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Impact of Frontline Ivosidenib on Volumetric Growth Patterns in Isocitrate Dehydrogenase (IDH) mutant Astrocytic and Oligodendroglial Tumors

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Abstract

Purpose: Isocitrate dehydrogenase (IDH) mutant gliomas are usually treated with radiotherapy and chemotherapy, which increases the risk for neurocognitive sequelae during patients' most productive years. We report our experience using off-label first-inclass IDH1mut-inhibitor ivosidenib and its impact on tumor volume in IDHmut gliomas.

Experimental design: We retrospectively analyzed patients aged ≥18 years with radiation/chemotherapy-naïve, IDH1mut, non-enhancing, radiographically active, grade 2/3 gliomas, and ≥2 pretreatment and ≥2 on-ivosidenib MRIs. T2/FLAIR-based tumor volumes, growth rates and PFS were analyzed. Log-linear mixed-effect modeling of growth curves adjusted for grade, histology and age was performed.

Results: We analyzed 116 MRIs of 12 patients (median age 46years [range:26-60]) 10 males, 8 astrocytomas (50% grade 3), 4 grade 2 oligodendrogliomas. Median on-drug follow-up was 13.2 months (interquartile range[IQR]:9.7-22.2). Tolerability was 100%. 50% of patients experienced ≥20% tumor volume reduction on treatment and absolute growth-rate was lower during treatment (-1.2±10.6cc/year) than before treatment (8.0±7.7cc/year; p≤0.05). Log-linear models in the Stable group (n=9) showed significant growth before treatment (53%/year; p=0.013), and volume reduction (- 34%/year; p=0.037) after 5-months on treatment. After-treatment volume curves were significantly lower than before treatment (after/before treatment ratio 0.5; p<0.01). Median-time-to-Best Response was 11.2(IQR:1.7-33.4) months, and 16.8(IQR:2.6-33.5) months in patients on drug for ≥1 year. PFS-9mo was 75%.

Conclusions: Ivosidenib was well-tolerated and induced a high volumetric response rate. Responders had significant reduction in tumor growth rates and volume reductions observed after a 5-month delay. Thus, ivosidenib appears useful to control tumor growth and delay more toxic therapies in IDH-mutant non-enhancing indolently growing gliomas.