ABSTRACT

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Molecular profile to guide personalized medicine in adult patients with primary brain tumors: results from the ProfiLER trial.

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Immunohistochemistry and recent molecular technologies progressively guided access to personalized anti-tumoral therapies. We explored the feasibility, efficacy, and the impact of molecular profiling in patients with advanced brain tumors. This multicentric prospective trial ProfiLER enrolled patients with primary brain tumors, who have been pre-treated with at least one line of anti-cancer treatment, and for whom molecular profiles had been achieved using next-generation sequencing and/or comparative genomic hybridization on fresh or archived samples from tumor, relapse, or biopsies. A molecular tumor board weekly analyzed results and proposed molecular-based recommended therapy (MBRT). From February 2013 to December 2015, we enrolled 141 patients with primary brain tumor and analyzed 105 patients for whom tumor genomic profiles had been achieved. Histology mainly identified glioblastoma (N = 46, 44%), low-grade glioma (N = 26, 25%), high-grade glioma (N = 12, 11%), and atypical and anaplastic meningioma (N = 8, 8%). Forty-three (41%) patients presented at least one actionable molecular alteration. Out of 61 alterations identified, the most frequent alterations occurred in CDKN2A (N = 18), EGFR (N = 12), PDGFRa (N = 8), PTEN (N = 8), CDK4 (N = 7), KIT (N = 6), PIK3CA (N = 5), and MDM2 (N = 3). Sixteen (15%) patients could not be proposed for a MBRT due to early death (N = 5), lack of available clinical trials (N = 9), or inappropriate results (N = 2). Only six (6%) of the 27 (26%) patients for whom a MBRT had been proposed finally initiated MBRT (everolimus (N = 3), erlotinib (N = 1), ruxolitinib (N = 1), and sorafenib (N = 1)), but discontinued treatment for toxicity (N = 4) or clinical progression (N = 2). High-throughput sequencing in patients with brain tumors may be routinely performed, especially when macroscopic surgery samples are available; nevertheless delays should be reduced. Criteria for clinical trial enrollment should be reconsidered in patients with brain tumors, and a panel of genes specifically dedicated to neurologic tumors should be developed to help decision-making in clinical practice.

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