Supplemental Table 1A. Subgroup analysis of overall survival

			Sorafenib	Placebo	HR	95% CI
	Patients	Events	Median OS (months)	Median OS (months)		
ITT Population	703	579	8.2	8.3	0.99	0.85-1.17
Region						
North America, Northern/Western Europe	241	211	6.6	8.0	1.19	0.91-1.56
South America, Eastern Europe, Asia-Pacific	462	368	9.4	8.6	0.89	0.72-1.09
Number of prior treatments						
2	386	317	8.3	7.8	0.84	0.67-1.05
3	317	262	8.0	9.9	1.16	0.91-1.48
Brain metastases						
No	592	482	8.3	9.0	0.99	0.83-1.19
Yes	110	97	7.3	5.7	0.85	0.57-1.27
Prior EGFR inhibitor treatment						
No	287	225	7.9	8.3	0.96	0.74-1.25
Yes	416	354	8.4	8.4	0.97	0.79-1.20
Age group						
<65 years	461	375	8.3	8.3	0.96	0.78-1.18
65 to 74 years	193	163	7.5	7.7	1.04	0.76-1.41
≥75 years	49	41	12.8	10.4	0.77	0.40-1.46
Sex						
Male	395	335	7.6	7.7	0.99	0.80-1.22
Female	308	244	9.4	9.4	0.97	0.75-1.25
ECOG PS						
0	214	157	13.5	11.7	0.93	0.68-1.28
1	483	417	7.3	7.7	0.98	0.81-1.19
Duration of prior EGFR treatment						
<12 weeks	453	376	7.7	7.8	0.98	0.80-1.20
≥12 weeks	245	199	10.7	10.2	0.93	0.71-1.23
Prior EGFR treatment with PR or CR as best overall						
Yes	115	101	9.5	10.0	0.91	0.62-1.36
No	583	474	8.1	8.2	0.97	0.81-1.17
East Asian vs non East Asian						
East Asian	304	248	9.7	8.9	0.84	0.66-1.08
Non East Asian	399	331	7.2	8.0	1.10	0.89-1.36
Smoking status						
Never smoker	295	237	9.7	8.8	0.91	0.70-1.17
Past/present smoker	397	336	7.2	8.2	1.03	0.83-1.28

Supplemental Table 1B. Subgroup analysis of progression-free survival

			Sorafenib	Placebo	HR	95% CI
	Patients	Events	Median PFS (months)	Median PFS (months)		
ITT Population	703	624	2.8	1.4	0.61	0.51-1.72
Region						
North America, Northern/Western Europe	241	212	2.5	1.6	0.80	0.61-1.05
South America, Eastern Europe, Asia-Pacific	462	412	2.8	1.4	0.53	0.44-0.64
Number of prior treatments						
2	386	342	2.8	1.4	0.53	0.43-0.66
3	317	282	2.7	1.4	0.71	0.56-0.90
Brain metastases						
No	592	527	2.8	1.4	0.63	0.53-0.75
Yes	110	97	2.7	1.4	0.45	0.30-0.68
Prior EGFR inhibitor treatment						
No	287	252	2.8	1.4	0.55	0.43-0.71
Yes	416	372	2.7	1.4	0.65	0.53-0.80
Age group						
<65 years	461	409	2.8	1.4	0.51	0.42-0.62
65 to 74 years	193	170	2.7	1.5	0.74	0.54-1.00
≥75 years	49	45	4.1	2.8	0.90	0.49-1.66
Sex						
Male	395	355	2.7	1.4	0.61	0.50-0.76
Female	308	269	2.8	1.4	0.61	0.48-0.77
ECOG PS						
0	214	191	2.8	1.5	0.68	0.51-0.91
1	483	431	2.7	1.4	0.58	0.48-0.70
Duration of prior EGFR treatment						
<12 weeks	453	406	2.7	1.4	0.67	0.55-0.81
≥12 weeks	245	217	2.8	1.4	0.51	0.38-0.66
Prior EGFR treatment with PR or CR as best overall						
Yes	115	110	2.0	1.4	0.64	0.44-0.94
No	583	513	2.8	1.4	0.61	0.51-0.72
East Asian vs non East Asian						
East Asian	304	279	2.8	1.4	0.46	0.36-0.59
Non East Asian	399	345	2.7	1.6	0.73	0.59-0.90
Smoking status						
Never smoker	295	258	2.8	1.4	0.55	0.43-0.70
Past/present smoker	397	357	2.7	1.4	0.63	0.51-0.77

