ORIGINAL

The Relationship Between Expression of HIF-1α and Clinical Response in Cervical Cancer Patients with Neoadjuvant Chemotherapy at Dr. Soetomo Surabaya Hospital

La relación entre la expresión HIF- 1α y la respuesta clínica en pacientes con cáncer de cuello uterino con quimioterapia neoadyuvante en el Dr. Hospital Soetomo Surabaya

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ABSTRACT

This investigation aims to analyze the relationship between expression of Hypoxia Inducible factors-1 αlfa (HIF-1α) to assess the response to neoadjuvant chemotherapy in cervical cancer patients. This research is a Quast Experimental Non-Randomized Before and After with no control design with a sample size of 30 stage IIIB cervical cancer patients by inclusion and exclusion criteria, with pretest and posttest treatment, namely biopsy for immunohistochemical examination and abdominal ultrasound to evaluate lesion diameter cervix after three cycles of chemotherapy. This study showed a decrease in HIF-1α expression before and after chemotherapy (p=0,003) and a decrease in the diameter of cervical lesions before and after chemotherapy (p=0,000). Correlation between decreased HIF-1α expression and decreased diameter of cervical lesions (p=<0,05). Response to neoadjuvant chemotherapy: 25 patients (83,3 %) showed a negative response and 5 patients (16,7 %) showed a positive response. Strong HIF-1α expression before chemotherapy gave a negative response 23 and 25 subjects with a negative response after neoadjuvant chemotherapy. This study found a relationship between high HIF-α expression before chemotherapy with a negative chemotherapy response and low HIF-1α expression after neoadjuvant chemotherapy with a positive chemotherapy response in cervical cancer patients at Dr Soetomo Hospital, Surabaya.

Keywords: Cervical Cancer; HIF-1α; Response to Chemotherapy.

RESUMEN

Este estudio tiene como objetivo analizar la relación entre la expresión del factor-1 alfa inducible por hipoxia (HIF-1 α) para evaluar la respuesta a la quimioterapia neoadyuvante en pacientes con cáncer de cuello uterino. Esta investigación es un estudio cuasi experimental no aleatorizado de antes y después sin un diseño de control con un tamaño de muestra de 30 pacientes con cáncer de cuello uterino en estadio IIIB según criterios de inclusión y exclusión, con tratamiento previo y posterior a la prueba, a saber, biopsia para examen inmunohistoquímico y ultrasonido abdominal para evaluar la lesión. diámetro cervical después de tres ciclos de quimioterapia. Este estudio mostro una disminución en la expresión de HIF-1α antes y después de la quimioterapia (p=0,003) y una disminución en el diámetro de las lesiones cervicales antes y después de la Quimioterapia (p=0,000). Correlación entre la disminución de la expresión de HIF-1α y la disminución del diámetro de la lesión cervical (p=<0,05). Respuesta a la quimioterapia neoadyuvante: 25 pacientes (83,3 %) mostraron una respuesta negativa y 5 pacientes (16,7 %) mostraron una respuesta positiva. La fuerte expresión de HIF-1α antes de la quimioterapia dio una respuesta negativa en 23 y 25 sujetos con una respuesta negativa después de la quimioterapia neoadyuvante. Este estudio encontró una relación entre una alta expresión de HIF-α antes de la quimioterapia con una respuesta negativa a la quimioterapia y una

baja expresión de HIF-1α después. Quimioterapia neoadyuvante con respuesta positiva a la quimioterapia en pacientes con cáncer de cuello uterino en el Hospital Dr. Soetomo de Surabaya.

Palabras clave: Cáncer de Cuello Uterino; HIF-1α; Respuesta a la Quimioterapia.

INTRODUCTION

Cervical cancer is a malignant tumor that develops in the uterus, which occurs because cervical cells are multiplying, resulting in abnormalities and the majority of them occur at the fertile age between 30-45 years. The cause of cervical cancer is the Human Papilloma Virus (HPV) and other risk factors such as sexual relations at a young age or under 18 years, multiple partners, smoking, having many children, low socioeconomic status, using contraceptive pills, and being negative for the Human PapillomaVirus (HPV). Or positive, STIs, and immune disorders.[1] 99,7 % of cervical cancer is caused by the transmission of Human papillomavirus (HPV) types 16 and 18. Indonesia is known for its risk of cervical cancer with around 93 million women, out of a total of 21,000 new cases diagnosed each year cervical cancer is the second most common cancer in Indonesia which occupies the eighth position as the country with the highest number of cases or cervical cancer in Southeast Asia which reached 32,469 or 17,2 % of cases and with a total death rate of 18,279 per year.[2]

