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 Pharmaceuticals Inc.	
Study Number:	13162	NCT00865709 EudraCT 2008-005025-11
Study Phase:	IIb	
Official Study Title:	A phase 2b, double blind, randomized study evaluating the efficacy and safety of sorafenib compared with placebo when administered in combination with chemotherapy (modified FOLFOX6) for the treatment of metastatic colorectal cancer in subjects who have not been previously treated for stage IV disease	
Therapeutic Area:	Oncology	
Test Product		
Name of Test Product:	Sorafenib (Nexavar, BAY43-9006)	
Name of Active Ingredient:	Sorafenib tosylate	
Dose and Mode of Administration:	Two 200 mg tablets were given twice daily (approximately every 12 hours), orally. The background anticancer treatment was mFOLFOX6 (5-FU, LLV, and oxaliplatin) every 14 days at the following doses: • Oxaliplatin 85 mg/m^2 on Day 1 • Levo-leucovorin 200 mg/m^2 on Day 1. If LLV was not available, then an equivalent dose of leucovorin (LV) (400 mg/m^2) was administered in place of LLV. • 5-Fluorouracil 400 mg/m^2 bolus on Day 1 immediately following LLV infusion • 5-Fluorouracil 2400 mg/m^2 continuous infusion for approximately 46 to 48 hours	
Reference Therapy/Placebo		
Reference Therapy:	Matching placebo	
Dose and Mode of Administration:	Two 200 mg tablets were given twice daily (approximately every 12 hours), orally. The back ground treatments were given following same dose/frequency as test drug.	
Duration of Treatment:	Subjects continued treatment on a daily basis until disease progression or unacceptable toxicity occurred.	
Studied period:	**Date of first subjects' first visit:**	11 MAR 2009
	Date of last subjects' last visit:	15 FEB 2012
Premature Study Suspension / Termination:	No	
Substantial Study Protocol Amendments:	Amendment no. 1 (dated 29 MAY 2009) was implemented to make three substantial changes: • Clarify inclusion and exclusion criteria for study subject eligibility requirements. • Clarify dosing regimens (route and time of administration) for the	

	modified FOLFOX6 (mFOLFOX6) components (5-fluorouracil [5-FU], levo-leucovorin [LLV], oxaliplatin). • Change the sample size of the study from 300 to 220 subjects, including the required number of subjects experiencing disease progression, for determination of the primary endpoint (progression-free survival [PFS]) and the required number of deaths for determination of overall survival (OS) in the study. Amendment no. 2 (dated 25 JAN 2010) was implemented to make the following substantial changes: • Change the sample size of the study from 220 to 180 subjects, including the required number of subjects experiencing disease progression for determination of the primary endpoint (PFS), the required number of deaths for determination of OS in the study, and study duration. • Clarify that the original intent of the exclusion criterion for placement of central venous access port was to reduce the risk of thrombosis and hemorrhage immediately following injury to a major vein that might occur as a result of exposure to sorafenib. There was no intent to restrict the use of chemotherapy immediately following insertion of a central venous access port. • Clarify that for subjects with Grade 3 or 4 allergic reactions to sorafenib or placebo, only sorafenib or placebo, and not all study treatment, were to be discontinued. • Clarify that for the list of assessments that were to be conducted on the day of mFOLFOX6 infusion before study drug administration, mFOLFOX6 infusion was to be provided only when treatments were not discontinued. Amendment No. 3 (dated 08 SEP 2010) was implemented after the end of study enrollment to change the required number of subjects experiencing disease progression for determination of the primary endpoint (PFS) from 100 to 120 subjects. The upper bound of number of deaths to be observed for determination of OS in the study was changed from 100 to 120 subjects, and the study duration was also increased so that the observed difference between the treated and placebo arms in this study would be a more precise estimate of the true difference.
Study Centre(s):	This study was planned in 116 centers in 10 countries worldwide, and 43 study centers randomized patients in 6 countries (UK [8 sites], US [1 site], Belgium [1 site], Spain [9 sites], Russia [20 sites], and Romania [4 sites]).
Methodology:	The goal of this study was to evaluate the antitumor activity and safety and tolerability of sorafenib versus palcebo when used in combination with mFOLFOX6 in subjects with metastatic colorectal cancer (CRC). This study consisted of a Screening Period, a Treatment Period, an Active Follow-up Period, and a Long-term Follow-up (LTFU) Period. The study was to end at the time of the 120th death or approximately 41 months after randomization of the first subject, whichever occurred first. Once subjects met all eligibility criteria, they were randomly assigned to receive mFOLFOX6 + sorafenib or mFOLFOX6 + placebo in a 1:1 ratio within 3 days before the Cycle 1, Day 1 infusion. During randomization, subjects were stratified based on liver involvement

