Liposomal iRInotecan, Carboplatin or oXaliplatin in the first line treatment of esophagogastric cancer: a randomized phase 2 study (LyRICX)

Published: 27-09-2018
Last updated: 21-12-2024

This study has been transitioned to CTIS with ID 2023-509287-26-00 check the CTIS register for the current data. To compare the progression free survival and neurotoxity of first line treatment with F-Nal-IRI, CapCar and CapOx.

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

Summary

ID

NL-OMON54618

Source
ToetsingOnline

Brief title
LyRICX

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
cancer of esophagus and stomach, Metastatic upper gastrointestinal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC

Source(s) of monetary or material Support: Servier

Intervention

Keyword: efficacy, metastatic esophagogastric cancer, palliative chemotherapy, toxicity

Outcome measures

Primary outcome

Progression free survival (PFS1) and neurotoxicity

Secondary outcome

Secondary endpoints

* Overall survival

* Response rate according to RECIST 1.1

* Adverse events according to NCI CTC version 5.0

* Quality of life

* Percentage of patients proceeding to subsequent lines of treatment after progression and describe the types of treatment

* Reasons for forgoing subsequent treatment after progression

- To compare the primary objective and above mentioned secondary objectives for patients treated with and without nivolumab

- To compare the progression free survival 2: time from reintroduction carboplatin, oxaliplatin or Nal-IRI after first moment of disease progression, untill disease progression.

Exploratory endpoints

• Relative abundance of stroma and tumor immune infiltrate in metastatic tumor tissue as predictor of response to treatment and survival.

• Stromal markers, including ADAM12 in metastatic tumor tissue and blood as predictor of response to treatment and survival.

• Patient derived tumor organoids to assess markers of response to treatment and identify resistance pathways.

• Baseline ctDNA levels and changes in ctDNA as a marker of response to treatment.

• Baseline characteristics of and changes in the fecal microbiome as a biomarker for response to treatment and toxicity.

• Cost effectiveness.

Study description

Background summary

No globally accepted standard first-line treatment regimen exists.
In deciding on an optimal first-line treatment regimen, not only (progression free) survival should be taken into account, but also the effects of a first-line regimen on the possibility to undergo subsequent treatments. In this respect, side effects are of crucial importance: if a side-effect does not readily resolve after stopping the treatment this may hamper the start of second-line treatment. This issue particularly arises with neurotoxicity, a well-known side effect of the F-oxaliplatin combination. F-oxaliplatin is a frequently used doublet in many countries, and, in fact, in the Netherlands even the most frequently used doublet. [publication in preparation]
Neurotoxicity may last for prolonged periods of time, and may prevent the start of second line paclitaxel. Replacing oxaliplatin by another platinum compound such as carboplatin, or a non-neurotoxic compound such as liposomal irinotecan, may resolve this issue.

Therefore, in this study we will set out to compare three F-doublets, both in terms of efficacy and toxicity, more particularly neurotoxicity, to identify the most optimal first-line cytotoxic treatment regimen for future use.

As of spring 2022 nivolumab will be added to the treatment of patients with a PD-L1 CPS of 5 or higher, but this isonly applicable for patients treated with CapOX or CapCar. For this reason, patients with a CPS of 5 or higher will no

longer be randomized to F-Nal-IRI from that moment on, but only to CapOx and CapCar and they will also receive nivolumab in addition to chemotherapy.

Study objective

This study has been transitioned to CTIS with ID 2023-509287-26-00 check the CTIS register for the current data.

To compare the progression free survival and neurotoxity of first line treatment with F-Nal-IRI, CapCar and CapOx.

Study design

multi-center, open label, randomized phase II trial using a pick the winner design

Intervention

1. Nal-IRI 70 mg/m² (water free base), folinic acid 400 mg/m², fluorouracil 2400 mg/m² over 46 h, every 2 weeks.
2. Capecitabine 1000 mg/m2 and carboplatin AUC5 with/without Nivolumab, every three weeks.
3. Capecitabine 1000 mg/m2 and oxaliplatin 130 mg/m2 with/without Nivolumab, every three weeks.

Study burden and risks

Burden
Extra VENA PUNCTION: baseline, week 4 and at progression: 55 ml blood (translational research)
Extra QUESTIONNAIRE: every 3 weeks, neurotoxicity 5-10 min
Extra QUESTIONNAIRE: every 9 weeks 20-30 min
Extra FECES collection and diet diary during 3 days: baseline, week 4, week 10
OPTIONAL: baseline: biopsies primary gastroesophagel tumor and /or metastases (liver maximal 2-3 extra biopsies, skin 3-4 biopsies)

In regular treatment, a biopsy will performed to diagnose metastatic cancer. Also every 3 weeks, a physical examination and a venapunction will take place to assure that the next cycle can be administered.
The blood and tumor tissue for biomarkers, feces collection and questionnaires are extra.

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

* Patients with histologically confirmed diagnosis of metastatic or irresectable HER2 negative adenocarcinoma of the stomach or oesophagus, patients with HER2 positive disease are eligible when treatment with trastuzumab is contraindicated.
* Patients with metastatic or irresectable adenocarcinoma of the stomach or oesophagus not pre-treated with chemotherapy or radiotherapy for irresectable or metastatic disease. Palliative radiotherapy on the primary tumor or a metastatic lesion is allowed if other untreated lesions for RECIST evaluation are present. Chemoradiation with carboplatin area under the curve (AUC) 2 and paclitaxel 50 mg/m2 for irresectable disease is allowed if subsequent disease progression is proven on radiological imaging.
* Measurable/evaluable disease as assessed by RECIST 1.1

* ECOG (WHO) performance status 0-2
* Adequate hepatic, renal and hematological function

Exclusion criteria

* Serum total bilirubin >=1.5 x ULN (biliary drainage is allowed for biliary obstruction) * Severe renal impairment (CLcr <= 30 ml/min) * 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 * Current use or any use in last two weeks of strong CYP3A-enzyme, CYP2C8, and/or strong UGT1A inhibitors/inducers * Known complete dihydropyrimidine dehydrogenase (DPD) deficiency * Treatment within 4 weeks with DPD inhibitors, including sorivudine or its chemically related analogues such as brivudine * Pre-existing motor or sensory neurotoxicity greater than CTCAE grade 1

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):	04-09-2019
Enrollment:	320
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Carboplatin
Generic name:	Carboplatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	fluorouracil
Generic name:	fluorouracil
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Leucovorin
Generic name:	Leucovorin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Onivyde
Generic name:	Nanoliposomaal irinotecan
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Xeloda
Generic name:	capecitabine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-09-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-06-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-07-2019

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-11-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-07-2020

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2022

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-12-2022
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	02-01-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	11-06-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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Approved WMO
Date: 10-07-2023

Application type: Amendment

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Approved WMO
Date: 25-07-2023

Application type: Amendment

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Approved WMO
Date: 27-07-2023

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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Application type:	Amendment
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Approved WMO Date:	15-01-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	22-04-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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Approved WMO
Date: 25-04-2024

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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Approved WMO
Date: 12-08-2024

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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Approved WMO
Date: 03-10-2024

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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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	CTIS2023-509287-26-00
EudraCT	EUCTR2018-002767-26-NL
ClinicalTrials.gov	NCT03764553
CCMO	NL66783.018.18