Signs and symptoms of cervical cancer are fluor albus which increasingly smell bad due to increased infection and tissue necrosis, bleeding after intercourse, irregular menstrual cycles, amenorrhea and hypermenorrhea, intermenstrual bleeding, pain that spreads to the lower extremities and sometimes mucoid blood comes out and other signs include signs include post-coital bleeding, smelly vaginal discharge, vaginal bleeding continuously without stopping and pain which is an early sign of cervical cancer.[3]

Cancer treatment can be done in several ways, including surgery, radiotherapy, and chemotherapy. Chemotherapy is a systematic therapy that spreads throughout the body and can reach cancer cells that have spread far or metastasized to other places at the same time, which is called combination chemotherapy.[4]

Chemotherapy is a method of treating cancer by eradicating cancer cells through drugs that enter the body by killing and preventing the spread and inhibiting the development of developing cancer cells. chemotherapy is a systematic treatment method to kill cancer cells. Cisplatin is an anti-tumor and chemotherapy drug that is most widely used for various malignant treatment programs and increases survival rates and is used as a hope for a cure because cisplatinus combined with capecitabine induction chemotherapy so that it can improve the quality of life and reduce the possibility of recurrence and metastasis in patients.[5]

The way cisplatin works is that it can reduce tumor size, increase tumor sensitivity to radiation, and reduce the occurrence of micrometastases because cisplatin works systemically so that not only cancer cell share affected but normal cells are also affected and the use of cisplatin in chemotherapy drugs shows a Response Rate of 15- 47 %. [5,6]

The most common side effects are feeling tired, hair loss, dry mouth, nausea, vomiting, fertility problems, diarrhea, and weakened memory, so this is sometimes the reason why patients do not comply with chemotherapy.[7]

Hypoxia is a condition where the oxygen supply cannot meet the needs of organisms, organs, and cells, so in this situation, the organism or cells must activate various mechanisms to maintain energy levels. Hypoxia inducible factors (HIF) is a protein with a basic loop-helix-loop that forms a heterodynamic complex that acts as a transcription regulator of genes containing hypoxia response consensus sequences (HREs). The basic form of the structure is Hypoxia Inducible Factor (HIF-1) which consists of 2 subunits, namely Hypoxia Inducible Factor 1 alpha (HIF-1α) which is a subunit regulator of oxygen and Hypoxia Inducible Factor 1 beta (HIF-1β) which is expressed directly throughout the body. a network called Aryl hydrocarbon Receptor Nuclear Translocator or ARNT to degrade transcription factors. The synthesis of the (HIF-1α) protein is regulated by an oxygen-independent mechanism that is influenced by oxygen. (HIF-1α) is a transcription factor that targets genes involved in three main groups in low oxygen homeostasis: vascular development, blood cell production, or changing energy metabolism.[8]

Immunohistochemistry or IHC is a method that is widely used to test anatomical pathology to classify and diagnose cells by using antibodies targeted against certain antigens in tissues and cells to determine cell type. Ultrasound examination is the main imaging modality to evaluate patients with various symptoms, including patients with various symptoms including pelvic pain, pelvic infections, abnormal vaginal bleeding, endocrine abnormalities, and the presence of pelvic masses. Ultrasound imaging can identify the primary site for various pelvic pathologies and enforce management in patients, including the role of pelvic ultrasound as a first-line gynecological imaging modality for detection, making it easier to establish the diagnosis and appropriate management of patients. Ultrasound imaging along

with other modern imaging methods and in the assessment of cervical cancer patients with ultrasound is recommended for detecting renal pelvic dilatation ultrasound has undergone many technical developments that

are comparable to Magnetic Resonance Imaging (MRI) for detecting the pelvic area thereby increasing the high number of ultrasound users. Ultrasound also has many advantages, one of which is that it is cheaper, cheaper and does not disturb the patient's comfort. Imaging examination to accurately plan the size and location of the tumor (tumor topography), the presence of infiltrates, and the status of lymph nodes.[8,9]

