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Supplemental online content for:

Differential Radiographic Appearance of *BRAF* V600E–Mutant Metastatic Colorectal Cancer in Patients Matched by Primary Tumor Location

Chloe E. Atreya, MD, PhD; Claire Greene, BA; Ryan M. McWhirter, BS; Nabia S. Ikram, MD; I. Elaine Allen, PhD; Katherine Van Loon, MD, MPH; Alan P. Venook, MD; Benjamin M. Yeh, MD; and Spencer C. Behr, MD

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eAppendix 1. Supplemental Methods

Patients

The primary pool for matching comprised of patients seen by 2 authors from March 1, 2014, to March 1, 2015. For reference, 152 patients with metastatic colorectal cancer were seen by these 2 authors over the course of 1 year: 60 (39%) were female, 55 (36%) were younger than 50 years at diagnosis, 48 (32%) had right-sided colon primaries, 59 (39%) had left-sided colon primaries, and 42 (28%) had rectal primaries; 58 (38%) tumors harbored a known *RAS* mutation and 12 (8%) harbored a known *BRAF* V600E mutation. If no match was identified, a third author's panel was searched, and the interval was later extended to September 2015. Extension beyond the original patient pool was necessary, in particular, to match females with right-sided colon primaries. A total of 224 patient records were searched. Follow-up was extended to August 2016, specifically to update the status of surviving patients and to review radiology reports and/or images for interval development of ascites.

Image Analysis

For patients with only one CT study, liver metastases were considered present if greater than 1 cm. The cutoff point of 1 cm was chosen because subcentimeter lesions are too small to fully characterize on CT and have been found to be statistically benign even in patients with known malignancy.[1] For patients with multiple CTs, liver metastases were considered present if they were new or if 2 mm of growth had occurred for lesions less than 1 cm. Peritoneal or omental disease was considered present when soft tissue densities or nodular infiltration soft tissue were present that could not be attributed to a vessel, lymph nodes, or prior surgeries.

Unlike liver and other solid organs, the definition of peritoneal implants is not strictly defined in the radiology literature. Conversely, the overall sensitivity for detection of liver metastases is less than that of peritoneal implants. The overall sensitivity is 96% for peritoneal implants using multidetector-row CT[2] versus approximately 80% for liver metastases.[3]

References

1. Khalil HI, Patterson SA, Panicek DM. Hepatic lesions deemed too small to characterize at CT: prevalence and importance in women with breast cancer. Radiology 2005;235:872–878.
2. Schmidt S, Meuli RA, Achtari C, Prior JO. Peritoneal carcinomatosis in primary ovarian cancer staging: comparison between MDCT, MRI, and 18F-FDG PET/CT. Clin Nucl Med 2015;40:371–377.
3. Vialle R, Boucebci S, Richer JP, et al. Preoperative detection of hepatic metastases from colorectal cancer: prospective comparison of contrast-enhanced ultrasound and mutidetector-row computed tomography (MDCT). Diagn Interv Imaging 2016;97;851–855.

eAppendix 2. Individual Patient Clinicopathologic Characteristics

Study ID	BRAF 0=wild-type 1=mutant	Primary[a] 1=R colon 2=L colon 3=rectum	Sex 1=male 2=female	Age at diagnosis	RAS 0=wild-type 1=mutant	Expanded RAS[b] 0=no; 1=yes 3=NA	MSI 0=MSS; 1=MSI 3=NA	Ethincity 0=not Hispanic 1=Hispanic 3=unknown	Race 0=white 1=Asian[c] 2=black	Histology 0=adenoca 1=mucinous 3=signet ring	Grade[d]	Stage at Diagnosis	Resected Primary 0=no; 1=yes	Resected Metastasis 0=no; 1=yes	Confirmed Dead as of 07/2016 0=no; 1=yes	Survival From mCRC Diagnosis (mo)	*BRAF* Trial Participant 0=no; 1=yes	Notes
1	1	1	1	58	0	3	0	0	0	0	3	2	1	1	1	22.6	1	
2	1	1	1	59	0	3	3	0	1	0	0	4	1	1	1	27.4	1	
3	1	1	0	72	0	3	1	1	0	0	5	3	1	0	1	6.5	1	
4	1	2t	0	54	0	3	3	0	0	0	5	3	1	0	1	4.6	1	
5	1	3	0	57	0	3	3	3	1	0	0	4	0	0	1	8.6	0	
6	1	1	1	51	0	3	0	0	0	0	3	4	0	0	1	29.6	1	
7	1	3	1	77	0	3	1	0	0	0	5	4	1	0	0	37.1	1	
8	1	3	1	64	0	3	0	0	0	0	3	3	1	1	1	31.0	1	
9	1	2	0	59	0	3	0	0	0	0	0	4	0	0	1	15.6	0	
10	1	1	1	20	0	3	3	0	0	0	3	3	1	0	1	40.5	1	Familial polyposis coli
11	1	1	1	62	0	3	3	0	0	0	0	4	1	0	1	25.0	1	
12	1	1	1	64	0	3	1	0	0	1	5	3	1	0	1	3.8	1	
13	1	1	1	51	0	3	3	0	0	0	3	4	1	1	1	74.0	1	
14	1	1	1	58	0	3	3	0	0	0	3	4	1	0	1	24.8	0	
15	1	1	1	75	0	3	3	3		0	3	3	1	1	1	25.7	0	
16	1	2	1	45	0	3	0	0	0	0	5	4	1	0	1	31.4	1	
17	1	1	0	28	0	3	3	0	0	0	5	4	1	0	1	34.7	1	
18	1	1	1	57	0	3	3	0	0	0	5	3	1	0	1	40.0	1	
19	1	1	0	53	0	3	3	0	1	0	5	2	1	0	1	24.5	1	
20	1	1	0	27	0	3	0	1	0	0	3	4	1	0	1	8.5	1	
21	1	2t	1	66	0	3	3	0	0	0	3	4	1	0	1	20.7	0	
22	1	2	1	65	0	3	3	0		0	2	4	0	0	1	14.9	0	
23	1	2	0	62	0	3	0	0	0	1	1	4	0	0	1	23.7	1	
24	1	2t	0	61	0	3	3	0	1	0	3	4	1	0	1	22.5	1	
25	1	2	0	39	0	3	0	0	0	0	4	4	0	0	1	18.3	0	
26	1	1	1	57	0	3	3	3	0	1	3	4	1	0	1	32.1	1	
27	1	3	1	51	0	3	0	0	0	0	2	4	1	0	1	20.1	0	
28	1	1	1	70	0	3	3	0	0	0	3	4	1	0	1	21.8	0	
29	1	1	0	75	0	3	3	0	0	0	3	3	1	1	1	16.5	0	
30	1	1	0	65	0	3	1	0	1	0	3	2	1	1	0	7.9	0	
31	1	2	0	51	0	3	0	0	0	0	3	3	1	0	1	12.9	0	
32	1	2t	1	77	0	3	3	0	0	0	1	4	1	0	1	33.7	0	
33	1	1	1	45	0	3	0	0	0	0	3	4	1	0	0	32.7	1	
34	1	1t	1	48	0	3	0	0	0	1	2	4	1	0	0	25.0	1	
35	1	2	0	48	0	3	0	0	1	0	5	4	0	0	1	9.4	0	
36	1	1	0	60	0	3	0	0	0	0	5	4	1	0	0	30.9	0	
37	1	1	1	75	0	3	3	0	0	0	0	4	0	0	1	10.2	1	
38	1	1	0	66	0	3	1	0	0	2	2	4	0	0	1	4.4	1	
39	1	2t	1	27	0	3	0	0	0	1	0	4	0	0	0	23.5	1	
40	1	1	1	66	0	3	1	0	1		2	3	1	0	0	7.7	0	
41	0	2	0	48	0	1	1	0	0	0	3	4	1	1	0	29.5		Lynch syndrome, immunotherapy trial participant
42	0	1	0	46	0	0	1	0	1	0	5	3	1	0	0	41.8		Lynch syndrome, immunotherapy trial participant
43	0	1	1	65	1	3	0	0	0	2	4	4	1	1	1	15.8		
44	0	1	1	48	0	1	0	0	0	1	3	3	1	0	0	32.0		
45	0	1	1	45	1	3	0	3	0	0	3	4	0	0	1	11.9		
46	0	2	0	53	1	3	3	0	0	0	1	2	1	0	1	15.7		
47	0	2	0	85	0	0	0	0	0	0	2	4	1	0	1	24.2		
48	0	3	1	76	0	0	0	0	0	0	4	3	1	0	1	17.3		
49	0	1	1	88	1	3	0	0	0	0	3	3	1	1	0	55.2		
50	0	2	1	40	0	1	0	0	0	0	3	4	1	1	0	19.9		
51	0	1	0	53	1	3	0	0	2	1	3	4	1	0	1	16.4		
52	0	1	1	44	1	3	0	0	2	1	1	4	1	1	0	24.0		
53	0	2	0	67	0	0	0	0	0	0	3	2	1	1	0	65.6		
54	0	3	0	76	0	1	0	0	0	0	5	2	1	1	1	54.8		
55	0	1	0	66	1	3	0	0	0	0	3	3	1	1	0	32.2		
56	0	1	0	77	1	3	3	1		0	1	2	1	0	0	29.4		
57	0	2	1	57	0	1	0	0	1	0	3	4	1	0	0	15.6		
58	0	1	0	51	1	3	0	0	0	0	5	4	1	1	0	18.9		
59	0	1	1	55	1	3	0	0	2	0	0	4	1	0	1	22.9		
60	0	2	1	60	0	0	0	0	2	0	5	4	1	1	0	38.3		

