THE ROLE OF ANTIBODIES IN GYNECOLOGICAL TUMORS

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Annotation: During the last decades, several improvements in treating gynecological malignancies have been achieved. In particular, target therapies, mostly monoclonal antibodies, have emerged as an attractive option for the treatment of these malignancies. In fact, various molecular-targeted agents have been developed for a variety of malignancies with the objective to interfere with a precise tumor associated receptor, essential for cancer cell survival or proliferation, blocking its function, of the cancer cells. This article examines the role of antibodies in the diagnosis, treatment, and monitoring of gynecological tumors, including ovarian, cervical, and endometrial cancers. It highlights how monoclonal antibodies and antibody-based therapies, such as antibody-drug conjugates and immune checkpoint inhibitors, are being used to target tumor-specific antigens.

Key words: gynecological tumors, antibodies, monoclonal antibodies, antibody-drug conjugates, ovarian cancer, cervical cancer, immunotherapy, tumor markers, targeted therapy

Introduction: Alternatively, monoclonal antibodies have been developed to block immune suppression or enhance functions of immune effector cells. So far, several monoclonal antibodies have been tested for clinical efficacy for the treatment of gynecological cancers. Antibodies against Vascular Endothelial Growth Factor (VEGF) and Epidermal Growth Factor Receptor (EGFR) have been used in different neoplasms such as ovarian and cervical cancer. Catumazumab, a bivalent antibody against CD3 and EpCAM, is effective in the treatment of neoplastic ascites. Other antibodies are peculiar for specific cancer-associated antigen such as Oregovomab against CA125 or Farletuzumab against the folate receptor. Here we describe the

preclinical and clinical experience gained up to now with monoclonal antibodies in tumors of the female genital tract and trace future therapeutic and research venues.

Monoclonal Antibodies (MoAbs) represent the majority of target therapies which have been investigated and employed in clinical settings so far. These immunological reagents recognize molecular targets whose expression is tumor associated or/and are essential for the cancer cell survival and proliferation such as the Vascular Endothelial Growth Factor (VEGF), the Epidermal Growth Factor Receptor (EGFR) family, CA125, MUC1, and other signaling pathways which are aberrant in tumor tissue (EpCAM). Also, the targeting of immune cells by MoAbs has been proved to be an efficacious strategy to modulate immune system functions (anti-CTLA-4, anti-CD3, anti-CD40). To date, several MoAbs have been approved for the treatment of colorectal, breast, head and neck, nonsmall cell lung, and renal cell cancer. Encouraging results have being achieved also in gynecological tumors. Here, we review the most promising MoAbs that are under early or advanced investigation for the treatment of neoplasms of the lower genital tract.

Material and methods: Significant advances in gynecological cancer management have been recently achieved, including interesting progresses in surgical, chemotherapeutic, and concurrent chemo-radioterapeutic settings. However, more effective, specific, and less toxic approaches need to be investigated. Based on the promising results of preclinical studies, various targeted therapies are currently being evaluated in cancer patients. One of the most promising approaches, that may improve patient outcome, is the use of MoAbs. The use of MoAbs in cancer treatment is focused on the idea of selectively targeting tumor cells that express tumor-associated antigen [1], with the aim to specifically antagonize receptor signaling pathways, which are essential for proliferation, survival, and migration of tumor cells. Thus, MoAbs offer increasingly customized solutions based on the targeting of multiple specific pathways essential for cancer development and metastasis by attacking targeted tumor cells. Furthermore, the high specificity of the target reduces cytotoxic side effects on normal tissue, seen with traditional chemotherapeutic agents, and should permit the maintenance of a high quality of life. The first experience of MoAb administration in cancer patient was carried out in a patient affected by non-Hodgkin's lymphoma [2]. MoAbs are antibodies produced by hybridoma cells. In the sixties the conventional route to derive MoAbs was to immunize mice. It took 10 years to be translated to the patient with MoAb muromonab, a murine-derived antibody for acute organ rejection approved by FDA in 1986 [3]. Recently, recombinant engineering techniques permitted the construction of MoAbs with possible variation in size, valence, configuration, and effectors functions. This technology results in the development of fragment, chimeric, humanized, and fully humanized MoAbs.

In contrast to hematological malignancies and certain solid tumors such as breast and colorectal cancer, MoAbs have not been completely proven to be clinically effective in the treatment of ovarian cancer, although encouraging results are being achieving. Currently, the mostly investigated targets in ovarian cancer are (VEGF) and (EGFR) family members (EGFR1, EGFR2/ErbB2).

Results and discussion:

Monoclonal antibodies have demonstrated to be effective in both hematologic and solid malignancies. This family of antineoplastic agents have several different mechanisms, such as binding soluble ligands, blocking cell receptors, and activating ADCC.

In ovarian cancer, encouraging results have been observed with bevacizumab in first and second line settings, mostly in association to standard chemotherapy regimens. Currently, the primary goal in combining bevacizumab to standard chemotherapy is to test its efficacy in increasing the duration of first remission. Preliminary results of randomised trials carried out with this purpose seem to confirm a benefit in terms of progression-free survival, whereas data regarding overall survival remain currently less clear. Furthermore, on the basis of the Japanese experience [3], the GOG 262 is now testing the association between bevacizumab and paclitaxel in a dose dense front line regimen. The rational of combining bevacizumab to weekly paclitaxel in first line setting dates back to recent evidences showing that this association significantly improves progression-free survival in heavily pretreated recurrent epithelial ovarian cancer [3], thus confirming the role of weekly paclitaxel plus bevacizumab in synergistically inhibiting angiogenesis

Conclusion: antibodies play a vital and expanding role in the management of gynecological tumors. Their application ranges from diagnostics and prognostics to highly targeted therapeutic interventions. Monoclonal antibodies and antibody-drug conjugates have demonstrated promising results, especially in the treatment of ovarian and cervical cancers, by enhancing specificity and minimizing systemic toxicity. Furthermore, immune checkpoint inhibitors have opened new avenues for harnessing the immune system in combating tumor progression.

As research advances, antibody-based therapies are expected to become even more personalized, guided by molecular profiling and biomarker discovery. While challenges remain—such as cost, accessibility, and treatment resistance—the continued development of antibody technologies holds significant promise for improving survival rates and quality of life for patients with gynecological malignancies.

A multidisciplinary approach, combining immunology, oncology, and molecular medicine, will be essential in fully realizing the potential of antibodies in the fight against gynecological cancers.

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