Table 5-98 analysis of pulse rate (beats / min) (SS)
Table 5-99 analysis of measured pulse rate (SS)
Table 5-100 analysis of change value of respiration (time / min)
Table 5-101 analysis of measured value of respiration (time / min)
Table 5-102 analysis of systolic blood pressure (mmHg)
Table 5-103 analysis of measured systolic blood pressure (SS)
Table 5-104 analysis of diastolic blood pressure (SS)
Table 5-105 analysis of measured diastolic blood pressure (SS)
Table 5-106 analysis of changes in height (cm)
Table 5-107 analysis of measured height (cm)
Table 5-108 analysis of weight (kg)
Table 5-109 analysis of measured weight (kg) (SS)

5.5 Analysis of physical examination

Table 5-110 shift table of baseline and post medication evaluation of physical examination (SS)

index	baseline			
group	N	normal	abnormal	ND
Most extreme post-baseline visit value	n(%)	n(%)	n(%)	n(%)
N n(%)	XX	XX(X.X)	XX(X.X)	XX(X.X)
Normal n%	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
Abnormal n%	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)
ND n(%)	XX(X.X)	XX(X.X)	XX(X.X)	XX(X.X)

Note: the judgment of clinical significance after medication is recorded by the most serious judgment.

List 1: completion of subjects

List 1-1 subjects not enrolled (Screening subjects)

Screening number	Screening failure reason	Screening failure reason classification

List 1-2 trial completion (randomized subjects)

group	center	Random number	Gender	Age (yr)	Complete the test	Last treatment period	Completion date	Exit date	Reasons for exit	Other reasons	Details of adverse events
					Yes / no						

List1-3 follow up summary list (randomized subjects)

group	center	Random number	Gender	Age (yr)	Follow up end date	Reasons for the end of follow-up	Other reasons	Date of death	Lost date

List1-4 follow up (randomized subjects)

group	center	Random number	Gender	Age (yr)	follow-up	Follow up method	Follow up date	Survival state	KPS score	Whether adverse events occurred within 1 month after the last use of the trial drug	Any anti-tumor treatment	Anti tumor treatment details	To judge whether the disease progression	Progress day stage	Judging by evidence
					Yes / no						Yes / no				

List 1-5 subjects with protocol deviation (randomized subjects)

group	center	Random number	Gender	Age (yr)	Protocol deviation classification	Specific description of protocol deviation	Severity

…	…	…			…	…	…

List 1-6 details of subject population division (randomized subjects)

group	center	Random number	Gender	Age (yr)	PPS	FAS	SS	Cause classification	Detailed description of the cause

List 2 demographic data

List 2-1 subject data (FAS)

group	center	Random number	sign Informed date	Date of visit	date of birth	Age (yr)	Gender	Height (cm)	Weight (kg)	Body surface area (m^2)	nation	occupation	Native place

List medical history

List 3-1 surgical history (FAS)

group	center	Random number	gender	Age (yr)	History of surgery	Surgery type	Surgery time	Reasons for implementation	Selective surgery meter Draw	Elective surgery type	Elective surgery time	Implementation of elective surgery reason
					Yes / no							

List 2-2 current history of cancer (FAS)

group	center	Random number	Gender	Yr (age)	Date of first diagnosis	Course of disease (month)	Pathological type	Diagnosis type	Other types	Tumor site	TNM score stage	chemotherapy	Chemotherapy regimen	start time	End time	radiotherapy	Radiotherapy plan	start time	End time	Biliary obstruction
												yes / no				yes / no				yes / no

List 3-2 allergy history (FAS)

group	center	Random number	Drug allergy	Drug description
			Yes / no	

List 3-3 concomitant diseases (FAS)

group	center	Random number	Gender	Age (yr)	Concomitant diseases	Name of disease	start time	End time	At present, it continues
					Yes / no				Yes / no

List 3-4 concomitant treatment (FAS)

group	center	Random number	Gender	Age (yr)	Concomitant therapy	Generic name of drug	ATC1	ATC2	ATC5	Total daily dose	Reasons for use	start time	End time	Continue to use
					Yes/ nothing									Yes / no

