A Randomized, Double-Blind, Phase 3 Study of the JAK1/2 Inhibitor Ruxolitinib or Placebo in Combination With Capecitabine in Subjects With Advanced or Metastatic Adenocarcinoma of the Pancreas Who Have Failed or Are Intolerant to First-Line Chemotherapy (The JANUS 2 Study)

Published: 07-07-2014
Last updated: 20-04-2024

Primary Objectives:- To evaluate and compare the overall survival (OS) of subjects with advanced or metastatic adenocarcinoma of the pancreas when treated with JAK 1/2 Inhibitor in combination with capecitabine versus capecitabine alone.Secondary…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Exocrine pancreas conditions
Study type	Interventional

Summary

ID

NL-OMON41730

Source
ToetsingOnline

Brief title
Incyte INCB 18424-363 study (JANUS 2)

Condition

- Exocrine pancreas conditions

Synonym
adenocarcinoma of the pancreas, pancreatic cancer

Research involving
Human

Sponsors and support

Primary sponsor: Incyte Corporation
Source(s) of monetary or material Support: Incyte

Intervention

Keyword: Adenocarcinoma of pancreas, Capecitabine, Ruxolitinib

Outcome measures

Primary outcome

To evaluate and compare the overall survival (OS) of subjects with advanced or metastatic adenocarcinoma of the pancreas when treated with JAK 1/2 Inhibitor in combination with capecitabine versus capecitabine alone.

Secondary outcome

* Progression-free survival defined as the time from randomization until the earliest date of disease progression determined by investigator assessment of objective radiographic disease assessments per RECIST (v1.1), or death due to any cause, if sooner.

* Restricted mean survival time (RMST) estimated over the interval between the date of randomization and 12 months (365 days); if the last death in either treatment group is prior to study Day 365, then the earlier of the death in the placebo or the death in the ruxolitinib treatment group, truncated to the last full 30-day incremented prior the earlier death, will be used as the end of the RMST estimation interval in

both groups.

* Objective response rate and duration of response determined by

radiographic disease assessments per RECIST (v1.1), by investigator

assessment.

* Safety and tolerability of the treatment regimens through assessment

of adverse events and changes in safety assessments including

laboratory parameters.

Study description

Background summary

In this study it is investigated if the combination of Ruxolitinib and Capecitabine has beneficial effects in patients with advanced or metastatic adenocarcinoma of the pancreas who have failed or are intolerant to first-line chemotherapy.

Study objective

Primary Objectives:
- To evaluate and compare the overall survival (OS) of subjects with advanced or metastatic adenocarcinoma of the pancreas when treated with JAK 1/2 Inhibitor in combination with capecitabine versus capecitabine alone.

Secondary Objectives:
- To evaluate and compare the efficacy of the 2 treatment groups with respect to progression-free survival (PFS).
- To evaluate and compare the efficacy of the 2 treatment groups with respect to overall tumor response and duration of response.
- To evaluate and compare the safety and tolerability of JAK 1/2 Inhibitor in combination with capecitabine versus capecitabine alone.

Study design

This is a randomized, double-blinded, placebo-controlled, Phase 3 study.

Intervention

Patients will be randomized (1:1) to one of the following treatment groups:
- Treatment A (N = 135): Capecitabine 2000 mg/m2 daily (1000 mg/m2 twice daily [BID]) + JAK 1/2 Inhibitor
- Treatment B (N = 135): Capecitabine 2000 mg/m2 daily (1000 mg/m2 BID) + placebo

Study burden and risks

The study has a duration of 6 months, with a study cyclus of 21 days

Burden: Physical examinations, vital functions examinations, CT scans, bloodtests, questionnaires.

Risks: The most frequently reported side effects in patients with myelofibrosis (MF) who have been treated with ruxolitinib are: Anemia (low red blood cells), Thrombocytopenia (low platelets), Raised ALT (blood proteins that may indicate mild liver damage).

Also capecitabine can cause side effects, like anemia (low red blood cells), fatigue, diarrhea, etc.
The risks to an unborn human fetus or a nursing child from ruxolitinib are not known. Women who are pregnant or nursing a child may not participate in this study

Contacts

Public
Incyte Corporation

Route 141 & Henry Clay Road Building E336
DE Wilmington 19880
US
Scientific
Incyte Corporation

