The Ever Changing Treatments for Tumors of the Central Nervous System

In the past few years, celebrities like Gord Downie in Canada and Robert Kennedy of the United States were diagnosed with glioblastoma. This heightened the interest in central nervous system (CNS) tumors among the general public. This thematic issue covers different aspects of management for CNS tumors. Although CNS tumors are only at around the 14th position among the common tumors in the world, but mortality is high [1]. The current role and recent advances of imaging, staging, pathology, surgery, radiotherapy and systemic therapies are reviewed. Recent changes to the World Health Organization (WHO) classification published in 2016 have demonstrated the prognostic and predictive value of molecular profiling and have also defined a new tumor entity diffuse midline glioma, histone H3-K27M mutant, as WHO grade IV [2]. In 2017, the eighth edition of American Joint Commission on Cancer staging has been introduced [3].

We have invited authors from different departments (dept.) and universities (U.) of Canada, France and Hong Kong so that readers would have a balanced view of treatment approaches and resources available in different countries. The review from Hong Kong by Prof. Dora Kwong’s group summarized the local experience and clinical trials to see if new treatments can be applied to the Oriental population. Modern technologies with image-guided radiotherapy (RT) or stereotactic RT improve the precision of radiation treatment and minimize toxicity. This editorial highlights a few controversies and updates mentioned below.

Temozolomide (TMZ) emerged to be the cornerstone for glioblastoma treatment in 2005. In the landmark study of Stupp et al. 6 cycles of adjuvant TMZ were employed [4]. The duration of maintenance TMZ varies in different institutions, from 6-12 months [5]. Different dosages and timing of TMZ are described. Of interest, in the elderly patients with glioblastoma, the addition of TMZ improved overall survival (OS) by nearly six months (13.5 vs. 7.7 months), TMZ also appeared to improve survival in patients with MGMT-unmethylated tumors (but the magnitude of effect was smaller: 10 vs. 7.9 months) [6].

For newly diagnosed anaplastic gliomas without 1p19q co-deletion, interim results of the CATNON trial, indicate that patients who receive radiation plus 12 cycles of adjuvant TMZ have improved survival compared with those who do not receive adjuvant TMZ [7]. Currently, there is an ongoing randomized trial of 1p19q co-deleted tumors comparing RT plus PCV (procarbazine, lomustine, vincristine) with RT plus TMZ (“CODEL”) [8].

We are still waiting for better therapies of recurrent CNS tumors. The TAVAREC trial from the European Organization of Research and Treatment of Cancer (EORTC) showed that the addition of bevacizumab (BEV) to TMZ did not improve OS, PFS, or cognitive function in recurrent grade II and III 1p/19q intact gliomas; regardless of isocitrate dehydrogenase (IDH) mutational status [9]. EORTC 26101 did not demonstrate the addition of BEV to lomustine, benefiting patients with progressive glioblastoma [10]. CheckMate-143, a randomized Phase III clinical trial of nivolumab in patients with first recurrence of glioblastoma did not meet its primary endpoint of improved OS over BEV monotherapy [11]. The data were presented on May 7, 2017 at the World Federation of Neuro-Oncology Societies (WFNOS) meeting in Zurich, Switzerland.

Tumor-treating fields (TTFields) are produced from a patient-operated home-use device which delivers 200 kHz alternating electrical field to the brain. The treatment interferes with cell divisions and selectively disrupts mitosis by interfering with spatial alignment of polar macro-molecules within the cell. It also inhibits the repair of double strand breaks. It is gaining momentum as a therapeutic approach for glioblastoma with high therapeutic index but minimal side effects. Stupp et al. reported the results of a phase III randomized trial of 695 patients comparing the use of maintenance TTFields with TMZ vs. TMZ alone in newly diagnosed glioblastoma: median PFS of 7.1 vs. 4.0 months and OS of 20.5 vs.15.6 months, respectively [12].

Guidelines from the American National Comprehensive Cancer Network (NCCN) and European Association of Neuro-Oncology (EANO) are very useful [13, 14]. Clinicians are encouraged to watch the NCCN, EORTC and EANO website for new guidelines or updates [15, 16]. The entire thematic issue attempts to cover most common CNS tumors. It will be of great teaching value for clinicians in practice or in training.
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