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 Pharmaceuticals Inc.	
Study Number:	11961	NCT00300885
Study Phase:	III	
Official Study Title:	A randomized controlled trial comparing safety and efficacy of carboplatin and paclitaxel plus or minus sorafenib (BAY 43-9006) in chemonaïve patients with stage IIIB-IV non-small cell lung cancer (NSCLC)	
Therapeutic Area:	Oncology	
Test Product		
Name of Test Product:	Sorafenib (Nexavar, BAY43-9006)	
Name of Active Ingredient:	Sorafenib	
Dose and Mode of Administration:	Chemotherapy Phase (21-day cycle) Day 1: Paclitaxel 200 mg/m^2 intravenously (IV) over 2.5 to 4 hours followed by carboplatin IV dose that gives area under the curve (AUC) = 6 mg/mL*min^{-1} over 15 to 60 minutes. Day 2 - 19: Sorafenib 400 mg; 2 tablets (200 mg each) administered orally twice daily. Cycles were repeated every 3 weeks. Maintenance Phase (21-day cycle) Day 1 - 21: Sorafenib 400 mg; 2 tablets (200 mg each) administered orally twice daily.	
Reference Therapy/Placebo		
Reference Therapy:	Placebo + Carboplatin/Paclitaxel	
Dose and Mode of Administration:	Chemotherapy Phase (21-day cycle) Day 1: Similar to test therapy Day 2 - 19: Placebo tablets matching sorafenib 200 mg tablets, 2 placebo tablets administered orally twice daily. Cycles were repeated every 3 weeks. Maintenance Phase (21-day cycle) Day 1 - 21: Placebo tablets matching sorafenib 200 mg tablets, 2 placebo tablets administered orally twice daily.	
Duration of Treatment:	Each treatment cycle consisted of 21 days. Subjects received up to 6 cycles of carboplatin/paclitaxel with sorafenib or placebo in the Chemotherapy Phase. If the subject had radiographic evidence of stable disease (SD), partial response (PR), or complete response (CR) after completing up to 6 cycles in the Chemotherapy Phase, they were allowed to continue on to the Maintenance Phase. During the Maintenance Phase, the subject received daily sorafenib or placebo as a single agent until the criteria for withdrawal were met.	
Studied period:	**Date of first subjects' first visit:**	13 FEB 2006
	Date of last subjects' last visit:	05 FEB 2009
Premature Study Suspension / Termination:	The study could not meet its primary efficacy endpoint and in consequence the study was terminated early for futility on	

	01 OCT 2007. Efficacy data was analyzed from 13 FEB 2006 to 01 OCT 2007 and the cumulative safety data was analyzed from 13 FEB 2006 to 05 FEB 2009.
Substantial Study Protocol Amendments:	Amendment no. 1 (dated 31 JAN 2006) specified the following changes: • Cytological confirmation of malignant effusion in Stage IIIB subjects was required for inclusion. • Carboplatin and paclitaxel dosing was based on actual body weight on Day 1 of each cycle. • Weekly blood pressure monitoring was required for the first 6 weeks of sorafenib therapy. • If radiological imaging was not possible, then clinical progression was to be used (defined as cancer-related deterioration of ECOG status to 3 or more). • Functional Assessment of Cancer Treatment-Lung (FACT-L) would not be assessed at the end-of-treatment visit using Lung Cancer Subscale (LCS). • Biomarker plasma samples could be collected one day before Cycle 3 if more convenient. Amendment no. 2 (dated 19 JUN 2006) was applicable only to Site 22001 (Ospedale San Luigi, Italy). It specified addition of an ancillary study of medical imaging as a biomarker of anticancer activity performed by means of 18F-flourodeoxyglucose Positron Emission Tomography (18FDG PET). Amendment no. 3 (dated 01 NOV 2006) specified following changes: • Thoracentesis or pericardiocentesis was not necessary if a biopsy of the original tumor was available to confirm diagnosis of NSCLC. • "No prior chemotherapy" was removed from the inclusion criteria. • Range of activated partial thromboplastin time within 1.2 times the lower limit of normal to 1.2 times theupper limit of normal (ULN) was added. • A subject receiving the lowest dose level of carboplatin or paclitaxel, or sorafenib/placebo, who required a further dose reduction, was to be discontinued from the study. • Subjects requiring delays to chemotherapy cycles were allowed to continue taking sorafenib/placebo at the discretion of the investigator. • Adverse events (AEs) were collected up to 30 days after the stop of treatment for all AEs that were ongoing at the end of treatment. Amendment no. 4 (dated 19 DEC 2007) specified the following changes to the statistical analysis plan (SAP): • SAP included a less aggressive futility boundary to be utilized for the formal planned interim analysis. • Analyses with respect to subject reported outcomes (PRO) were summarized in a descriptive fashion. Amendment no. 5 (dated 18 APR 2008) was implemented as the study could not meet its primary efficacy endpoint and as a consequence, the study was terminated early for futility. It specified the following changes to the protocol: • For all subjects on placebo, the treatment was discontinued and they were followed every three months for overall survival (OS). • Squamous cell subjects who had oral study medication stopped

