**Supplementary Figure 1: IGV view of multiple variants within the 24-week cfDNA sample from patient 12**

Blue, brown and red colors indicate sequencing reads containing a *TP53* variant within the sequencing alignment. Variants affecting neighboring bases are not on the same DNA strand, suggesting that these variants originated from separate clones in the tumor.

IGV, integrative genomics viewer.
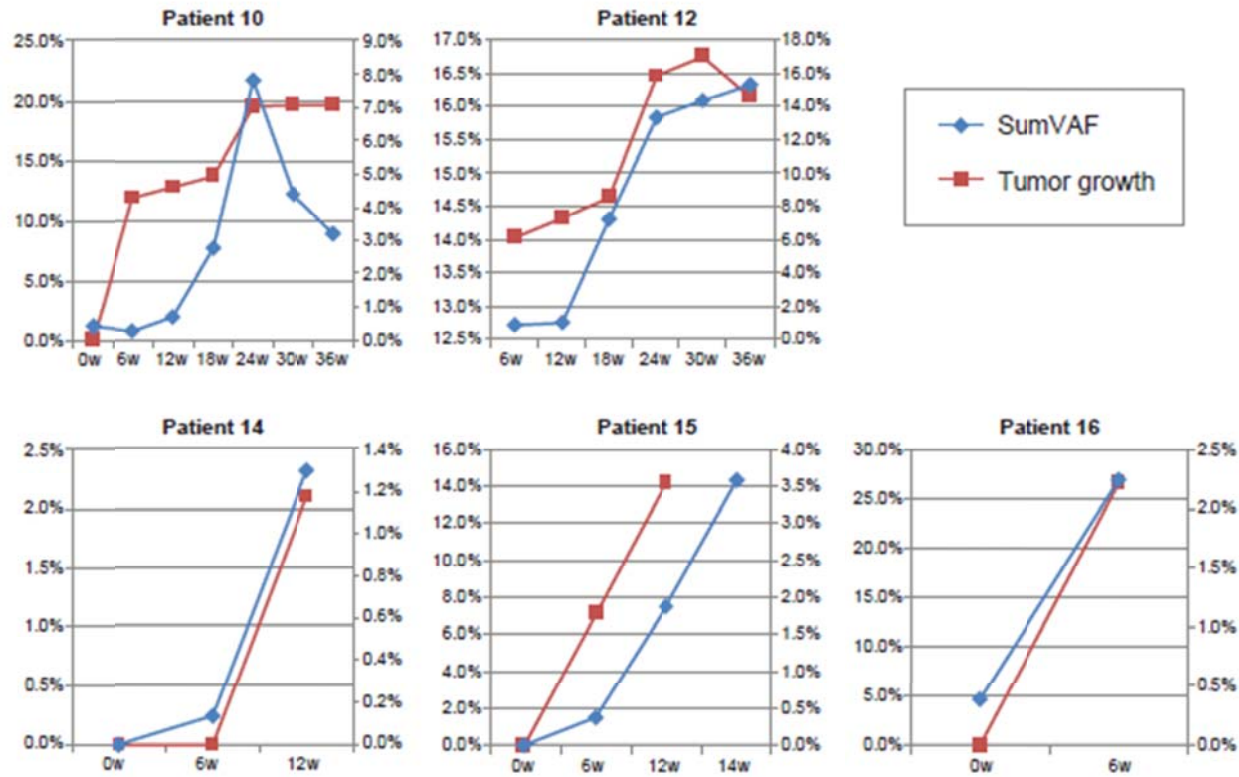
Supplementary Figure 2: Comparison of tumor growth and total *TP53* mutation burden in cfDNA

Tumor growth is presented as percentage change in tumor size by computed tomography measurement relative to baseline measurement (Y axis 1, left). Total *TP53* mutation burden is sum of all *TP53* variant allelic fractions (VAF; Y axis 2, right). X axis represents time on treatment (weeks).
