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COMMENTARY

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Current status of treatment with immune checkpoint inhibitors in the field of gynecological oncology

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In our living body, foreign objects are eliminated by the function of immunity. On the other hand, cancer cells are known to have a mechanism to break the immune cell system that is trying to attack cancer in order to escape from the attack of immune cells. "Immune checkpoint inhibitors" prevent cancer cells from breaking the immune system. Therefore, the "immune checkpoint inhibitor" is a drug that induces the immune function to attack the original cancer. Currently, PD-1 antibody, PD-L1 antibody and CTLA-4 antibody are used in clinical medicine as anti-cancer drugs. In this paper, the authors discuss the clinical use of immune checkpoint inhibitors in gynecological tumors.

Ovarian cancer is difficult to detect at early stage, therefor more than half of patients with ovarian cancer is advanced cancer in stages III to IV, so it is said to be a cancer with a poor prognosis even in the gynecology field [1]. By recent advances in medical technology, there are many cases of gynecological tumors where chemotherapy is effective, and the development of various anti-cancer drugs and progress of surgical treatment have significantly improved the short- and medium-term survival rates in the past 10 years. However, long-term survival rates have not improved much because of high recurrence rates and drug resistance. Dr. Ikuo Konishi, director of National Hospital Organization Kyoto Medical Center and Honorary professor at Kyoto University (Kyoto, Japan) said "the characteristic of immunotherapy is that long-term survival of patients can be expected when the anti-cancer drugs is effective against malignant tumors".

A platinum preparation is used as a standard clinical treatment for ovarian cancer. Konishi et al. [2] used the anti-PD-1 antibody, nivolumab for patients with platinum-resistant relapsed ovarian cancer, which has recurred within six months of platinum treatment. Anti-cancer effects of nivolumab were observed in 2 of 20 patients with ovarian cancer (Figure 1). Konishi et al. [2] has reported that patients survive for long periods without recurrence. This is the first time the safety and efficacy of nivolumab has been demonstrated in patients whose ovarian cancer was non-responsive to other clinical treatments. This was also the first women-only study on the efficacy of PD-1/PD-L1 signal inhibitors, providing valuable insight on the immune-related adverse event (irAE) unique to middle-age women who take PD-1 antibodies.

Most recently, the PD-1 inhibitors pembrolizumab and nivolumab have been approved for microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that

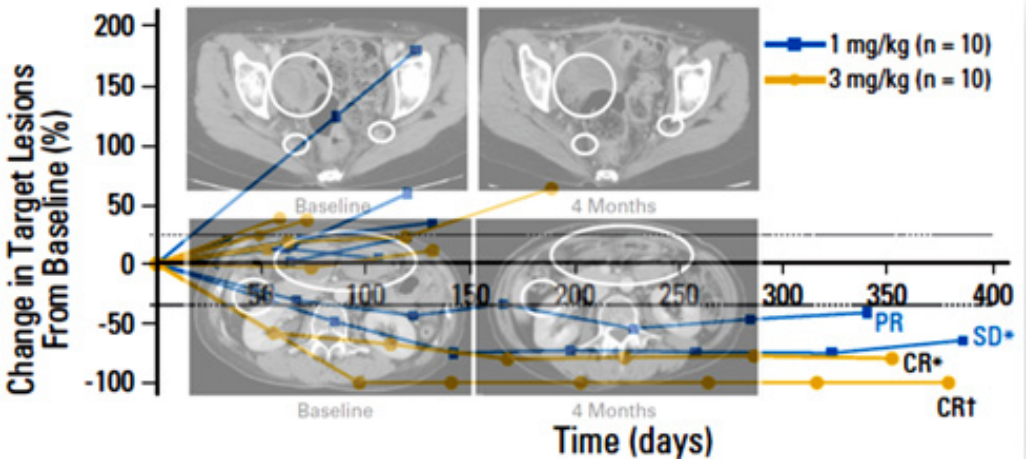

Figure 1. *PD-1 antibody, nivolumab, has in fighting the disease, ovarian cancer.*

have progressed after previous treatment, an approval that will provide a new option for women with MSI-H recurrent endometrial cancer (~20% will be MSI-H) and other MSI-H gynecological malignancies including ovarian cancer and sarcoma [3,4].

In the future, it will be necessary to study predictive biomarkers for the effects of immune checkpoint inhibitors, and to study combinations of immune checkpoint inhibitors with existing therapies. Currently, clinical trials using anti-PD-1 and anti-PD-L1 antibodies for gynecological tumors including ovarian cancer and sarcoma are in progress worldwide. With further clarification of the basic immune mechanism and development of biomarkers specific to immunity, immunotherapy with immune checkpoint inhibitors will be a major pillar of clinical treatment for cancer.

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