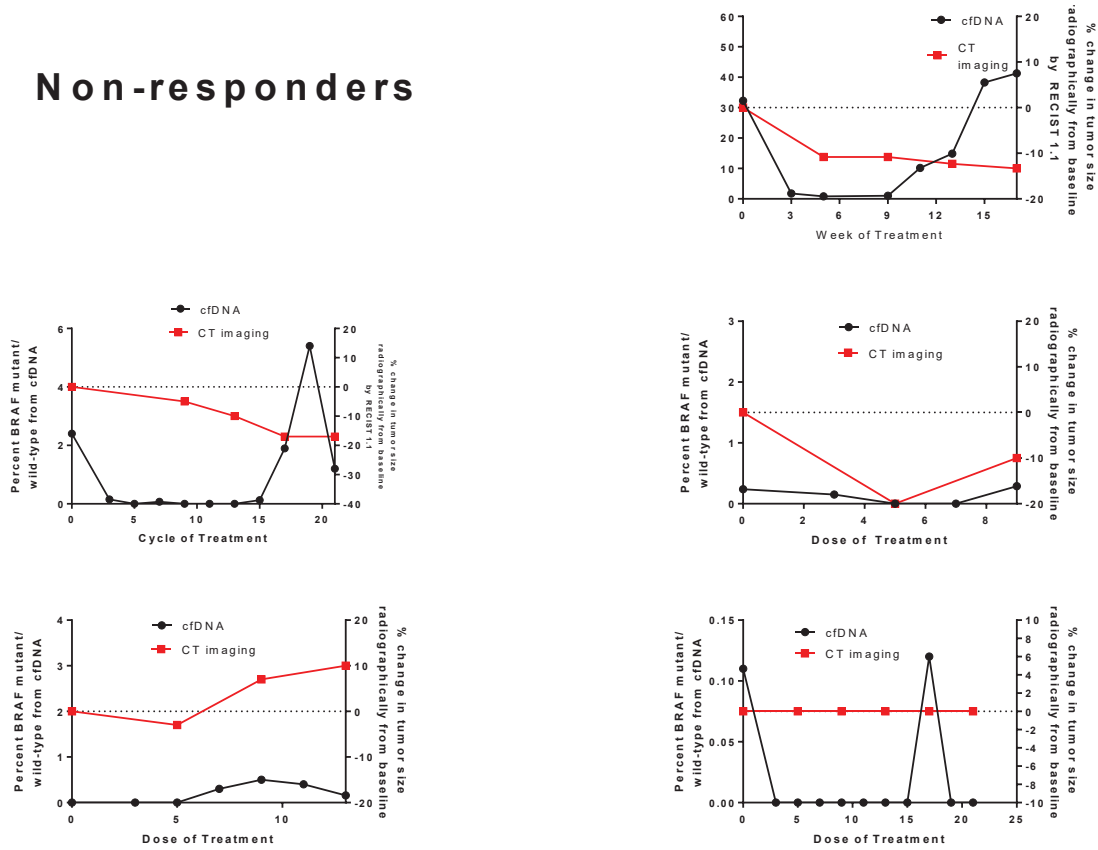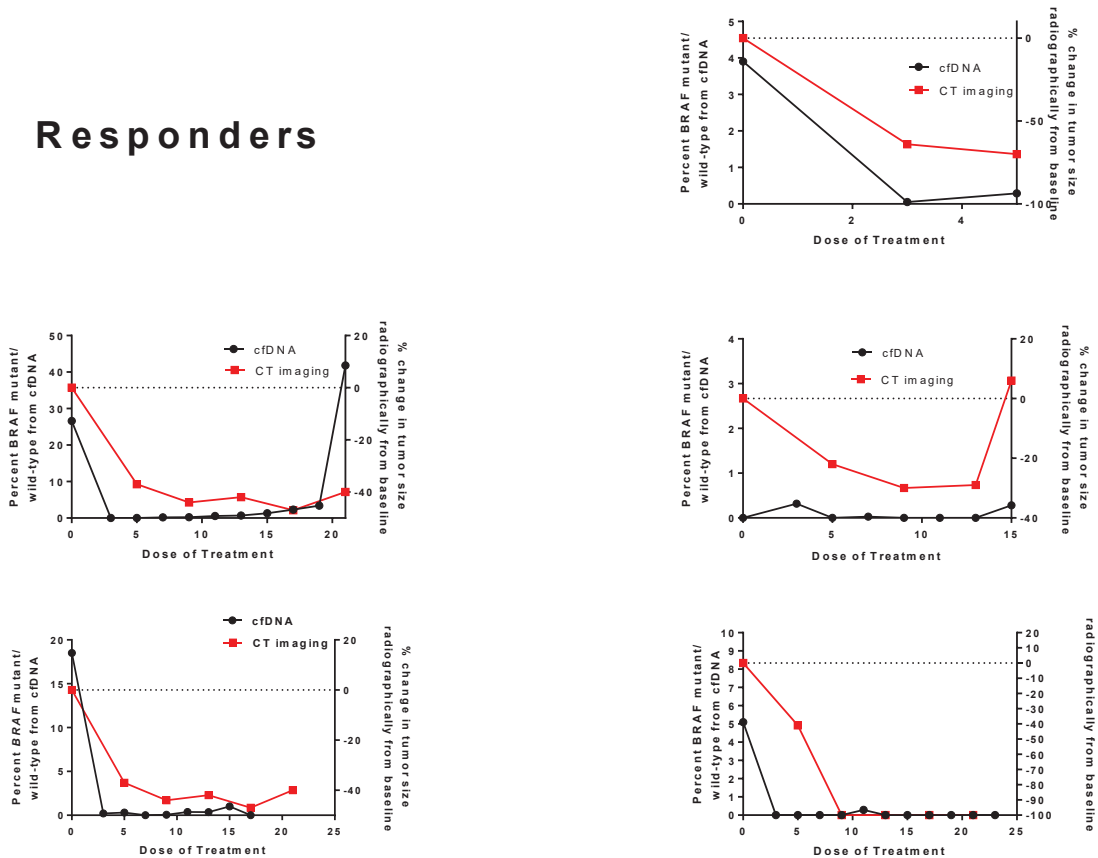**Supplementary Figure 1:** Trends in various mutation allele frequencies tracked serially over treatment course for two patients on study.
