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Abstract

Nintedanib (BIBF 1120) is a small, orally available, triple angiokinase inhibitor in phase III development (various indications) that targets VEGFR 1-3, FGFR 1-3, and PDGFR-α/β. This open-label, uncontrolled, phase II study assessed the efficacy and safety of nintedanib in patients with recurrent glioblastoma multiforme (GBM) who had previously failed radiotherapy plus temozolomide as first-line therapy (STUPP), or the same regimen with subsequent bevacizumab-based therapy as second-line treatment (BEV). Patients with a performance status of 0-1, histologically proven GBM, and measurable disease (by RANO) were enrolled. Nintedanib was given orally at a dose of 200 mg twice daily (bid), with magnetic resonance imaging undertaken every 8 weeks. The primary endpoint was objective response rate. The study was stopped prematurely following a preplanned futility analysis after inclusion of 13 patients in the STUPP arm and 12 in the BEV arm. Best response was stable disease (SD) in three patients (12 %); all other patients progressed within the first four 28-day cycles. One patient in the BEV arm has had SD for 17+ months. Median progression-free survival was 1 month and median overall survival was 6 months. Nintedanib had an acceptable safety profile, with no CTCAE grade 3-4 adverse events. Common adverse events were CTCAE grade 1-2 fatigue, loss of appetite, diarrhea, and nausea. Single-agent nintedanib (200 mg bid) demonstrated limited, but clinically non-relevant antitumor activity in patients with recurrent GBM who had failed 1-2 prior lines of therapy.