	were followed every three months for OS. • Non-squamous cell subjects who continued on sorafenib as monotherapy (if deemed clinically beneficial) maintenance were followed for safety and OS either in this study or in an ongoing extension program. • Subjects in the post-treatment follow-up phase of the study continued to be followed every three months for OS. Subjects on maintenance phase were followed for OS information.
Study Centre(s):	The study was conducted at 154 centers in 20 countries: United States (51), Brazil (18), Germany (15), Italy (9), Argentina (6), France (5), Spain (5), Poland (6), Australia (5), Canada (5), Belgium (3), Chile (4), Hungary (4), United Kingdom (4), Russia (3), Sweden (3), Taiwan (3), the Netherlands (2), Hong Kong (1), and South Korea (2).
Methodology:	Subjects were randomized in a double-blind fashion using a 1:1 allocation of subjects to sorafenib in combination with paclitaxel and carboplatin (sorafenib group) or placebo in combination with paclitaxel and carboplatin (placebo group). Stratification factors for randomization were Eastern Cooperative Oncology Group (ECOG) performance status (PS) (ECOG PS 0 versus 1), geographic region, disease histology (squamous versus non-squamous), and disease stage (Stage IIIB with pleural or pericardial effusion versus Stage IV). The study comprised of 3 periods: Screening, Treatment Period (Chemotherapy Phase and Maintenance Phase), and Post-treatment Follow-up Period. Radiologic assessments were performed every 6 weeks ±5 days (after the first dose of study drug) for the first 18 weeks of the study and thereafter every 12 weeks ±5 days, regardless of whether the subject was in the Chemotherapy Phase or the Maintenance Phase. All subjects who discontinued treatment due to any reason entered a Post-treatment Follow-up Period for collection of OS data until death. In addition to ongoing monitoring of fatal bleeding events for all treated subjects during the study, a formal interim safety analysis was also performed to monitor fatal bleeding events in subjects with squamous cell histology treated with sorafenib to determine whether enrollment of squamous cell subjects was to be continued. For safety measurements all AEs were collected up to 30 days after termination of treatment and were reported and graded according to Common Terminology Criteria for Adverse Events (CTCAE) version 3.0.
Indication/ Main Inclusion Criteria:	Indication: Non Small Cell Lung Cancer (Unresectable Stage IIIB or IV NSCLC) Main Inclusion Criteria: • Male and female subjects of ≥18 years of age with Stage IIIB (with cytologically confirmed malignant pleural or pericardial effusion) or Stage IV histological or cytological confirmation of NSCLC. • ECOG PS of 0 or 1 and a life expectancy of at least 12 weeks. • No prior chemotherapy for NSCLC allowed. • Adequate bone marrow, liver, and renal function as assessed by clinical laboratory tests.
Study Objectives:	**Overall:** To evaluate the efficacy and safety of carboplatin and paclitaxel plus or minus sorafenib in chemonaive subjects with Stage IIB (with effusion) and Stage IV NSCLC.

	Primary: To evaluate overall survival between subjects treated with sorafenib versus placebo in combination with paclitaxel and carboplatin. **Secondary:** To evaluate tumor response, duration of response, progression-free survival (PFS) and subject reported outcome between subjects treated with sorafenib versus placebo in combination with paclitaxel and carboplatin. **Other evaluations:** To evaluate biomarkers that may relate the pharmacological mechanism of action of sorafenib to its anti-tumor activity. **Safety:** Evaluation of safety between subjects treated with sorafenib vs placebo in combination with paclitaxel and carboplatin.
Evaluation Criteria:	**Efficacy (Primary):** The primary efficacy variable was OS. The investigator assessed tumor response and disease progression based on a blinded review of computed tomography (CT) scans of the chest and abdomen. Tumor response and disease progression were evaluated based on Response Evaluation Criteria in Solid Tumors (RECIST) criteria (version 1.0). Non-target lesions were also recorded. Primary analysis of the efficacy data was based on the intent-to-treat (ITT) population, i.e., all subjects randomized to treatment. **Efficacy (Secondary):** Secondary efficacy variables included progression-free survival, best tumor response, duration of response, PRO using the FACT-L and LCS instruments. **Safety:** Safety was assessed based on results of physical examinations including ECOG performance status, vital signs, electrocardiogram (ECG) data, weight, laboratory values and AEs up to 30 days after termination of treatment. The study used the National Cancer Institute (NCI) CTCAE Version 3.0 for assessment of toxicity and serious adverse events (SAEs) reporting. Safety analyses were based on the Valid-for-Safety population, i.e., all subjects randomized to treatment who received any study medication.
Statistical Methods:	**Efficacy (Primary):** The primary efficacy endpoint was OS. All randomized subjects (the ITT population) were included in the primary analyses. OS was defined as the time from randomization to death due to any cause. In the analysis of OS, the two treatment groups (sorafenib and placebo) were compared using a one-sided log-rank test with an overall alpha of 0.025 stratified by the same stratification factors as randomization. Kaplan-Meier estimates and survival curves were also presented for each treatment group. In addition to the final analysis of OS, one formal interim analysis of

	OS was planned during the study. The interim analysis of overall survival was conducted when approximately 383 deaths had been observed. A Lan-Demets alpha spending function determined the monitoring boundaries for early stopping for efficacy so that the overall false positive rate, alpha, was less than or equal to 0.025 (one-sided). The alpha spending function was the O'Brien-Fleming type boundary specified. The actual monitoring boundaries applied to the formal OS analyses were based on the actual number of events observed at the time of analysis. Interim OS analysis was based on 384 actual events (deaths) observed up to the data cut-off of 01 OCT 2007 and according to the protocol specified O'Brien-Fleming type alpha spending function, the one-sided alpha value for this interim analysis was 0.0046. **Efficacy (Secondary):** Secondary efficacy endpoints also presented were PFS, best tumor response, duration of response, and health-related quality of life (HRQOL) of subjects in the two treatment groups using the FACT-L and LCS instruments. The two treatment groups were compared with respect to each secondary efficacy parameter using a one-sided alpha of 0.025. PFS was calculated as the time (days) from date of randomization to date of first observed disease progression (radiological or clinical, whichever was earlier) or death due to any cause, if death occurred before progression was documented. The two treatment groups were compared using a log-rank test stratified by the same stratification factors as randomization. Kaplan-Meier estimates and Kaplan-Meier curves were also presented for each treatment group. **Safety:** Treatment-emergent AEs, drug-related AEs, and safety laboratory parameters were summarized by treatment group and CTCAE grade. One formal interim analysis of OS was planned during study.
Number of Subjects:	A total of 1043 subjects were enrolled: 117 subjects failed screening and 926 subjects were randomized between 15 FEB 2006 and 09 MAY 2007 at 150 centers in 20 countries. The population valid for ITT analyses comprised of the 926 randomized subjects (462 in the placebo + C/P group and 464 in the sorafenib + C/P group) Four subjects did not receive the study drug, and were not considered valid for the safety analysis. Thus, 922 subjects began double-blind treatment (459 in the placebo + C/P group and 463 in the sorafenib + C/P group) and were included in the population valid for the safety analyses. Post-treatment follow-up was entered by 793 subjects: 383 from the sorafenib + C/P group and 410 from the placebo + C/P group.

Study Results
Results Summary — Subject Disposition and Baseline
Of the 926 randomized subjects, 922 received at least one dose of study medication: 463 in

the sorafenib + carboplatin/paclitaxel (sorafenib + C/P) group and 459 in the placebo + carboplatin/paclitaxel (placebo + C/P) group.

Of the 4 subjects, who did not receive study drug, three were randomized to placebo + C/P and one to sorafenib + C/P treatment.

Of the 926 subjects in the ITT population, 581 subjects (63%) were male and 345 were female (37%). Eight hundred-and-two subjects (87%) were White. Mean age at enrollment was 61.2 years (range: 34 to 86 years). The treatment groups were similar with regard to the demographic characteristics.

