ABSTRACT

Drugs. 2022 Apr;82(5):491-510. doi: 10.1007/s40265-022-01702-6. Epub 2022 Apr 9.

Pharmacotherapeutic Treatment of Glioblastoma: Where Are We to Date?

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The clinical management of glioblastoma (GBM) is still bereft of treatments able to significantly improve the poor prognosis of the disease. Despite the extreme clinical need for novel therapeutic drugs, only a small percentage of patients with GBM benefit from inclusion in a clinical trial. Moreover, often clinical studies do not lead to final interpretable conclusions. From the mistakes and negative results obtained in the last years, we are now able to plan a novel generation of clinical studies for patients with GBM, allowing the testing of multiple anticancer agents at the same time. This assumes critical importance, considering that, thanks to improved knowledge of altered molecular mechanisms related to the disease, we are now able to propose several potential effective compounds in patients with both newly diagnosed and recurrent GBM. Among the novel compounds assessed, the initially great enthusiasm toward trials employing immune checkpoint inhibitors (ICIs) was disappointing due to the negative results that emerged in three randomized phase III trials. However, novel biological insights into the disease suggest that immunotherapy can be a convincing and effective treatment in GBM even if ICIs failed to prolong the survival of these patients. In this regard, the most promising approach consists of engineered immune cells such as chimeric antigen receptor (CAR) T, CAR M, and CAR NK alone or in combination with other treatments. In this review, we discuss several issues related to systemic treatments in GBM patients. First, we assess critical issues toward the planning of clinical trials and the strategies employed to overcome these obstacles. We then move on to the most relevant interventional studies carried out on patients with previously untreated (newly diagnosed) GBM and those with recurrent and pretreated disease. Finally, we investigate novel immunotherapeutic approaches with special emphasis on preclinical and clinical data related to the administration of engineered immune cells in GBM.

DOI: 10.1007/s40265-022-01702-6
PMID: 35397073