Hyperthermia and PARP-1 inhibition in recurrent head&neck or bladder cancer

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Primary:To establish a recommended phase II dose of the PARP-inhibitor olaparib in combination with hyperthermia in a) patients with recurrent HNC in previously irradiated area and in b) patients with primary irresectable or local recurrent bladder...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON44022

Source
ToetsingOnline

Brief title
Hyppi

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
head and neck cancer and bladder cancer

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Astra Zeneca,farmaceutische industrie

Intervention

Keyword: hyperthermia, PARP-inhibition

Outcome measures

Primary outcome

The primary study parameter is toxicity graded according to the International Common Toxicity Criteria (CTC), version 4.0.

Secondary outcome

The response rate of olaparib in combination with hyperthermia in patients with previously irradiated recurrent carcinoma of the head and neck or in patients with primary irresectable or recurrent bladder cancer unfit for or who progressed after platinum-based chemotherapy.

HRD induced by hyperthermia in vivo as measured by degradation of the BRCA2 protein or decreased formation of RAD51 foci.

Study description

Background summary

In patients with recurrent squamous cell carcinoma of the head and neck as in patients with primary irresectable or local recurrent bladder cancer major problems, such as pain (often neuralgic) and severe bleeding may occur, which are often difficult to control and result in substantial morbidity and poor quality of life. Few treatment options are available for these patients, also because of their frail conditions.
Hyperthermia transiently induces HRD in recurrent squamous cell carcinoma of the head and neck or in primary irresectable or local recurrent bladder cancer leading to impaired DSB repair, which sensitizes these cancer cells to treatment with PARP-inhibitors.
We therefore hypothesize that hyperthermia (inducing transient HRD) combined with a PARP-inhibitor (inducing DSB) in patients with recurrent squamous cell

carcinoma of the head and neck or local recurrent bladder cancer will result in tumor cell apoptosis, thereby leading to clinical response and palliation.

Study objective

Primary:To establish a recommended phase II dose of the PARP-inhibitor olaparib in combination with hyperthermia in a) patients with recurrent HNC in previously irradiated area and in b) patients with primary irresectable or local recurrent bladder cancer using the maximum tolerated dose (MTD).

Study design

Phase 1 dose-escalation trial

Intervention

Five hyperthermia treatment combined with olaparib twice daily

Study burden and risks

During study treatment (5 weeks) and two weeks thereafter patients have to visit the clinic, are being seen by the medical oncologist. During these visits two tubes of blood are taken. When approved by the medical oncologist and hyperthermia physician hyperthermia takes place. During 4,5 weeks olaparib is described in different doses in different cohort. No toxicity is to be expected from hyperthermia or olaparib during a short period of use is being expected, but no data are known about the combination. As local recurrence often needs palliation, benefit from treatment may result in relief of symptoms.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Groene Hilledijk 301
Rotterdam 3075EA
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Groene Hilledijk 301
Rotterdam 3075EA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Recurrent squamous cell carcinoma of the head and neck in previously irradiated area or primary irresectable stage T4 or a local recurrent bladder cancer (urothelial carcinoma or squamous cell carcinoma) in patients unfit for or who progressed after platinum-based chemotherapy and for whom no other treatments are available.
• Age > 18 years
• Performance status WHO 0-1
• Life expectancy of at least 3 months

Exclusion criteria

Curative treatment options available
• Treatment according to guideline available
• Contra-indications for hyperthermia, i.e. patients with a pacemaker or metal implant in the heated area of > 2 cm , multiple sclerosis

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-07-2016
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	16-12-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-05-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-04-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 28959
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2015-003450-40-NL
CCMO	NL54543.078.15
OMON	NL-OMON28959