Results Summary — Efficacy

A total of 384 actual events (deaths) were reported as of the data cut-off date of 01 OCT 2007 and were included in the formal interim efficacy analysis of OS.

The sorafenib + C/P groups demonstrated no survival benefit compared to the placebo + C/P group in terms of the efficacy data with no significant differences between the treatment groups. Subgroup analyses (non-squamous vs squamous subjects) revealed an increased hazard for almost all efficacy variables in squamous subjects after treatment with sorafenib compared to placebo.

For the OS analysis, the median OS was 322 days for placebo + C/P and 324 days for sorafenib + C/P, with a hazard ratio of 1.15 (sorafenib/placebo) representing a 15% increase in hazard with sorafenib. The stratified log-rank test had a one-sided p-value of 0.915. Based on these results, the estimated hazard ratio had crossed the futility monitoring boundary (for lack of efficacy) of 1.0515, thus, it was determined that the study would not meet its primary efficacy endpoint.

For the non-squamous subgroup, the median OS was 309 days for placebo + C/P and 350 days for sorafenib + C/P, with a hazard ratio of 0.98. For the squamous subgroup, the median OS was 415 days for placebo + C/P and 272 days for sorafenib + C/P, with a hazard ratio of 1.85, representing an 85% increase in hazard with sorafenib.

Subgroup OS results reported trends favoring placebo + C/P treatment for subgroups such as sex, age, baseline ECOG, disease stage at entry or smoking history. A hazard ratio favoring sorafenib + C/P treatment was observed for subjects with a disease stage at entry of IIIB only, although the number of subjects in this subgroup was limited. In squamous subjects, trends mainly favored placebo + C/P treatment.

The two treatment groups did not differ significantly in terms of overall PFS based on the investigator's assessment. The median PFS was 163 days for the placebo + C/P group and 139 days for the sorafenib + C/P group with a hazard ratio of 0.99, representing no trend in favor of either treatment arm. Histology subgroup analysis of PFS showed similar trends to the OS subgroup outcome.

The overall response rate (PR + CR) according to RECIST criteria was 24% for the placebo + C/P group and 27% for the sorafenib + C/P group. For the non-squamous subgroup, the overall response rate was 20% for the placebo + C/P group and 28% for the sorafenib + C/P group. For the squamous subgroup, the overall response rate was 35% for the placebo + C/P group and 25% for the sorafenib + C/P group.

The overall disease control rate (Stable Disease or better) was 72% for the placebo + C/P group and 73% for the sorafenib + C/P group.

Further analysis of PRO revealed that there were no differences in observed means by cycle or mean changes of LCS scores between two treatments throughout the study period. In addition both treatment arms had similar total scores on FACT-L representing no notable

difference in quality of life between the two arms.

In summary, efficacy data from this double-blind, multi-center, multinational, and placebo controlled study could not demonstrate significant prolongation of OS or PFS in subjects with Stage IIIB-IV NSCLC treated with sorafenib. Additionally, an increase in hazard was observed in squamous subjects treated with sorafenib.

Results Summary — Safety

Exposure to study drug was comparable between the two treatment groups with median treatment duration of 17 weeks for sorafenib + C/P and of 18 weeks for placebo + C/P.

One or more treatment-emergent AEs were reported in >99% of the subjects in each of the two treatment groups. One or more drug-related AEs were reported for 84% of the subjects in the sorafenib + C/P group and 68% of the subjects in the placebo + C/P group. SAEs were reported for 59% (drug-related 17%) of the subjects in the sorafenib + C/P group and 43% (drug-related 9%) of the subjects in the placebo + C/P group. AEs leading to discontinuation of study drug were reported for 33% of the subjects in the sorafenib + C/P group and 22% of the subjects in the placebo + C/P group. AEs leading to death, including death within 30 days of end of treatment, occurred in 21.8% of the subjects in the sorafenib + C/P group and 13.5% of the subjects in the placebo + C/P group.

Overall, the following AEs were more common in subjects treated with sorafenib + C/P: rash/desquamation (52% vs 17%), diarrhea (44% vs 24%), low platelet counts (31% vs 15%), hand-foot skin reaction (24% vs 5%), weight loss (22% vs 12%), fever (21% vs 14%), hypertension (20% vs 10%), mucositis (clinical exam), oral cavity (17% vs 7%), pruritus (14% vs 8%), heartburn (10% vs 6%), and hypokalemia (10% vs 5%).

In the non-squamous and squamous subgroups, >99% of the subjects reported one or more treatment-emergent AEs. In the non-squamous subgroup, one or more drug-related AEs were reported for 86% of the subjects in the sorafenib + C/P group and 70% of the subjects in the placebo + C/P group. SAEs were reported for 59% of the subjects in the sorafenib + C/P group and 43% of the subjects in the placebo + C/P group. Treatment-emergent AEs leading to death, including death within 30 days of end of treatment occurred in 7% of the subjects in the sorafenib + C/P group and in 6% of the subjects in the placebo + C/P group.

Analysis of treatment-emergent AEs in non-squamous subjects revealed higher frequencies in the sorafenib + C/P group compared to the placebo + C/P group for rash/desquamation (55% vs 18%), diarrhea (45% vs 25%), low platelets (32% vs 14%), hand-foot skin reaction (25% vs 5%), fever (21% vs 13%), hypertension (21% vs 10%), weight loss (20% vs 13%), mucositis (clinical exam), oral cavity (17% vs 7%), pruritus (14% vs 8%), hemorrhage pulmonary – nose (11% vs 5%), heartburn (11% vs 6%), and hypokalemia (10% vs 6%). Infections were also more common in the sorafenib + C/P group compared to the placebo + C/P group (43% vs 31%) with no site specific pattern. Also pulmonary/upper respiratory events were more common in the sorafenib + C/P group (57% vs 49%).

In the squamous subgroup, one or more drug-related AEs were reported for 77% of the subjects in the sorafenib + C/P group and 63% of the subjects in the placebo + C/P group. SAEs were reported for 58% of the subjects in the sorafenib + C/P group and 40% of the subjects in the placebo + C/P group. Treatment-emergent AEs leading to death, including death within 30 days of end of treatment occurred in 8% of the subjects in the sorafenib + C/P group and in 6% of the subjects in the placebo + C/P group.

