ABSTRACT

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Immunotherapy as a New Therapeutic Approach for Brain and Spinal Cord Tumors.

Medikonda R(1), Pant A(1)(2), Lim M(3).

Author information:
(1)Department of Neurosurgery, Stanford University School of Medicine, Palo Alto, USA.
(2)Department of Neurosurgery, Johns Hopkins School of Medicine, Baltimore, USA.
(3)Department of Neurosurgery, Stanford University School of Medicine, Palo Alto, USA. mklim@stanford.edu.

Historically, the central nervous system (CNS) was considered an immune-privileged organ. However, recent studies have shown that the immune system plays a significant role in the CNS. Thus, there is renewed interest in applying cancer immunotherapy to CNS malignancies with the hope of generating a robust anti-tumor immune response and creating long-lasting immunity in patients. There has been some work with non-specific immunotherapy such as IL-2 for brain metastasis. Unfortunately, the results from non-specific immunotherapy studies were lackluster, so the focus has shifted to more specific CNS immunotherapies including cancer vaccines, immune checkpoint inhibitors, oncolytic virus therapy, and chimeric antigen receptor (CAR) T cell therapy. With respect to cancer vaccines, rindopepimut has been well-studied in glioblastoma (GBM) patients with the EGFRvIII mutation, with early results from phase II trials showing possible efficacy in carefully selected GBM patients. Other antigen-specific CNS tumor vaccines are still in the early stages. Immune checkpoint inhibitors are amongst the most promising and widely studied CNS immunotherapy strategies. Anti-PD-1 showed promising results in many non-CNS solid tumors, however, results from early clinical trials show poor efficacy for anti-PD-1 in GBM patients. Anti-PD-1 is also under investigation for CNS metastasis and showed some efficacy in non-small cell lung cancer and renal cell carcinoma patients. Anti-PD-1 is under early stage investigation for other CNS tumors such as chordoma. Oncolytic virus therapy is the strategy of infecting tumor cells with a virus that in turn triggers an innate immune response leading to tumor cell lysis. Oncolytic viruses currently under investigation include several adenovirus-based therapies and a herpes simplex virus-based therapy. Phase I studies have demonstrated the safety of oncolytic virus therapies in GBM patients. Current studies are evaluating the efficacy of these therapies both alone and in combination with other immunotherapy approaches such as checkpoint inhibition in patients with CNS tumors. CAR T cell therapy is a newer immunotherapy approach. CAR T cell therapies, directed against EGFRvIII mutation and HER-2 mutation, demonstrate an acceptable safety profile, although there is no conclusive evidence of the survival benefit of these therapies in early trials. Studies are currently underway to determine optimal tumor-specific antigen selection and modality of administration for CAR T cell therapy. Overall, the prognosis is generally poor for patients with CNS malignancies. The promising results of cancer immunotherapy for non-CNS tumors have created significant interest in applying these therapies for CNS malignancies. Preliminary results have not demonstrated robust efficacy for CNS immunotherapy. However, it is important to keep in mind that the field is still in its infancy and many clinical trials are still early-phase. Several, clinical trials are currently underway to further explore the role of immunotherapy for CNS malignancies.

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