

## Immune checkpoint inhibitors efficacy in cervical cancer

Luo Jianwei<sup>1,a,\*</sup>

<sup>1</sup>Leshan vocational and Technical College, Leshan, 614000, China

<sup>a</sup> 512076491@qq.com

\*corresponding author

**Keywords:** Immune checkpoint inhibitors; immunotherapy; cervical cancer

**Abstract:** To explore the clinical effects of immune checkpoint inhibitors in the treatment of cervical cancer patients. [Methods] A total of 218 patients with cervical cancer admitted to our hospital were included. It is administered according to the clinical treatment plan of immunotherapy, including single administration such as Nivolumab and Ipilimumab and combined administration with chemotherapy. [Results] The effective rate of treatment was 78%; after treatment, the positive rate of vaginal resection margin was 4.00%, the positive rate of lymph node metastasis was 3.00%, the positive rate of parauterine involvement was 6.00%, and the positive rate of vascular infiltration was 2.00%; After treatment, the tumor size was significantly reduced. The maximum diameter of the tumor before treatment is 5.24 cm, and the maximum diameter of the tumor after treatment is 3.06 cm; After immune checkpoint inhibitor treatment, the 1, 2 and 3 year tumor-free survival rates were 93.50%, 83.42%, and 79.63%, respectively, the median progression-free survival was 35.4 months, and the median overall survival was 78.2 months. The adverse reaction rate is low and the adverse reactions are mainly minor reactions. Three patients had grade III reactions. [Conclusion] Immune checkpoint inhibitors have relatively satisfactory clinical effects for patients with cervical cancer. They can significantly shorten the maximum tumor diameter, enhance the therapeutic effect and reduce the incidence of pathological positives, and are worthy of clinical application.

### 1. Introduction

Cervical cancer is the most common gynecological malignant tumor for women in my country, which seriously threatens women's health. The 5-year survival rate of patients with early cervical cancer receiving surgery, radiotherapy and chemotherapy exceeds 90%, while the 5-year survival rate of patients with advanced cervical cancer is less than 20%, and the 5-year survival rate of patients with recurrent cervical cancer is less than 5% [1]. The treatment of advanced, recurrent and metastatic cervical cancer is still a huge challenge faced by gynecological oncologists, and there is an urgent need to explore more effective treatment methods.

Reports showed that the expression rate of programmed death ligand 1 in cervical intraepithelial neoplasia cells reached 95% (20 /21), while the expression rate of programmed death ligand 1 in cervical squamous cell carcinoma was 80% (56 / 70). There are high levels of programmed death ligands in the metastatic lymph nodes 1 positive antigen presenting cells and regulatory T cells [2]. The above data shows that immune checkpoint inhibitors have great potential in the treatment of cervical cancer.

At present, driven by the continuous advancement of biomedical and clinical technology, immunotherapy has become the most promising new treatment model, and immune checkpoint inhibitors have played an active role in the clinical treatment of tumors. Immune checkpoint inhibitors have been approved by the US Food and Drug Administration for the clinical treatment of some malignant tumors (such as lung cancer and melanoma) or have entered clinical trials [3]. However, the current data on the treatment of cervical cancer immune checkpoint inhibitors are still limited, and most reports are individual cases. Therefore, this article mainly describes the therapeutic effects of immune checkpoint inhibitors in cervical cancer, and discusses the latest research progress of new immune checkpoints in cervical cancer.

## **2. Clinical data and research methods**

### **2.1. General information**

Cervical cancer patients admitted in our hospital from March 2017 to March 2019 are the research objects. The calculation of the sample size is based on the data obtained in the preliminary survey. Inclusion criteria of the study subjects: diagnosis of cervical cancer by pathological and histological diagnosis. Between 18 and 65 years old; normal listening, speaking, reading and writing skills; no cognitive impairment, no mental illness; informed consent and voluntary participation in the study. The exclusion criteria are: presence of other cancers or serious diseases; participating in other research. In the end, 218 patients were included in this study. The average age was  $45.17 \pm 9.43$  years. The growth types included 41 cases of endogenous cervical cancer, 69 cases of exogenous type, 63 cases of squamous cell carcinoma, 28 cases of adenocarcinoma, and 17 cases of squamous adenocarcinoma. This study complies with the relevant requirements of the Declaration of Helsinki of the World Medical Association.

### **2.2. Mode of administration**

It is administered according to the clinical treatment plan of immunotherapy, including single administration such as Nivolumab and Ipilimumab and combined administration with chemotherapy. Tumor PD-L1 score  $\geq 1$  point and received at least 1 course of chemotherapy. The treatment regimen is 200 mg intravenously every 3 weeks until unacceptable toxicity or disease progression occurs.

### **2.3. Observation indicators**

Observe the treatment effect of patients, and evaluate the treatment effect according to the evaluation standard of solid tumor. Complete remission: After treatment, the patient's tumor marker levels returned to normal, and all target and non-target lesions disappeared. Partial remission: After treatment, the longest diameter of the patient's baseline lesion was reduced by  $\geq 30.00\%$  compared to before treatment. Stable: After treatment, the total length of the patient's baseline lesions decreased to a certain extent, but did not achieve partial remission or increased to a certain extent but did not achieve progress. Progress: After treatment, the patient has new lesions or the total length of the baseline lesions has increased by  $20.00\%$  compared to before treatment. Effective rate = (complete remission + partial remission)/total number of cases  $\times 100.00\%$ .