Response Evaluation Criteria in Solid Tumor (RECIST) method to measure lesions or measurable lesions at least 1 lesion with a minimum size of 10 mm with a spiral CT Scan or 20 mm with a conventional CT Scan. Lesions that cannot be measured or non-measurable lesions are lesions with a size of <20 mm/10mm such as ascites, pleural/pericardial effusion, cystic lesions, and other non-target lesions that are part of the disease. Neoadjuvant chemotherapy is chemotherapy given before main interventions such as radiation and surgery to inhibit the growth of tumor mass and facilitate surgery, radiation, or other procedures.[9]

METHOD

This research was conducted at the Oncology Poly clinic at Dr. Soetomo Hospital Surabaya from 24 October to 13 March 2024, using the Quast Experimental Non Randomized Before & After research method with no control without randomization stages, by the inclusion and exclusion criteria, all research objects were pretested with biopsy and ultrasound and posttest with biopsy and ultrasound after receiving 3 cycles of chemotherapy, followed by immunohistochemical examination to assess the expression of HIF-1α and the data were tabulated and analyzed.

The population in this study were women suffering from cervical cancer who underwent examination and the sample was 30 with the inclusion criteria of IIIB cervical cancer patients with inclusion criteria who had never received chemotherapy and had PA results at the Oncology Clinic at Dr. Soetomo Hospital, Surabaya.

Data obtained from the research were age, education, age at marriage, parity, histology, response to chemotherapy, HIF-1α expression before and after chemotherapy using immunohistochemical techniques, measurement of expression levels using the IRS/Remmle Score system with weak, medium, strong staining. and diameter of cervical lesions before and after neoadjuvant chemotherapy. Ethical Approval Number: 0812/KEPK/X/2023

RESULTS

Characteristics of research subjects

The characteristics of the research subjects based on age were 4 people aged less than 40 years (13,3 %), 21 people aged 40-60 years (21 %), and 5 people aged> 60 years (16,7 %). The characteristics of the research subjects based on education were 12 people (40,0 %) had elementary school education, 13 people (43,3 %) had junior high school education and 5 people (16,7 %) had high school education. The characteristics of research subjects based on age at marriage were 19 people aged <20 years (63,3 %), 2 people aged 20 years (6,7 %), and 9 people aged >20 years (30,0 %). The characteristics of research subjects based on parity were parity <3 as many as 17 people (56,7 %), parity 3as many as 11 people (36,7 %) and >3 as many as 2 people (6,7 %). The characteristics of the research subjects based on histology were 25 people (83,3 %) with Squamous cell carcinoma (SCC) and 5 (16,7 %) with Adenocarcinoma (ADC). The characteristics of research subjects based on chemotherapy response were Partial Response in 5 subjects (16,7 %), and Stable Disease in 25 subjects (83,3 %)

Table 1. Characteristics of research subjects		
	Category	**Amount**
Age	< 40 years	4 (13,3 %)
	40-60 years	21 (70,0 %)
	>60 years	5 (16,7 %)
Education	Elementary School	12 (40,0 %)
	Junior high School	13 (43,3 %)
	Senior high School	5 (16,8 %)
Marriage age	<20 years	19 (63,3 %)
	20 years	2 (6,7 %)
	>20 years	9 (30,0 %)
Parity	<3	17 (56,7 %)
	3	11 (36,7 %)
	>3	2 (6,7 %)
Histology	SCC	25 (83,3 %)
	ADC	5 (16,7 %)
Chemotherapy Response	PR	5 (16,7 %)
	SD	25 (83,3 %)

Differences in HIF-1α expression in cervical cancer patients before and after neoadjuvant chemotherapy. Analysis of the HIF-1α tissue expression variable using the Wilcoxon test before giving neoadjuvant chemotherapy and after giving neoadjuvant chemotherapy was normally distributed with a value of p<0,001

Table 2. Normality test of HIF-1α tissue expression before andafter administration of neoadjuvant chemotherapy

Variable	Wilcoxon
Expression HIF-1α pre and post	p=0,000
*Significant p <0,05 (p=0,000)	

Because the tissue HIF-1α expression data was normally distributed, a difference test was carried out using the paired t-test. It can be seen in the table that the mean tissue HIF- 1α expression before administering neoadjuvant chemotherapy was higher (7,23) compared to after administering neoadjuvant chemotherapy (5,73) with a value of p = 0,003 (p<0,05). This shows a significant difference between tissue HIF-1α expression before chemotherapy and after neoadjuvant chemotherapy and means that neoadjuvant chemotherapy effectively reduces HIF-1α expression.