	(yes or no) and the number of metastatic sites (<3 or ≥3) as assessed on radiological findings. Subjects received the assigned treatment until disease progression. Sorafenib or matching placebo was given twice daily. Tumor response and progressive disease (PD) were evaluated based on Response Evaluation Criteria in Solid Tumors (RECIST) criteria. Symptom deterioration was considered disease progression in this study. Throughout the Treatment Period, the same lesions as those identified and measured at Baseline were evaluated using the same technique. Tumor assessment was done ≤28 days before randomization, every 8 weeks (± 7 days) during each treatment cycle (until PD was documented), and at the end of the study treatment visit. The primary efficacy variable, PFS, was measured from the date of randomization to the date of first documented disease progression (i.e., the date on which a radiological procedure or clinical evaluation was performed) or the date of death due to any cause, if the death was before disease progression. Safety parameters, including adverse events (AEs), laboratory parameters, and vital signs, were also evaluated. Tolerability, quality of life (QOL) and tissue biomarkers were also assessed in this study. Tumor tissue sample for Kirsten rat sarcoma viral oncogene homolog/v-raf murine sarcoma viral oncogene homolog B1 (KRAS/BRAF) assessment was done ≤28 days before randomization. Quality of life assessment was done ≤7 days before randomization, every 8 weeks during each treatment cycle, and at end of the study treatment visit. If a subject was discontinued from study treatment but had not experienced PD, the subject entered Active Follow-up, in which clinic visits and disease assessments continued every 8 weeks (± 7 days) until PD or until completion of the study was documented. Evaluations during this time included tumor assessment and reporting of any additional anticancer therapy administered. If a subject experienced PD, the subject was contacted every three months to ascertain survival status and need for additional anticancer therapies.
Indication/ Main Inclusion Criteria:	Indication: Metastatic colorectal cancer Inclusion criteria: • Age ≥ 18 years • Histological confirmation of adenocarcinoma of the colon or rectum • Tumor tissue sample available for KRAS and BRAF assessments • Measurable metastatic Stage IV disease documented within 28 days before randomization • No prior chemotherapy for metastatic CRC • At least one measurable metastatic lesion that had not been

	irradiated. The lesion was measured according to RECIST (version 1.0) and was documented by radiological evaluation within 28 days before randomization • Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 • Life expectancy of at least 12 weeks • Prior radiation therapy was allowed but was required to be completed at least 28 days before randomization (if applicable) • Adequate bone marrow, liver, and renal function Women of childbearing potential were required to have a negative serum pregnancy test performed within seven days before randomization. • Subject were required to have the ability, in the opinion of the investigator, to comply with all study procedures and follow-up examinations. • Subjects (and/or legal guardian[s]) were required to understand and be able and willing to sign an ICF that was required to be appropriately obtained before undertaking any study specific procedures.
Study Objectives:	**Primary:** The primary objective was to compare PFS in subjects who received sorafenib in combination with mFOLFOX6 versus subjects who received placebo in combination with mFOLFOX6. **Secondary:** The secondary objectives were to compare the treatment groups in terms of: • Overall survival (OS) • Time to progression (TTP) • Tumor response (TR) • Duration of overall response (DOR) • Safety and tolerability **Tertiary:** The tertiary objectives of this study were: • To compare the treatment groups in terms of change from Baseline in QOL assessments based upon the EuroQol 5-dimensional (EQoL-5D) validated instrument • To evaluate possible and potentially predictive assays of clinical benefit through an assessment of the correlation between relevant biomarkers (KRAS, BRAF) and clinical endpoints
Evaluation Criteria:	**Efficacy (Primary):** Tumor response and PD were evaluated based on RECIST tumor response criteria (version 1.0). Symptom deterioration was considered as disease progression. Progression-free survival was defined as the time from the date of randomization to disease progession or the date of death due to any cause, whichever occurred first. It was assessed from randomization of the first subject until 23 months later. For subjects without documented progression or death at the time of analysis, PFS was censored at the last date of tumor assessment. If a subject had no tumor assessments after Baseline, then the subject was censored at

