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Evaluating the effectiveness of combining intensity-modulated radiotherapy technique and paclitaxel plus cisplatin chemotherapy into the treatment of high-risk inoperable cervical cancer

Submission date 14/10/2021	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 25/10/2021	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 17/11/2023	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Cervical cancer is a type of cancer that occurs in the cells of the cervix - the lower part of the uterus that connects to the vagina.
Radiation therapy (also called radiotherapy) is a cancer treatment that uses high doses of radiation to kill cancer cells and shrink tumors.
In recent decades, intensity-modulated radiotherapy (IMRT) has become the mainstream treatment for patients with prostate, rectal, neck, and several other cancers. Such a technique allows for an escalated prescription dose to target areas while sparing normal tissues from excessive radiation.
This study aims to recruit 50 patients to determine whether the incorporation of the IMRT technique and adjuvant paclitaxel plus cisplatin chemotherapy would improve the survival of inoperable locally advanced cervical cancer. The goal is to find a more effective treatment strategy with less toxicity for this group of patients, and the study's findings should help to improve the well-being of patients who suffer from cervical cancer.

Who can participate?
Patients who have biopsy-proven stage III-B- IV-A squamous cervical cancer or patients who have stage II-B disease and metastatic regional nodes.

What does the study involve?
If a patient is enrolled, she will be treated with concurrent chemoradiation. After that, adjuvant chemotherapy will be administered. Radiotherapy consists of external-beam radiotherapy and brachytherapy. External-beam radiotherapy will be delivered with an intensity-modulated technique with dynamic multileaf collimators. Brachytherapy is initiated nearly 3 weeks after the initiation of external beam radiotherapy.
Adjuvant chemotherapy will be scheduled within 4 weeks after the completion of CCRT and

repeated 3 weeks later.
Acute complications such as bone marrow suppression will be monitored twice every week during the treatment. Late complications, as well as treatment outcomes, will be recorded at 3-month intervals for 2 years, every 6 months during the next 3 years, and annually thereafter. At each follow-up visit, pelvic examination, including Pap smear and HPV detection, was routinely performed, whereas imaging, including ultrasound, chest X-ray, CT, or MRI, was prescribed at the physician's discretion.

What are the possible benefits and risks of participating?
Participants treated with such a technique might have improved outcomes. If such a treatment strategy is proven to be an effective option, it will influence how patients with inoperable cervical cancer will be treated in the future. In addition, part of the participants' examination and follow-up will be funded by the sponsor.
The main risks for the participants may be the uncertainty of the superiority of such a treatment plan over traditional treatment. That is, the treatment outcomes of the participants may not be superior to or may even be inferior to conventional CCRT. In addition, chemotherapy-related toxicities, including allergies, bone marrow suppression, hair loss, and liver or renal function impairment, might be another concern.

Where is the study run from?
The study is being run by the National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences, and Peking Union Medical College, and takes place in National Cancer Center/National Clinical Research Center for Cancer /Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (China)

When is the study starting and how long is it expected to run for?
February 2010 to September 2017

Who is funding the study?
National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences, and Peking Union Medical College (China)

Who is the main contact?
1. Dr. Gongyi Zhang
samuel000816@sina.com
2. Prof. Lingying Wu
wulingying@csco.org.cn

Contact information

Type(s)
Public

Contact name
Mr Gongyi Zhang

ORCID ID
https://orcid.org/0000-0002-7264-1232

Contact details

NO.17 Panjiayuan
Chaoyang District
Beijing
China
100021
+86-010-87787210
samuel000816@sina.com

Type(s)
Scientific

Contact name
Dr Lingying Wu

Contact details
NO.17 Panjiayuan
Chaoyang District
Beijing
China
100021
+86-010-87788996
wulingying@csco.org.cn

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
LC2010B33

Study information

Scientific Title
Concurrent definitive chemoradiation incorporating intensity-modulated radiotherapy followed by adjuvant chemotherapy in high risk locally advanced cervical squamous cancer: A phase II study.

Study objectives
Incorporating both intensity-modulated radiotherapy and adjuvant chemotherapy into the concurrent definitive chemoradiation for patients with high risk locally advanced cervical squamous cancer might improve their survival.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 03/04/2010, Ethics Committee of National Cancer Center/Cancer Hospital (Chinese Academy of Medical Sciences and Peking Union Medical College, NO.17 Panjiayuan, Chaoyang District, Beijing, China; +86(0)10-87788495; cancergcp8495@163.com), ref: 10/171-2633

Study design
Single-center interventional single-armed nonrandomized noncomparative phase II trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
High-risk locally advanced cervical squamous cancer

Interventions
Radiotherapy consists of intensity-modulated external-beam radiotherapy and brachytherapy. IMRT is delivered with dynamic multileaf collimators using 6 MV photon beams. Clinical target volume (CTV) is defined as the gross tumor plus areas potentially containing microscopic disease. The CTV is expanded by 5 mm uniformly to create the planning target volume (PTV). Prescription for PTV ranges from 45.0~50.0 Gy at 1.8 Gy~2.0 Gy/fraction in 25 fractions. Involved nodes are contoured separately and are defined as GTV nodes. A tailored margin of 3 mm is added to GTV nodes to generate PTV nodes, which are treated with a simultaneous integrated boost (SIB) technique to a total dose of 50.0–65 Gy at 2.0- 2.6Gy/fraction in 25 fractions. Brachytherapy is initiated when 27.0~30.0 Gy of external beam is delivered to PTV. The aim of brachytherapy boost is to deliver cumulative EQD2 doses (combined external beam radiotherapy (EBRT) and brachytherapy delivered in 2 Gy equivalent doses) of ≥80 Gy to point A for stage B-A disease and ≥90 Gy for stage B-A disease. Specifically, a total dose of 28~35 Gy high-dose-rate (HDR) brachytherapy is prescribed to point An in 4~5 weekly fractions using an iridium-192 source. An additional fraction of 5-7 Gy brachytherapy will be delivered if a residual cervical tumor is suspected by pelvic examination or MRI.
Chemotherapy consists of 4~6 cycles of concurrent cisplatin infusions and 2 cycles of adjuvant TP regimen. Concurrent weekly intravenous cisplatin at 30 mg/m² is initiated on the first day of radiotherapy for over 1 hour during EBRT.
Adjuvant chemotherapy was scheduled within 4 weeks after the completion of CCRT and repeated 3 weeks later. Paclitaxel 150 mg/m2 was given as a 3-hour infusion on day 1, followed by cisplatin 35 mg/m2 with a 1-hour infusion on days 1-2 (70 mg/m2 in total). Discontinuation of chemotherapy is allowed in the event of grade 3-4 hematological or gastrointestinal toxicities. It will resume when patients' absolute neutrophil count recovers to ≥1500/mm3 and their platelet count improves to ≥100,000/mm3; however, doses of all agents should be subsequently reduced by 20%.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Disease-free survival (DFS) and overall survival (OS) are measured from the time of diagnosis to the time of first evidence of relapse or death from any cause. Patients without documented evidence of recurrence are censored at the date of last follow up visit. The cumulative survival rate is calculated with the Kaplan-Meier method using SPSS.

Key secondary outcome(s))
1. Patterns of failure measured in terms of locoregional recurrence (LRR) and distant metastasis (DM) at the time of first evidence of relapse.
2. Toxicities are measured according to the Common Terminology Criteria for Adverse Events (CTCAE) v4.0 and Radiation Therapy Oncology Group (RTOG) Late Radiation Morbidity Scoring Scheme every week during the treatment, every 3-months after the completion of treatment for 2 years, and every 6 months during the next 3 years.

Completion date
01/09/2017

Eligibility

Key inclusion criteria
1. Biopsy proven stage III-A- IV-A squamous cervical cancer or stage II-B disease with metastatic regional nodes.
2. Age 18-70 years
3. Eastern Cooperative Oncology Group (ECOG) performance status (PS) ≤1
4.No previous history of chemotherapy or radiotherapy
5. Sufficient bone marrow, including leukocyte count ≥4,000/mm^3, neutrocyte count ≥2,100 /mm^3, platelet count ≥100,000/mm^3, hemoglobin ≥90 g/L.
6. Adequate renal and hepatic functions.
7. Normal cardiovascular function.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
70 years

Sex
Female

Total final enrolment
52

Key exclusion criteria
1. Patients with synchronous malignancies
2. Patients with distant metastases
3. Patients with known hypersensitivity to cisplatin or paclitaxel
4. Patients with poorly controlled medical conditions

5. Patients with previous chemotherapy or radiotherapy treatment.
6. Patients who were pregnant or lactating.

Date of first enrolment
01/06/2010

Date of final enrolment
01/01/2013

Locations

Countries of recruitment
China

Study participating centre
National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College
NO.17 Panjiayuan
Chaoyang District
Beijing
China
100021

Sponsor information

Organisation
Cancer Hospital of Chinese Academy of Medical Sciences

ROR
https://ror.org/03x937183

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Cancer Hospital of Chinese Academy of Medical Sciences

Results and Publications

Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		20/12/2022	17/11/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Preprint results		07/07/2021	18/07/2022	No	No
Protocol file			25/10/2021	No	No