Table 3. Test of difference in mean tissue HIF-1α expression before and after administration of neoadjuvant chemotherapy

Group	N	Average of HIF-1	SD	p expression
Before Chemotherapy	30	7,23	1,54	0,001
After Chemotherapy	30	5,73	1,43	
*Significant p<0,05 (p=0,001)				

Diameter of Cervical Lesions Before and After Neoadjuvant Chemotherapy in Cervical Cancer Patients

Analysis of the variable of the largest diameter of cervical lesions using the normality test (Shapiro-Wilk) before giving neoadjuvant chemotherapy and after giving neoadjuvant chemotherapy was normally distributed with a value of p=902 (p>0,005) for the results before giving chemotherapy and p=192 (p>0,005). for results after administration of chemotherapy.

Table 4. Normality test of the largest diameter of cervical lesions before and after administration of neoadjuvant chemotherapy

Variable	Kolmogorov-Smirnov	Shapiro-Wilk
Pre lesion diameter	0,20*	902
Post lesion diameter	0,20*	120
Sig. 0,200* p > 0,05		

Because data on the largest diameter of cervical lesions was normally distributed, a difference test was carried out using the paired t-test. From the table above, it can be seen that the mean largest diameter of cervical lesions before chemotherapy was given was higher (5,61) than after chemotherapy (3,87) with a value of p=0,000. This shows that there is a very significant difference between the largest diameter of cervical lesions and after giving neoadjuvant chemotherapy and it can be concluded that giving neoadjuvant chemotherapy is very effective in reducing the diameter of cervical lesions.

Table 5. Test for differences in the largest diameter of cervical lesions before and after neoadjuvant chemotherapy

Group	N	Average of HIF-1 α	SD	p expression
Before Chemotherapy	30	5,61	1,77	0,001
After Chemotherapy	30	3,87	2,28	
*Significant p<0,05 (p=0,001)				

DISCUSSION
Epidemiological Characteristics

Hypoxia Inducible Factor-1 (HIF-1) is a transcription factor that plays an important role in maintaining oxygen balance, both at the cellular and systemic levels. The HIF-1 molecule is a heterodimer consisting of an α subunit and a β subunit. However, only the α subunit had its stability and activity enhanced under hypoxic conditions. Thus, the α subunit is believed to be a marker of hypoxic tissue. [10,11]

HIF-1α is a transcription factor that targets genes involved in three main groups of low oxygen homeostasis namely vascular development, blood cell production, or altered energy metabolism and HIF-1α can act as a malignant tumor suppressor gene.[12]

The expression of HIF-1α in tissue increases due to hypoxic conditions in tumor tissue and is by the results of this study that neoadjuvant chemotherapy can reduce the size of the lesion thereby reducing oxygen demand in the tissue because it has decreased after being given neoadjuvant chemotherapy. The basic form of the structure is HIF-1α which consists of 2 subunits, namely HIF-1α which is a regulatory subunit and HIF-1ß which is expressed directly throughout the tissue called Aryl hydrocarbon Receptor Nuclear Translocator (ARNT) and synthesized from the HIF-1α protein are regulated by an oxygen-independent mechanism where the expression of HIF-1α is influenced by tissue oxygen levels.[13]

In this study, the expression HIF-1α decreased significantly after administering neoadjuvant chemotherapy because one of the aims was to shrink the size of the lesions on the cervix there by reducing the oxygen demand of cancer cells and the expression of HIF-1α, and has a role in reducing hypoxic conditions by increasing the expression of Vascular Endothelial Growth Factor (VEGF) and inhibiting p53 expression.HIF-1α has a role as an independent prognostic factor for the number of Survival has also been tested in univariate and multivariate analysis tests.[14]

Based on the results of this research, the majority of their education is in junior high school with 13 subjects, which is the result of this research in line with research that there is a relationship between education and the incidence of cervical cancer because insight or the level of education, a person will shape their personality. who are more critical in dealing with various things because the higher a person's education, the broader their insight so they can think and behave positively, especially for health-related to reproductive hygiene to reduce the risk of developing cervical cancer and this is by the results of research that the majority of women with cervical cancer have a lower level of education, so adequate education is needed so that there are no misunderstandings about the disease or health and treatment, making it easier for patients to accept it with a positive attitude and it is also easier to convey to the family what is happening, on the other hand. On the other hand, education also increases a person's awareness of the symptoms of disease so that they can be treated more quickly.[14,15]