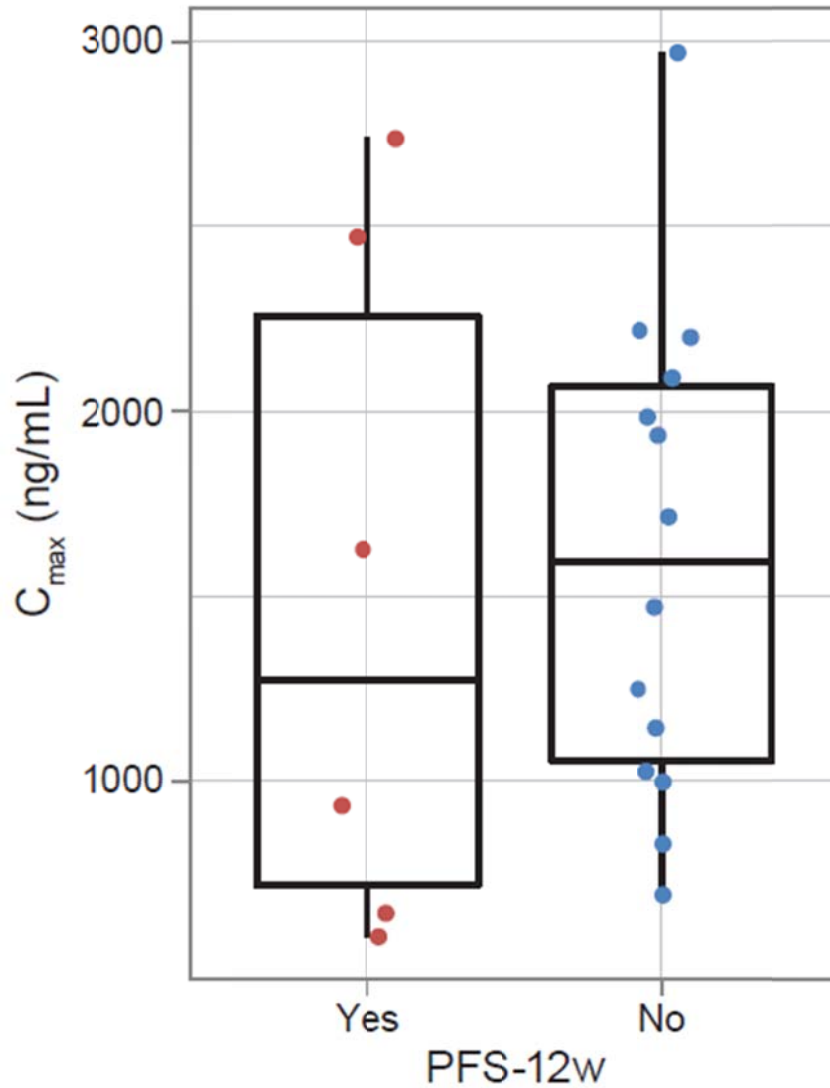
**Supplementary Figure 3: Comparison of C_{max} at baseline (Cycle 1, Day 1) for patients with and without progression-free survival at 12 weeks (PFS-12w)**

Box plots with actual data points are shown (n = 20). Center line indicates median value. Bottom and top of the whiskers represent the smallest and largest non-outlier values respectively. Lower and top end of the box indicate the 1st and 3rd quartile respectively.

