Durable Complete Responses in Some Recurrent High Grade Glioma Patients Treated with Toca 511 & Toca FC.


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BACKGROUND: Vocimagene amiretrorepvec (Toca 511) is an investigational gamma-retroviral replicating vector encoding cytosine deaminase that, when used in combination with extended-release 5-fluorocytosine (Toca FC), results preclinically in local production of 5-fluorouracil, depletion of immune-suppressive myeloid cells, and subsequent induction of anti-tumor immunity. Recurrent high grade glioma (rHGG) patients have a high unmet need for effective therapies that produce durable responses lasting more than 6 months. In this setting, relapse is nearly universal and most responses are transient.

METHODS: In this Toca 511 ascending-dose phase I trial (NCT01470794), HGG patients who recurred after standard of care underwent surgical resection, received Toca 511 injected into resection cavity wall followed by orally administered cycles of Toca FC.

RESULTS: Among 56 patients, durable complete responses were observed. A subgroup was identified based on Toca 511 dose and entry requirements for the follow-up phase III study. In this subgroup, which included both IDH1-mutant and -wildtype tumors, the durable response rate is 21.7%. Median duration of follow-up for responders is 35.7+ months. As of August 25, 2017, all responders remain in response and are alive, 33.9+ to 52.2+ months after Toca 511 administration, suggesting a positive association of durable response with overall survival.

CONCLUSIONS: Multi-year durable responses have been observed in rHGG patients treated with Toca 511 & Toca FC in a phase I trial and the treatment will be further evaluated in a randomized phase III trial. Among IDH1 mutant patients treated at first recurrence, there may be an enrichment of complete responders.

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