Route 141 & Henry Clay Road Building E336
DE Wilmington 19880
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Male or female, 18 years or older.
- Histologically or cytologically confirmed adenocarcinoma of the pancreas.
- Advanced adenocarcinoma of the pancreas that is inoperable or metastatic.
- mGPS of 1 or 2 as defined below:
o mGPS of 1: C-reactive protein (CRP) > 10 mg/L and albumin * 35 g/L
o mGPS of 2: CRP > 10 mg/L and albumin < 35 g/L
**Received 1 prior chemotherapy regimen for advanced or metastatic disease (not including neoadjuvant and/or adjuvant therapy).
o Use of a fluoropyrimidine-containing regimen (eg, FOLFIRNOX, FOLFOX, CapeOx, chemoradiation,etc) in
the first-line setting is permitted provided the subject discontinued treatment for reasons other
than disease progression and the subject received * 8 weeks of therapy. Subjects who received
single-agent capecitabine as first-line therapy are not eligible.
- * Neoadjuvant regimens will be considered first-line therapy if the subject has disease progression during treatment. Adjuvant regimens will be considered first-line therapy if the subject has disease progression during treatment or * 6 months after the last dose.
o There is no restriction on the use of fluoropyrimidine-containing regimens in the neoadjuvant
or adjuvant setting.
o *History of palliative radiotherapy to disease sites is allowed provided there are other sites of
disease or subsequent progression of the disease in the radiation field, and * 4 weeks have elapsed since the completion of radiotherapy and all treatment-related toxicities have resolved
or are at a new stable baseline.
- Able to tolerate and benefit from therapy as evidenced by:
o Absolute neutrophil count * 1.5 × 109/L with white blood cell count < 20 × 109/L.
o Platelets * 75 × 109/L.
o Hemoglobin * 9 g/dL (transfusions are permitted to achieve baseline hemoglobin level).
o Alanine aminotransferase (ALT)/aspartate aminotransferase (AST) * 2.5 × upper limit of

normal (ULN); or * 5 × ULN in the presence of liver metastases.
o Total bilirubin * 1.5 × ULN; if total bilirubin is > 1.5 × ULN then direct bilirubin must be * 1.5 × ULN (use of biliary stent to achieve bilirubin levels is permitted).
o Alkaline phosphatase < 3 × ULN.
o Lactate dehydrogenase (LDH) < 3 × ULN in the absence of hemolysis.
o Creatinine clearance * 50 mL/min measured or calculated by Cockroft-Gault equation.
o ECOG performance status 0 to 2.
o Body mass index (BMI) > 16 kg/m2.
o Absence of significant concurrent, uncontrolled medical condition including, but not limited to renal, hepatic, hematological, gastrointestinal, endocrine, pulmonary, cardiac, neurological, cerebral, or psychiatric disease.
o Able to swallow and retain oral medication.
- * 2 weeks elapsed from the completion of previous treatment regimen and subjects must have
recovered or be at a new stable baseline from any related toxicities.
- Radiographically measurable or evaluable disease (based on local evaluation), per RECIST (v1.1).

Exclusion criteria

- Received more than 1 prior regimen (eg chemotherapy, biologic, targeted, immune, investigational therapies alone or in combination) for advanced or metastatic disease.
- Chronic or current active infectious disease requiring systemic antibiotics, antifungal, or antiviral treatment.
- Known brain or central nervous system metastases or history of uncontrolled seizures.
- Clinically significant or uncontrolled cardiac disease, including unstable angina, acute myocardial infarction within 6 months from Day 1 of study drug administration, New York Heart Association Class III or IV congestive heart failure, and arrhythmia requiring therapy.
- Ongoing radiation therapy or radiation therapy administered within 30 days of enrollment.;- Concurrent anticancer therapy (eg, chemotherapy, radiation therapy, surgery, immunotherapy, biologic therapy, hormonal therapy, investigational therapy, or tumor embolization).
- Subjects who participated in any other study in which receipt of an investigational study drug occurred within 28 days or 5 half-lives (whichever is longer) prior to the first dose.
- Current or previous other malignancy within 2 years of study entry, except cured basal or squamous cell skin cancer, superficial bladder cancer, prostate intraepithelial neoplasm, carcinoma in situ of the cervix, or other noninvasive or indolent malignancy without sponsor approval.
- Recent (* 3 months) history or ongoing partial or complete bowel obstruction, unless surgically corrected.
- Prior severe reaction to fluoropyrimidines, known DPD deficiency, or other known hypersensitivity to active substances, including fluorouracil (5-FU), or ruxolitinib, or any of their excipients.
- Known history of human immunodeficiency virus infection.
- Active hepatitis B or C infection that requires treatment.

- Unwilling to be transfused with blood components.
- Prior treatment with a JAK inhibitor for any indication.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-01-2015
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Accord
Generic name:	Capecitabine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Actavis
Generic name:	Capecitabine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Jakafi
Generic name:	ruxolitinib

Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	07-07-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-11-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-05-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-05-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	29-06-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2014-000294-39-NL
ClinicalTrials.gov	NCT02119663
CCMO	NL48685.018.14

Study results

Date completed: 11-02-2016

Actual enrolment: 12

Summary results
Trial is onging in other countries