Supplementary Figure 4: cfDNA yields in patients with DDLPS receiving SAR2405838
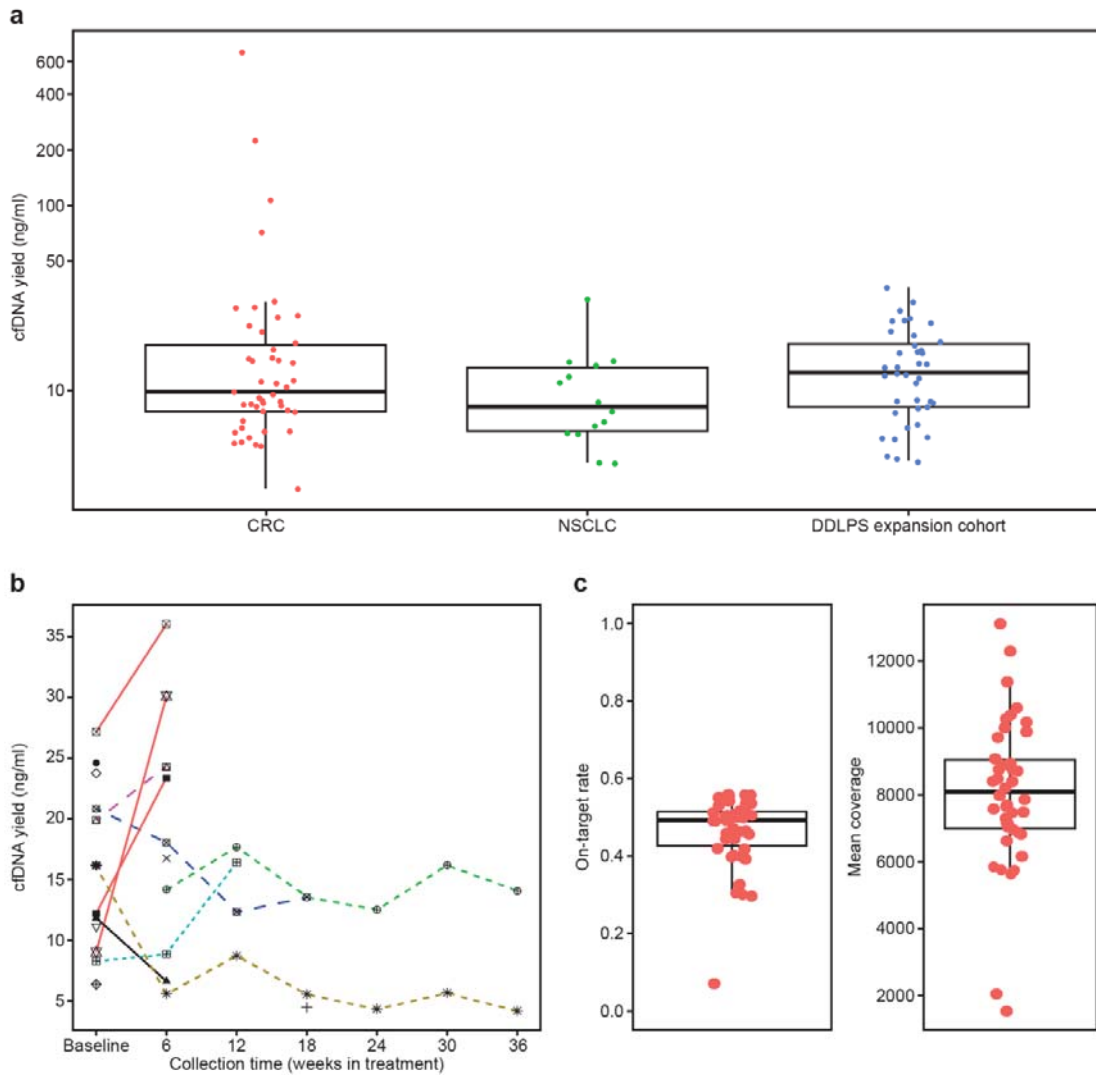
(a) Plasma cfDNA was isolated from patients participating in the DDLPS expansion cohort. The cfDNA yield was similar to that observed in the 60 matched CRC and NSCLC tumor and plasma pairs. Box plots with actual data points are shown. CRC, colorectal cancer (n = 46); DDLPS, de-differentiated liposarcoma (n = 39); NSCLC, non-small cell lung cancer (n = 14). (b) The plasma cfDNA yield from patients participating in the DDLPS expansion cohort did not consistently increase or decrease over time. (c) cfDNA sequencing QC results from the DDLPS expansion cohort suggest that most libraries met our targets of 40% on-target rate and 8000X mean sequence coverage. Box plots with actual data points are shown (n = 39).

cfDNA, cell-free DNA; CRC, colorectal cancer; DDLPS, de-differentiated liposarcoma; NSCLC, non-small cell lung cancer.