Abbreviations: mCRC, metastatic colorectal cancer; MSI, microsatellite instability; MSS, microsatellite stable; NA, not applicable.

[a]t=transverse colon.

[b]Mutation testing covered KRAS and NRAS codons 12, 13, 61, 117, and 146.

[c]Asian, Native Hawaiian, or Other Pacific Islander.

[d]0=unknown; 1=low; 2=low/intermediate; 3=intermediate; 4=intermediate/high; 5=high.

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eAppendix 2. Individual Patient Clinicopathologic Characteristics (cont.)

Study ID	BRAF 0=wild-type 1=mutant	Primary[a] 1=R colon 2=L colon 3=rectum	Sex 1=male 2=female	Age at diagnosis	RAS 0=wild-type 1=mutant	Expanded RAS[b] 0=no; 1=yes 3=NA	MSI 0=MSS; 1=MSI 3=NA	Ethincity 0=not Hispanic 1=Hispanic 3=unknown	Race 0=white 1=Asian[c] 2=black	Histology 0=adenoca 1=mucinous 3=signet ring	Grade[d]	Stage at Diagnosis	Resected Primary 0=no; 1=yes	Resected Metastasis 0=no; 1=yes	Confirmed Dead as of 07/2016 0=no; 1=yes	Survival From mCRC Diagnosis (mo)	*BRAF* Trial Participant 0=no; 1=yes	Notes
61	0	1	1	68		3	3	0	1	1	3	4	0	0	1	16.1		
62	0	1	1	28	1	3	0	1		1	3	4	1	1	0	91.2		
63	0	1	0	53	0	1	0	0	0	0	1	2	1	1	0	42.2		
64	0	2	0	52	0	1	0	0	0	0	2	2	1	0	0	32.1		
65	0	3	1	74	1	3	3	0	0	0	3	4	0	0	1	28.6		
66	0	2	0	50	0	1	0	0	1	0	2	4	1	1	1	68.2		
67	0	1	0	55	1	3	0	0	0		0	4	1	1	0	67.4		
68	0	1	1	54	1	3	3	0	0	0	1	4	1	1	1	58.3		
69	0	2	1	51	0	1	0	3		0	0	3	1	0	1	50.9		
70	0	1	1	42	1	3	1	3		0	1	3	1	0	0	8.1		Lynch syndrome
71	0	1	0	47	1	3	0	0	0	1	3	2	1	0	1	25.7		
72	0	1	0	48	0	0	1	0	0	0	0	3	1	1	0	62.7		Lynch syndrome
73	0	3	0	65	1	3	0	0	0	0	3	4	1	1	0	51.1		
74	0	3	1	64	1	3	0	0	1	0	3	3	1	0	1	23.7		
75	0	1t	1	67	0	0	3	3	0	0	5	4	0	0	1	9.4		
76	0	1	0	67	1	3	3	0	1	0	3	3	1	0	1	25.2		
77	0	1	1	38	1	3	0	0	1	0	3	4	1	0	1	44.9		