	Day 1. **Efficacy (Secondary):** Tumor response and PD were evaluated based on RECIST tumor response criteria (version 1.0) for the secondary efficacy variables. Symptom deterioration was considered as disease progression. • Overall survival was defined as the time from the date of randomization to death due to any cause. Overall survival was assessed from randomization of the first subject until 33 months later. Subjects still alive at the time of analysis were censored at their last date of tumor evaluation. • Time to progression was defined as the time from the date of randomization to disease progression. Time to progression was assessed from randomization of the first subject until 23 months later. • Tumor response: The tumor response for each treatment group was calculated as the proportion of subjects achieving complete response (CR) or partial response (PR) as the best overall response. Tumor response was assessed from randomization of the first subject until 23 months later. • Duration of response: The duration of response was defined as the time from the date of the first documentation of PR or CR to the first date of PD or death due to any cause. Duration of response was assessed from randomization of the first subject until 23 months later. **Safety:** Results of physical examinations, vital signs assessments, electrocardiogram (ECG) data, weight, AEs, laboratory values, and concomitant medication used were evaluated. Reasons for dose delays, modifications, or omissions were documented.
	Other: • The EQoL-5D instrument was used to assess quality of life (QOL) and correlation of QOL with clinical endpoints. • Genotype analysis of the status of tumor KRAS and BRAF (wild-type or mutant) were determined using archived tumor samples.
Statistical Methods:	**Population:** All subjects who were randomized to study treatment, regardless of the treatment received, were included in the intent-to-treat (ITT) population. All primary analyses of the efficacy data were conducted using the ITT population. All subjects in the ITT population who had no major protocol deviations were included in the per-protocol population (PPP). All subjects who were randomized and who received any study treatment were included in the safety population. **Efficacy (Primary):** The primary analysis for PFS was a log-rank test with the randomization stratification factors provided by the interactive voice response system by the principal investigator (IVRS PI): liver involvement (yes versus no) and number of metastatic disease sites (<3, ≥3), as strata to detect differences between the treatment

	groups in the ITT population. For these analyses, one-sided p-value from the stratified log-rank test was presented. The relative risk (sorafenib to placebo) was estimated by the hazard ratio from stratified Cox regression with a 95% confidence interval (CI). Kaplan-Meier estimates for quartiles of PFS and Kaplan-Meier curves were presented for each treatment group. The PFS rate at several time points was estimated for each treatment group using the Kaplan-Meier method. The difference of PFS rate between two treatment arms was calculated with the 95% CI based on normal approximation. One-sided p-value for the difference was calculated based on normal approximation. **Efficacy (Secondary):** Analyses of all secondary efficacy variables were based on the ITT population. Only responders (CR or PR) were included in the analysis of duration of response. For time-to-event variables (TTP and OS), one-sided p-value from stratified log-rank test was presented. The relative risk (sorafenib to placebo) was estimated by the hazard ratio (HR) from the stratified Cox regression with the randomization stratification factors provided by IVRS (PI): liver involvement and number of metastatic sites as stratum. Kaplan-Meier estimates for the quartiles and Kaplan-Meier curves were also presented for each treatment group. The best overall response (OR) was summarized for each treatment group. The tumor response was estimated with a 95% CI for each treatment group. The treatment groups were compared with respect to tumor response using the Cochran-Mantel-Haenszel test, adjusting for the stratification factors. **Safety:** Analysis of all safety variables was based on safety population. Extent of exposure, laboratory parameters, vital signs, and ECG data were summarized using descriptive stastics. In addition to summaries of AEs classified according to MedDRA (v 13.1) preferred term and SOC, safety analyses included evaluation of clinically significant laboratory test results and vital signs. The toxicity grades of selected laboratory values were determined using the CTCAE v3.0.
	Other: Changes from Baseline in the EQoL-5D instrument assessments and correlation between relevant biomarkers (KRAS and BRAF) and clinical endpoints were also included in the analyses.
Number of Subjects:	Number of subjects enrolled in the study: 230 Number of subjects randomized: 198 (101 subjects assigned to placebo arm and 97 subjects to sorafenib arm)
Study Results	
This report, including the final analysis of PFS, was based on the database cut-off of when approximately 120 PFS events occurred, in accordance with the power calculations specified in the protocol.	
Results Summary — Subject Disposition and Baseline	