Supplementary Table 1: Summary of prior treatments, progression-free survival at 12 weeks (PFS-12w), tumor volume at baseline and tumor volume changes during treatment

Patient ID	Prior treatments	PFS-12w	Tumor vol at baseline (cm³)	base line	Tumor volume change (%)										Plasma available for this study
					6w	12w	18w	24w	30w	36w	42w	48w		
3	Adriamycin, ifosfamide, antineoplastic agents	No	10.15	0	28.94737									*TP53* VAF ≥ 1.0%
4	Doxorubicine, Endoxan	No	289.6	0	14.92537									
5		Yes	310.7	0	-8.374384	-15.27094	-19.21182	-23.64532	-24.13793	-23.64532	-24	-24		
6	Doxorubicin, trabectedin	Yes	27.3	0	-0.9771987	4.560261	1.954397	11.07492						
7	Doxorubicin	No	64.4	0	22.73099									
8	Cytoxan, adriamycin, vincristine, ifosfamide, etoposide, mesna, gemcitabine, taxotere, protein kinase inhibitors	No	385.8	0	11.45308	30.02018								
9	Doxorubicine, gemcitabine, docetaxel, trabectedin, DTIC, Gemzar, Taxotere, protein kinase inhibitors	No	27.3	0	15.53218	33.04456								
10	Gemcitabine, docetaxel, doxorubicin, ifosfamide	Yes	224.97	0	11.85468	12.81071	13.67113	19.50287	19.59847	19.59847				
11		No	347	0	23.57195									
12	Docetaxel, gemcitabine, sorafenib, antineoplastic agents.	Yes	124.8	0	14.02439	14.32927	14.63415	16.46342	16.76829	16.15854				
13	Doxorubicin, cyclophosphamide	No	2281.5	0	5.252525									
14		Yes	191	0	0	2.094241								
15	Dexamethasone, gemcitabine, docetaxel, antineoplastic agents, palbociclib	Yes	1006.3	0	7.094594	14.18919	33.10811							
16	gemcitabine, palbociclib, alisertib, vismodegib, antineoplastic agents	No	1795	0	26.6171									
17	Palbociclib, gemcitabine	No	606	0	22.76451									
18		No	80.6	0	23.73737									
19	Palbociclib	No	91.2	0	16.54135									
20	Evofosfamide, doxorubicin, gemcitabine, navelbine	No		0										

Supplementary Table 2: *TP53* probe sequences

Name	Sequence
Hs_TP53_e1_1	/5Biosg/TGTCCAGCTTTGTGCCAGGAGCCTCGCAGGGGTTGATGGGATTGGGGTTTTCCCCTCCCATGTGCTCAAGACTGGCGCTAAAAGTTTTGAGCTTCTCAAAAGTCTAGAGCCACCGTCCAG
Hs_TP53_e1_2	/5Biosg/GGAGCAGGTAGCTGCTGGGCTCCGGGGACACTTTGCGTTCGGGCTGGGAGCGTGCTTTCCACGACGGTGACACGCTTCCCTGGATTGGGTAAGCTCCTGACTGAACTTGATGAGTCCTCT