78	0	2	0	53	1	3	0	0	0	0	3	4	1	1	0	42.7		
79	0	1	0	71	0	1	0	0	0	0	0	4	1	1	1	22.9		
80	0	2	0	34	0	0	0	0	0	0	1	4	1	1	0	43.2		
81	0	2	0	56	0	0	0	0	0	0	1	4	1	0	1	31.1		
82	0	1	1	50	1	3	0	0	0	0	3	4	0	0	1	20.9		
83	0	1	1	72	1	3	0	0	0	0	3	4	1	0	0	37.2		
84	0	1	0	53	1	3	0	0	0	1	1	4	1	0	1	8.4		
85	0	1	1	82	1	3	0	0	1	0	3	4	1	0	1	10.9		
86	0	2	0	74	1	3	3	3	2	0	3	4	1	0	1	22.3		
87	0	1	1	70	1	3	3	0	0	0	3	4	1	0	1	17.9		
88	0	1	0	42	1	3	3	3		0	3	3	1	1	1	32.6		
89	0	1	1	56	1	3	3	0	0	0	3	3	1	1	1	45.0		
90	0	1	1	67	1	3	3	3		0	1	3	1	0	1	48.7		
91	0	1	1	51	0	0	0	3		0	4	4	1	0	1	17.4		
92	0	2	0	73	0	1	0	0	0	0	4	4	1	1	0	27.9		
93	0	1t	1	67	1	3	3	0	2	1	5	4	1	0	1	35.2		
94	0	1	1	54	1	3	0	0	0	1	3	3	1	0	0	15.3		
95	0	3	1	64	1	3	0	1	0	0	3	3	1	1	1	23.0		
96	0	2	0	30	1	3	0	0	0	0	5	4	1	0	1	12.8		
97	0	1	1	44	1	3	0	0	1	0	3	4	1	1	0	28.1		
98	0	2	0	58	1	3	3	0		0	2	4	1	1	0	38.1		
99	0	2	1	38	0	1	0	0	1	0	5	4	1	0	1	17.2		
100	0	3	1	69	0	1	0	0	0	0	3	3	1	0	0	19.4		
101	0	3	1	56	0	0	3	0	0	0	2	3	1	0	0	35.3		
102	0	1	1	43	0	1	0	0	0	0	5	3	1	0	0	23.1		
103	0	2	1	71	0	0	3	0	0	0	5	4	1	1	0	17.8		
104	0	2	0	47	1	3	0	0	1	0	3	4	1	1	1	31.5		
105	0	1	0	60	1	3	3	0	1	0	4	4	1	0	1	23.1		
106	0	1	1	64	1	3	3	3		0	3	4	0	0	0	16.4		
107	0	2	1	47	1	3	0	0	0	0	3	4	1	1	0	22.0		
108	0	1	1	52	0	1	3	0	0	2	0	4	1	1	1	18.4		
109	0	1	1	53	0	0	0	0	0	0	5	3	1	0	0	29.5		
110	0	2	1	48	0	1	0	0	1	0	3	4	1	0	0	18.0		
111	0	1	0	70	1	3	3	0	0	0	1	3	1	0	1	12.1		
112	0	2	1	50	1	3	0	0	0	0	1	2	1	1	0	64.8		
113	0	1	1	65	1	3	0	0	0	0	2	4	0	0	0	8.8		
114	0	1	0	58	0	1	0	0	0	2	0	4	0	0	0	19.6		
115	0	1	1	72	1	3	3	1		0	2	3	1	0	1	14.8		
116	0	1t	1	51	0	1	0	0	1	1	3	4	1	1	0	13.3		
117	0	2	1	52	1	3	0	0	0	0	1	3	1	0	1	64.5		
118	0	1	1	68	1	3	3	0	0	0	3	4	0	0	0	6.5		
119	0	1	1	68	0	0	3	1		0	0	4	1	0	1	50.8		
120	0	1	1	75	1	3	0	0	0	0	3	4	1	0	0	16.1		

Abbreviations: mCRC, metastatic colorectal cancer; MSI, microsatellite instability; MSS, microsatellite stable; NA, not applicable.
[a]t=transverse colon.
[b]Mutation testing covered KRAS and NRAS codons 12, 13, 61, 117, and 146.
[c]Asian, Native Hawaiian, or Other Pacific Islander.
[d]0=unknown; 1=low; 2=low/intermediate; 3=intermediate; 4=intermediate/high; 5=high.

eAppendix 3. Individual Patient Patterns of Metastatic Disease

Study ID	*BRAF* 0=wild-type 1=mutant	Liver Metastases 0=no; 1=yes	Lung Metastases	Bone Metastases	Lymph Node Metastases	Ascites	Peritoneal Metastases	Other Metastatic Sites	Number of Metastatic Sites	RECIST 1.1 Measureable 0=no; 1=yes	Time to Ascites (mo)[a]
1	1	0	1	0	0	0	0		1	0	
2	1	1	1	1	0	0	1	Soft tissue, adrenal, muscular, renal	8	1	
3	1	0	0	0	1	0	0		1	1	
4	1	0	0	0	1	1	0		2	1	0.0
5	1	1	0	0	0	1	0		2	1	8.6
6	1	1	1	0	1	0	1		4	1	
7	1	0	0	0	1	0	0		1	1	
8	1	1	0	0	0	1	0	Soft tissue, pancreas	4	1	29.5
9	1	1	0	0	0	1	1		3	1	9.2
10	1	1	1	1	1	1	1		6	1	30.4
11	1	1	0	0	0	1	1	Pleura	4	0	23.1
12	1	0	0	0	1	1	0	Soft tissue	3	1	0.0
13	1	0	1	0	0	0	1		2	1	
14	1	1	0	0	1	1	1		4	1	24.0
15	1	0	0	0	0	1	1		2	0	21.8
16	1	0	0	1	1	0	0		2	1	
17	1	1	0	0	1	0	1		3	1	
18	1	0	1	0	1	0	0		2	1	
19	1	0	0	1	0	1	1		3	0	0.3
20	1	1	0	0	1	1	1		4	1	4.6
21	1	1	1	0	1	1	0		4	1	19.6
22	1	1	1	0	1	0	0		3	1	
23	1	0	0	0	1	1	1		3	0	0.0
24	1	1	1	0		0	0		2	1	
25	1	1	0	0	1	1	1		4	1	2.8
26	1	1	0	0	1	0	0		2	1	
27	1	0	1	0	0	0	1		2	1	
28	1	1	0	0	1	1	0		3	1	21.4
29	1	1	0	0	0	0	0		1	1	
30	1	0	0	0	0	0	0		0	0	
31	1	0	1	0	1	0	0		2	1	
32	1	0	0	0	0	0	1		1	1	
33	1	1	1	0	0	0	0	Brain	3	1	
34	1	0	0	0	0	1	1		2	0	0.0
35	1	0	0	0	1	1	0		2	1	0.0
36	1	0	0	0	1	0	1		2	1	
37	1	1	0	0	0	1	1		3	1	7.0
38	1	1	0	0	0	1	1		3	1	0.0
39	1	0	0	0	0	1	1		2	0	7.0
40	1	1	0	0	1	0	0		2	1	
41	0	1	0	0	1	0	0		2	1	
42	0	0	0	0	1	0	0		1	1	
43	0	1	0	0	0	1[a]	0		1	1	15.4[b]
44	0	0	1	0	1	0	0		2	1	
45	0	1	0	0	0	0	0		1	0	
46	0	0	1	1	0	0	0	Brain	3	1	
47	0	1	1	0	1	1	0		4	1	21.3
48	0	1	0	0	1	0	0		2	1	
49	0	0	0	0	0	0	1		1	0	
50	0	1	0	0	0	0	0		1	1	
51	0	1	0	0	1	1	0		3	1	1.6
52	0	0	0	0	0	1	1		2	0	0.0
53	0	1	1	0	0	0	0		2	1	
54	0	1	1	0	0	0	0		2	1	
55	0	1	0	0	0	0	0		1	1	
56	0	0	0	1	0	0	0	Pleura	2	0	
57	0	1	0	0	0	0	1		2	1	

[a]Time to radiograpic detection of ascites from diagnosis with metastatic colorectal cancer.

[b]Ascites detected only after extended follow-up (through 8/2016).

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eAppendix 3. Supplemental Methods (cont.)

Study ID	*BRAF* 0=wild-type 1=mutant	Liver Metastases 0=no; 1=yes	Lung Metastases	Bone Metastases	Lymph Node Metastases	Ascites	Peritoneal Metastases	Other Metastatic Sites	Number of Metastatic Sites	RECIST 1.1 Measureable 0=no; 1=yes	Time to Ascites (mo)[a]
58	0	1	0	0	1	0	0		2	1	
59	0	1	1	0	1	1	0		4	1	8.1
60	0	0	0	0	0	0	0		0	0	
61	0	1	1	0	1	1	1		5	1	0.0
62	0	1	0	0	0	0	0		1	1	
63	0	1	0	0	0	1[a]	0		1	1	40.5[b]
64	0	1	1	0	0	0	0	Brain	3	1	
65	0	1	1	0	0	1[a]	0		2	1	26.8[b]
66	0	1	1	1	1	0	0		4	1	
67	0	1	0	0	1	0	0		2	1	
68	0	1	0	0	0	0	1		2	1	
69	0	1	1	1	1	0	0		4	1	
70	0	1	0	0	1	0	0		2	1	
71	0	0	0	0	0	1	1		2	0	23.2
72	0	0	0	0	1	0	1		2	0	
73	0	0	1	0	0	0	0		1	1	
74	0	0	1	1	1	0	0		3	1	
75	0	1	0	0	1	0	1		3	1	
76	0	0	1	0	1	0	0		2	1	
77	0	0	1	0	1	1	0		3	1	28.1
78	0	1	1	0	1	0	0		3	1	
79	0	1	0	0	1	0	0		2	1	
80	0	1	0	0	1	0	0		2	1	
81	0	1	0	0	1	0	0		2	1	
82	0	1	1	0	1	0	0		3	1	
83	0	0	0	0	0	1	1		2	0	2.2
84	0	1	1	0	0	1	1	Pleura	5	1	0.2
85	0	1	1	0	0	0	0		2	1	
86	0	1	0	0	0	0	0		1	1	
87	0	1	0	0	1	0	0		2	1	
88	0	1	1	0	1	0	0		3	1	
89	0	1	1	0	0	1	1		4	1	0.0
90	0	0	1	0	0	0	0		1	1	
91	0	1	0	0	1	0	1		3	1	
92	0	1	0	0	0	0	0		1	1	
93	0	0	1	0	1	1	1		4	1	32.3
94	0	1	0	0	0	0	0		1	1	
95	0	0	0	0	0	0	1		1	0	
96	0	1	0	0	0	0	1		2	1	
97	0	1	0	0	1	0	1	Ovary	4	1	
98	0	1	0	0	1	0	0		2	1	
99	0	1	0	1	1	1	0		4	1	0.0
100	0	1	1	0	0	0	0		2	1	
101	0	0	1	0	0	0	0		1	1	
102	0	1	1	0	1	0	0	Spleen	4	1	
103	0	0	0	0	1	0	1		2	1	
104	0	1	1	0	0	0	0		2	1	
105	0	1	1	0	1	1	0		4	1	12.8
106	0	1	1	0	0	1	1		4	1	16.2
107	0	1	0	0	0	0	0		1	1	
108	0	1	0	0	1	1	1		4	1	0.1
109	0	0	0	0	1	0	0		1	1	
110	0	0	1	0	1	0	0		2	0	
111	0	0	0	0	0	1	1		2	0	0.0
112	0	0	1	0	0	0	0		1	1	
113	0	1	0	0	0	0	0		1	1	
114	0	0	0	0	0	1	1		2	0	0.0
115	0	1	1	0	0	0	0	Brain	3	1	
116	0	0	0	0	0	1	1		2	0	0.0
117	0	1	1	0	1	1	1		5	1	1.8
118	0	1	0	1	0	0	1		3	1	
119	0	0	0	0	0	0	0		0	0	
120	0	1	0	0	0	0	1		2	1	

[a]Time to radiograpic detection of ascites from diagnosis with metastatic colorectal cancer.

[b]Ascites detected only after extended follow-up (through 8/2016).

eAppendix 4. Patterns of Metastasis by MSI Status

Metastatic Sites	MSI[a] (N=10)	MSS[a] (N=68)	*P* Value
Liver	4 (40%)	44 (65%)	.13
Lung	0 (0%)	26 (38%)	.017
Bone	0 (0%)	5 (7%)	.37
Lymph node	8 (80%)	31 (46%)	.042
Peritoneal	2 (20%)	23 (34%)	.38
Ascites	3 (30%)	19 (28%)	.89

Abbreviations: MSI, microsatellite instability (or mismatch repair deficient); MSS, microsatellite stability (or mismatch repair proficient).
[a]The MSI/MMR status of 42 patients was unknown.

eAppendix 5. Patterns of Metastasis by *BRAF* Mutation Status and Location of Colorectal Cancer Primary With Omission of Transverse Colon Primaries

	Entire Cohort			Right Colon Primaries			Left Colon Primaries		
Metastatic Sites	Mutant (N=34)	Wild-Type (N=77)	*P* Value	Mutant (N=23)	Wild-Type (N=45)	*P* Value	Mutant (N=7)	Wild-Type (N=24)	*P* Value
Liver	19 (56%)	53 (69%)	.19	14 (61%)	30 (67%)	.64	3 (43%)	19 (79%)	.063
Lung	10 (29%)	32 (42%)	.22	7 (30%)	15 (33%)	.81	2 (29%)	11 (46%)	.41
Bone	4 (10%)	7 (9%)	.66	3 (13%)	2 (4%)	.20	1 (14%)	4 (17%)	.88
Lymph node	19 (56%)	35 (45%)	.31	12 (52%)	21 (47%)	.67	6 (86%)	12 (50%)	.092
Peritoneal	20 (50%)	22 (29%)	.029	13 (56%)	17 (38%)	.14	3 (43%)	4 (17%)	.14
Ascites	16 (47%)	17 (22%)	.0079	10 (43%)	14 (31%)	.31	4 (57%)	3 (12%)	.013

Six patients with *BRAF*-mutated transverse colon primaries (1 classified as originating in the right colon, 5 classified as originating in the left colon) and 3 patients with *BRAF* wild-type transverse colon primaries (all classified as originating in the right colon) were excluded from this analysis.

eAppendix 6. Univariate and Multivariate Predictors of Survival in *BRAF*-Mutant Metastatic Colorectal Cancer

N		Survival (mo)	HR	CI Lower	CI Upper	LR *P* Value
Primary location (left or right colon)						
	L: 12	18.3	0.47	0.21	1.04	.07
	R: 24	25.0				
Sex						
	M: 16	15.6	0.37	0.18	0.76	.009
	F: 24	27.4				
Stage at diagnosis						
	II/III: 13	22.6	0.87	0.41	1.83	.71
	IV: 27	23.7				
Grade (low or high)						
	Low: 23	23.7	1.01	0.44	2.27	.99
	High: 11	24.5				
Age category, y						
	<50: 9	31.4	1.56	0.63	3.86	.31
	≥50: 31	22.6				
Primary resected						
	(–): 10	14.9	0.30	0.13	0.70	.009
	(+): 30	25.0				
Metastasis resected						
	(–): 33	22.5	0.61	0.23	1.60	.29
	(+): 7	25.7				
Metastatic sites						
Liver						
	(–): 19	24.5	1.42	0.70	2.88	.33
	(+): 21	22.5				
Lung						
	(–): 28	23.7	0.54	0.24	1.24	.13
	(+): 12	22.6				
Lymph node						
	(–): 18	24.5	1.02	0.50	2.10	.95
	(+): 21	23.7				
Peritoneum						
	(–): 20	21.8	0.62	0.31	1.27	.20
	(+): 20	25.0				
Ascites						
	(–): 20	29.6	2.35	1.14	4.83	.02
	(+): 20	20.7				
RECIST measureable						
	(P): 8	24.5	0.93	0.34	2.53	--
	(+): 32	21.8				
Trial participant						
	(P): 16	18.3	0.50	0.23	1.05	--
	(+): 24	27.4				
Adjusted for Ascites						
Sex, peritoneal metastasis, location, age, stage, grade, resection, metastasectomy[a]			6.15	1.74	21.79	.0007
Sex, peritoneal metastasis, location, age, stage, grade, resection			5.85	1.76	19.40	.0003
Sex, peritoneal metastasis, location, age, stage, grade			7.06	2.21	22.54	.0003
Sex, peritoneal metastasis, location, age, stage			7.53	2.54	22.32	.0001
Sex, peritoneal metastasis, location, age			6.81	2.41	19.22	<.0001
Sex, peritoneal metastasis, location			5.85	2.16	15.87	.0001
Sex, peritoneal metastasis			3.59	1.63	7.92	.0001
Sex			2.51	1.19	5.28	.0017

Abbreviations: F, female; HR, hazard ratio; L, left; LR, likelihood ratio; M, male; R, right.

[a]Adjustment for sex, peritoneal metastases, location of primary tumor (left or right colon), age and stage at diagnosis, tumor grade, resection of primary tumor, and metastases. Based on diagnostic plots (not shown) and the Schoenfeld test (*P*=.68), the assumption of proportional hazards for primary tumor location effect is reasonable in this dataset.

eAppendix 7. Timing of Radiographic Detection of Ascites

Time of Ascites Detection	*BRAF*-mut (N=20)	*BRAF* wt (N=22)
Median time after mCRC diagnosis (range), mo	7 (0–30)	2 (0–40)
Within 3 mo of mCRC diagnosis	8 (40%)	12 (54%)
Within 3 mo of death from mCRC	7 (20%)	7 (32%)

Abbreviations: mCRC, metastatic colorectal cancer; mut, mutant; wt, wild-type.