Of the 198 subjects randomized in this study, 101 were randomly assigned to placebo and 97 to sorafenib. Of the 97 subjects randomized to the sorafenib arm, 67 subjects continued treatment at data cut-off or discontinued treatment due to PD or death. Of the 101 subjects in the placebo arm, 83 subjects continued treatment at data cut-off or discontinued treatment due to PD or death. As of the cut-off date for PFS, 170 subjects had discontinued Active Treatment. Forty-one subjects (25 subjects in the sorafenib arm and 16 subjects in the placebo arm) who discontinued Active Treatment but who had not experienced PD entered Active Follow-up. A total of 32 subjects (sorafenib arm: 17 subjects, placebo arm: 15 subjects) completed the Active Follow-up. The most common reason for discontinuation of Active Treatment was PD (65 subjects in the placebo arm and 49 subjects in the sorafenib arm). Other than PD, the reasons for discontinuation of Active Treatment included withdrawal by subject (17 subjects), AEs (15 subjects), surgery (11 subjects), death (8 subjects), and investigator decision (5 subjects).

Once subjects experienced PD, they entered the LTFU period: 82 subjects from the placebo arm and 70 subjects from the sorafenib arm entered the LTFU period. In the sorafenib arm, 24 subjects, and in the placebo arm, 33 subjects completed LTFU.

Subjects in this study were predominantly white (99.0%); mean age at enrollment was 59.8 ± 9.3 years (sorafenib arm: 59.2 ± 10.3 years, placebo arm: 60.3 ±8.3 years). Male subjects outnumbered female subjects (53% [42 males in sorafenib arm and 63 males in placebo arm] versus 47% [55 females in sorafenib arm and 38 females in placebo arm], respectively).

The number of subjects with ECOG score 0 was 34 in the sorafenib arm and 36 in the placebo arm; and with ECOG score 1 was 63 in the sorafenib arm and 65 in the placebo arm. The mean time from initial diagnosis of metastatic CRC to randomization into the study was 9.5 ± 16.6 months for the study population (9.8 ± 16.2 months in the sorafenib arm and 9.2 ± 16.9 months in the placebo arm). The mean time since most recent disease progression or relapse was 1.8 months in the placebo arm and 2.4 months in the sorafenib arm. A majority of the subjects' most recent disease relapse (93.1% of placebo and 92.8% of sorafenib) had been less than 12 months prior to randomization to the study drug. The most common site of metastasis was the liver, which comprised about 82% of the metastatic sites overall. The number of subjects with liver metastases was 79 in the sorafenib arm and 81 in the placebo arm. The number of subjects without liver metastases was 18 in the sorafenib arm and 20 in the placebo arm. The number of subjects with <3 metastatic sites was 71 in both the sorafenib and placebo arms. The number of subjects with ≥3 metastatic sites was 26 in the sorafenib arm and 30 in the placebo arm. The number of subjects with mutant KRAS type was 33 in the sorafenib arm and 43 in the placebo arm, and the number of subjects with wild-type KRAS was 42 in the sorafenib arm and 41 in the placebo arm. Information about type of KRAS was missing in 22 subjects in the sorafenib arm and in 17 subjects in the placebo arm.

The mean weight of the placebo arm (73.5 kg) was higher than the sorafenib arm (68.5 kg).

The concomitant medications used by 100% of subjects were serotonin (5ht3) antagonists and glucocorticoids. Medications that were used by > 20% of subjects were propulsives, antipropulsives, anilides, and heparins. Laxatives, nutritional supplements, proton pump inhibitors, proponic acid inhibitors, electrolyte solutions, and colony stimulating factors were used by > 10% of subjects.

Results Summary — Efficacy

Progression-free survival: The primary study endpoint was PFS. A total of 149 subjects had PD or died as of the PFS data cut-off date, including 82 subjects (81.2%) in the placebo arm

and 67 subjects (69.1%) in the sorafenib arm (p = 0.2309, one-sided). The median PFS was 265 days (8.7 months) (95% CI: 224 days [7.4 months] to 290 days [9.5 months]) for the placebo arm and 276 days (9.1 months) (95% CI: 230 days [7.6 months] to 294 days [9.7 months]) for the sorafenib arm. The estimated HR risk of progression/death with sorafenib versus placebo) was 0.884 (95% CI: 0.635 to 1.231), representing an 11.6% reduction in hazard with sorafenib versus placebo.

