PROTECT: on-line adaptive proton therapy for cervical cancer to reduce the impact on morbidity and the immune system

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23395

Source
NTR

Brief title
PROTECT

Health condition

Cervical cancer

Sponsors and support

Primary sponsor: LUMC
Source(s) of monetary or material Support: Varian consortium-confined call 2019

Intervention

Outcome measures

Primary outcome

- Detect a difference of 4.3 Gy in mean dose to pelvic bones (whole pelvic contour), and a

difference of 364cc in the mean V15-bowelbag dose (according to EMBRACE bowel bag definition)

Secondary outcome

- Compare (IMRT/VMAT) photon with Proton Therapy (IMPT) on:
o Dosimetric parameters (target volumes and organs at risk)
o Clinical outcomes (response after 3 months, overall survival, pelvic- and distant recurrence-free survival)
o Health-related quality of life (EORTC QLQC30 and EORTC QLQCX24/EN25)
o Safety & tolerability, grade ≥2 according to NCI-CTCAE version 5.0
- Determine the effect of IMPT and IMRT/VMAT on the immune system and possible differences, as measured by the number and function of circulating leukocytes (myeloid and lymphocytes).

Study description

Background summary

Rationale:
The current standard treatment for locally advanced cervical cancer is external beam radiotherapy (EBRT) with concurrent chemotherapy followed by MRI-guided intracavitary/interstitial brachytherapy. This combination of treatment modalities is very effective for locoregional control. As most patients have the prospect of long-term survival, they will also have to live with treatment-related morbidity. This has substantial impact on many domains of their life (physical, sexual, emotional, social, economic). Since most patients are diagnosed in their early decades (peak incidence: 35-45 yrs), morbidity has a major societal impact as well.
Severe late morbidity (grade 3-4) which requires medical intervention (grade 3) and/or can be life-threatening (grade 4), occurs in 8-11% of patients and concerns most often the gastro-intestinal and urogenital tract and, less frequently, insufficiency fractures of the pelvic bones in the irradiated area. Moreover, the number and functioning of circulating leukocytes (myeloid and lymphocytes) can be reduced by pelvic radiotherapy, which might reduce efficacy and feasibility of adjuvant chemo/immunotherapy.
Radiotherapy-related morbidity is a result of the dose to organs at risk (OAR) and is both dose and volume dependent. With proton therapy (PT), OAR dose can be further reduced by highly localized dose-deposition using its finite range. The biggest dose reductions are observed in low-dose regions, such as bowel and bone(marrow). For treatments that included both the pelvic and para-aortic regions the dosimetric advantage of PT is even bigger.
This clinical study will be the first prospective comparative trial to directly compare adaptive photon therapy (IMRT/VMAT) with adaptive PT (IMPT) on dosimetric parameters and clinical outcomes. All participating patients will undergo the current state-of-the-art treatment for LACC (primary chemoradiation with concurrent cisplatin followed by image-guided adaptive brachytherapy). With this study design we will create a homogenous population wherein only

the type of EBRT (IMRT/VMAT or IMPT) is different. Such a study will yield a wealth of information on differences in the effects on dose-volume parameters and both short-term and long-term morbidities. Moreover, it creates a unique opportunity to study the effects of both types of EBRT on local and systemic immune response.

Hypothesis:
I. Daily adaptive IMPT for locally advanced cervical cancer is clinically feasible and will be able to spare the organs at risk to a significantly greater extent than photon-based IMRT/VMAT, while maintaining coverage of the target volume.
II. There are subgroups of patients with locally advanced cervical cancer that will have a clinically relevant reduction of acute and late bowel morbidity if treated with IMPT instead of IMRT/VMAT
III. With IMPT the suppression of the number of circulating leukocytes (myeloid and lymphocytes) will be lower compared to IMRT/VMAT

Study objective

I. Daily adaptive IMPT for locally advanced cervical cancer is clinically feasible and will be able to spare the organs at risk to a significantly greater extent than photon-based IMRT/VMAT, while maintaining coverage of the target volume.
II. There are subgroups of patients with locally advanced cervical cancer that will have a clinically relevant reduction of acute and late bowel morbidity if treated with IMPT instead of IMRT/VMAT
III. With IMPT the suppression of the number of circulating leukocytes (myeloid and lymphocytes) will be lower compared to IMRT/VMAT

Study design

Baseline
During treatment: week 1 and 4 of external beam radiotherapy, at time of brachytherapy
End of treatment
Follow up: 4 and 8 weeks, 3, 6, 9 and 12 months.

Intervention

Multicentre, prospective, clinical, non-randomised phase 2 trial to compare photon and proton therapy in patients with locally advanced cervical cancer who are treated with pelvic and peri-aortic adaptive radiotherapy combined with concurrent chemotherapy with curative intent

Contacts

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Eligibility criteria

Inclusion criteria

- Histologically confirmed diagnosis of cervical cancer (squamous cell carcinoma, adenocarcinoma or adenosquamous carcinoma, HPV positive or negative) with an indication for curative treatment with primary chemoradiation with concurrent cisplatin followed by 3D image-guided adaptive brachytherapy.
- Indication to include the common iliac region or the common iliac and para-aortic regions into the elective clinical target volume of the external beam radiotherapy.
- No distant metastasis beyond the para-aortic lymph node chain as determined by diagnostic imaging (PET-CT scan)
- Age > 18 years
- WHO 0-1
- Adequate systemic organ function:
o Creatinine clearance (> 50 cc/min)
o Adequate bone marrow function : white blood cells (WBCs) ≥3.0 x 109/l, neutrophils ≥1.5 x 109/l, platelets ≥100 x 109/l
- Patients must be accessible for treatment and follow-up
- Written informed consent according to the local Ethics Committee requirements

Exclusion criteria

- Small cell cancer, melanoma and other rare histological types of the cervix.
- History of another primary malignancy that could conceivably be active evaluated by the study physician. Examples of exception include, but are not limited to:
o Malignancy treated with curative intent and with no known active disease ≥5 years.
o Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease.
- Other severe diseases such as recent myocardial infarction, clinical signs of cardiac failure or clinically significant arrhythmias
- Previous pelvic or abdominal radiotherapy
- History of active primary immunodeficiency

- Active or prior documented autoimmune or inflammatory disorders (including inflammatory bowel disease [e.g. colitis or Crohn’s disease])
- The use of immunosuppressive drugs at baseline
- Contraindications for weekly Cisplatin (or Carboplatin)
- Contraindications for the use of MRI

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2021
Enrollment:	30
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description

-

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL9567
Other	METC Leiden – Den Haag – Delft : Holland PTC project code: 2019008

Study results