Clinical Study Synopsis

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The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

Bayer HealthCare

Clinical Trial Results Synopsis

Study Design Description		
Study Sponsor:	Bayer Healthcare AG	
Study Number:	12782	NCT00678288
Study Phase:	II	
Official Study Title:	A Phase II, Randomized, Open-label, MultiCenter Study Evaluating the Efficacy of Sorafenib Alone and Sorafenib in Combination with Low Dose Interferon Alpha-2a as Second-line Treatment of Sunitinib Failure in Patients with Metastatic Renal Cell Carcinoma (RCC)	
Therapeutic Area:	Oncology	
Test Product		
Name of Test Product:	Sorafenib (Nexavar, BAY46-4006)	
Name of Active Ingredient:	4-{4-[3-(4-chloro-3-trifluoromethyl-phenyl)-ureido]-phenoxy}-pyridine-2-carboxylic acid methylamide-4-methylbenzenesulfo-nate	
Dose and Mode of Administration:	400 mg (two 200 mg tablets) twice a day (bis in die [bid]) oral (per os [PO])	
Reference Therapy/Placebo		
Reference Therapy:	Sorafenib combined with interferon alpha-2a	
Dose and Mode of Administration:	Sorafenib 400 mg (two 200-mg tablets) bid PO Interferon alpha-2a 3 million international units (MIU) five times a week (FIW) from Monday to Friday subcutaneously (sc) Interferon alpha-2a was started at a dose of 1.5 MIU FIW 1 week after starting sorafenib, with the full dose (3 MIU) to be reached within the first 2 weeks of treatment	

Duration of Treatment:	Treatment continued in repeating 28 day cycles until one of the following occurred: • Unacceptable toxicity which required drug discontinuation. • Disease progression, unless the investigator believed the subject might benefit from dose escalation. In that case, final discontinuation occurred upon second progression under the higher dose. • Withdrawal of consent. • Sponsor decided to terminate the study for any reason.	
Studied period:	Date of first subjects' first visit:	16 Apr 2008
	Date of last subjects' last visit:	26 Jun 2009
Study Center(s):	The study was conducted at 31 centers in 7 countries: France (11), Italy (6), Spain (5), Poland (4), Ireland (2), United Kingdom (2), and Austria (1)	
Methodology:	This was a randomized, open-label, multicenter, Phase II study designed to evaluate the efficacy of sorafenib alone and sorafenib in combination with low-dose interferon alpha 2a after either sunitinib failure or sunitinib intolerability in patients with metastatic RCC. Concomitant treatment with other cytotoxic or cytostatic agents, as well as biological agents, was prohibited. Palliative radiation therapy was allowed only for symptomatic, nontarget lesions. All subjects who met the entrance criteria were randomized to receive either: • The approved sorafenib dosage (400 mg bid PO) until progression (at which time the dosage could be escalated to 600 mg bid PO) OR • The approved sorafenib dosage (400 mg bid PO) plus interferon alpha-2a (3 MIU FIW sc) until progression or unacceptable toxicity. If progression occurred, the dosage of sorafenib (monotherapy) could be escalated to 600 mg bid, at the discretion of the investigator. Every 28 days constituted 1 cycle of treatment. Dose reduction was possible for both sorafenib and interferon alpha 2a if toxicities thought to be related to the study drug were observed.	
Indication/ Main Inclusion Criteria:	Adult (≥ 18 years old) subjects with histologically confirmed metastatic RCC with predominant clear cell histology (clear cell component more than 50%), Eastern Cooperative Oncology Group (ECOG) performance 0 or 1, Memorial Sloan Kettering Cancer Center (MSKCC) score low or intermediate, and for whom treatment with sunitinib had failed (disease progression as defined by Response	

