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A Multicenter Phase II Study of Pazopanib in Patients with Unresectable Dermatofibrosarcoma Protuberans

Julie Delyon [1], Raphael Porcher [2], Maxime Battistella [3], Nicolas Meyer [4], Henri Adamski [5], François Bertucci [6], Bernard Guillot [7], Thomas Jouary [8], Marie-Thérèse Leccia [9], Sophie Dalac [10], Laurent Mortier [11], Zineb Ghrieb [12], Laetitia Da Meda [13], Eric Vicaut [14], Florence Pedeutour [15], Samia Mourah [16], Celeste Lebbe [17]

Affiliations

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Abstract

Dermatofibrosarcoma protuberans (DFSP) is a soft-tissue sarcoma characterized by a high risk of local infiltration. The identification of the COL1A1-PDGFB t(17;22) translocation activating the PDGF pathway led to the use of imatinib in unresectable DFSP, with a response rate of 36-80%. Pazopanib is a multitarget tyrosine kinase inhibitor approved for soft-tissue sarcomas. We conducted a phase II study of patients with unresectable DFSP to evaluate the efficacy and safety of pazopanib. Patients received 800 mg of pazopanib daily. The primary endpoint was the objective response rate defined as the reduction of the largest diameter of the tumor by ≥30% at 6 months or at surgery. A total of 23 patients, including one pretreated with imatinib, were enrolled. With a median follow-up of 6.2 months (interquartile range = 5.6-7.8 months), five patients (22%, 95% confidence interval = 7-22%) had a partial response to pazopanib. The best objective response rate was 30% (95% confidence interval = 13-53%) using Response Evaluation Criteria in Solid Tumors. One patient with metastatic DFSP previously treated with imatinib died after 2.4 months. Nine patients (39%) discontinued the treatment owing to adverse events. Pharmacodynamics analyses of tumor samples were conducted: the enrichment of EGF and the EGFR-associated gene panel was associated with resistance, suggesting that EGFR-targeted therapies could be a therapeutic option to explore in DFSP. TRIAL REGISTRATION: ClinicalTrials.gov identifier: NCT01059656.

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