Analysis of AEs in squamous subjects revealed higher frequencies of treatment-emergent AEs in the sorafenib + C/P compared to the placebo + C/P group for diarrhea (41% vs 21%), rash/desquamation (44% vs 17%), constipation (29% vs 14%), low platelets (28 % vs 18%), weight loss (27% vs 11%), hand-foot skin reaction (23% vs 6%), hypertension (18% vs 12%), mucositis (clinical exam), oral cavity (16% vs 8%), pruritus (15% vs 5%), bone

pain (10% vs 5%), hypokalemia (10% vs 4%), hypotension (9% vs 4%), hemorrhage pulmonary – respiratory tract NOS (8% vs 4%), pulmonary – other (8% vs 5%), heartburn (8% vs 4%), death (8% vs 4%), haemorrhage pulmonary – nose (6% vs 4%), and pneumothorax (4% vs 0%). Infections were also more common in the sorafenib + C/P compared to the placebo + C/P group (44% vs 33%), however, there was no site-specific pattern of infection.

One or more Grade ≥3 AEs were reported for 416 subjects (90%) in the sorafenib + C/P group and for 352 subjects (77%) in the placebo + C/P group. The most commonly reported Grade 3 or 4 AEs in the sorafenib + C/P group were low neutrophils (33%), low platelets (15%), fatigue (12%), dyspnea (11%), and low leukocytes (10%) with no other Grade ≥3 AEs reported for more than 10% of the subjects. Similar overall incidences of Grade ≥3 AEs were reported in non-squamous and squamous subjects. In addition, in the squamous subjects treated with sorafenib + C/P, a higher incidence of Grade ≥3 dyspnea (21% compared to 12% in placebo + C/P subjects) was apparent.

The AEs frequently associated with the use of sorafenib include neutrophils/granulocytes, leukopenia, platelets, hemoglobin, hypertension, fatigue, weight loss, diarrhea, nausea, mucositis, hemorrhage/bleeding, febrile neutropenia, hypophosphatemia, sensory neuropathy, pain, hand-foot skin reaction, rash/desquamation, pruritus and thrombus/embolism.

There was a higher incidence of low platelets in the sorafenib + C/P group than in the placebo + C/P group, particularly in Grade ≥3 thrombocytopenia (15% versus 5%, respectively). About one-third of the events in the blood/bone marrow category were considered related to study drug.

Hypertension occurred in 20% of subjects in the sorafenib + C/P group and in 11% of the subjects in the placebo + C/P group. Nineteen (4%) subjects in the sorafenib + C/P group experienced hypertension of Grade ≥3 as did 8 (2%) subjects in the placebo + C/P group. Investigators considered hypertension to be related to study drug in 13% of subjects in the sorafenib + C/P group and in 6% of subjects in the placebo + C/P group.

Fatigue occurred in 50% of the subjects in the placebo + C/P group and in 54% of subjects in the sorafenib + C/P group. Fifty-five subjects (12%) in the sorafenib + C/P group experienced fatigue of Grade ≥3, as did 33 (7%) subjects in the placebo + C/P group.

Weight loss occurred about twice as often in the sorafenib + C/P group compared to the placebo + C/P group (22% vs 12%).

Diarrhea occurred more frequently among subjects in the sorafenib + C/P group (44% same) than among subjects receiving placebo + C/P (24%), but that is not unexpected; diarrhea is associated with sorafenib treatment. Mucositis (oral cavity, by clinical investigation) occurred in 17% of the subjects of the sorafenib + C/P group compared to 7% of subjects of the placebo + C/P, and was judged as drug-related in 10% of sorafenib + C/P-treated subjects and in 2% of placebo + C/P-treated subjects.

Hemorrhage/bleeding events occurred in 110 subjects (24%) receiving sorafenib + C/P and 85 subjects (19%) receiving placebo + C/P, the majority of which were of Grade 1 or 2 severity in both treatment groups. Except for hemorrhage pulmonary, nose (10% vs 5%) and hemorrhage pulmonary - lung events (5% vs 4%) there were no important differences between groups among types of hemorrhages. Fatal bleeding events were significantly more frequent in sorafenib-treated subjects in the squamous histology subgroup (6%) compared to the non-squamous subgroup (1.1%). A similarly higher incidence of fatal bleeding events in the squamous subgroup was observed among placebo-treated subjects (4.4%) compared to the non-squamous subgroup (no cases). This difference between histological subgroups is partly accounted for by the higher incidence of fatal lung bleedings: 3.7% in squamous vs

0.8% in non-squamous subgroup in the sorafenib + C/P arm; 12.6% in squamous vs. no cases in non-squamous in the placebo + C/P arm. Therefore, overall, squamous histology was associated with a higher incidence of fatal bleeding events (including fatal pulmonary hemorrhage) in this study population irrespective of treatment with sorafenib or placebo.

Infection occurred with higher overall frequency in the sorafenib + C/P group (43%) than in the placebo + C/P group (31%), but there were no important differences between groups among types of infections except for infections affecting the upper airways, which tend to occur in higher frequencies in the sorafenib + C/P group. The incidence rates of febrile neutropenia were higher in the sorafenib + C/P group compared to the placebo + C/P group (5% vs 2%).

Vascular, neurological, and pain AEs occurred with similar frequencies in both treatment groups. Of the metabolic/laboratory events, hypokalemia, hypomagnesemia, and hypophosphatemia were reported more frequently in the sorafenib + C/P group compared to the placebo + C/P group.

Dermatology events occurred more often in the sorafenib + C/P group (80%) than in the placebo + C/P group (60%) with a significantly higher percentage of Grade ≥3 events in the sorafenib + C/P group (19% vs 2%). Rash/desquamation, hand-foot skin reaction, and pruritus were reported more frequently under sorafenib treatment, (52%, 24% and 14%, vs 17%, 5%, and 8%, respectively).

Pulmonary/upper respiratory events were equally distributed in both groups and were reported for 51% of the subjects in the placebo + C/P group and for 56% of the subjects in the sorafenib + C/P group, which was expected due the underlying disease of NSCLC. There were no important differences between groups among types of pulmonary events except for hypoxia, pneumonitis, and pneumothorax, which tended to occur in higher frequencies in the sorafenib + C/P group.

There were 163 subjects with AEs resulting in death up to within 30 days of last dose of study drug: 101 (21.8%) in the sorafenib + C/P group and 62 (13.5%) in the placebo + C/P group. The most common cause of death within 30 days of study drug was underlying disease. Excess mortality compared to non-squamous subjects has been reported for deaths due to disease progression and deaths NOS for squamous subjects in the sorafenib + C/P group.

