Multi-Drug Therapy Including Immune Checkpoint Inhibitors in Ovarian Cancer

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Abstract

Ovarian cancer has the worst prognosis among gynecological cancers. Since only a few cases of ovarian cancer could be treated effectively with immune checkpoint inhibitor monotherapy, to improve the prognosis of ovarian cancer, multi-drug therapy including immune checkpoint inhibitors is necessary. In this short commentary, we highlight the need for studies on novel treatment strategies.

Keywords: Microsatellite instability; Ovarian cancer; Immune checkpoint inhibitor; Immunohistochemistry; Mismatch repair protein

Abbreviations: PD-1: Programmed Cell Death-1; PD-L1: Programmed Cell Death-Ligand 1; MSI: Microsatellite Instability; MMR: Mismatch Repair; PFS: Progression-Free Survival

Content

Ovarian cancer has the poorest prognosis of all gynecological cancers, and therefore new therapies are needed to improve the prognosis [1]. Currently, new drugs such as immune checkpoint inhibitors and poly (ADP-ribose) polymerase inhibitors (PARP inhibitors) are in the spotlight. Anti-programmed cell death-1 (PD-1)/ programmed cell death-ligand 1 (PD-L1) antibody, one of immune

inhibitors have been reported to upregulate PD-L1 expression [17,18]. From these results, combined treatment of immune checkpoint inhibitors with chemotherapy or PARP inhibitors is expected to be useful. Long-term treatment with PARP inhibitors, even in ovarian cancer patients with HRD, can sometimes weaken the anti-tumor effects of PARP inhibitors. Even with PARP inhibitor monotherapy resistance, the combination of immune checkpoints and PARP inhibitors may contribute to tumor shrinkage in ovarian cancer with HRD.

Currently, many clinical trials have been performed to evaluate the efficiency of multi-drug therapies together with immune checkpoint inhibitors and various anti-cancer drugs and molecular targeted therapies in ovarian cancer patients [19]. Recently, we are examining the effects of multi-drug therapies along with immune checkpoint inhibitors in ovarian cancer using immunocompetent mice. We believe that new treatments for platinum-resistant ovarian cancer might be discovered by administering platinum-resistant cell lines to mice and verifying the potency of combination therapy. In addition, in order to discover new treatments for PARP inhibitors resistant ovarian cancer with HRD, we would like to create PARP inhibitors resistant cell lines using BRCA mutant cell lines and evaluate the effectiveness of immune checkpoint inhibitors.

In summary, ovarian cancer has only a few cases of MSI. Therefore, there are few ovarian cancer patients who can be expected to benefit from immune checkpoint inhibitor monotherapy. For better prognosis of ovarian cancer, multi-drug therapy together with immune checkpoint inhibitors is necessary. New therapeutic strategies for ovarian cancer may be found.

Conflict of Interest

The authors declare no potential conflicts of interest.

References

1. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, et al. (2018) Global surveillance of trends in cancer survival 2000-14(CONCORD-3): Analysis of individual records for 37,513,025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet 391: 1023-1075.
2. Topalian SL, Hodi FS, Brahmer JR, Gettinger SN, Smith DC, et al. (2012) Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. N Engl J Med 366: 2443-2454.
3. Alexandrov LB, Nik-Zainal S, Wedge DC, Aparicio SA, Behjati S, et al. (2013) Signatures of mutational processes in human cancer. Nature 500: 415-421.
4. Aysal