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Study with intensity modulated radiation therapy with cisplatin to treat stage I-IVA cervical cancer

Submission date 02/04/2012	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 27/04/2012	**Overall study status** Completed	
Last Edited 17/01/2020	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Cervical cancer is a leading cause of death by cancer in women. Despite the successes of screening and vaccination, a large proportion of women dont take preventative steps and are diagnosed with locally advanced stages of cancer. Concurrent chemotherapy and radiation therapy (RT) is the standard treatment for patients in addition to standard cisplatin-based chemotherapy. When patients received this combination treatment, there are side effects and sometimes the cancer returns. Therefore, strategies to reduce the side effects and allow treatment intensification are needed. Conventional pelvic RT results in a box-shaped radiation dose to the pelvis that covers both tumor tissues and normal tissues. Intensity modulated radiation therapy (IMRT) is a modern RT technique that differs from conventional techniques in many ways. First, patients undergo computed tomography (CT) simulation so that customized radiation doses can be delivered. IMRT treatment planning involves multiple beam angles and uses computerized treatment planning to reduce radiation to surrounding normal tissues. This would be the first international study to test IMRT for both postoperative and definitive treatment of cervical cancer.

Who can participate?
Patients with cervical cancer (invasive squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma) will be enrolled in the study.

What does the study involve?
After signing an informed consent form, patients will receive radiation therapy daily (Monday to Friday) for 5 to 5½ weeks. Once a week on study days 1, 8, 15, 22, and 29 patients will also receive intravenous infusions of cisplatin prior to radiation therapy. In addition, once a week some evaluations and tests will be done. After chemotherapy and radiation is complete patients will be followed up at the following times: 1 week, 2 weeks, 1, 2, 4, 8, 12, 18, 24, 30, and 36 months. The assessments at these visits will be part of the patients routine care for their cancer and will include a physical examination, review of side effects, testing and a quality of life evaluation.

What are the possible benefits and risks of participating?
Standard treatment for cervical cancer may involve risks and discomforts. Patients will be at risk for side effects whether or not you choose to participate in this study. There may also be other side effects that we cannot predict. Medicines and other treatments can be given to make the side effects less serious and uncomfortable. Many side effects go away shortly, but in some cases, side effects may be serious, long-lasting, and may even cause death.
Patients participating in this study may receive a direct medical benefit. IMRT reduces radiation doses to normal organs and tissues, which previous studies have indicated may reduce side effects compared to standard radiation therapy. However, the benefits of IMRT are unknown. Others may also benefit from the information learned from this research study.

Where is the study run from?
The University of California, San Diego Moores Cancer Center is coordinating the study between approximately 14 countries and 25 sites.

When is the study starting and how long is it expected to run for?
Patient enrollment started in September 2011 and is expected to continue until December 2014.

Who is funding the study?
United States of America National Institute of Health and University of California, San Diego Moores Cancer Center

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01554397

Protocol serial number

INTERTECC, NIH grant R21CA162718-01

Study information

Scientific Title
Phase II/III clinical trial of intensity modulated radiation therapy with concurrent cisplatin for stage I-IVA cervical carcinoma

Study objectives
Compared to conventional RT techniques, IMRT will reduce acute hematologic and gastrointestinal toxicity for cervical cancer patients treated with concurrent cisplatin

Ethics approval required
Old ethics approval format

Ethics approval(s)
University of California, San Diego Human Research Protection Program, 08 August 2011, ref: 110808

Primary study design
Interventional

Study design
Randomised phase II/III trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Biopsy-proven, invasive squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the cervix

Interventions
Phase II Open Label (1 Arm) Expected Enrollment = 91 Patients
Cisplatin 40 mg/m2 given weekly (for 5 weeks starting day 1) over 60 minutes IMRT, 45.0 (intact) or 50.4 Gy (postoperative high-risk) in 1.8 Gy daily fractions over 5-5.5 weeks
Optional: Intracavitary Brachytherapy for Postoperative Patients
Follow-up: patients will followed up every 4 months for a year, then every 6 months for 2 years (total 36 months)

Phase III Expected Enrollment = 334 Patients
1. Arm A:
Cisplatin 40 mg/m2 given weekly (for 5 weeks starting day 1) over 60 minutes
IMRT, 45.0 (intact) or 50.4 Gy (postoperative high-risk) in 1.8 Gy daily fractions over 5-5.5 weeks
Optional: Intracavitary Brachytherapy for Postoperative Patients
Follow-up: patients will followed up every 4 months for a year, then every 6 months for 2 years (total 36 months)