Treatment-emergent SAEs were reported more frequently under sorafenib + C/P treatment (59% vs 43%). The most common treatment-emergent SAEs for sorafenib + C/P compared to placebo + C/P were infection lung (pneumonia) (25 subjects, 5.4%), dyspnea (shortness of breath) (24 subjects, 5.2%) and constitutional symptoms-other (19 subjects, 4.1%). Subgroup analyses of SAEs in squamous vs all subjects treated with sorafenib + C/P revealed an apparent increase of hemorrhage/bleeding events (10% vs 5%), attributable to increased incidences of pulmonary lung (5% vs 2%) and pulmonary respiratory tract (NOS) hemorrhages (4% vs 1%), dyspnea (8% vs 5%) as well as more frequent vascular events (6% vs 4%) with a higher incidence of thrombosis/thrombus/embolism events (6% vs 4%). Blood/bone marrow events and constitutional symptoms showed trends of similar or lower frequencies compared to all subjects of the sorafenib + C/P group. In nonsquamous subjects treated with sorafenib + C/P, the incidences of SAEs were generally similar or lower compared to the overall sorafenib + C/P-treated population.

One or more AEs that led to the discontinuation of at least one study drug were reported for 22% of the subjects in the placebo + C/P group and for 33% of the subjects in the sorafenib + C/P group.

The only laboratory tests for which the treatment groups differed by at least 5% regarding the incidence of Grade 3 or 4 toxicity were low leukocytes, lymphopenia, hypophosphatemia, hyponatremia, and hypokalemia (all higher incidence in the sorafenib + C/P group). The only

laboratory test for which the treatment groups differed by at least 5% regarding the incidence of Grade 4 toxicity was low leukocytes (higher incidence in the sorafenib + C/P group). Analyses of Grade 3 and 4 abnormal laboratory values in squamous and non-squamous subjects treated with sorafenib + C/P showed similar results compared to all sorafenib + C/P-treated subjects.

Conclusion(s)

In this study, distinction between treatment-emergent AEs associated with sorafenib and events associated with the underlying lung disease or C/P treatment was demonstrated.

The results demonstrated a comparable overall incidence in treatment-emergent AEs for sorafenib + C/P and placebo + C/P. Higher incidences of drug-related and/or SAEs were reported for the sorafenib + C/P group. Most AEs were tolerable, and, in the majority of subjects, did not result in many dose reductions or interruptions, or increased hospitalization.

Due to the lack of overall efficacy in NSCLC for the combination therapy evaluated in this study, and increased mortality of squamous cell subjects treated with sorafenib, this study was prematurely terminated. Future clinical trials with sorafenib in NSCLC should carefully evaluate the inclusion or exclusion of the squamous subtype and focus mainly on subjects of non-squamous subtype.

Publication(s):	Scagliotti G et al. Phase III study of carboplatin and paclitaxel alone or with sorafenib in advanced non-small cell lung cancer. J Clin Oncol 2010, 28:1835-42.		
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Investigational Site List

Marketing Authorization Holder in Germany	
Name	Bayer Pharma AG
Postal Address	D-13342 Berlin
Sponsor in Germany	
Legal Entity Name	Bayer Healthcare AG
Postal Address	D-51368 Leverkusen

List of Investigational Sites

No	Facility Name	Street	ZIP Code	City	Country
1	Centro Especializado ISIS	Urquiza 3077	S3000FFV	Santa Fé	ARGENTINA
2	Hospital General de Agudos Dr. Carlos G. Durand	Hospital de Día Avda. Diaz Velez 5044	C1405DCS	Buenos Aires	ARGENTINA
3	Hospital Nacional Professor A. Posadas	Oncology Av. Presidente Illia y Marconi s/n	1684	El Palomar - Morón	ARGENTINA
4	Hospital Privado de la Comunidad	Cordoba 4545	B7602CBM	Mar del Plata	ARGENTINA
5	Instituto Medico Especializado Alexander Fleming	Cramer 1180	C1426ANZ	Capital Federal-Buenos Aires	ARGENTINA
6	Instituto Médico Platense	Boulevard 51 Nº 315	B1900AVG	La Plata	ARGENTINA

7	Peninsula Oncology Centre	Peninsula Oncology Centre Frankston Private 24-28 Frankston-Flinders Road	3199	Frankston	AUSTRALIA
8	Port Macquarie Base Hospital	Oncology Unit Port Macquarie Base Hospital Wrights Road	2444	Port Macquarie	AUSTRALIA
9	Royal Brisbane & Women's Hospital	Department Medical Oncology Level 5 West Block Butterfield Street Herston	4029	Brisbane	AUSTRALIA
10	Southeast Oncology	Suite 19 183 Wattletree Road Malvern	3144	Melbourne	AUSTRALIA
11	Southern Medical Day Care Centre	410 Crown Street	2500	Wollongong	AUSTRALIA
12	CHU de Liège	Hôpital du Sart Tilman Domaine Universitaire du Sart Tilman Bâtiment B35	4000	LIEGE	BELGIUM
13	CU Saint-Luc/UZ St-Luc	Service Pneumology/ Dienst Pneumologie Avenue Hippocrate 10 Hippocrateslaan	1200	BRUXELLES - BRUSSEL	BELGIUM

14	Grand Hôpital de Charleroi	Site Clinique Notre-Dame Grand'Rue 3	6000	CHARLEROI	BELGIUM
15	Biocor Hospital de Doenzas Cardiovasculares Ltda	Avenida Alameda da Serra, 217- Vila da Serra	34000000	Nova Lima	BRAZIL
16	Centro de Oncologia do Paraná	Rua Saldanha Marinho #2167	80730-180	Curitiba	BRAZIL
17	Centro Regional Integrado de Oncologia - CRIO	Rua Francisco Calaça, 1300	60336-550	Fortaleza	BRAZIL
18	Clínica Vila Rica	SHL/S 716, Centro Clínico Sul, Torre II, sala W423/431	70390907	Brasília	BRAZIL
19	Conjunto Hospitalar de Sorocaba	Oncology Rua Dos Andradas, 23	18030-510	Sorocaba	BRAZIL
20	Fundação Pio XII – Hospital de Câncer de Barretos	Rua Antenor Duarte Villela 1331 Bairro: Dr. Paulo Prata	14784400	Barretos	BRAZIL
21	Hosp. Araujo Jorge da Associação de Combate ao Câncer	Rua 239, 181, Bairro Universitário	74605-180	Goiânia	BRAZIL
22	Hospital Amaral Carvalho	Rua das Palmeiras 122 Villa Assis	17210-120	Jaú	BRAZIL
23	Hospital das Clínicas da Faculdade de Medicina da USP	Instituto de Radiologia INRAD Av. Dr. Enéas de Carvalho Aguiar #255 3º andar – sala 7.21	05403-000	São Paulo	BRAZIL

