# Study on the relationship between plasma MRD and cfDNA HPV and the efficacy and prognosis of locally advanced cervical cancer after concurrent chemoradiotherapy

Project Title: Relationship between plasma MRD and cfDNA HPV and efficacy and prognosis after concurrent chemoradiotherapy for locally advanced cervical cancer

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A.、Purpose of the study

1. Main objective: To detect the expression levels of MRD and plasma HPV before and after concurrent chemoradiotherapy for cervical cancer based on cfDNA liquid biopsy, and to evaluate the efficacy and recurrence risk of cervical cancer after concurrent chemoradiotherapy by the expression levels of MRD and plasma HPV

2. Secondary objectives: To facilitate clinical decision-making on whether to adjuvant chemotherapy, as well as the timing of adjuvant chemotherapy and the benefits of adjuvant chemotherapy through the expression levels of MRD and plasma HPV.

B.、Types of study design, principles and procedures

1. study design

This is a prospective, observational, single-center study

2. Study population and sample size considerations

Study population: Cervical cancer patients diagnosed with initial visit to Guizhou Provincial People's Hospital from November 2022 to November 2024 were collected.

Sample content estimation

There were about 30 cases in the experimental group, and the sample estimation was estimated by Power and Sample Size Program software, α 0.05, Power 0.8, δ and σ were obtained according to the literature review, m was 0.5.

2.1 Inclusion Criteria:

(1) Age: ≥ 18 years old, ≤ 75 years old.

(2) Pathological histologic confirmation of cervical cancer.

(3) Imaging or PET/CT examination can be performed to understand the tumor

and complete all follow-up.

(4) Measurable lesions before treatment.

(5) Good physical condition: ECOG score 0-1 (or KPS score 70-100).

(6) Estimated survival≥ 6 months.

(7) The baseline blood routine and biochemical indexes before radiotherapy and chemotherapy met the following standards: hemoglobin ≥ 80g/L, absolute neutrophil count (ANC) ≥ 1.5×109/L, platelet ≥ 100×109/L, ALT, AST ≤ 2.5 times the normal upper limit; Serum albumin ≥ 30 g/L.

(8) There are three preoperative items: if the patient has syphilis, plum repellent therapy is required before treatment.

(9) The patient has no history of allergy to rubber products.

(10) Cardiopulmonary function is basically normal

**2.2 Exclusion criteria:**

(1) Those who are allergic to rubber products.

(2) Those with severe acute infection and uncontrolled or purulent and chronic infection wounds that do not heal, chronic hepatitis B active stage, active tuberculosis, syphilis outbreak and AIDS.

(3) Patients with pre-existing severe heart disease, including: congestive heart failure, uncontrollable high-risk arrhythmia, unstable angina, myocardial infarction, severe valvular heart disease, and intractable hypertension.

(4) Those with neurological or psychiatric diseases or mental disorders that are not easy to control, poor compliance, unable to cooperate with and describe treatment responses, uncontrolled primary brain tumors or central

nervous system metastases, and those with obvious cranial hypertension signs or neuropsychiatric symptoms.

(5) with malignant serous effusion.

(6) History of severe enteritis and cystitis, bleeding, intestinal perforation, rectovaginal fistula, rectoval bladder fistula, etc.

(7) Those who have participated in other clinical trials.

(8) Other situations in which the investigator believes that the subject is not suitable to participate in this experiment.

**2.3Exit criteria:**

(1) The subject asked to withdraw from the study.

(2) An irreversible accident occurs.

(3) Unable to effectively follow up with participants.

(4) The investigator considers it necessary for the subject to abort the study from a medical point of view.

(5) Other unforeseen circumstances.

**2.4 Termination of study criteria**

(1) The patient's condition is aggravated.
(2) Occurrence of serious adverse events.
(3) Poor patient compliance.

**3. Duration of the study**

November 2022 to November 2024

**4. Research interventions**

This study was non-interventional.

**5. Study steps and related checks**

Before treatment: clear cervical pathology is required to confirm cervical cancer, complete imaging data, hematological data, laboratory test results

and comprehensive medical history.

Treatment period: Complete standard treatment of cervical cancer (concurrent chemoradiotherapy).

Follow-up period: Regular review at 4, 12 and 24 weeks after the end of treatment

### 6. Use and preservation of biological samples

Cervical tumor tissue was taken twice and made into wax blocks before treatment and during treatment (before the start of the first post-loading treatment); Clinically observe tumor retraction and monitor efficacy.

5ml of peripheral blood was drawn 5 times, respectively, before treatment, during treatment (before the start of the first after-loading treatment), 4 weeks, 12 weeks and 24 weeks after treatment, and serum and white blood cells were retained after treatment; Tested at Nanjing Shihe Medical Laboratory No. 128 Huakang Road, Jiangbei New District, Nanjing

### 7. Evaluation indicators/study endpoints

The main endpoint indicators: the expression level and expression status of MRD and plasma HPV before, during, and 4, 12 and 24 weeks after treatment, the relationship between the expression level of MRD and plasma HPV expression status and the efficacy of concurrent chemoradiotherapy for cervical cancer, and the risk of recurrence after concurrent chemoradiotherapy for cervical cancer was predicted.

Secondary endpoints: decision on whether to give adjuvant chemotherapy after the end of concurrent chemoradiotherapy for cervical cancer by the expression level of MRD and the expression status of plasma HPV, as well as the timing of chemotherapy and the benefit of chemotherapy

8. Visiting arrangements and data collection during the study

From November 01, 2022 to November 31, 2024, 30 patients with newly treated cervical cancer admitted to Guizhou Provincial People's Hospital were included, 30 cervical cancer tissue samples were collected before treatment and during treatment (before the start of the first afterload), and 5ml of peripheral blood of cervical cancer patients was collected before, during treatment (before the start of the first afterload), and 4 weeks, 12 weeks and 24 weeks after the end of treatment to detect MRD expression levels. The relationship between the expression level of MRD and the expression status of HPV in plasma and the efficacy of cervical cancer treatment was analyzed.

Thirty cases of cervical cancer were treated with concurrent chemoradiotherapy, and the efficacy was evaluated 4 weeks after the end of chemoradiotherapy, and the value of MRD expression level and plasma HPV expression status for clinically guided adjuvant chemotherapy and adjuvant chemotherapy time node and clinical benefit were evaluated.

MRD and plasma HPV tests were performed 4 weeks, 12 weeks and 24 weeks after the end of concurrent chemoradiotherapy in 30 cases of cervical cancer to understand the risk of recurrence and predict prognosis. The expression level of MRD and the expression status of HPV in plasma and the clinical value of imaging results in predicting recurrence risk were compared.