2. Arm B:
Cisplatin 40 mg/m2 Weeks 1-5

Conventional RT, 45.0 (intact) or 50.4 Gy (postoperative high-risk) in 1.8 Gy daily fractions over 5-5.5 weeks
Optional: Intracavitary Brachytherapy for Postoperative Patients
Follow-up: patients will followed up every 4 months for a year, then every 6 months for 2 years (total 36 months)

Intervention Type
Other

Phase
Phase II/III

Primary outcome(s)
To test whether IMRT will reduce the rate of acute grade ≥ 3 hematologic or clinically significant grade ≥ 2 gastrointestinal toxicity compared to conventional RT techniques for cervical cancer patients treated with concurrent cisplatin

Key secondary outcome(s)
1. To estimate and compare the probability of acute and late adverse events
2. To estimate and compare efficacy of cisplatin/IMRT in terms of locoregional failure, disease-specific survival, disease-free survival, and overall survival

Completion date
12/01/2017

Eligibility

Key inclusion criteria
1. Biopsy-proven, invasive squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the cervix
2. Biopsy result positive for carcinoma within 60 days prior to registration
3. FIGO clinical stage I-IVA disease, based on standard diagnostic workup, including:History /physical examination and/or Examination under anesthesia (if indicated)
4. If the patient is status post hysterectomy, one or more of the following conditions must be present: positive lymph nodes, positive margins, parametrial invasion, or non-radical surgery (i.e., simple hysterectomy).
5. If the patient is inoperable, one or more of the following conditions must be present: clinical stage IB2-IVA, positive lymph nodes on nodal sampling or frozen section, and/or parametrial invasion
6. Within 42 days prior to registration, the patient must have any of the following, if clinically indicated: examination under anesthesia, cystoscopy, sigmoidoscopy, rigid proctoscopy, or colonoscopy.
7. X-ray (PA and lateral), CT scan, or PET/CT scan of the chest within 42 days prior to registration;
8. CT scan, MRI, or PET/CT of the pelvis within 42 days prior to registration
9. Karnofsky Performance Status 60-100
10.1. Absolute neutrophil count (ANC) ≥ 1500 cells/mm3
10.2. Platelets ≥ 100,000 cells/mm3
10.3. Hemoglobin ≥ 10.0 g/dl (Note: The use of transfusion or other intervention to achieve Hgb ≥ 10.0 g/dl is acceptable)
10.4. Creatinine clearance ≥ 50 mg/dl
10.5. Bilirubin < 1.5 mg/dl

10.6. WBC ≥ 3,000/µl
10.7. ALT/AST < 3 x ULN
10.8. INR ≤ 1.5
11. Negative serum pregnancy test for women of child-bearing potential

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Prior invasive malignancy (except non-melanomatous skin cancer), unless disease free for a minimum of 3 years
2. Prior systemic chemotherapy within the past three years
3. Prior radiotherapy to the pelvis or abdomen that would result in overlap of radiation therapy fields;
4. Para-aortic, inguinal, or gross (unresected) pelvic nodal metastasis. Gross pelvic nodal metastasis is defined as either: Radiographic evidence of nodal metastasis on CT or MRI (node having short axis diameter > 1 cm)OR Radiographic evidence of nodal metastasis on diagnostic FDG-PET or PET/CT scan (abnormally increased FDG uptake as determined and documented by the radiologist)OR Biopsy-proven metastasis (e.g. needle biopsy) in undissected node
5. Distant metastasis
6. Unstable angina and/or congestive heart failure requiring hospitalization within the past 6 months
7. Hepatic insufficiency resulting in clinical jaundice and/or coagulation defects
8. Uncontrolled diabetes, defined as diabetes mellitus, which in the opinion of any of the patient's physicians requires an immediate change in management
9. Uncompensated heart disease or uncontrolled high blood pressure
10. Acquired Immune Deficiency Syndrome (AIDS) based upon current CDC definition

Date of first enrolment
09/01/2011

Date of final enrolment
12/01/2017

Locations

Countries of recruitment
United Kingdom

Brazil

Canada

China

Czech Republic

India

Korea, South

Taiwan

Thailand

Türkiye

United States of America

Study participating centre
University of California
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Sponsor information

Organisation
University of California, San Diego

ROR
https://ror.org/0168r3w48

Funder(s)

Funder type
Government

Funder Name
National Institutes of Health

Alternative Name(s)
US National Institutes of Health, Institutos Nacionales de la Salud, NIH, USNIH

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	phase II results	01/03/2017	11/04/2019	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes