

Commentary

Glioblastoma Multiforme - A Report on its Long-standing Standard of Care Treatment to Future Perception

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ABSTRACT

Cancer is a leading cause of Morbidity and Mortality. Currently, It is a second leading cause of death followed by Cardiovascular diseases. Despite the fact that cancer can occur at any age, the older adults are more susceptible for tumor spread and contribute for its largest increase in incident cases worldwide.

Keywords: glioblastoma multiforme, cancer

INTRODUCTION

Cancer is a leading cause of Morbidity and Mortality. Currently, It is a second leading cause of death followed by Cardiovascular diseases. Despite the fact that cancer can occur at any age, the older adults are more susceptible for tumor spread and contribute for its largest increase in incident cases worldwide. There were 14.9 million incidences of cancer cases reported largest increase in incident cases worldwide¹.

According to U.S. National Cancer Institute, Glioblastoma multiforme (GBM) is the most aggressive brain tumor which shows microscopic regions of necrosis, hemorrhage and contributes to 15.4% of all primary brain tumors and about 60% – 75% of all astrocytoma. Being the complex nature of the tumor itself, it thus resists therapeutic interventions². Taking into considerations the epidemiology of GBM which may occur at any age, however, study showed that the peak incidence was at age 70–74 years in males and at age 75–79 years in females. Males are predominant with a ratio of about 1.2:1 M:F. Non-Latino whites had the highest incidence rates (2.5 per 100,000) followed by Latino whites (1.8 per 100,000), and blacks (1.5 per 100,000)³. GBM can easily metastasize within the meninges or spinal cord through the CSF however; autopsy studies showed that GBM metastases in the meninges and spinal cord occur in 20% of GBM patients which in contrast to extra-cranial GBM metastases which occur in only about 0.4% to 2.0% of GBM patients⁴.

DISCUSSION

The standard treatment for GBM has been the same since many decades—surgical removal of tumor mass as much as possible, followed by radiation therapy and chemotherapy⁵. The patients have restricted care of

treatment and trials are being intensely conducted and reported with the aim of increasing the patient survival. Recently conducted phase III cohort study on 440 stage IV recurrent GBM patients failed to demonstrate the survival benefits in GBM patients. The study was designed to compare nivolumab monotherapy with Bevacizumab. The study concluded that GBM patients recurred following radiation therapy and temozolomide, could not survive longer when treated with opdivo compared to standard of care treatment with Bevacizumab⁶. The time where researchers have vigorously exploring the new technologies and therapeutics to better cure the tumor if not to have the better survival rate. The studies are being conducted successfully and the treatment is now catching the eyeballs. One of the clinical trials “EF-14” reported this year during the American Association of Cancer Research (AACR) Annual Meeting is an exciting breakthrough for treatment of GBM. The study was multicentred Phase III which enrolled a total of 695 grade IV GBM patients who had undergone standard care of treatment involving surgery, temozolomide, and radiation. The patients were randomized into two arms, one arm represent temozolomide with TTFields and second arm represents temozolomide alone. The trial involved TTFields (Optune; Novocure) which are low-intensity electric fields operating at frequency 200kHz that considered to exert their anticancer effects by blocking the cell division. The patients with GBM, receive the TTFields continuously in the brain by a patient-operated, medical device which needs to be worn continuously (at least 18 hours) throughout the day. The trial’s primary and secondary endpoints were progression-free survival (PFS) and Overall Survival (OS) respectively. There was a noticeable difference in PFS, OS and the life expectancy in patients

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Table 1: Progression free survival, overall survival and life expectancy of patients randomized in Arm 1 and 2.

Arms	PFS (Months)	Median (Months)	PFS (Months)	Median (Months)	OS	Life Expectancy				
						Post 1 Yr	Post 2 Yr	Post 3 Yr	Post 4 Yr	Post 5 Yr
Arm 1 (TT fields+Temozolomide)	6.7	11.2		20.9		73	43	26	20	13
Arm 2 (temozolomide-only).	4	8		16.0		65	31	16	08	05

randomized in arm 1 as compared to arm 2 as shown below in the table 1.

Researcher also concluded that the age was not a matter with the treatment. The median age in both groups was 56.5 years and OS was found better in both groups suggesting the oncologists should consider the device for use in elderly patients. Moreover; Interim results of the trial, led to the FDA's approval of this device in 2015 for the use in newly diagnosed GBM patients followed by standard treatment. The conclusion of this study as whole is that the electric fields therapy should be considered as part of the standard of care for newly diagnosed GBM patients⁷. Another study reported on newly diagnosed, elderly GBM patients, age ≥ 70 years. The study showed promising survival benefits in patients treated with bevacizumab and temozolomide followed by surgical resection⁸.

CONCLUSION

As the researchers are continuously in search of the better treatment, new drugs are coming up to the market which can assure better future for GBM patients. The drugs which are under phase III are TRC-105, VB-111, TOCA 511, DCVax-Brain, Rindopepimut (CDX-110) are inclined to provide enhanced efficacy, shorter onset of action and fewer side effects as compared to the currently available GBM treatment. Large number of investigational drugs belongs to immunotherapy category are expected to change the overall perspective of the market. Hence, in view of future commercialization of these molecules in the forecast period 2016 – 2022 is anticipated to have an insightful impact on the growth of the overall GBM market⁹.

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