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Phase II Trial of Afatinib in Patients With *EGFR*-Mutated Solid Tumors Excluding Lung Cancer: Results From NCI-MATCH ECOG-ACRIN Trial (EAY131) Subprotocol A

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Abstract

Purpose: National Cancer Institute-Molecular Analysis for Therapy Choice (NCI-MATCH) was a multicohort phase 2 trial that assigned patients with advanced pretreated cancers to molecularly targeted therapies on the basis of tumor genomic testing. NCI-MATCH Arm A evaluated afatinib, an EGFR tyrosine kinase inhibitor (TKI) approved for advanced non-small cell lung cancer, in patients with tumors other than lung cancer harboring *EGFR* mutations.

Methods: Patients with advanced pretreated cancers other than lung cancer found to have selected actionable *EGFR* mutations were offered participation in Arm A. Previous therapy with an EGFR TKI was not allowed. Patients received afatinib 40 mg once daily continuously until disease progression or unacceptable toxicity. The primary end point was objective response rate (ORR). Secondary end points included progression-free survival (PFS), 6-month PFS, and overall survival (OS).

Results: Seventeen patients received protocol therapy. Tumor types included glioblastoma multiforme (GBM) (13), gliosarcoma (1), adenocarcinoma not otherwise specified (NOS) (2), and adenosquamous carcinoma of the breast (1). Fifty-nine percent of patients received ≥2 lines of previous therapy. The ORR was 11.8% (90% CI, 2.1 to 32.6), with one complete response lasting 16.4 months (GBM harboring a rare exon 18 *EGFR-SEPT14* fusion) and one partial response lasting 12.8 months (adenocarcinoma NOS with the classic *EGFR* mutation, p.Glu746_Ala750del). Three patients had stable disease. The 6-month PFS was 15% (90% CI, 0 to 30.7); the median OS was 9 months (90% CI, 4.6 to 14.0). Rash and diarrhea were the most common toxicities.

Conclusion: Afatinib had modest activity in a cohort of patients with heavily pretreated cancer with advanced nonlung, *EGFR*-mutated tumors, but the trial's primary end point was not met. Further evaluation of afatinib in GBM with *EGFR* exon 18 fusions may be of interest.