List 3-5 KRAS gene mutation detection (FAS)

group	center	Random number	Gender	Age (yr)	Name of visit	Inspection date	Inspection results

List 4 details of medication compliance and combined drug use

List 4-1 details of test drug medication compliance (SS)

group	center	random number	gender	year age (yr)	body heavy (kg)	Administration	Drug number	Dosage	Recovery medicine	At the time of administration	Administration dosage	Is the medication administered during administration	down regulation dosage	Down regulation time	The dosage of down regulating agent	Reasons for downward adjustment	Is it suspended during administration drug	Start time of drug suspension	End time of drug suspension	Reasons for drug suspension
						Yes/ no														

List 4-2 details of gemcitabine medication compliance (SS)

group	center	random number	gender	year age (yr)	body heavy (kg)	Administration	At the time of administration	Dosage Administration	During the administration, whether the dosage is down	Dosage down time	Dosage after down the administration	Reasons for down dosage	Is the Administration suspended Medication	Start time of drug suspension	End time of drug suspension	Reasons for drug suspension
						Yes/ no										

List 4-3 details of previous medication (SS)

List 4-4 details of combined medication (SS)

group	center	Random number	Gender	Yr (age)	Body weight (kg)	neric name of drug	ATC 1	ATC 2	ATC 5	Dosage per time	Specifications	requency of administration	Route of administration	Reasons for medication	Date of medication	End date of medication	The last visit is still taking

Note: it is arranged by group, center, random number, start date, end date and drug name.

List 5 relevant indicators for efficacy evaluation

List 5-1 clinical benefit response (FAS)

TFLs for Statistical Analysis Plan

group	center	Random number	gender	Age (yr)	weight (kg)	Name of visit	Whether to carry out clinical benefit Reaction evaluation	Pain intensity (mm)	Analgesics name	Analgesics consume	KPS score	Clinical benefit assessment classification

List 5-2 tumor imaging assessment-1 (FAS)

group	center	Random number	Gender	Age (yr)	weight (kg)	Name of visit	Target lesion	Target lesion site	Date of determination	measuring method	Other methods	Measurement type	measurement result (mm)	The lesions had special changes	Details of changes	Sum of measurement results (mm)
							Yes/no							Yes / no		

List5-3 tumor imaging assessment-2 (FAS)

group	center	Random number	Gender	Age (yr)	weight (kg)	Name of visit	Non-target lesions	Non target lesion site	Date of determination	measuring method	Other methods	Measurement type	measurement result (mm)	Lesion changes	New lesions	Date of discovery	New diseases Details
							Yes / no								Yes/nothing		

List 5-4 efficacy evaluation (FAS)

group	center	Random number	nature other	Age (yr)	weight (kg)	Name of visit call	Daily assessment stage	Target lesion assessment	Target lesion He assessed	Non-target lesions assessment	Non target lesions He assessed	Overall efficacy assessment	The other-side overall effect

List5-5 overall survival (OS) and related lists (FAS)

group	center	Random number	Gender	Age (yr)	Weight (kg)	Random date	Calculate OS date	Censored status	OS(month)	Date of death	Final confirmation of survival date	Reasons for censoring

List5-6 progression free survival (PFS) and related lists (FAS)

group	center	Random number	gender	Age (yr)	weight (kg)	random date	Calculate PFS date	censored state	PFS(month)	progress date	death date	Last valid Imaging examination date	New anti-tumor therapy Treatment start date	censored reason

List 5-7 TTP and FAS

group	center	Random number	nature other	Age (yr)	weight (kg)	random date	Calculate TTP date	censored state	TTP(month)	progress date	Last valid shadow Date of imaging examination	New antitumor therapy Start date	censored reason

