ABSTRACT

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Genome-driven medicine for patients with recurrent glioma enrolled in early phase trials.

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BACKGROUND: Recent studies showed that patients with glioma can safely participate in early phase clinical trials; however, clinical benefits in this population were limited. We aimed to evaluate the benefit of molecular profiling to guide enrolment in early phase trials for patients with recurrent glioma.

METHODS: Records of patients enrolled in early phase trials of cytotoxic therapies, small molecule inhibitors or monoclonal antibodies from 2008 to 2018 were reviewed for clinico-pathological characteristics, toxicity, response, progression-free survival and overall survival (OS). The primary objective was to evaluate response rates in molecularly-oriented versus non-molecularly-oriented patients.

RESULTS: Eighty-eight patients were enrolled, of whom 45 (51.1%) patients were molecularly-oriented. Targets included IDH1/2 (n = 15), BRAF (n = 11), and FGFR1 (n = 3) mutations, FGFR2-3 fusions (n = 9), and mismatch repair deficiency (n = 7). Among patients with high-grade glioma (n = 74), the rate of stable disease ≥6 months and partial or complete response was 25.7% in molecularly-oriented versus 5.1% in non-molecularly-oriented patients (p = 0.02). Upon multivariable adjustment, baseline steroid use ≥20 mg prednisone equivalent per day was associated with shorter OS (OR 3.15 [95% CI 1.62-6.13], p = 0.0008), while molecular enrichment strategy was associated with longer OS (OR 0.40 [95% CI 0.22-0.73], p = 0.003). Nine (10.2%) patients

experienced grade 3-4 toxicity and no dose limiting toxicity (DLT) occurred in both cohorts.

CONCLUSION: The use of molecular profiling to guide enrolment in early phase trials is feasible and might provide benefits to selected patients with glioma. Further studies are warranted to confirm these results in larger randomised settings and identify the patients most likely to benefit from this approach.

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