24	Hospital IGESP	Rua Silvia 276 Bella Vista	01331010	São Paulo	BRAZIL
25	Hospital Luxemburgo	Quimioterapia Rua Gentios 1350	30380490	Belo Horizonte	BRAZIL
26	Hospital Municipal Sao José	Rua Placido Gomes 488 3rd. Floor	89202-050	Joinville	BRAZIL
27	Hospital Nossa Senhora da Conceicao	Rua Francisco Trein, 596 Cristo Redentor - Sala 2046B - 2° Andar	91350-200	Porto Alegre	BRAZIL
28	Hospital Sao Lucas da Pontificia Universidade Catolica do RS	Serviço de Ginecología Av. Ipiranga 6690 Sala 220 - 2 andar	90619900	Porto Alegre	BRAZIL
29	Instituto do Cancer do Ceará	Rua Papi Junior #1222 - 4º andar Rodolfo Teófilo	60430-230	Fortaleza	BRAZIL
30	Irmandade da Santa Casa de Misericordia - Sao Paulo	Instituto do Câncer Arnaldo Vieira de Carvalho (ICAVC) Rua Largo do Arouche, 66		São Paulo	BRAZIL
31	Santa Casa de Misericórdia da Bahia Hospital Santa Izabel	Unidade de Oncologia Praça Conselheiro Almeida Couto 500 Bairro: Nazaré	40050410	Salvador	BRAZIL
32	Santo Andre Diagnostico e Terapeutica	Rua das Bandeiras #175 3.0 andar	09090-780	Santo Andre	BRAZIL
33	Allan Blair Cancer Centre	4101 Dewdney Avenue	S4T 7T1	Regina	CANADA

34	Office of Dr. Sandeep Sehdev, MD	157 Queen Street East Suite 102	L6W 3X4	Brampton	CANADA
35	Royal Victoria Hospital	Cancer Care Program Room 1193-A 201 Georgian Drive	L4M 6M2	Barrie	CANADA
36	Sir Mortimer B. Davis Jewish General Hospital	Division of Pulmonary Diseases G-203 3755 Ch. Cote Ste-Catherine	H3T 1E2	Montreal	CANADA
37	University of British Columbia	Lions Gate Hospital Chemotherapy Clinic 231 East 15th Street	V7L 2L7	North Vancouver	CANADA
38	Centro de Cancer Nuestra Señora de la Esperanza	Diagonal Paraguay 319		Santiago	CHILE
39	Hospital Clínico San Borja Arriarán	Unidad de Hemato-Oncología Santa Rosa 1234 CDT 2° piso	836-0156	Santiago	CHILE
40	Hospital DIPRECA	Comité Oncología 5to piso Vital Apoquindo 1200 Las Condes	760 0448	Santiago	CHILE
41	Instituto Nacional del Cancer	Av. Profesor Zañartu 1010 Independencia	838-0455	Santiago	CHILE
42	Centre Antoine Lacassagne - Nice	Centre Antoine LACASSAGNE 33 avenue de Valombrose	06102	NICE CEDEX 2	FRANCE

43	Centre d'Oncologie de Gentilly - Nancy	Centre d'Oncologie de Gentilly Service d'Oncologie Médicale 2, rue Marie Marvingt	54100	NANCY	FRANCE
44	Centre François Baclesse - CLCC - Caen	Centre François Baclesse Avenue du Général Harris B.P. 5026	14073	CAEN	FRANCE
45	Hopital Avicenne - Bobigny	Hopital Avicienne Service d'Oncologie Médicale 125 route de Stalingrad	93009	BOBIGNY CEDEX	FRANCE
46	Hopital Lyautey - Strasbourg	Hopital Lyautey 1 rue des Canonniers	67100	STRASBOURG	FRANCE
47	Asklepios Fachkliniken München Gauting	Zentrum für Pneumologie und Thoraxchirurgie Robert-Koch-Allee 2	82131	Gauting	GERMANY
48	Asklepios Klinik Harburg	Lungen und Bronchialheilkunde Eißendorfer Pferdeweg 52	21075	Hamburg	GERMANY
49	Charité Campus Benjamin Franklin	Medizinische Klinik III (WE 24) Hämatologie, Onkologie und Transfusionsmedizin Hindenburgdamm 30	12200	Berlin	GERMANY

50	Johannes-Gutenberg-Universität Mainz	III. Medizinische Klinik und Poliklinik Schwerpunkt Pneumologie Langenbeckstraße 1	55131	Mainz	GERMANY
51	Kliniken der Medizinischen Hochschule Hannover	Klinik für Pneumologie Carl-Neuberg-Str. 1	30625	Hannover	GERMANY
52	Kliniken Essen - Mitte	Evang. Huyssens-Stiftung Klinik für Innere Medizin IV / Internistische Onkologie / Hämatologie Zentrum für Palliativmedizin Henricistr. 92	45136	Essen	GERMANY
53	Klinikum Innenstadt der Ludwigs-Maximilians-Universität	Medizinische Klinik - Pneumologie Ziemssenstr. 1	80336	München	GERMANY
54	Klinikum Leverkusen gGmbH	Medizinische Klinik III Onkologie / Hämatologie Am Gesundheitspark 11	51375	Leverkusen	GERMANY
55	Klinikum Mannheim gGmbH	Chirurgische Klinik Interdisziplinäre Thoraxonkologie Theodor-Kutzer-Ufer 1-3	68167	Mannheim	GERMANY

56	Krankenhaus Großhansdorf	Zentrum für Pneumologie und Thoraxchirurgie Onkologischer Schwerpunkt Wöhrendamm 80	22927	Großhansdorf	GERMANY
57	Krankenhaus Hofheim am Taunus	Medizinische Klinik III Pneumologie Lindenstr. 10	65719	Hofheim	GERMANY
58	Lungenklinik Hemer	Zentrum für Pneumologie und Thoraxchirurgie Theo-Funccius-Str. 1	58675	Hemer	GERMANY
59	Thoraxklinik Heidelberg	Onkologie Amalienstr. 5	69126	Heidelberg	GERMANY
60	Universitätsklinikum Essen	Klinik und Poliklinik für Innere Medizin Tumorforschung Hufelandstr. 55	45122	Essen	GERMANY
61	Universitätsmedizin der Georg-August-Universität Göttingen	Zentrum Innere Medizin Abt. Hämatologie und Onkologie Robert-Koch-Str. 40	37075	Göttingen	GERMANY
62	Queen Elizabeth Hospital	Department of Oncology 30 Gascoigne Road		Hong Kong	HONG KONG

