A randomised phase III trial comparing a strategy based on molecular analysis to the empiric strategy in patients with carcinoma of an unknown primary;A la carte CUP treatment using the CancerTYPE ID test

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Determine wether or not a strategy based on molecular analysis is effective in improving the PFS

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON39511

Source
ToetsingOnline

Brief title
CUP

Condition

- Other condition

Synonym
Carcinoma of unknown primay

Health condition

oncologische aandoening

Research involving
Human

Sponsors and support

Primary sponsor: Viecuri Medisch Centrum voor Noord-Limburg
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: - cancerTYPE ID test, - Carcinoma of unknown primary, - Strategy

Outcome measures

Primary outcome

Progression free survival

Secondary outcome

Objective respons rate, Tolerance, Overall survival

Study description

Background summary

GEFCAPI 01 randomized phase II trial was conducted from 1999 to 2001 and demonstrated that the combination of cisplatin and gemcitabine (40 patients) results in a promising antitumor activity (response rate: 55%, median survival: 8 months) and a favorable pattern of tolerance in patients with CUPs (Culine, J Clin Oncol 2003). Based on these data, the randomized GEFCAPI 02 trial was conducted from 2004 to 2007 and tested cisplatin with or without gemcitabine in patients with CUP and a non-unfavorable prognosis. A median survival rate of 11 months was obtained in the combination arm (27 patients), as compared to 8 months in the single arm (25 patients) (Gross-Goupil 2008). Taken together, results from the GEFCAPI 01 and 02 trials indicate that the cisplatin-gemcitabine association is a reasonable empiric chemotherapy regimen in patients with CUPs.
In recent years, several groups have shown that cancers can be identified with a high reproducibility by their microarray signature. In the meantime, important therapeutic progresses have been made in a number of metastatic cancers using specific treatments (chemotherapy and/or targeted agents), leading to improvement in progression-free survival and in some cases, overall survival.

Therefore, it becomes more tempting to identify a primary cancer before treating a patient with CUP, so that a more specific treatment can be used.
In an effort to develop such a strategy, the GEFCAPI embarked in 2008 in a feasibility study in which RNA was extracted from tissue samples of 20 patients with CUP and a microarray analysis was performed to compare their gene expression with that of known primary cancer signatures (Gross-Goupil 2008).
The results indicated that:
a clinically acceptable delay (median: 10 days) could be achieved between tissue sample shifting and receipt of the molecular analysis by the investigator, making this strategy feasible in practice;
almost half of the primary cancers suspected by microarray analysis (colo-rectal cancer, hepatocarcinoma, renal cell carcinoma, breast cancer, melanoma) would not be treated appropriately by an empiric chemotherapy regimen like the cisplatin-gemcitabine combination.
This clearly supports the study of gene microarray analysis followed by suspected primary cancer-tailored specific therapy in patients with CUP

Study objective

Determine wether or not a strategy based on molecular analysis is effective in improving the PFS

Study design

European randomised phase III multi centric study comparing a diagnostic and therapeutic strategy based on molecular analysis followed by suspected primary cancer tailored specific therapy to an empiric strategy in patients with carcinoma of unknown primary.

Intervention

Molecular analysis test

Study burden and risks

No additional risk for the patient. The moleculary analysis will be performed on the sample that has been done for standard of care.

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

1) Patients presenting with carcinoma of an unknown primary, confirmed by histo-pathological analysis (including an immunohistochemical analysis) and corresponding to one of the following histologic types: moderately or welldifferentiated adenocarcinoma, poorly-differentiated adenocarcinoma, undifferentiated carcinoma, squamous-cell carcinoma
2) Diagnostic work-up in keeping with Standard Options Recommandations des CAPI (Lesimple et al., 2003),
3) Age>18 years,
4) Performance status 0, 1 or 2 according to ECOG
5) Good or poor prognosis CUP classified according to the GEFCAPI classification
6) CUP with at least one measurable lesion
7) Tumour sample available for molecular analysis.
8) CUP not belonging to a subgroup requiring a specific treatment,
9) Satisfactory haematological, renal and hepatic function
10) Cardiac, respiratory and neurological function compatible with the administration of cisplatin chemotherapy,
11) No previous chemotherapy for CUP,
12) Previous radiotherapy is acceptable, but it should be completed at least 4 weeks before the start of systemic treatment. Randomisation can be performed during this time frame,
13) All patients with reproductive potential must practice an effective method of birth control

throughout the study. Female patients with childbearing potential must have a negative pregnancy test within 7 days before study treatment
14) Information delivered to patient and informed consent form signed by the patient or legal representative.

Exclusion criteria

1) Patients in whom the diagnosis has not been histologically confirmed (a cytological analysis alone does not permit patient entry onto the trial),
2) Patients with known HIV infection
3) Patients with symptomatic brain metastases,
4) Associated disease likely to prevent the patient from receiving the treatment,
5) Previous history of cancer (excepted skin basocellular epithelioma or epithelioma in situ of the uterine cervix) during the 5 years before study entry,
6) Patients already included in another clinical trial with an experimental therapy,
7) Pregnant women, and women who are breastfeeding,
8) Compliance with trial medical follow-up impossible due to geographic, social or psychological reasons.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-03-2014
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO Date:	17-07-2013
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-09-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
Other	2011-A01202-39
CCMO	NL40415.068.12