List 6 detailed adverse events

list 6-1 TEAE details (SS)

list 6-2 ADR details (SS)

list 6-3 SAE details (SS)

list 6-4 SADR details (SS)

list 6-5 TEAEs leading to reduction or suspension of study drug

list 6-6 ADRs causing reduction or suspension of study drug (SS)

list 6-7 TEAEs leading to withdrawal of study drug (SS)

list 6-8 ADRs leading to study drug withdrawal (SS)

list 6-9 TEAEs leading to death (SS)

list 6-10 ADRs causing death (SS)

list 6-11 TEAEs leading to withdrawal of trial (SS)

list 6-12 ADRs leading to withdrawal of trial (SS)

group	center	Random number	Gender	Age (Yr)	Body weight (kg)	AE name	PT	SOC	Start date	NCI-CTCAE4.0 classification	Measures taken for the study medication	Other drugs Treatment	Correlation with study drug	SAE	Adverse event outcome	Date of recovery	Recovery date	Sequela	Remission date	Date of death	AE sign out
														Yes / no							yes / no

Note: it is arranged by group, center, random number, AE start date and AE name.
MedDRA 23.0 or above is used for coding.

List 6-13 SAE detailed -1 (SS)

group					
center					
Random number					
Report type					
Reporting time					
Name of medical institution and specialty					
Telephone					
Name of sponsor					

Telephone number of sponsor unit					
Chinese name of trial drug					
English name of trial drug					
Drug category					
What kind of drugs					
Clinical study staging					
Drug dosage form					
Subject abbreviation					
Gender					
date of birth					
national					
Subject disease diagnosis					
SAE situation					
Time of SAE occurrence					
SAE response severity					
Measures for the trial drug					
SAE outcome					
sequela					
Time of death					
Relationship between SAE and trial drug					
Breaking blindness					
Domestic reports of SAE					
Foreign reports of SAE					

List 6-14 SAE detailed-2 (SS)

group	center	Random number	Report type	Detailed description of SAE

List 7 abnormal value list of laboratory examination

list 7-1 abnormal blood routine values (normal baseline → abnormal after treatment) (SS)
list 7-2 abnormal value list of blood routine (baseline NCS → CS after treatment) (SS)
list 7-3 measured blood routine values (SS)

group	center	Random number	Gender	Age (yr)	Weight (kg)	Name of visit	Sampling date	Inspection index	Detection value	Company	Determination of clinical significance

Note: examination index: white blood cell, neutrophil, hemoglobin, platelet, C-reactive protein.
NCS: abnormal without clinical significance, CS: abnormal with clinical significance.

List 7-4 abnormal urine routine values (normal baseline → abnormal after treatment) (SS)
List 7-5 abnormal urine routine values (baseline NCS → CS after treatment) (SS)
List 7-6 measured urine routine values (SS)

group	center	Random number	Gender	Age (yr)	Weight (kg)	Name of visit	Sampling date	Inspection index	Check value	Company	Determination of clinical significance

Note: examination indexes:Urine, white blood cell test.
NCS: abnormal without clinical significance, CS: abnormal with clinical significance.

List 7-7 blood biochemical abnormal values (normal baseline → abnormal after treatment) (SS)
List 7-8 abnormal blood biochemical values (baseline NCS → CS after treatment) (SS)
List 7-9 blood biochemical measured values (SS)

group	center	Random number	Gender	Age (yr)	Weight (kg)	Name of visit	Sampling date	Inspection index	Check value	Company	Determination of clinical significance

Note: examination indexes: alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, Total bilirubin, direct bilirubin, urea nitrogen, creatinine.
NCS: abnormal without clinical significance, CS: abnormal with clinical significance.

List 7-10 electrolyte abnormal value (baseline normal → abnormal after treatment) (SS)
List 7-11 electrolyte abnormal value (baseline NCS → CS after treatment) (SS)
List 7-12 electrolyte measured value (SS)

group	center	Random number	Gender	Age (yr)	Weight (kg)	Name of visit	Inspection date	Inspection index	Check value	Company	Determination of clinical significance

Note: examination index: potassium, sodium, chlorine, calcium and magnesium.
NCS: abnormal without clinical significance, CS: abnormal with clinical significance.

List 7-13 abnormal value of tumor index examination (normal baseline → abnormal after treatment) (SS)
List 7-14 abnormal value of tumor index examination (baseline NCS → CS after treatment) (SS)
List 7-15 measured value of tumor index examination (SS)

group	center	Random number	Gender	Age (yr)	Weight (kg)	Name of visit	Sampling date	CA19-9 (carbohydrate antigen) detection value	Company	Other units	Determination of clinical significance

Note: NCS: abnormal has no clinical significance, CS: abnormal has clinical significance.

