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Investigational treatment strategies in glioblastoma: progress made and barriers to success

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Abstract

Introduction: Glioblastoma, isocitrate dehydrogenase wildtype (IDHwt), remains an incurable disease despite considerable research effort. The current standard of care since 2005 comprises maximal safe resection followed by radiation with concurrent and adjuvant temozolomide; more recently, the addition of tumor treating fields was approved in the newly diagnosed and recurrent disease settings.

Areas covered: Searches of PubMed, Cochrane Library, and ClinicalTrials.gov provided a foundation for this review. We first describe early research including carmustine wafers, brachytherapy, anti-angiogenesis, and immune checkpoint inhibition for glioblastoma. Next, we discuss challenges precluding the translation of preclinical successes. This is followed by a description of promising treatments such as chimeric antigen receptor T-cell therapy as well as the recent qualified successes of cancer vaccinations. Non-immunotherapy trials are also highlighted, and ongoing or pending phase 2 and 3 clinical trials are codified in study tables.

Expert opinion: Unfortunately, hundreds of trials, including of agents effective in systemic malignancy, have not drastically changed management of glioblastoma. This may reflect unique resistance mechanisms and highlights a need for multimodality treatments beyond surgery, radiation, and conventional chemotherapy. Novel techniques, such as those in the emerging field of cancer neuroscience, may help uncover tolerable and effective regimens for this lethal malignancy.

Keywords: Cancer neuroscience; Chimeric antigen receptor T-cell therapy; cancer vaccination; glioblastoma; immunotherapy.