A randomized Phase II study of second line treatment with liposomal irinotecan and S1 versus liposomal irinotecan and 5-fluorouracil in patients with metastatic pancreatic cancer who failed on first line gemcitabine-based chemotherapy

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This study has been transitioned to CTIS with ID 2023-509463-24-01 check the CTIS register for the current data. The main objective of this study is to determine the optimal second line treatment strategy in Caucasian patients with metastatic...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON55645

Source
ToetsingOnline

Brief title
Second line treatment with nal-IRI and S1 in pancreatic cancer.

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
pancreatic cancer

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Servier,Shire

Intervention

Keyword: liposomal irinotecan, pancreatic cancer, S1, second line

Outcome measures

Primary outcome

Run in phase: Dose limiting toxicity (DLT) and Maximal tolerated dose (MTD) of nal-IRI when co-administered with fixed dose S1 in patients with metastatic pancreatic cancer.

Phase II part: Efficacy between the treatment arms in terms of progression free survival

Secondary outcome

Overall survival

Response rate according to RECIST 1.1

Adverse events according to NCI CTC version 4.0

Quality of life

Study description

Background summary

The 5-year survival of patients with pancreatic cancer is less than 5%. Despite improvements over the past years with the introduction of FOLFIRINOX (5-fluorouracil, irinotecan, oxaliplatin and leucovorin) and gemcitabine + nab-paclitaxel, the vast majority will have disease recurrence or progression within 6 months. Single-arm phase II studies have been conducted after

gemcitabine-based therapy. Randomized clinical trial data are limited in this setting, but the conclusion was up to recently that there is no superior chemotherapeutic regimen after gemcitabine failure. However, the NAPOLI trial altered the treatment landscape. In this trial, patients with metastatic pancreatic cancer that progressed after treatment with gemcitabine-based chemotherapy received liposomal irinotecan (nal-IRI) either as single agent or in combination with 5-fluorouracil/ leucovorin (5-FU/LV), or 5-FU/LV alone. Patients treated with the combination of nal-IRI plus 5-FU/LV experienced a median survival of 6.1 months versus 4.2 months for the 5-FU/LV group. Recently, two studies on the clinical use of S-1 for pancreatic cancer have been reported from Japan. In the first study, S-1 demonstrated non-inferiority to gemcitabine in overall survival (OS) for advanced pancreatic cancer. In the second study, S-1 showed superiority to adjuvant chemotherapy with gemcitabine in OS. In addition to gemcitabine, S-1 is now regarded as the key drug in the management of pancreatic cancer in Japan. Phase II studies of S-1 in patients with gemcitabine-resistant pancreatic cancer have demonstrated moderate activity with acceptable toxicity. Although there has been no confirmed evidence based on phase III trials, S-1 would be a feasible treatment option in this patient population. However, given the lack of data from prospective studies on S-1 in combination with nal-IRI as second line treatment in metastatic pancreatic cancer in the Western population, this study is designed to compare nal-IRI combined with S-1 and nal-IRI combined with 5-FU/LV in terms of safety and efficacy, in metastatic pancreatic cancer patient

Study objective

This study has been transitioned to CTIS with ID 2023-509463-24-01 check the CTIS register for the current data.

The main objective of this study is to determine the optimal second line treatment strategy in Caucasian patients with metastatic pancreatic cancer, whereby the hypothesis is, based on studies conducted in the Asian population, that the combination of S-1 and nal-IRI will be superior compared to 5-FU/ LV and nal-IRI , in terms of progression free survival. Therefore, patients will be randomized, after the optimal dose of S1 and nal-IRI has been determined in the run in phase, between S-1 in combination with nal-IRI and 5-FU/LV in combination with nal-IRI during the phase II part of the study.

Study design

This is a multi-center, open label, randomized phase I/II trial

Intervention

Arm 1:
S1 will be given for 14 consecutive days, twice daily, followed by 2 weeks

rest. Nal-IRI will be administered as an intravenous infusion on day 1 and 15. Courses of treatment will be repeated every 4 weeks.

Arm 2:
Nal-IRI 80 mg/m2 will be administered first, followed by LV 400 mg/m2, followed by 5-FU 2400 mg/m2 as an IV infusion over 46-hours on days 1. Each cycle consists of 14 days. Courses of treatment will be repeated every 2 weeks.

Study burden and risks

The burden for the patient is 3 extra blood samples that will be taken on the same day of, but additive to routine blood samples. Risks include side effects related to chemotherapy, which include (depending on the chemotherapy) nausea, diarrhoea, low blood cell counts, hand foot syndrome, loss of appetite, fatigue and anorexia.
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Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Able to understand and provide written informed consent
>= 18 years of age
Histologically or cytologically confirmed adenocarcinoma of exocrine pancreas
Documented metastatic disease
Previously treated with gemcitabine or gemcitabine containing therapy, or progression within 6 months of adjuvant gemcitabine treatment
Adequate hepatic, renal and hematological function

Exclusion criteria

WHO 0-1
Any clinically significant gastrointestinal disorder, including hepatic disorders, bleeding, inflammation, occlusion, or diarrhea > grade 2
Severe arterial thromboembolic events (myocardial infarction, unstable angina pectoris, stroke) in last 6 months
NYHA Class III or IV congestive heart failure, ventricular arrhythmias or uncontrolled blood pressure. Or known abnormal ECG with clinically significant abnormal findings
Active infection or an unexplained fever >38.5°C (excluding tumor fever), which in the physician*s opinion might compromise the patient*s health
Current use or any use in last two weeks of strong CYP3A-enzyme inducers/inhibitors and/or strong UGT1A inhibitors
Known hypersensitivity to any of the components of liposomal irinotecan (nal-IRI) other liposomal irinotecan formulations, irinotecan, fluoropyrimidines, or leucovorin.
Hypersensitivity to any of the active substances (tegafur, gimeracil, and oteracil)
Previous treatment with fluoropyrimidine therapy
Known dihydropyrimidine dehydrogenase (DPD) deficiency
Breast feeding, known pregnancy, positive serum pregnancy test or unwillingness to use a reliable method of birth control, during therapy and for 3 months following the last dose of liposomal irinotecan (nal-IRI).
Treatment within 4 weeks with DPD inhibitors, including sorivudine or its chemically related analogues such as brivudine

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-12-2019
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	5 fluorouracil
Generic name:	5 fluorouracil
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	onyvide
Generic name:	irinotecan hydrochloride trihydrate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	teysuno
Generic name:	tegafur/gimeracil/oteracil
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	18-10-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-11-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-05-2021
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
EU-CTR	CTIS2023-509463-24-01
EudraCT	EUCTR2017-004675-31-NL
CCMO	NL64126.018.17