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

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28959

Source
NTR

Brief title
HYPPI

Health condition

recurrent squamous cell carcinoma of the head and neck in previously irradiated area or primary irresectable stage T4 bladder cancer (urothelial carcinoma or squamous cell carcinoma) or a local recurrent bladder cancer after radical cystectomy unfit for or who progressed after platinum-based chemotherapy and for whom no other treatments

Sponsors and support

Primary sponsor: Erasmus University Medical Center
Source(s) of monetary or material Support: Astra Zeneca

Intervention

Outcome measures

Primary outcome

Recommended phase II dose of olaparib combined with hyperthermi

Secondary outcome

toxicities according to CTCAE version 4.0
translational

Study description

Background summary

Background of the study:

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.

Objective of the study:

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

Study population:

Patients with recurrent squamous cell carcinoma of the head and neck in previously irradiated area or primary irresectable stage T4 bladder cancer (urothelial carcinoma or squamous cell carcinoma) or a local recurrent bladder cancer after radical cystectomy unfit for or who progressed after platinum-based chemotherapy and for whom no other treatments are available.

Intervention:

Five hyperthermia treatment combined with olaparib twice daily

Primary study parameters/outcome of the study:

The primary study parameter is toxicity graded according to the International Common Toxicity Criteria (CTC), version 4.0.
Secundary study parameters/outcome of the study (if applicable):

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.
Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

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.

Study objective

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 design

during the treatment period (5 weeks) and 4 weeks after.

Intervention

Hyperthermia and PARP-inhibition

Contacts

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Eligibility criteria

Inclusion criteria

• Recurrent squamous cell carcinoma of the head and neck in previously irradiated area or primary irresectable stage T4 bladder cancer (urothelial carcinoma or squamous cell carcinoma) or a local recurrent bladder cancer after radical cystectomy 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

• Minimum required laboratory data - within 7 days prior to enrollment:

Hematology: hemoglobin ≥ 6.2 mmol/L, no blood transfusion within the last 28 days

absolute granulocytes ≥ 1.5 x 109/L

platelets ≥ 100 x 109/L

Biochemistry: total bilirubin: ≤1.5 x upper normal limit

AST (SGOT), ALT (SGPT): ≤2.5 x upper normal limit;

Creatinine: ≤1.5 x upper normal limit.

• Before patient enrollment, written informed consent must be given according to ICH/GCP, and national/local regulations to any study specific procedures

• Postmenopausal or evidence of non-childbearing status for women of childbearing potential: negative urine or serum pregnancy within 28 days of study treatment and confirmed prior to treatment on day 1

• Patient is willing and able to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits and examinations.

Exclusion criteria

• Curative treatment options available

• Treatment according to guideline available

• Contra-indications for hyperthermia, e.g. patients with a pacemaker or multiple sclerosis. When the patient has multiple metal implants of <1 cm (staples) then the distance between the implants must be at least 1 cm. A metal implant >2 cm very close to the tumor volume (target) is a contraindication.

• Any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial

• Any grade 3/4 toxicity according to CTCAE version 4.0 or any serious concomitant disease or symptom considered by the study coordinator to constitute to a high risk for study participation, except for (chemo)radiotherapy related long-term toxicity (like trismus, xerostomia etc.)

• Patients with a known hypersensitivity to olaparib or any of the excipients of the product

• Resting ECG with QTc > 470 msec on 2 or more time points within a 24 hour period or family history of long QT syndrome

• Patients receiving any systemic chemotherapy or radiotherapy within 3 weeks prior to study treatment

• Concomitant use of known potent CYP3A4 inhibitors such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, telithromycin, clarithromycin and nelfinavir

• Patients with myelodysplastic syndrome/acute myeloid leukemia

• Patients with symptomatic uncontrolled brain metastases. A scan to confirm the absence of brain metastases is not required.

• Breast feeding woman

• Immunocompromised patients, e.g. patients who are known to be serologically positive for human immunodeficiency virus (HIV)

• Patients with known active hepatitis

• Previous bone marrow transplant

• Unable to swallow

• The use of anti-coagulants as warfarin or heparins.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-06-2016
Enrollment:	8
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	24-05-2016
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 44022
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL5603
NTR-old	NTR5842
CCMO	NL54543.078.15
OMON	NL-OMON44022

Study results