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Preliminary findings of German-sourced ONC201 treatment in H3K27 altered pediatric pontine diffuse midline gliomas

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Abstract

Purpose: H3K27 altered pediatric pontine diffuse midline gliomas (pDMG) have a poor prognosis, and conventional treatments offer limited benefits. However, recent advancements in molecular evaluations and targeted therapies have shown promise. The aim of this retrospective analysis was to evaluate the effectiveness of German-sourced ONC201, a selective antagonist of dopamine receptor DRD2, for the treatment of pediatric H3K27 altered pDMGs.

Methods: Pediatric patients with H3K27 altered pDMG treated between January 2016 and July 2022 were included in this retrospective analysis. Tissue samples were acquired from all patients via stereotactic biopsy for immunohistochemistry and molecular profiling. All patients received radiation treatment with concurrent temozolomide, and those who could acquire GsONC201 received it as a single agent until progression. Patients who could not obtain GsONC201 received other chemotherapy protocols.

Results: Among 27 patients with a median age of 5.6 years old (range 3.4-17.9), 18 received GsONC201. During the follow-up period, 16 patients (59.3%) had progression, although not statistically significant, the incidence of progression tended to be lower in the GsONC201 group. The median overall survival (OS) of the GsONC201 group was considerably longer than of the non-GsONC201 group (19.9 vs. 10.9 months). Only two patients receiving GsONC201 experienced fatigue as a side effect. 4 out of 18 patients in the GsONC201 group underwent reirradiation after progression.

Conclusion: In conclusion, this study suggests that GsONC201 may improve OS in pediatric H3K27-altered pDMG patients without significant side effects. However, caution is warranted due to retrospective design and biases, highlighting the need for further randomized clinical studies to validate these findings.

Keywords: Diffuse midline glioma; H3K27 alteration; ONC201; Stereotactic pontine biopsy.