List 8 abnormal value list of ECG examination

List 8-1 ECG abnormal value (baseline normal → abnormal after treatment) (SS)
List 8-2 ECG abnormal value (baseline NCS → CS after treatment) (SS)
List 8-3 ECG measured value (SS)

group	center	Random number	Gender	Age (yr)	Weight (kg)	Name of visit	Inspection date	HR (times / min)	R-R(ms)	P-R(ms)	QRS(ms)	QT(ms)	QTc(ms)	Results description	Determination of clinical significance

Note: NCS: abnormal has no clinical significance, CS: abnormal has clinical significance.

List 9 vital signs

List 9-1 measured values of vital signs (SS)

group other	center	random number	gender	Age (yr)	Visit name	Date of visit	Body temperature (℃)	Pulse rate (times / min)	breathing (minutes)	systolic pressure (mmHg)	diastolic pressure (mmHg)	height (cm)	Weight (kg)	Body surface area (m^2)

List 10 physical examination list

List 10-1 abnormal values of physical examination (baseline normal → abnormal after treatment) (SS)
List10-2 measured values of physical examination (SS)

group	center	Random	Gender	Age (yr)	Weight (kg)	Name of visit	Physical examination	Description of abnormal physical

		number					results	examination

List 11 pregnancy tests

List 11-1 pregnancy tests (SS)

group	center	Random number	Age (yr)	Weight (kg)	Name of visit	Inspection date	Inspection results

List 11-2 pregnancy report form (SS)

Group					
Center					
Random number					
Pregnancy during the trial					
Report type					
Follow up times					
Researcher					
Contact number					
Subject abbreviation					
Gender					
Date of birth					
Random number					
Date of diagnosis of pregnancy					
Date of last menstruation					
Pregnancy outcome					
Date of termination of pregnancy					
Date of birth					
Sex of fetus					
Other supplements					

Is the outcome of the fetus or infant for SAE					
SAE reasons					
Contraceptive methods of subjects					
Previous pregnancies (beyond this time)					
abortion					
Other risk factors					
Did SAE happen before the trial of subjects					
SAE descriptions					
Drugs taken by subjects during the first 6 months of pregnancy (including research use) Drug package number) information					
Other supplementary information					

Note: only pregnant women during the trial were listed.

Supplement 1, OS subgroup analysis (study drug use times)

Supplement table 1-1 OS increases by the subgroup analysis (study drug administration times) (FAS)

index	Experimental group	Control group
Number of study drug administration		
< 6 times		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
HR(95%CI)	X.X(X.X~X.X)	
>= 6 times		
N	XX	XX
Censored(%)	XX(XX.X)	XX(XX.X)
Number of deaths	XX(XX.X)	XX(XX.X)
Kaplan Meier estimation (month)		
25%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
50%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
75%(95%CI)	XX.X (XX.X~XX.X)	XX.X (XX.X~XX.X)
HR(95%CI)	X.X(X.X~X.X)	

Supplement 2. RMSTREG

In this model, the stratification factor is also considered.

Table 2-1 OS RMST analysis results considering stratification factor (FAS)

Analysis of Parameter Estimates						
Parameter	DF	Estimate	SE	95% Confidence Limits	Chi-Square	Pr > ChiSq

Intercept	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Tumor location	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Surgery history	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Management for biliary obstruction	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Adjuvant chemotherapy	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Group (trial group)	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX

Note: link = log, estimation method = PV, tau = 75.

Supplement Table 2-2 RMST analysis results of OS considering stratification factor (PPS)

Analysis of Parameter Estimates

Parameter	DF	Estimate	SE	95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Tumor location	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Surgery history	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Management for biliary obstruction	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Adjuvant chemotherapy	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Group (trial group)	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX

Note: link = log, estimation method = PV, tau = 75.

Table 2-3 PFS RMST analysis results considering stratification factor (FAS)

Analysis of Parameter Estimates

Parameter	DF	Estimate	SE	95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Tumor location	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Surgery history	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX

Management for biliary obstruction	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Adjuvant chemotherapy	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Group (trial group)	X	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX

Link = log, estimation method = PV, tau = 31.