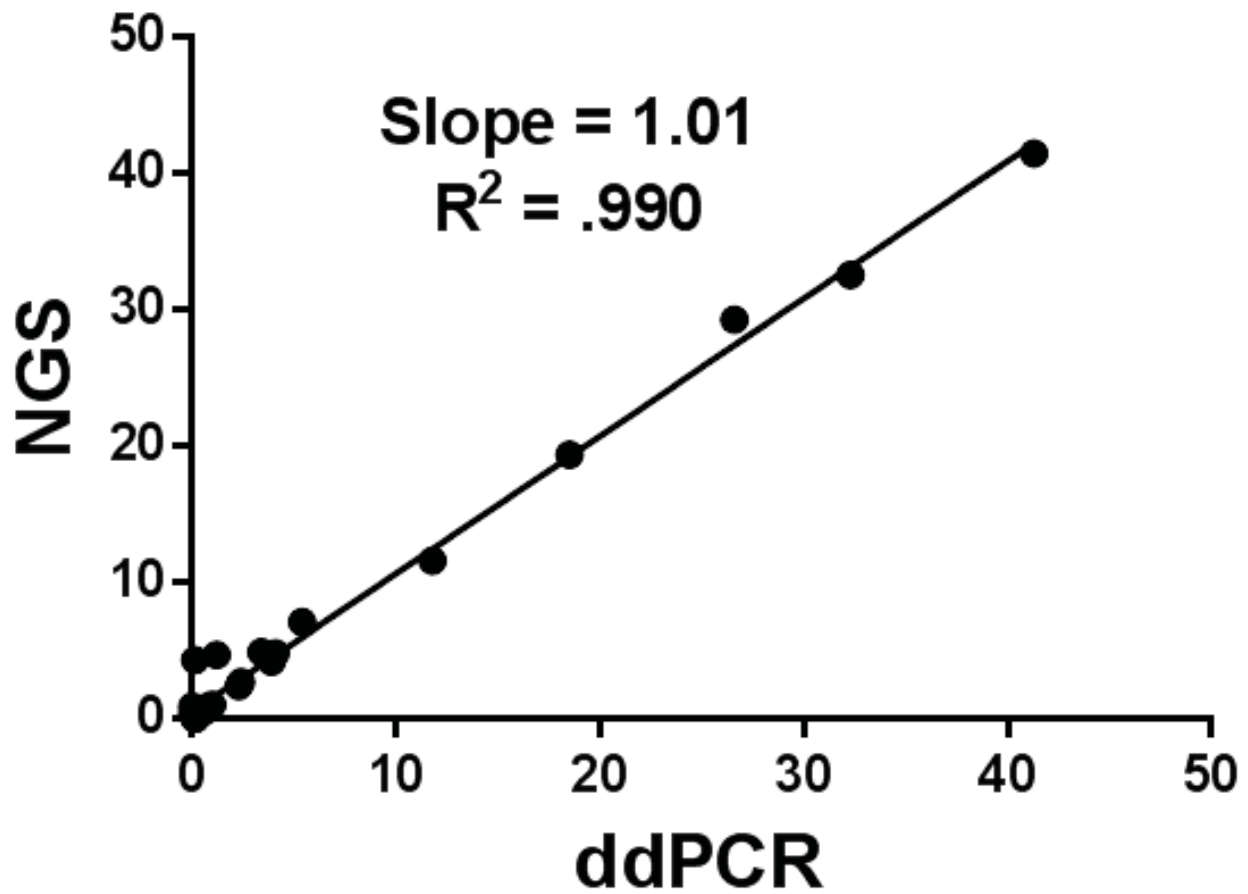
Supplementary Figure 2: Trends in cfDNA fraction (black) and radiographic changes (red) for ten other patients on study.