A subgroup analysis of PFS indicated that gender and baseline ECOG status may have had some effect on PFS outcomes. KRAS status did not have an apparent effect on PFS when subjects were treated with sorafenib. For the 76 subjects with wild-type KRAS, the HR for sorafenib to placebo was 0.895 (95% CI: 0.529 to 1.512). For the 83 subjects with mutant KRAS, the HR was 0.786 (95% CI 0.474 to 1.303).

Overall survival: The secondary endpoint of OS was analyzed based on the data cut-off 01 DEC 2011, after the 120 deaths required to reach the endpoint had occurred. Overall, 123 deaths occurred. The HR of sorafenib treatment to placebo for OS was 1.127 (95% CI: 0.787 to 1.614), which indicates a 12.7% increase in hazard for the sorafenib subjects. This increase was not statistically significant (p = 0.2565). The median OS was 552 days (95% CI: 453 days to 651 days) for the placebo arm and 535 days (95% CI: 437 days to 613 days).

Time to progression: A total of 136 events of disease progression had occurred, which included 77 subjects in the placebo arm (76.2%) and 59 subjects in the sorafenib arm (60.8%). The comparison of two treatment arms for TTP was not statistically significant (p = 0.1437, one-sided). The median TTP was 273 days (9.0 months) (95% CI: 230 days [7.6 months] to 317 days [10.4 months]) for the placebo arm and 281 days (9.2 months) (95% CI: 236 days [7.8 months] to 335 days [11.0 months]) for the sorafenib arm. The estimated HR (risk of progression with sorafenib versus placebo) was 0.829 (95% CI: 0.586, to 1.174), representing a 17.1% reduction in hazard with sorafenib versus placebo.

Tumor response: The best overall response of CR or PR was achieved in 106 subjects, including 61 placebo subjects (60.4%) and 45 sorafenib subjects (46.4%). Statistically, significantly fewer subjects had a tumor response in the sorafenib arm than the placebo arm (p = 0.0230, one-sided).

Duration of response: The median DOR was 205 days (6.7 months) (95% CI: 168 days [5.5 months] to 246 days [8.1 months]) for the placebo arm and 229 days (7.5 months) (95% CI: 173 days [5.7 months] to 287 days [9.4 months]) for the sorafenib arm.

Results Summary — Safety

No unexpected differences in safety profile between the two treatments were observed in the study. The total subject exposure to placebo was greater than to sorafenib. The mean daily dose of placebo arm was equivalent to 728.1 mg compared to 553.1 mg in the sorafenib arm. The median duration of treatment was shorter in the sorafenib arm than in the placebo arm; the median duration of placebo was 33 weeks (range 1.6 to 62). The median duration of sorafenib was 32 weeks (range 1.3 to 77). More subjects in the sorafenib arm had dose reductions and interruptions than the placebo arm, which corresponded to the lower daily dose for sorafenib subjects. Similar trends were observed for the components of mFOLFOX6, although the magnitude of the difference between treatment arms was less pronounced. Overall, 9.4% of the subjects discontinued study treatment due to AEs in the sorafenib arm compared with 5.9% in the placebo arm.

A total of 99 subjects in the placebo arm (98.0%) and 96 subjects in the sorafenib arm (99.0%) reported ≥one treatment-emergent AEs. The most common AEs in the placebo arm

were nausea (48.5%), diarrhea (38.6%), neutropenia (38.6%), peripheral sensory neuropathy (24.8%), and thrombocytopenia (24.8%). The most common AEs in the sorafenib arm were neutropenia (61.9%), palmar-plantar erythrodysaesthesia syndrome ([PPES] also known as hand-foot skin reaction, 53.6%), diarrhea (50.5%), and nausea (37.1%).

One or more drug-related AEs were reported for 96 subjects in the placebo arm (95.0%) and 95 subjects in the sorafenib arm (97.9%). The most common drug-related AEs in the placebo arm were nausea (46.5%), neutropenia (37.6%), diarrhea (34.7%), peripheral sensory neuropathy (24.8%), and thrombocytopenia (23.8%). The most common drug-related AEs in the sorafenib arm were neutropenia (61.9%), PPES (53.6%), diarrhea (47.5%), and nausea (36.1%).

Grade 3 and higher AEs were more common in the sorafenib arm (87.6% of the subjects) than the placebo arm (73.3% of the subjects). Neutropenia represented the highest proportion of Grade 3 and higher events for both arms (21.8% of the placebo subjects, 48.5% of the sorafenib subjects). The rate of Grade 3 and higher neutropenia when subjects were treated with sorafenib + mFOLFOX6 (48.5%) was more than twice that of the mFOLFOX6 alone (21.8%). For the placebo arm, the second most commonly observed Grade 3 AE was peripheral sensory neuropathy (11.9% of the placebo subjects) and in the sorafenib arm, the second most commonly observed Grade 3 AE was PPES (19.6% of the sorafenib subjects).

Eighteen AEs led to discontinuation of treatment in 15 subjects (6 placebo, 9 sorafenib). No single AE term led to more than one discontinuation.

As of cut-off for PFS, 61 subjects died and a similar proportion of subjects had died in the placebo arm (31.7%) as in the sorafenib arm (29.9%). The most common cause of death was disease progression in nine subjects. Within 30 days post treatment, nine subjects died in the sorafenib arm (9.3%) and 7 in the placebo arm (6.9%). Beyond 30 days post-treatment, 54 subjects (53.5%) died in the placebo arm and 54 subjects (55.7%) died in the sorafenib arm.

Treatment-emergent serious adverse events (SAEs) occurred in 56 subjects: 27 placebo (26.7%) and 30 sorafenib subjects (30.9%). Drug-related SAEs were reported for 16 subjects in the placebo arm (15.8%) and 21 subjects in the sorafenib arm (21.6%). The SAEs that occurred in three subjects were device-related infection (two placebo subjects, one sorafenib subject), diarrhea (one placebo subject, two sorafenib subjects), intestinal obstruction (three placebo subjects), and pulmonary embolism (two placebo subjects, one sorafenib subject).

Most of the laboratory values were similar between the treatment arms. However, subjects in the sorafenib arm had higher frequencies of Grade ≥ 3 and higher levels in the following laboratory tests:

- Neutrophils: Grade 3 low neutrophil count was reported in 7.4% of the subjects in the sorafenib arm, compared to 2.0% of the subjects in the placebo arm.
- Phosphorus: Grade 3 and Grade 4 low phosphate levels were reported in 26% and 1.1% of the subjects in the sorafenib arm; compared to 6.0% and 0% of the subjects in the placebo arm. Hypophosphatemia was a common adverse drug reaction of sorafenib.
- Potassium: Grade 3 and Grade 4 low potassium was reported in 12% and 5.3% of the subjects in the sorafenib arm; compared with 7% and 0% of the subjects in the placebo arm.

The dose modifications were evenly distributed between the placebo and sorafenib arms. The most common reasons for dose reductions or delays were AEs followed by logistical

difficulties.

Analysis of vital sign data and electrocardiograms were not performed at the PFS cut-off date.

Results Summary — Other

All other results pertaining to this study (EQoL-5D, KRAS and BRAF, and biomarker analyses) will be reported in in an addendum or addenda to this report..

Conclusion(s)

In this study, it was concluded that the addition of sorafenib to first-line chemotherapy of mFOLFOX6 in the study population of metastatic CRC subjects did not result in a significant PFS or OS benefit compared with mFOLFOX6 alone. The data reported here indicate that KRAS status does not have an apparent effect on PFS when subjects were treated with sorafenib in this population. There were no unexpected toxicities associated with the addition of sorafenib, but there were increases in the rates of some Grade 3/4 AEs, most notably neutropenia and PPES. The increased incidence of AEs was associated with increased rates of dose modifications. Overall, the exposure to each of the mFOLFOX6 components was less in the sorafenib arm than in the placebo arm.

Publication(s):	Tabernero J, Garcia-Carbonero R, Cassidy J, Sobrero A, Van Cutsem E, Köhne CH et al. sorafenib in combination with oxaliplatin, leucovorin, and fluorouracil (modified FOLFOX6) as first-line treatment of metastatic colorectal cancer: The RESPECT Trial. Clin Cancer Res. 2013 May 1;19(9):2541-2550.		
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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

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