External beam radiotherapy for unresectable hepatocellular carcinoma. A multicenter phase I/II trial.

Published: 04-05-2009
Last updated: 06-05-2024

Trial objectivesThe objective of the phase I is to assess the feasibility and safety of radiotherapy (RT) in hepatocellularcarcinoma (HCC).The objective of the phase II is to assess the efficacy and safety of RT in HCC.Additional research...

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

Summary

ID

NL-OMON39363

Source
ToetsingOnline

Brief title
Radiotherapy in HCC

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary neoplasms malignant and unspecified

Synonym
hepatocellular carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: SAKK - Swiss Group for Clinical Cancer Research
Source(s) of monetary or material Support: SAKK (Swiss Group for Clinical Cancer

research)

Intervention

Keyword: dosis escalation, External radiotherapy, hepatocellular carcinoma, respons assesment

Outcome measures

Primary outcome

Primary endpoint of phase I

• Dose limiting toxicity (DLT) of RT

Primary endpoint of phase II

• Best objective response of target liver lesions according to RECIST

Secondary outcome

Secondary endpoints of phase I

• Best objective response of target liver lesions according to RECIST

• Adverse events (AEs)

Secondary endpoints of phase II

• Volumetric response of target liver lesions at 5 months

• Time to progression of target liver lesions

• Duration of response of target liver lesions

• Stable disease of target liver lesions

• Time to liver event

• Progression-free survival (PFS)

• Overall survival (OS)

• Compensatory liver tissue hypertrophy

• Child-Pugh Score

• Adverse events (AEs)

• Serum alpha fetoprotein (AFP) level

Study description

Background summary

RATIONALE
HCC is the fifth most common cancer worldwide with increasing incidence rates in Europe and high mortality
rates. The symptoms, disease progression and thus prognosis are primarily defined by the size and localization
of the tumor and accessibility to therapy. The standard care for non-resectable liver cancer is TACE. Alternative
methods are radiofrequency ablation (RFA), nuclear therapy with intra-arterial radioactive beads and ionizing
radiation. Ionizing radiation is a highly effective single agent against HCC. Radiotherapy has been underused in
the past due to technical inadequacy. More recent technical developments such as image-guided radiotherapy,
CT-based RT planning, and 3D-conformal dose delivery allow minimizing the dose to non-target tissue such as
non-affected liver tissue, kidneys and the gut. Thus, less collateral dose delivery to healthy neighboring tissue
allows dose escalation to the diseased segments. The present trial is the first to investigate and define the
potential role of high dose external beam RT for non-resectable HCC in Switzerland and a few centers abroad,
seeking to establish RT as a potential experimental arm in a subsequent phase III trial.

Study objective

Trial objectives
The objective of the phase I is to assess the feasibility and safety of radiotherapy (RT) in hepatocellular
carcinoma (HCC).
The objective of the phase II is to assess the efficacy and safety of RT in HCC.
Additional research question

The subproject of the phase II of this trial is a proteomics analysis of blood serum samples taken before and
after RT. The objectives are the generation of reproducible peptide patterns, assessment of changes in the
proteome and the detection of peptides that discriminate between the situation before and after RT.

Study design

Phase I:
- dose escalation of radiotherapy (RT)
- 5 levels (level 1/2/3: 3 patients, level 4/5: 5 patients)
- determination of the maximum tolerated dose (MTD)

Phase II:
- radiotherapy at MTD-level (if >= 62 Gy)
- sample size: 43 evaluable patients
- assessment of efficacy and safety

Intervention

Once daily RT sessions with 2 Gy, five days a week (on weekdays), will be performed.

Phase I: Dose finding according to the following escalation table:
Dose level Radiotherapy dose (1 x 2 Gy session/day, 5 sessions/week)
1 (3 patients) 27 x 2 Gy = 54 Gy
2 (3 patients) 29 x 2 Gy = 58 Gy, with optional field reduction after a dose of 54 Gy
3 (3 patients) 31 x 2 Gy = 62 Gy, with optional field reduction after a dose of 54 Gy
4 (5 patients) 33 x 2 Gy = 66 Gy, with optional field reduction after a dose of 54 Gy
5 (5 patients) 35 x 2 Gy = 70 Gy, with optional field reduction after a dose of 54 Gy

Phase II: The dose for phase II will be recommended according to the MTD determined in phase I, if the MTD is
62 Gy or higher. If the MTD is 58 Gy or lower, the phase II part of the trial will not be performed.

Study burden and risks

Phase

during RT:

- daily (5/week) RT for 6-7 week, depending on the dosis level (27, 29, 31, 33 or 35 sessions)
- weekly physical examination and bloodexamination

During FU (11 months)
- 1 m after RT: bloodexaminiation
- 1, 2, 3, 5, 8 en 11 m after RT physical examination
- CT or MRI liver 2, 5, 8 en 11 m after RT or until progression

fase II
during RT:
- daily (5/week) RT during 6- 7 weeks, dosis depending on the results of fase I
- weekly physical examination and bloodexamination

during FU (35 months)
- 1 m after RT: bloodexamination
- 1, 2, 3, 5, 8, 11, 15, 19, 23, 29 and 35 months after RT physical examination
- CT or MRI liver 2, 5, 8, 11 , 15, 19, 23, 29 and 35 months after RT or until progression

Contacts

Public
SAKK - Swiss Group for Clinical Cancer Research

Effingerstrasse 40
Bern CH-3008
CH
Scientific
SAKK - Swiss Group for Clinical Cancer Research

Effingerstrasse 40
Bern CH-3008
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1.patient must give informed consent before registration
2.confirmed diagnosis of HCC
3.stage: cT2-4, cN0-1, M0 or unresectable cT1,cN0-1,M0
4.cirrhosis Child-Pugh class A or B
5.measurable disease
6.residual liver volume: >= 800 ml or >= 40% of total liver volume
7.WHO 0-2
8.adequate hematological volumes
9.adequate hepatic functions
10.adequate coagulation parameter
11.adequate renal function
12.age >= 18
13.ability to tolerate proton-pump inhibitors or H2 antagonists during RT
14.women:not pregnant and adequate contraception must be used; men: agree not to father a child during/ within 4 months after trial
15. compliance and geographic proximity to allow proper staging and follow-up
16. phase I only:adequate pancreatic function

Exclusion criteria

1.previous malignancy within 5 years
2.previous RT to the abdomen or caudal chest
3.TACE, RFA or RT within 8 weeks before registration
4. concurrent treatment with other experimental drugs or other anti-cancer therapy
5.operable disease (curative intent) or planned liver transplantation
6.nutritional intake < 1500 kcal/day
7.weight loss > 15%
8.presence of clinical ascites
9.presence of encephalopathy
10.recent myocard infarction
11.esophageal varices >or = gr 3
12.syptoms of colitis, enteritis, esophagitis, fistula, gastristis, ileus, necrosis, perforation, stricture or ulcer
13.severe anorexia, constipation, dehydration, diarrhea or vomiting
14.any serious underlyuing condition which could impair teh ability of the patient to

participate in the trial
15.concommitant treatment with steroids or NSAIDs durinng RT
16.psychiatric disorder precluding understanding of information on trial related topics or giving informed consent

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):	18-11-2010
Enrollment:	18
Type:	Actual

Ethics review

Approved WMO Date:	04-05-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	05-06-2013
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	NCT00777894
CCMO	NL25647.068.08