Supplemental Table 1C. Subgroup analysis of time to progression

			Sorafenib	Placebo	HR	95% CI
	Patients	Events	Median TTP (months)	Median TTP (months)		
ITT Population	703	541	2.8	1.4	0.54	0.45-0.65
Region						
North America, Northern/Western Europe	241	182	2.8	1.6	0.68	0.50-0.91
South America, Eastern Europe, Asia-Pacific	462	359	3.9	1.4	0.50	0.41-0.62
Number of prior treatments						
2	386	296	3.5	1.4	0.46	0.37-0.58
3	317	245	2.8	1.4	0.68	0.53-0.87
Brain metastases						
No	592	462	3.5	1.4	0.57	0.47-0.68
Yes	110	79	2.7	1.4	0.44	0.28-0.70
Prior EGFR inhibitor treatment						
No	287	214	4.1	1.4	0.47	0.36-0.62
Yes	416	327	2.8	1.4	0.61	0.49-0.77
Age group						
<65 years	461	350	2.9	1.4	0.46	0.37-0.57
65 to 74 years	193	153	2.8	1.5	0.69	0.50-0.95
≥75 years	49	38	5.5	2.8	0.90	0.49-1.66
Sex						
Male	395	301	2.9	1.4	0.55	0.43-0.69
Female	308	240	2.8	1.4	0.57	0.44-0.74
ECOG PS						
0	214	175	4.0	1.5	0.61	0.45-0.82
1	483	365	2.8	1.4	0.53	0.43-0.65
Duration of prior EGFR treatment						
<12 weeks	453	343	2.8	1.4	0.61	0.49-0.75
≥12 weeks	245	198	4.1	1.4	0.46	0.34-0.61
Prior EGFR treatment with PR or CR as best overall						
Yes	115	100	2.7	1.4	0.57	0.38-0.86
No	583	441	2.9	1.4	0.56	0.46-0.67
East Asian vs non East Asian						
East Asian	304	254	2.8	1.4	0.44	0.34-0.57
Non East Asian	399	287	3.5	2.5	0.62	0.49-0.78
Smoking status						
Never smoker	295	223	2.8	1.4	0.51	0.39-0.67
Past/present smoker	397	309	3.9	1.4	0.55	0.44-0.69

Supplemental Table 2. Patient demographic characteristics relative to EGFR mutation status*

	EGFR mutation		**EGFR wild-type**	
Demographic characteristic, n (%)	**Sorafenib, n=44 (%)**	**Placebo, n=45 (%)**	**Sorafenib, n=122 (%)**	**Placebo, n=136 (%)**
Median age, yr	57.5	56.0	62.5	62.5
Male	17 (38.6)	24 (53.3)	71 (58.2)	83 (61.0)
Smoking status				
Non-smoker	28 (63.6)	23 (51.1)	40 (32.8)	32 (23.5)
Past or present smoker	15 (34.1)	22 (48.9)	80 (65.6)	104 (76.5)
Passive smoker	0 (0)	0 (0)	1 (0.8)	0 (0)
Missing	1 (2.3)	0 (0)	1 (0.8)	0 (0)
ECOG PS				
0	12 (27.3)	18 (40.0)	45 (36.9)	52 (38.2)
1	31 (70.5)	27 (60.0)	77 (63.1)	84 (61.8)
2	1 (2.3)	0 (0)	0 (0)	0 (0)
Brain metastasis present	9 (20.5)	13 (28.9)	16 (13.1)	20 (14.7)
Prior EGFR systemic therapy	37 (84.1)	37 (82.2)	68 (55.7)	72 (52.9)
No. of prior regimens				
2	21 (47.7)	27 (60.0)	66 (54.1)	73 (53.7)
3	22 (50.0)	18 (40.0)	53 (43.4)	63 (46.3)
EGFR mutational status - Source				

Tumor	6	6	29	49
Plasma	42	43	124	137
Combined*	44	45	122	136

* In the combined tumor/plasma data set, a patient was considered to have an EGFR mutation if the mutation was present in either the tumor sample or the plasma sample.**Supplemental Table 3**. Investigator assessed tumor response as a function of EGFR and KRAS status

	Mutation Positive		**Wild-type**	
	Placebo + BSC, %	Sorafenib + BSC, %	Placebo + BSC, %	Sorafenib + BSC, %
EGFR				
ORR	0	6.8	1.5	7.4
DCR	2.2	40.9	25.8	46.7
KRAS				
ORR	0	2.9	1.4	8.3
DCR	7.6	44.1	20.4	45.4

BSC, best supportive care; ORR, overall response rate; DCR, disease control rate

Supplemental Table 4. Drug-related treatment-emergent adverse events occurring in >5% of either treatment group

	Sorafenib (n=346)			Placebo (n=351)		
Event, n (%)	**All**	**Grade 3**	**Grade 4**	**All**	**Grade 3**	**Grade 4**
Rash/Desquamation	132 (38.2)	14 (4.0)	0	37 (10.5)	0	0
Diarrhea	104 (30.1)	10 (2.9)	0	23 (6.6)	0	0
Fatigue	74 (21.4)	14 (4.0)	0	41 (11.7)	5 (1.4)	0
Hypertension	56 (16.2)	15 (4.3)	1 (0.3)	12 (3.4)	1 (0.3)	0
Mucositis, oral cavity	48 (13.9)	3 (0.9)	0	11	(3.1)	0
Nausea	36 (10.4)	5 (1.4)	0	34 (9.7)	1 (0.3)	0
Vomiting	30 (8.7)	4 (1.2)	0	15 (4.3)	1 (0.3)	0
Pruritis	21 (6.1)	0	0	11 (3.1)	0	0
Proteinuria	19 (5.5)	1 (0.3)	0	6 (1.7)	1 (0.3)	0
ALT	19 (5.5)	5 (0.9)	0	6 (1.7)	1 (0.3)	0
AST	18 (5.2)	2 (0.6)	0	4 (1.1)	0	0

ALT, alanine transaminase; AST, aspartate transaminase

Supplemental Figure 1. Progression-free survival (PFS) and overall survival (OS) for patients with KRAS mutations and KRAS wild-type. (A) PFS KRAS mutations, (B) PFS KRAS wild-type, (C) OS KRAS mutations, (D) OS KRAS wild-type.