63	Csongrad Megyei Onkormanyzat Mellkasi Betegsegek Szakkorhaza	Alkotmany u. 36	6772	Deszk	HUNGARY
64	Matrai State Hospital	Szanatorium u. 4	3233	Matrahaza	HUNGARY
65	Orszagos Koranyi TBC es Pulmonologiai Intezet	Pulmonologiai Itezet Piheno u. 1	1529	Budapest	HUNGARY
66	Pest County Lung Institute	Tudogyogyintezet Munkacsy Mihaly u. 70	2045	Torokbalint	HUNGARY
67	A.O. di Perugia	Oncologia Medica Ufficio Operativo Ricerche Cliniche (Piano -1) Località S. Andrea delle Fratte	06156	Perugia	ITALY
68	A.O. Ospedali Riuniti Bergamo	Largo Barozzi, 1	24128	Bergamo	ITALY
69	A.O. Osp Niguarda Ca' Granda	Oncologia Medica Falck Piazza Ospedale Maggiore, 3	20162	Milano	ITALY
70	A.O. San Camillo-Forlanini	Oncologia Medica Circonvallazione Gianicolense, 87	00152	Roma	ITALY
71	A.O.U. di Parma	Via Gramsci, 14	43100	Parma	ITALY
72	A.O.U. San Giovanni Battista	Oncologia Medica Corso Bramante, 88	10126	Torino	ITALY

73	A.O.U. San Luigi Gonzaga	Oncologia Ospedale San Luigi Gonzaga Regione Gonzole, 10	10043	Orbassano	ITALY
74	IRCCS Ist Nazionale Tumori GE	Oncologia Medica Largo R. Benzi, 10	16132	Genova	ITALY
75	IRCCS Policlinico San Matteo	Urologia Ambulatorio Andrologia - Padiglione C2 Viale Golgi, 19	27100	Pavia	ITALY
76	Asan Medical Center	# 388-1, Pungnap-dong, Songpa-gu	138736	Seoul	KOREA, REPUBLIC OF
77	Samsung Medical Center	Devision of Hematology/Oncology, Department of Medicine, School of Medicine, Sungkyunkwan University , Samsung Medical Center, 50 Ilwon-dong, Kangnam-ku, Seoul 135-710, Korea	135710	Seoul	KOREA, REPUBLIC OF
78	Catharina	Afd. Longgeneeskunde en Tuberculose Michelangelolaan 2	5623 EJ	EINDHOVEN	NETHERLANDS
79	Isala Klinieken, lokatie Weezenlanden	Afd. Longziekten en tuberculose, Groot Wezenland 20	8011 JW	Zwolle	NETHERLANDS

80	Centrum Onkologii - Instytut im. M.Sklodowskiej-Curie	Klinika Nowotworów Pluca i Klatki Piersiowej ul. Roentgena 5	02-781	Warszawa	POLAND
81	Centrum Onkologii Instytut im. M. Sklodowskiej-Curie	Klinika Leczenia Systemowego ul. Garncarska 11	31-115	Krakow	POLAND
82	Dolnoslaskie Centrum Chorób Pluc	ul. Grabiszynska 105	53-439	Wroclaw	POLAND
83	Uniwersyteckie Centrum Kliniczne	Klinika Onkologii i Radioterapii ul. Debinki 7	80-952	Gdansk	POLAND
84	Wojskowy Instytut Medyczny	Klinika Onkologii CSK MON ul. Szaserow 128	04-141	Warszawa	POLAND
85	ZOZ MSWiA z Warminsko-Mazurskim Centrum Onkologii	Oddzial Chemioterapii ul. Wojska Polskiego 37	10-228	Olsztyn	POLAND
86	City Clinical Oncology Center	Department of Thoracic surgery Veteranov prospect 56	198255	St. Petersburg	RUSSIA
87	Russian Oncological Scientific Center n.a. N.N. Blokhin RAMS	Department of Combined Methods of treatment and Chemotherapy 18th floor 24, Kashirskoye shosse	115478	Moscow	RUSSIA

88	Russian Oncological Scientific Center n.a. N.N. Blokhin RAMS	Department of Chemotherapy 19th floor 24, Kashirskoe shosse	115478	Moscow	RUSSIA
89	Complejo Hospitalario de Zamora	Servicio de Oncología C/ Hernán Cortés,40	49021	Zamora	SPAIN
90	Hospital Clínic i Provincial de Barcelona	Servicio de Oncología Médica C/ Villarroel, 170	08036	Barcelona	SPAIN
91	Hospital General de Elche	Servicio de Oncología Camino de la Almazara, 11	03202	Elche	SPAIN
92	Hospital Ruber Internacional	Unidad de Oncología Médica C/ La Masó, 38, Mirassierra	28034	Madrid	SPAIN
93	Hospital Universitario Clinica Puerta de Hierro	Servicio de Oncología Médica C/ Manuel de Falla, 1 Consultas Externas	28222	Majadahonda	SPAIN
94	Akademiska Sjukhuset	Lung- och Allergikliniken	751 85	Uppsala	SWEDEN
95	Karolinska Universitetssjukhuset i Solna	Radiumhemmet Kliniken för onkologi	171 76	Stockholm	SWEDEN
96	Länssjukhuset Gävle-Sandviken	Kliniken för medicinsk onkologi	801 87	Gävle	SWEDEN
97	Chang-Guang Memorial Hospital	5 Fu-Hsin Rd, Kueishan, Taoyuan 333, Taiwan	333	Taoyuan	TAIWAN

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98	National Taiwan University Hospital	Research Ethics Committee B4, AB Building No.7.Chung Shan South Road	110	Taipei	TAIWAN
99	Taichung Veterans General Hospital	160,Sec 3,Tai-Chung-Kang Rd	40705	Taichung	TAIWAN
100	Derriford Hospital	Clinical Trials Unit Plymouth Oncology Centre Derriford Road Crownhill	PL6 8DH	Plymouth	UNITED KINGDOM
101	Leicester Royal Infirmary	Department of Oncology 2nd Floor Osborne Building Infirmary Square	LE1 5WW	Leicester	UNITED KINGDOM
102	Royal Bournemouth General Hospital	Department of Clinical Oncology Castle Lane East	BH7 7DW	Bornemouth	UNITED KINGDOM
103	Wythenshawe Hospital	North West Lung Centre Clinic Southmoor Road Wythenshawe	M23 9LT	Manchester	UNITED KINGDOM
104	Arkansas Oncology Associates	9600 Lile Drive Suite 200	72205	Little Rock	UNITED STATES
105	Arlington Cancer Center	2800 Highway 114 Suite 200	76262	Trophy Club	UNITED STATES
106	Berkshire Hematology/Oncology, PC	8 Conte Drive	01201	Pittsfield	UNITED STATES