	Evaluation Criteria in Solid Tumors [RECIST] or toxicity) were eligible for enrollment. Subjects must have had measurable disease (by RECIST) and must not have received prior systemic anticancer therapy other than sunitinib. Prior nephrectomy was strongly encouraged.
Study Objectives:	Primary: The aim of the study was to evaluate if the addition of low doses of interferon alpha-2a to sorafenib would be beneficial, by estimating the median progression-free survival (PFS), in patients who previously either had progressed or were intolerant to sunitinib. Secondary: Secondary objectives were to estimate response rate, time to progression (TTP), duration of response, and overall survival (OS).
Evaluation Criteria:	Efficacy: Because the study was terminated early, efficacy was not assessed. Safety: Adverse events, changes in laboratory (hematology, clinical chemistry, and clinical urinalysis) values, changes in vital signs (blood pressure, heart rate, respiratory rate, and temperature), and electrocardiogram (ECG) findings were evaluated for safety. The intensity of adverse events was graded according to the National Cancer Institute (NCI) Common Toxicity Criteria for Adverse Events (CTCAE), version 3.0.
Statistical Methods:	Efficacy: Because the study was terminated early, efficacy was not analyzed as described in the protocol or statistical analysis plan.
Number of Subjects:	The planned enrollment was 120 subjects in the 2 treatment groups (60 subjects per group). The study, however, was terminated prematurely because of slow accrual, at which time 16 subjects were enrolled and randomized. A total of 24 subjects were screened and 16 subjects were enrolled and randomized; 10 (63%) randomized to sorafenib alone and 6 (37%) randomized to sorafenib + interferon. All 16 randomized subjects received at least 1 dose of study drug and were included in the safety analysis population.

Study Results

Results Summary — Subject Disposition and Baseline

The study was terminated early due to slow accrual of subjects.

Results Summary — Efficacy
Because the study was terminated early, efficacy was not analyzed as described in the protocol or statistical analysis plan.
Results Summary — Safety
All 16 subjects (100%) randomized and treated in the study experienced at least 1 treatment emergent adverse event. Although the data from the small number of subjects treated in this study do not allow for definitive conclusions regarding safety, the incidence of subjects with treatment emergent adverse events was the same for the sorafenib (100% [10 subjects]) and sorafenib + interferon (100% [6 subjects]) groups. The most commonly reported adverse events overall were fatigue (8 [80%] subjects and 5 [83%] subjects in the sorafenib and sorafenib + interferon groups, respectively), pain (8 [80%] and 4 [67%] subjects, respectively), diarrhea (5 [50%] and 3 [50%] subjects, respectively), and rash/desquamation (5 [50%] and 3 [50%] subjects, respectively). Hand foot skin reaction was reported only in the sorafenib group (5 subjects; 50%). A higher proportion of subjects in the sorafenib + interferon group (100% [6 subjects]) than in the sorafenib group (50% [5 subjects]) had adverse events that were assessed by the investigator as ≥ Grade 3 in intensity. Among the 6 subjects in the sorafenib + interferon group, 4 (67%) subjects had a worst grade of 3, and 1 (17%) subject each had a worst grade of 4 or 5. All 5 (50%) subjects in the sorafenib group had a worst grade of 3; none had a worst grade of 4 or 5. The only ≥ Grade 3 events reported for more than 1 subject in each treatment group were fatigue (3 [50%] subjects in the sorafenib + interferon group), hand foot skin reaction (2 [20%] subjects in the sorafenib group), and erythema multiforme and pain (each, 2 [33%] subjects in the sorafenib + interferon group). Two subjects (1 each in the sorafenib [10%] and sorafenib + interferon [17%] treatment groups) died within 30 days of the last dose of study medication; the cause was reported as disease progression. Treatment emergent serious adverse events were reported for 5 (50%) subjects in the sorafenib group and 3 (50%) subjects in the sorafenib + interferon group. Study medication was discontinued due to adverse event for 2 (20%) sorafenib subjects (fatigue and bone pain) and 2 (33%) sorafenib + interferon subjects (fatigue in 2 subjects and vomiting in 1 subject). There were no notable differences between treatment groups in laboratory events. The most common ≥ Grade 3 biochemical abnormality was hypophosphatemia.
Conclusion(s)
Because the study was terminated early, efficacy was not analyzed and the number of subjects was too small to make definitive conclusions regarding safety. Based on the available safety data from 16 subjects with metastatic renal cell carcinoma, sorafenib and sorafenib + interferon appeared to be similarly tolerated.

Publication(s):	None
Date Created or Date Last Updated:	17 May 2010

Product Identification Information

Product Type	Drug
US Brand/Trade Name(s)	Nexavar
Brand/Trade Name(s) ex-US	Nexavar
Generic Name	Sorafenib
Main Product Company Code	BAY43-9006
Other Company Code(s)	BAY54-9085
Chemical Description	**(1)** 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-**(2)** 4-(4-{3.[4-chloro-3-(trifluoromethyl)phenyl]ureido}phenoxy)-N2-methylpyridine-2-carboxamide
Other Product Aliases	Sorafenib tosylate

Date of last Update/Change: 28 Apr 2012