Based on the age of marriage in this study, the majority were <20 years as many as 19 subjects. where the results of this study are in line with the results of research by Chairani that there is a significant influence between the age of first sexual intercourse on the incidence of cervical cancer due to age at first having sexual intercourse for ≤20 years increases the risk of cervical cancer and women who have had sexual intercourse for the first time <20 years are estimated to have a 3,3 times risk of suffering from cervical cancer compared to women who have had sexual intercourse>20 years and there are many factors that influence women's susceptibility to cervical cancer, including the age at which they first have sexual intercourse, education, and lifestyle and the age at which they first get married is 20 years old. 2,4 times higher risk of experiencing cervical cancer compared to those with a first marriage age of >20 years, as well as women who have sexual intercourse for the first time at a young age or less than 20 years, have multiple partners, have a history of STIs, HIV/AIDS, family history of cervical cancer and smoking.[16,17]

Based on parity in this study, there were <3 as many as 17 subjects or 56,7 %, where the results of this study are in line with which states that there is no significant relationship between parity and the incidence of cervical cancer and is also in line with the results of the study. states that there is no relationship between parity and the incidence of cervical cancer because there are still other things that may be a factor in the occurrence of cervical cancer.[18]

Based on histology, there were SCC, 25 subjects or 83,3 %, which the results of this study are in line with the results of research from with the largest number of sufferers being SCC histopathology and based on the results of SCC has a greater chance of survival. better than other histopathology because this result is also supported by other research, namely the high number of sufferers with SCC histopathology results of up to 83,3 %, much greater than the others because it also has a better survival rate.[19]

The most frequently encountered histopathological type is squamous cell carcinoma, which is around 80 %, followed by adenocarcinoma at 20 %, while other histopathological types are rare and in research at Al-Ihsan Regional Hospital, Bandung, 2017, there were 58 people (70,7 %) Of the 82 people included in the squamous cell carcinoma group.[20]

These results are also supported by previous research at RSUD Dr. Zainoel Abidin Banda Aceh, 2012 found that 17 people (77,28 %) out of 22 people had the histopathological type of squamous cell carcinoma and based on research at Sardjito General Hospital Yogyakarta, 2016 from 105 cervical cancer patients, 76 had squamous cell carcinoma type and the results of research found that 320 cases of 447 cases of cervical cancer were squamous cell carcinoma type. In Osman's study, from a total of 1760 cases, around 1680 cases were included in the squamous cell carcinoma group, followed by 55 cases in the adenocarcinoma group and in line with the results of the Endo study in 2011of 85 cancer patients. cervix, 76 patients were in the squamous cell carcinoma

group.

This is supported by research 2011 of 275 patients, the most common histopathological type was the squamous cell carcinoma group with a total of 221 patients, and research results from Alcazar et al were also obtained from 56 tumor cases, 49 cases came from squamous cell carcinoma and was followed by 9 cases by adenocarcinoma.

Differences in HIF-1a expression before and after neoadjuvant chemotherapy in cervical cancer patients

In this study, the expression HIF-1α decreased significantly after administering neoadjuvant chemotherapy from 7,23 before chemotherapy and 5,73 after chemotherapy, thisis because one of the aims of administering neoadjuvant chemotherapy is to shrink or reduce the size of the lesions on the cervix. thus reducing the need for oxygen in cancer cells and being able to be a therapy for cancer and a tumor suppressor. The results of other research also found that HIF 1-α in breast cancer patients, HIF1-α is an independent prognostic factor with its ability to form new lymphatic channels that it can be used as a target for therapy against tumor progression and metastasis and the results of other studies show that there is a significant difference between the expression of HIF-1α before and after the administration of neoadjuvant chemotherapy because the administration of neoadjuvant chemotherapy can reduce and there are significant results ($p = 0,000$) because the expression of HIF-1α is an important transcription factor in regulating neovascularization and maintaining oxidative metabolism to remain stable.