Hs_TP53_e2_1	/5Biosg/GGCCCAGGTGACCCAGGGTTGGAAGTGTCTCATGCTGGATCCCCACTTTTCCTCTTGCAGCAGCCAGACTGCCTTCCGGGTCACTGCCATGGAGGAGCCGCAGTCAGATCCTAGCGTCGA
Hs_TP53_e2_2	/5Biosg/GCCCCCTCTGAGTCAGGAAACATTTTCAGACCTATGGAAACTGTGAGTGGATCCATTGGAAGGGCAGGCCCACCACCCCCACCCCAACCCCAGCCCCCTAGCAGAGACCTGTGGGAAGCG
Hs_TP53_e2_3	/5Biosg/AAAATTCCATGGGACTGACTTTCTGCTCTTGTCTTTCAGACTTCCTGAAAACAACGTTCTGGTAAGGACAAGGGTTGGGCTGGGGACCTGGAGGGCTGGGGACCTGGAGGGCTGGGGGGC
Hs_TP53_e3_1	/5Biosg/GAGGACCTGGTCCTCTGACTGCTCTTTTCACCCATCTACAGTCCCCCTTGCCGTCCCAAGCAATGGATGATTTGATGCTGTCCCCGGACGATATTGAACAATGGTTCACTGAAGACCCAG
Hs_TP53_e3_2	/5Biosg/GTCCAGATGAAGCTCCCAGAATGCCAGAGGCTGCTCCCCCCGTGGCCCCTGCACCAGCAGCTCCTACACCGGCGGCCCCTGCACCAGCCCCCTCCTGGCCCCTGTCATCTTCTGTCCCTT
Hs_TP53_e3_3	/5Biosg/CCCAGAAAACCTACCAGGGCAGCTACGGTTTCCGTCTGGGCTTCTTGCATTCTGGGACAGCCAAGTCTGTGACTTGCACGGTCAGTTGCCCTGAGGGGCTGGCTTCCATGAGACTTCAAT
Hs_TP53_e4_1	/5Biosg/GCTGAGGTGGGAAGATCACTTGAGGCCAGGAGATGGAGGCTGCAGTGAGCTGTGATCACACCACTGTGCTCCAGCCTGAGTGACAGAGCAAGACCCTATCTCAAAAAAAAAAAAAAAAAAA
Hs_TP53_e4_2	/5Biosg/GAAAAGCTCCTGAGGTGTAGACGCCAACTCTCTCTAGCTCGCTAGTGGGTTGCAGGAGGTGCTTACGCATGTTTGTTTCTTTGCTGCCGTCTTCCAGTTGCTTTATCTGTTCACTTGTGC
Hs_TP53_e4_3	/5Biosg/CCTGACTTTCAACTCTGTCTCCTTCCTCTTCCTACAGTACTCCCCTGCCCTCAACAAGATGTTTTGCCAACTGGCCAAGACCTGCCCTGTGCAGCTGTGGGTTGATTCCACACCCCCGCC
Hs_TP53_e4_4	/5Biosg/CGGCACCCGCGTCCGCGCCATGGCCATCTACAAGCAGTCACAGCACATGACGGAGGTTGTGAGGCGCTGCCCCCACCATGAGCGCTGCTCAGATAGCGATGGTGAGCAGCTGGGGCTGGA
Hs_TP53_e5_1	/5Biosg/TTAGGTCTGGCCCCTCCTCAGCATCTTATCCGAGTGGAAGGAAATTTGCGTGTGGAGTATTTGGATGACAGAAACACTTTTCGACATAGTGTGGTGGTGCCCTATGAGCCGCCTGAGGTC
Hs_TP53_e6_1	/5Biosg/TCCTAGGTTGGCTCTGACTGTACCACCATCCACTACAACTACATGTGTAACAGTTCCTGCATGGGCGGCATGAACCGGAGGCCCATCCTCACCATCATCACACTGGAAGACTCCAGGTCA
Hs_TP53_e7_1	/5Biosg/TAGGACCTGATTTCCTTACTGCCTCTTGCTTCTCTTTTCCTATCCTGAGTAGTGGTAATCTACTGGGACGGAACAGCTTTGAGGTGCGTGTTTGTGCCTGTCCTGGGAGAGACCGGCGCA
Hs_TP53_e7_2	/5Biosg/CAGAGGAAGAGAATCTCCGCAAGAAAGGGGAGCCTCACCACGAGCTGCCCCCAGGGAGCACTAAGCGAGGTAAGCAAGCAGGACAAGAAGCGGTGGAGGAGACCAAGGGTGCAGTTATGC
