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Letter to the Editor

In reply: "H3K27M-mutant glioma: clinical characteristics and outcomes"

Conflict of interest statement. No conflicts of interest are reported.

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We thank Wang et al for their comments and interest in our study. The median survival of H3K27M-mutant adult diffuse midline glioma (DMG) in our series was 19.6 months,[1] which is consistent with the 4.3 to 18.6 months median survival reported in recent series of adult H3K27M-mutant DMG.[2–5] We found no significant difference between the median survival of adult H3K27M-mutant DMG and that of H3/isocitrate dehydrogenase (IDH) wild-type gliomas (whether non-midline or midline), even when the comparison, as suggested by Wang et al, was restricted to H3/IDH wild-type glioblastomas. Consistent with our findings, 3 studies have shown that the prognosis of adult H3K27M-mutant DMG was similar to or even slightly better than that of midline H3/IDH wild-type gliomas.[3–5] Therefore, in adults, in contrast to the pediatric population, where H3K27M-mutant DMGs are associated with a poorer prognosis than their H3 wild-type counterpart,[6] the prognosis of H3K27M-mutant DMG appears to be poor yet not necessarily poorer than that of patients with H3/IDH wild-type midline gliomas. The presence of a telomerase reverse transcriptase (*TERT*) promoter mutation has been reported as a feature of particularly poor prognosis in adult midline diffuse gliomas, while the presence of an activating fibroblast growth factor receptor 1 (*FGFR1*) mutation was associated with a better outcome.[3] The prognostic value of these alterations in adult H3K27M-mutant DMG remains to be fully assessed. We agree with Wang et al that the comparison of survival in our study was limited by the fact that it did not take into account the type of surgery or other treatment modalities. Further studies will be needed to address this question. Finally, we agree with Wang et al that H3K27 mutations can occur in brain tumors that do not correspond to H3K27M-mutant DMG and that our knowledge regarding these cases needs to be expanded. Wang et al refer to a case of H3K27M-mutant diffuse glioma with a non-midline location.[7] H3K27M mutations have also been reported in some cases of pilocytic astrocytomas, pediatric diffuse gliomas, gangliogliomas, ependymomas, or subependymomas that can have a favorable outcome.[8] Given these observations, the cIMPACT-NOW consortium has recommended that the diagnosis of "DMG H3K27M-mutant, grade IV" should only be made in gliomas that are diffuse and have a midline location.[8]

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