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In Reply to “Rathod et al.”

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Abstract:	

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To the Editor:

We thank Dr. Rathod and colleagues for their insightful reply[1] to our article[2] "Radiation for Glioblastoma in the Era of COVID-19: Patient Selection and Hypofractionation to Maximize Benefit and Minimize Risk" and appreciate the opportunity to respond.

For patients with glioblastoma (GBM) who have a very poor performance status (PS) with Karnofsky PS < 50, there are multitude of treatment options available during the COVID-19 pandemic. Based on prospective data, 34 Gy in 10 fractions, 25 Gy in 5 fractions, temozolomide (TMZ) alone, or best supportive care (BSC) are potential options, albeit patients with KPS<50 (ECOG 3-4) were not necessarily well-represented among the accrued patients in these trials[3,4]. We agree with Rathod et al. and recognize the immunosuppressive side-effects of TMZ such as neutropenia, which may increase risk of COVID infection or COVID-related severe illness / death. Consistent with other published neuro-oncology guidelines for the COVID era[5], TMZ is an option for consideration, particularly among those patients with hypermethylation of the O[6]-methylguanine-DNA methyltransferase (*MGMT*) promoter. Yet, the use of TMZ even among patients with *MGMT* methylation (who are most likely to benefit from TMZ) is cautioned in the context of known TMZ hematologic toxicity. While TMZ has known hematologic toxicity, there is growing evidence that radiation has also been found to have immunosuppressive effects in GBM through the killing of circulating lymphocytes[6]. Thus, the advantages and limitations of each treatment modality must be carefully weighed, especially during the ongoing COVID-19 crisis.

In conclusion, the integration of prospective trial-level data with clinical context, individualized patient considerations, multidisciplinary discussions, and shared decision-making with patients and their families is paramount to the discussion of the treatment of vulnerable patients with GBM during the COVID-19 pandemic.

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