Dokumenttyp: journal article

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Titel des Beitrags:
Efficacy and safety of motesanib, an oral inhibitor of VEGF, PDGF, and Kit receptors, in patients with imatinib-resistant gastrointestinal stromal tumors.

Abstract:
This multicenter phase 2 study assessed the tolerability and efficacy of motesanib, an oral inhibitor of Kit, platelet-derived growth factor receptor (PDGFR), and vascular endothelial growth factor receptors (VEGFR), in patients with imatinib-resistant gastrointestinal stromal tumors (GIST). Patients with advanced GIST who failed imatinib mesylate after>=8 weeks of treatment with>=600 mg daily received motesanib 125 mg orally once daily continuously for 48 weeks or until unacceptable toxicity or disease progression occurred. The primary endpoint was confirmed objective tumor response per RECIST and independent review. Secondary endpoints included progression-free survival (PFS), time to progression (TTP); objective response by (18)FDG-PET and by changes in tumor size and/or density (Choi criteria); pharmacokinetics and safety. In the patients evaluable for response (N = 102), the objective response rate was 3%; 59% of patients achieved stable disease, with 14% achieving durable stable disease>=24 weeks; 38% had disease progression. Higher objective response rates were observed per (18)FDG-PET (N = 91) (30%) and Choi criteria (41%). The median PFS
was 16 weeks (95% CI = 14-24 weeks); the median TTP was 17 weeks (95% CI = 15-24 weeks). The most common motesanib treatment-related grade 3 adverse events included hypertension (23%), fatigue (9%), and diarrhea (5%). Motesanib did not accumulate with daily dosing. In this study of patients with imatinib-resistant GIST, motesanib treatment resulted in acceptable tolerability and modest tumor control as evident in the proportion of patients who achieved stable disease and durable stable disease.

Zeitschriftentitel / Abkürzung: Cancer Chemother Pharmacol
Jahr: 2011
Band: 68
Heft / Issue: 1
Seiten: 69-77
Sprache: eng
Print-ISSN: 0344-5704
TUM Einrichtung: III. Medizinische Klinik und Poliklinik
Occurences: - Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > III. Medizinische Klinik und Poliklinik (Hämatologie / Onkologie) > 2011
entries: