

Supplementary Online Content

Cremolini C, Rossini D, Dell'Aquila E, et al. Rechallenge for patients with *RAS* and *BRAF* wild-type metastatic colorectal cancer with acquired resistance to first-line cetuximab and irinotecan: a phase 2 single-arm clinical trial. *JAMA Oncol*. Published online November 21, 2018. doi:10.1001/jamaoncol.2018.5080

eTable 1. List of Oncogenes and Tumour Suppressor Genes analyzed in ctDNA

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. List of Oncogenes and Tumour Suppressor Genes analyzed in ctDNA

<i>ABL1</i>	<i>AKT1</i>	<i>ALK</i>	<i>APC</i>	<i>ATM</i>
<i>BRAF</i>	<i>CDH1</i>	<i>CDKN2A</i>	<i>CSF1R</i>	<i>CTNNB1</i>
<i>EGFR</i>	<i>ERBB2</i>	<i>ERBB4</i>	<i>EZH2</i>	<i>FBXW7</i>
<i>FGFR1</i>	<i>FGFR2</i>	<i>FGFR3</i>	<i>FLT3</i>	<i>GNA11</i>
<i>GNAS</i>	<i>GNAQ</i>	<i>HNF1A</i>	<i>HRAS</i>	<i>IDH1</i>
<i>IDH2</i>	<i>JAK2</i>	<i>KDR/VEGFR2</i>	<i>KIT</i>	<i>KRAS</i>
<i>MET</i>	<i>MLH1</i>	<i>MPL</i>	<i>NOTCH1</i>	<i>NPM1</i>
<i>NRAS</i>	<i>PDGFRA</i>	<i>PIK3CA</i>	<i>PTEN</i>	<i>PTPN11</i>
<i>RB1</i>	<i>RET</i>	<i>SMAD4</i>	<i>SMARCB1</i>	<i>SMO</i>
<i>SRC</i>	<i>STK11</i>	<i>TP53</i>	<i>VHL</i>	

eTable 2. Baseline Patients' and Disease Characteristics

Characteristic	Study population (N=28)
Age in years (median (range))	69 (45-79)
Sex	
Male	19 (68%)
Female	9 (32%)
ECOG PS^a	
0	18 (64%)
1-2	10 (36%)
Synchronous Metastases	
Yes	20 (71%)
No	8 (29%)
Prior Adjuvant Chemotherapy	
Yes	8 (29%)
No	20 (71%)
Primary Tumor Site	
Right	9 (32%)
Left	13 (47%)
Rectum	6 (21%)
Number of Metastatic Sites	
1	7 (25%)
>1	21 (75%)
Liver Only Metastases	
Yes	5 (18%)
No	23 (82%)
Resected Primary Tumor	
Yes	25 (89%)
No	3 (11%)
Mucinous Histology	
Yes	1 (4%)
No	27 (96%)
Time from diagnosis of mCRC	
<18 months	5 (18%)
≥18 months	23 (82%)
^a ECOG PS, Eastern Cooperative Oncology Group Performance Status.	

eTable 3. Most Common Grade 3/4 Adverse Events

G3/4 Adverse Event	Study population (N=28)
Diarrhoea	5 (18%)
Skin Toxicity	4 (14%)
Neutropenia	4 (14%)
Hand and Foot Syndrome	2 (7%)
Febrile neutropenia	1 (4%)
Stomatitis	1 (4%)
Nausea	1 (4%)
Conjunctivitis	1 (4%)
Hypomagnesemia	1 (4%)

eTable 4. RAS Status on ctDNA Collected at Rechallenge Baseline and Best Response According to RECIST 1.1

Patients	RAS status on ctDNA	Objective Response
#1	Wild-type	Confirmed PR
#2	KRAS G12D	PD
#3	Wild-type	Confirmed PR
#4	Wild-type	PD
#5	Wild-type	SD
#6	KRAS G12D	PD
#7	Wild-type	SD
#9	Wild-type	Confirmed PR
#10	Wild-type	Unconfirmed PR
#11	Wild-type	PD
#12	KRAS G12D	PD
#13	KRAS G12V	PD
#15	NRAS Q61L	SD
#16	Wild-type	SD
#17	KRAS G12V/ Q61H	PD
#18	KRAS G12V	PD
#19	Wild-type	Confirmed PR
#21	KRAS G12D	SD
#22	KRAS G12V	SD
#23	KRAS G12V	PD
#24	KRAS G12D	Unconfirmed PR
#25	KRAS G12D	SD
#26	Wild-type	SD
#27	Wild-type	PD
#28	Wild-type	SD

eFigure. Kaplan-Meier Estimates of Progression-Free Survival and Overall Survival in the Study Population