### **2.4. Statistical methods**

SPSS19.0 statistical software was used for statistical analysis. Measurement data are expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ), using  $t$  test; Count data is expressed as rate (%), using  $\chi^2$  test.  $P < 0.05$  indicates that the difference is statistically significant.

## **3. Result**

### **3.1. Treatment effect**

The effective rate of treatment with immune checkpoint inhibitors is 78%. 8% of the cases progressed, 14% were stable, the partial remission rate was 14%, and the complete remission was 64%.

### **3.2. Pathologically positive occurrence**

After treatment, the positive rate of vaginal resection margin was 4.00%, the positive rate of lymph node metastasis was 3.00%, the positive rate of parauterine involvement was 6.00%, and the positive rate of vascular infiltration was 2.00%.

### **3.3. Comparison of tumor diameter before and after treatment**

After treatment, the tumor body was significantly reduced. The maximum diameter of the tumor before treatment was 5.24 cm, and the maximum diameter of the tumor after treatment was 3.06 cm.

The difference was statistically significant ( $P<0.05$ ). See Table 1.

Table 1 Comparison of tumor diameter before and after treatment

	Number	Diameter of tumor
Before treatment	218	$4.11 \pm 0.45\text{cm}$
After treatment	218	$3.24 \pm 0.31\text{cm}$
t	-	5.245
p	-	$<0.05$

### 3.4. Tumor-free survival rate of patients with cervical cancer

after immune checkpoint inhibitor treatment, patients with 1, 2 and 3 year tumor-free survival rates were 93.50%, 83.42%, and 79.63%, respectively, the median progression-free survival was 35.4 months, and the median overall survival was 78.2 months.

### 3.5. Adverse reaction rate

Among patients treated with ipilimumab monoclonal antibody, 24% developed rash, and when treated with nivolumab, the incidence of rash adverse reactions was 15%. The incidence of immune-related hepatitis was 2%, and the incidence of diarrhea was 25%. The reaction was mainly mild, and only three patients had grade III reactions.

## 4. Discussion

In recent years, with the in-depth study of immunomodulatory molecules in the immune system and tumor microenvironment, tumor immunotherapy has once again become a hot spot in clinical research. Among them, the most extensive clinical researches are immune checkpoint inhibitors, such as cytotoxic T lymphocyte-associated protein 4 (CTLA-4), programmed cell death receptor-1 (programmed cell death protein 1, PD -1) and its ligand (programmed cell death 1 ligand 1, PD-L1) inhibitors have been applied to the clinical treatment of a variety of tumors [4].

Surgery and radiotherapy are conventional treatments for cervical cancer. Although they have a significant role in promoting the recovery of the disease, they cannot achieve absolutely effective control of the subclinical lesions around the main lesions, which will lead to a very high recurrence rate in patients [5]. After surgical treatment, the patient's vaginal-related functions and ovaries can be preserved to a certain extent, but the effect of controlling metastases and surrounding subclinical lesions is relatively poor, and the postoperative recurrence rate is generally high; Patients' vaginal and ovarian functions will be severely damaged after radiotherapy. At the same time, patients are prone to disease recurrence and metastasis. These reasons will reduce the survival rate of cervical cancer patients after 5 years. Therefore, it is very important to actively explore efficient, stable and safe treatment methods for the early diagnosis, prevention and prognosis of the disease. Immune checkpoint inhibitor drugs act on the activation pathway of T cells and activate T cells by inhibiting the negative immune regulation mechanism, thereby exerting an immune killing function and significantly reducing the rate of disease recurrence. Studies have found that immune checkpoint inhibitors combined with chemotherapy and radiotherapy can not only eliminate micrometastases, but also reduce the scope and volume of tumors and improve surgical results.

Nivolumab and Ipilimumab are immune checkpoint inhibitor monoclonal antibodies that have been approved by the FDA for clinical use. They are extremely widely used in the immunotherapy of cervical cancer patients. The results of this study found that immune checkpoint inhibitors combined with chemotherapy or radiotherapy can significantly improve the efficacy in cervical cancer, significantly reduce the incidence of positive pathology, and significantly shorten the maximum tumor diameter. It is helpful for improving the effect of radiotherapy or surgery. In summary, immune checkpoint inhibitors have relatively satisfactory clinical effects for patients with cervical cancer. However, the current efficacy evaluation system for immune checkpoint inhibitors needs to be further refined, and the evaluation process for patients needs to be further improved. In future research, we will explore the combined application of immune checkpoint inhibitors and

traditional therapies, and screen out patients with reasonable immunotherapy applications. It will bring more survival benefits to patients with cervical cancer, especially patients with advanced and recurrent cervical cancer.

## References

- [1] Chen Tong. Analysis of the cervical cancer incidence in China from 1990 to 2017[J]. Modern Health B, 2019, 000(010):47-49.
- [2] Zong Liju, Xiang Yang. Research progress and future of immunotherapy for advanced and recurrent cervical cancer [J]. Chinese Journal of Practical Gynecology and Obstetrics, 2018, 34(11):31-36.
- [3] Gao Lili, Wang Yuzhu, Yang Jinbo. Case introduction of PD-1 immune checkpoint inhibitor combination drug approved by FDA[J]. Chinese Journal of New Drugs, 2019(16).
- [4] Ji Xiaohui, Li Dairong, Yang Dan, et al. Progress in drug therapy for cervical cancer[J]. Medical Review, 2019, 25(07):66-71+79.
- [5] Zhou Lijun, Li Wen, Liu Junjuan, et al. Cervical cancer immunotherapy and application prospects[J]. Advances in Modern Obstetrics and Gynecology, 2018, 27(09):709-712.