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Phase I clinical study of a multi-kinase inhibitor TG02 capsule for the treatment of recurrent high-grade gliomas with failed temozolomide treatment in Chinese patients

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Abstract

Introduction: Here, we report the safety, tolerability, pharmacokinetic characteristics and preliminary efficacy of a multi-kinase inhibitor (TG02 capsule) as a new therapy for patients with recurrent high-grade gliomas in China.

Methods: This is a single-center, dose-escalation, open-label phase I study, which enrolled patients with recurrent high-grade gliomas who failed to temozolomide. Patients were assigned sequentially into different dose groups and received TG02 every 4 weeks. The dose was increased in a traditional 3+3 design. Primary endpoints were the dose-limited toxicity (DLT) and the maximum tolerated dose (MTD).

Results: Twelve patients (8 glioblastomas, 4 diffuse astrocytoma) were enrolled between May 2019 and November 2021. Three patients received 100 mg and 9 received 150 mg TG02 twice a week. The plasma concentration of TG02 reached the maximum at 2 hours after administration, and the elimination half-life was about 7 hours. No DLT occurred and MTD was not defined in this study. Eleven patients had one or more investigator-assessed treatment-related adverse events (TRAEs). The most frequent TRAEs were vomiting (91.7%) and diarrhea (75.0%), and 50% of the patients had grade 3 or 4 adverse events. There were no treatment-related deaths. The median progression-free survival and overall survival were 1.77 (95% confidence interval [CI]: 0.82-4.24) and 9.63 (95%CI: 2.66-not estimated) months, respectively.

Conclusions: TG02 capsule 150mg twice a week is safe and tolerable in Chinese patients with recurrent high-grade gliomas. Patients who failed to temozolomide showed obvious tumor reduction when switching to TG02 capsule. The efficacy for recurrent gliomas warrant further investigation.