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Phase II Study of Samotolisib in Children and Young Adults With Tumors Harboring Phosphoinositide 3-Kinase/Mammalian Target of Rapamycin Pathway Alterations: Pediatric MATCH APEC1621D

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Abstract

Purpose: Patients age 1-21 years with relapsed or refractory solid and CNS tumors were assigned to phase II studies of molecularly targeted therapies on the National Cancer Institute-Children's Oncology Group (NCI-COG) Pediatric Molecular Analysis for Therapy Choice (MATCH) trial. Patients whose tumors harbored predefined genetic alterations in the phosphoinositide 3-kinase (PI3K)/mammalian target of rapamycin (mTOR) pathway and lacked mitogen-activated protein kinase pathway activating alterations were treated with the PI3K/mTOR inhibitor samotolisib.

Methods: Patients received samotolisib twice daily in 28-day cycles until disease progression or unacceptable toxicity. A rolling 6 limited dose escalation was performed as, to our knowledge, this was the first pediatric study of samotolisib. The primary end point was the objective response rate; secondary end points included progression-free survival (PFS) and the recommended phase II dose and toxicity of samotolisib in children.

Results: A total of 3.4% (41/1,206) of centrally tested patients were matched to this arm. Seventeen patients were treated. Among treated patients, the most common diagnoses included osteosarcoma (n = 6) and high-grade glioma (n = 5) harboring alterations in phosphatase and tensin homolog (n = 6), *PIK3CA* (n = 5), and tuberous sclerosis complex 2 (n = 3). No objective responses or prolonged stable disease were observed. Three-month PFS was 12% (95% CI, 2 to 31). Two patients experienced dose-limiting toxicities (mucositis and pneumonitis). Dose level 2 (115 mg/m^2/dose twice daily) was determined to be the recommended phase II dose of samotolisib in children.

Conclusion: This nationwide study was successful at identifying patients and evaluating the efficacy of molecularly targeted therapy for rare molecular subgroups of patients in a histology-agnostic fashion. Unfortunately, there was no activity of samotolisib against tumors with PI3K/mTOR pathway alterations. Prospective trials such as the NCI-COG Pediatric MATCH are necessary to evaluate the efficacy of molecularly targeted therapies given their increasing use in clinical practice.