107	Cancer Care Associates	6475 South Yale Avenue Suite 201	74136	Tulsa	UNITED STATES
108	Cancer Centers of the Carolinas	Research Office 65 International Drive	29615	Greenville	UNITED STATES
109	Cancer Outreach Associates	104 Abingdon Place	24211	Abingdon	UNITED STATES
110	Candler Hospital/St. Joseph's Candler Health System	Office of Research 5353 Reynolds Street	31405	Savannah	UNITED STATES
111	Capital Comprehensive Cancer Care Clinic	1241 West Stadium Boulevard	65109	Jefferson City	UNITED STATES
112	Charleston Hematology & Oncology Associates, PA	125 Doughty Street Suite 280	29403	Charleston	UNITED STATES
113	Clintell, Inc.	8707 Skokie Boulevard Suite 206	60077	Skokie	UNITED STATES
114	Compassionate Cancer Care Medical Group, Inc.	260 E. Ontario Avenue Suite 101	92829	Corona	UNITED STATES
115	East Valley Hematology/Oncology Medical Group	2601 West Alameda Avenue Suite 218	91595	Burbank	UNITED STATES
116	EPIC Management, LP	Beaver Medical Group 7000 Boulder Avenue	92346	Highland	UNITED STATES
117	Fairfax-Northern Virginia Hematology/Oncology, PC	8503 Arlington Boulevard Suite 400	22031	Fairfax	UNITED STATES

118	Fort Wayne Medical Hematology & Oncology	4402 East Street Boulevard	46815	Fort Wayne	UNITED STATES
119	Guthrie Clinic	One Guthrie Square	18840	Sayre	UNITED STATES
120	Hackensack University Medical Center	NJ Cancer Center Suite 400 20 Prospect Avenue	07601	Hackensack	UNITED STATES
121	Hattiesburg Clinic	Department of Oncology 301 South 28th Avenue	39401	Hattiesburg	UNITED STATES
122	Hematology/Oncology Clinic	7777 Hennessy Boulevard Suite 501	70808	Baton Rouge	UNITED STATES
123	Hematology Oncology Consultants, Inc.	8100 Ravines Edge Ct. Suite 100	43235	Columbus	UNITED STATES
124	Hematology & Oncology Consultants, PA	2501 North Orange Avenue Suite 381	32804	Orlando	UNITED STATES
125	Hematology & Oncology of Dayton, Inc.	9000 North Main Street Suite G-36	45429	Dayton	UNITED STATES
126	Henry Ford Health System	Henry Ford Hospital 2799 West Grand Boulevard	48202	Detroit	UNITED STATES
127	Highlands Oncology Group	601 Maple Drive Suite 512	72764	Springdale	UNITED STATES
128	Indiana University	Cancer Center Pavilion 535 Barnhill Road Suite 473	46202	Indianapolis	UNITED STATES
129	Investigative Clinical Research of Indiana, LLC	6920 Parkdale Place Suite 203	46254	Indianapolis	UNITED STATES

130	Jayne Gurtler APMC	3939 Houma Boulevard Suite 6	70006	Metairie	UNITED STATES
131	Kansas City Cancer Centers, LLC	1000 East 101st Terrace	64131	Kansas City	UNITED STATES
132	Kentuckiana Cancer Institute, PLLC	4500 Churchman Avenue Suite 300	40215	Louisville	UNITED STATES
133	MD Anderson Cancer Center-Orlando	1400 South Orange Avenue MP-780	32806	Orlando	UNITED STATES
134	Metropolitan Hematology Oncology Medical Group	201 South Alvarado Suite A	90057	Los Angeles	UNITED STATES
135	Northwest Georgia Oncology Centers, PC	340 Kennestone Hospital Blvd. Suite 200	30060	Marietta	UNITED STATES
136	Office of Dr. William Tester, MD	Einstein Center One 9880 Bustleton Avenue Suite 208	19115	Philadelphia	UNITED STATES
137	Oklahoma University Health Science Center	Room WP-2080 920 Stanton L. Young Blvd.	73104	Oklahoma City	UNITED STATES
138	Oncology-Hematology of Lehigh Valley, PC	701 Ostrum Street Suite 403	18015	Bethlehem	UNITED STATES
139	Peachtree Hematology & Oncology Consultants, PC	95 Collier Road NW Suite 4015	30309	Atlanta	UNITED STATES
140	Rocky Mountain Cancer Centers	1800 Williams Street Suite 200	80218	Denver	UNITED STATES

141	Sacred Heart Medical Oncology Group	6701 Airport Boulevard Bldg-B/ Terrace Level	36608	Mobile	UNITED STATES
142	Simon-Williamson Clinic, PC	833 Princeton Avenue SW	35211	Birmingham	UNITED STATES
143	Siouxland Hematology/Oncology Associates, LLC	230 Nebraska Street	51101	Sioux City	UNITED STATES
144	Space Coast Medical Associates	225 Cone Road	32952	Merritt Island	UNITED STATES
145	St. John's Mercy Medical Center	607 South New Ballas Road	63141	St. Louis	UNITED STATES
146	St. Joseph Mercy Hospital	Clinical Research Department 5301 East Huron River Drive	48106	Ann Arbor	UNITED STATES
147	Tenessee Cancer Specialists	101 Blount Avenue Suite 610	37920	Knoxville	UNITED STATES
148	Tower Hematology/Oncology Medical Group	Tower Cancer Research Foundation 9090 Wilshire Boulevard Suite 200	90211-1850	Beverly Hills	UNITED STATES
149	University of Chicago	University of Chicago Med. Ctr. MC-2115 5841 South Maryland Avenue	60637	Chicago	UNITED STATES
150	University of Utah Medical Center	Huntsman Cancer Institute 2000 Circle of Hope Suite 2160	84112	Salt Lake City	UNITED STATES
151	Virginia Cancer Institute	6605 West Broad Street Suite B	23230	Richmond	UNITED STATES

152	Virginia Commonwealth University	401 College Street PO Box 980037	23298-0037	Richmond	UNITED STATES
153	Virginia Oncology Care, PC	2951 West Front Street Suite 1200	24641	Richlands	UNITED STATES
154	Watson Clinic Center for Research	1730 Lakeland Hills Boulevard	33805	Lakeland	UNITED STATES

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