# 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 reviewApproved WMOStatusRecruitment stoppedHealth condition typeOther condition

**Study 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

1 - A randomised phase III trial comparing a strategy based on molecular analysis to ... 3-05-2025

## 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**

#### **Public**

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3 - A randomised phase III trial comparing a strategy based on molecular analysis to ... 3-05-2025

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#### **Scientific**

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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
  - 4 A randomised phase III trial comparing a strategy based on molecular analysis to ... 3-05-2025

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