Diameter of cervical lesions before and after administration of neoadjuvant chemotherapy in cervical cancer patients

The results of this study showed that the diameter of cervical lesions decreased significantly after administering neoadjuvant chemotherapy with the average diameter of cervical lesions before chemotherapy and after chemotherapy at 3,87 mm ($p=0,000$), which is in line with previous research that showed the response to neoadjuvant chemotherapy. in cervical cancer patients it influences tumor diameter, which is influenced by the response to chemotherapy and the larger the tumor size, the worse the response to chemotherapy given and tumors with a diameter of more than 4 cm will be at risk of a poor response, this is by international journals and Scientific Innovation review in May 2023 as well as other research conducted stated that the average diameter of the largest cervical lesion before neoadjuvant chemotherapy was greater than after with a comparison of 5,62 with 3,50 $p<0,001$).

Relationship between HIF-1a expression and cervical lesion diameter after neoadjuvant chemotherapy in cervical cancer patients

The results of this study showed a relationship between a decrease in HIF-1α expression and a decrease in the greatest diameter of cervical lesions after neoadjuvant chemotherapy, with a positive correlation at a moderate level of relationship with a p-value = 0,41, which means that the relationship between a decrease in HIF-1α expression and a decrease in diameter cervical lesions after administration of neoadjuvant chemotherapy is quite significant and this is in line with the results of previous research that the diameter of cervical lesions affects the results of chemotherapy which is followed by HIF-1α examination for immunohistochemical examination, the results of which are chemotherapy and HIF-1α is able to influence the diameter of cervical lesions and even when the cells die due to exposure to chemotherapy, there will no longer be any biomarker expression in the tissue so that the assessment is detected early and is supported by the results of research from Santoso and Askandar that administration of cisplatin, vincristine and bleomycin chemotherapy provides a success rate of 14,6 %

Relationship between HIF-1a expression before and after chemotherapy and response to neoadjuvant chemotherapy in cervical cancer patients

The results of this study showed a negative response from 25 subjects with responsive disease and a positive response from 5 subjects with Partial response, then the response to neoadjuvant chemotherapy was further categorized into positive response (Complete response and Partial response) and negative chemotherapy response (Stable disease and Progressive disease). Based on these results, it shows that the majority in this study were stable disease, namely 25 subjects (83,3 %) and the results of this study are in line with research by Grimaldi S, Terroir M and Caramella C, in The Quarterly Journal of Nuclear Medicine and Molecular Imaging that limitations in the use of recist to evaluate the response to chemotherapy based on changes in tumor size (size based evaluations), where with this application anti-angiogenic agents, immunotherapy and local treatment are not sufficient.

Cervical cancer with the SCC type which had a good response to chemotherapy was 32 % or 8 subjects and the rest responded well with the PR type, while the number of subjects who responded poorly to chemotherapy was greater, namely 16 subjects (68 %), of which 16 subjects, only one subject experienced a Progressive disease

response, the remaining 15 subjects were in the Stable disease type so that from the results of this study and supporting journals from the statement above that HIF-1α expression before chemotherapy is associated with a very low level of negative response in cervical cancer patients (p =0,004) Andalas Journal of Obstetrics and Gynecology, 2019 and in this case it is also supported by the results of research by He et al., 2018 that squamous cell carcinoma responds well to neoadjuvant chemotherapy by 80,2 % and the squamous cell carcinoma type has a good response to neoadjuvant chemotherapy better and significant survival rate.

Research limitations

In the research there are several limitations, namely:
- This research for RECIST assessment still uses ultrasound
- This study focuses on the relationship between HIF-1α expression and a decrease in cervical lesions and the response to chemotherapy in cervical cancer patients, whereas neoadjuvant chemotherapy cannot completely reduce the size of cervical cancer.
- This research uses a quasi-experimental pre and post-method which requires quite a long time to wait for the patient to return while still adjusting his return schedule and must be in place for those who dropout.

CONCLUSIONS

Based on the results of the research and discussion carried out, it can be concluded as follows: hypoxia Inducible Factor-1alpha (HIF-1α) expression decreased significantly with a moderate correlation in cervical cancer patients with response to neoadjuvant chemotherapy. The diameter of cervical lesions decreased significantly after administering neoadjuvant chemotherapy to cervical cancer patients. High HIF-1α expression before neoadjuvant chemotherapy is associated with a negative chemotherapy response and low HIF-1α expression after chemotherapy is associated with a positive chemotherapy response in cervical cancer patients. Expression of Hypoxia Inducible Factor-1alpha (HIF-1α) can be used as a biomarker in patients with cervical cancer

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