Hs_TP53_e8_1	/5Biosg/CACCTTTCCTTGCCTCTTTCCTAGCACTGCCCAACAACACCAGCTCCTCTCCCCAGCCAAAGAAGAAACCACTGGATGGAGAATATTTCACCCTTCAGGTACTAAGTCTTGGGACCTCTT
Hs_TP53_e9_1	/5Biosg/TTGTAGCTAACTAACTTCAGAACACCAACTTATACCATAATATATATTTTAAAGGACCAGACCAGCTTTCAAAAAGAAAATTGTTAAAGAGAGCATGAAAATGGTTCTATGACTTTGCCT
Hs_TP53_e9_2	/5Biosg/GATACAGATGCTACTTGACTTACGATGGTGTTACTTCCTGATAAACTCGTCGTAAGTTGAAAATATTGTAAGTTGAAAATGGATTTAATACACCTAATCTAAGGAACATCATAGCTTAGC
Hs_TP53_e10_1	/5Biosg/GCTGCAGATCCGTGGGCGTGAGCGCTTCGAGATGTTCCGAGAGCTGAATGAGGCCTTGGAACTCAAGGATGCCCAGGCTGGGAAGGAGCCAGGGGGGAGCAGGGCTCACTCCAGGTGAGT
Hs_TP53_e11_1	/5Biosg/CTTCTGTCTCCTACAGCCACCTGAAGTCCAAAAAGGGTCAGTCTACCTCCCGCCATAAAAAACTCATGTTCAAGACAGAAGGGCCTGACTCAGACTGACATTCTCCACTTCTTGTTCCCC
Hs_TP53_e11_2	/5Biosg/ACTGACAGCCTCCCACCCCCATCTCTCCCTCCCCTGCCATTTTGGGTTTTGGGTCTTTGAACCCTTGCTTGCAATAGGTGTGCGTCAGAAGCACCCAGGACTTCCATTTGCTTTGTCCCG
Hs_TP53_e11_3	/5Biosg/GGGCTCCACTGAACAAGTTGGCCTGCACTGGTGTTTTGTTGTGGGGAGGAGGATGGGGAGTAGGACATACCAGCTTAGATTTTAAGGTTTTTACTGTGAGGGATGTTTGGGAGATGTAAG
Hs_TP53_e11_4	/5Biosg/AAATGTTCTTGCAGTTAAGGGTTAGTTTACAATCAGCCACATTCTAGGTAGGGGCCCACTTCACCGTACTAACCAGGGAAGCTGTCCCTCACTGTTGAATTTTCTCTAACTTCAAGGCCC
Hs_TP53_e11_5	/5Biosg/ATATCTGTGAAATGCTGGCATTTGCACCTACCTCACAGAGTGCATTGTGAGGGTTAATGAAATAATGTACATCTGGCCTTGAAACCACCTTTTATTACATGGGGTCTAGAACTTGACCCC
Hs_TP53_e11_6	/5Biosg/CTTGAGGGTGCTTGTTCCCTCTCCCTGTTGGTCGGTGGGTTGGTAGTTTCTACAGTTGGGCAGCTGGTTAGGTAGAGGGAGTTGTCAAGTCTCTGCTGGCCCAGCCAAACCCTGTCTGAC
Hs_TP53_e11_7	/5Biosg/AACCTCTTGGTGAACCTTAGTACCTAAAAGGAAATCTCACCCCATCCCACACCCTGGAGGATTTCATCTCTTGTATATGATGATCTGGATCCACCAAGACTTGTTTTATGCTCAGGGTCA
Hs_TP53_e11_8	/5Biosg/ATTTCTTTTTTCTTTTTTTTTTTTTTTTTTTCTTTTTCTTTGAGACTGGGTCTCGCTTTGTTGCCCAGGCTGGAGTGGAGTGGCGTGATCTTGGCTTACTGCAGCCTTTGCCTCCCCGGCT
Hs_TP53_e11_9	/5Biosg/CGAGCAGTCCTGCCTCAGCCTCCGGAGTAGCTGGGACCACAGGTTCATGCCACCATGGCCAGCCAACTTTTGCATGTTTTGTAGAGATGGGGTCTCACAGTGTTGCCCAGGCTGGTCTCA
Hs_TP53_e11_10	/5Biosg/AACTCCTGGGCTCAGGCGATCCACCTGTCTCAGCCTCCCAGAGTGCTGGGATTACAATTGTGAGCCACCACGTCCAGCTGGAAGGGTCAACATCTTTTACATTCTGCAAGCACATCTGCA
Hs_TP53_e11_11	/5Biosg/TTTTCACCCCACCCTTCCCCTCCTTCTCCCTTTTTATATCCCATTTTTATATCGATCTCTTATTTTACAATAAAACTTTGCTGCCACCTGTGTGTCTGAGGGGTGAACGCCAGTGCAGGC