Supplementary Figure 3: Analysis of *BRAF*[V600E] allele fraction by cfDNA was validated using two separate methodologies.

NGS Panel

Complete* or Critical Exon Coverage in 68 Genes

POINT MUTATIONS

AKT1	ALK	**APC**	**AR**
AFAR	**ARID1A**	ATM	**BRAF**
BRCA1	**BRCA2**	**CCDN1**	**CCND2**
CCNE1	CDH1	**CDK4**	**CDK6**
CDKN2A	**CDKN2B**	CTNNB1	**EGFR**
ERBB2	ESR1	EZH2	FBXW7
FGFR1	**FGFR2**	FGFR3	GATA3
GNA11	GNAQ	GNAS	HNF1A
HRAS	IDH1	IDH2	JAK2
JAK3	**KIT**	**KRAS**	MAP2K1
MAP2K2	**MET**	MLH1	MPL
MYC	**NF1**	NFE2L2	NOTCH1
NPM1	**NRAS**	NTRK1	**PDGFRA**
PIK3CA	**PTEN**	PTPN11	**RAF1**
RET	RHEB	RHOA	RIT1
ROS1	SMAD4	SMO	SRC
STK11	TERT	**TP53**	VHL

AMPLIFICATIONS

AR
BRAF
CCNE1
CDK4
CDK6
EGFR
ERBB2
FGFR1
FGFR2
KIT
KRAS
MET
MYC
PDGFRA
PIK3CA
RAF1

FUSIONS

ALK
RET
ROS1
NTRK1

INDELS

EGFR exon 19 deletions
EGFR exon 20 insertions

Supplementary Figure 4: 68-gene panel for which mutation, amplification, deletion, and fusion profiling was available.

*Complete exon coverage for genes in **bold**

Age (median), range	63 (42-73)
Gender	
Male	10 (53%)
Female	9 (47%)
ECOG PS	
0	4 (21%)
1	14 (74%)
2	1 (5%)
Ethnicity	
White	15 (79%)
Hispanic	2 (11%)
Asian	2 (11%)
Prior Lines of Treatment (range)	2 (1-4)
Prior Irinotecan	
Yes	14 (74%)
No	5 (26%)
Prior Cetuximab	
Yes	8 (42%)
No	11 (58%)
Prior BRAF inhibitor	1 (5%)
Prior MEK inhibitor	1 (5%)

Supplementary Table 1: Demographic information