Table S1: Complete NGS results with time points. * - Treatment naïve collection; **- End of treatment collection. NA = Not Assessed. ND = ND

Patient ID	Variant detected in ctDNA	Treatment Naïve Collection #1 and VAF	Treatment Naïve Collection #2 and VAF	On-Treatment Collection #1 and VAF	On-Treatment Collection #2 and VAF	On-Treatment Collection #3 and VAF	End-of-Treatment Collection and VAF	Post-Treatment Collection #1 and VAF	Post-Treatment Collection #2 and VAF	Post-Treatment Collection #3 and VAF	Post-Treatment Collection #4 and VAF	Post-Treatment Collection #5 and VAF	Post-Treatment Collection #6 and VAF	Post-Treatment Collection #7 and VAF	Post-Treatment Collection #8 and VAF	Post-Treatment Collection #9 and VAF	Post-Treatment Collection #10 and VAF	Post-Treatment Collection #11 and VAF	Post-Treatment Collection #12 and VAF	Post-Treatment Collection #13 and VAF	Post-Treatment Collection #14 and VAF
1							**Day 111**	**Day 280**	**Day 371**												
	TP53 R175H	NA	NA	NA	NA	NA	ND	0.67%	ND												
2		**Day 5**					**Day 48**	**Day 69**	**Day 96**	**Day 278**	**Day 327**	**Day 348**	**Day 378**	**Day 448**	**Day 503**	**Day 585**	**Day 615**	**Day 656**			
	RB1 splice site	42.27%	NA	NA	NA	NA	ND	ND	ND	8.31%	ND	ND	ND	ND	18.07%	92.01%	27.91%	46.20%			
	TP53 Q192*	38.48%	NA	NA	NA	NA	ND	ND	ND	12.60%	ND	ND	ND	ND	20.06%	93.08%	28.59%	42.78%			
	NOTCH1 V2443L	31.27%	NA	NA	NA	NA	ND	ND	ND	10.36%	ND	ND	ND	ND	22.96%	47.58%	20.79%	29.13%			
	NOTCH2 amplification	2.77X	NA	NA	NA	NA	ND	ND	ND	ND	ND	ND	ND	ND	ND	2.84X%	2.65X	2.85			
	PIK3CA amplification	3.87X	NA	NA	NA	NA	ND	ND	ND	ND	ND	ND	ND	ND	ND	3.04X%	ND	3.27			
	PTEN del	Detected	NA	NA	NA	NA	ND	ND	ND	ND	ND	ND	ND	ND	Detected	Detected	Detected	Detected			
	RB1 del	Detected	NA	NA	NA	NA	ND	ND	ND	Detected	ND	ND	ND	ND	Detected	Detected	Detected	Detected			
	TP53 del	Detected	NA	NA	NA	NA	ND	ND	ND	ND	ND	ND	ND	ND	ND	Detected	Detected	Detected			
	BRAF amplification	ND	NA	NA	NA	NA	ND	ND	ND	ND	ND	ND	ND	ND	ND	3.22X	ND	ND			
	TP53 R175H	ND	NA	NA	NA	NA	ND	ND	ND	ND	ND	0.69%	ND	ND	ND	ND	0.23%	0.22%			
3		**Day 32**		**Day 60**			**Day 109**	**Day 145**	**Day 200**	**Day 256**											
	TP53 R65*	32.20%	NA	3.27%	NA	NA	ND	ND	1.73%	75.70%											
	TP53 del	Detected	NA	ND	NA	NA	ND	ND	ND	Detected											
	RB1 del	Detected	NA	ND	NA	NA	ND	ND	ND	Detected											
4		**Day 7**		**Day 29**	**Day 49**		**Day 70**	**Day 93**	**Day 161**	**Day 231**	**Day 296**	**Day 413**	**Day 538**	**Day 651**	**Day 842**	**Day 1017**	**Day 1197**				
	MYCL1 Amplification	Detected	NA	ND	ND	NA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND				
5				**Day 57**			**Day 76**	**Day 105**	**Day 153**	**Day 272**	**Day 356**	**Day 414**	**Day 440**	**Day 475**	**Day 482**	**Day 517**	**Day 573**	**Day 628**	**Day 657**	**Day 693**	**Day 719**
	NOTCH1 R2272H	NA	NA	ND	NA	NA	ND	ND	ND	ND	0.18%	ND	ND	ND	0.16%	ND	ND	ND	ND	ND	ND
	TP53 Y234C	NA	NA	ND	NA	NA	ND	ND	ND	ND	ND	0.30%	ND	ND	ND	ND	ND	ND	ND	0.61%	ND
	NOTCH4 Splice	NA	NA	ND	NA	NA	ND	ND	ND	ND	ND	0.40%	ND	ND	ND	ND	ND	ND	ND	ND	ND
	NOTCH3 P1343A	NA	NA	ND	NA	NA	ND	ND	ND	ND	ND	0.60%	ND	ND	ND	ND	ND	ND	ND	ND	ND
6				**Day 39**			**Day 59**	**Day 153**	**Day 480**	**Day 564**	**Day 620**	**Day 690**	**Day 811**								
	TP53 G245V	NA	NA	0.24%	NA	NA	ND	ND	3.14%	ND	1.01%	11.35%	51.38%								
	RB1 splice	NA	NA	ND	NA	NA	ND	ND	1.09%	ND	ND	4.85%	44.32%								
	KIT amplification	NA	NA	ND	NA	NA	ND	ND	ND	ND	ND	ND	4.67								
	PIK3CA amplification	NA	NA	ND	NA	NA	ND	ND	ND	ND	ND	ND	3.68								
	PTEN deletion	NA	NA	ND	NA	NA	ND	ND	ND	ND	ND	ND	Detected								
	BRAF K601E	NA	NA	ND	NA	NA	0.65%	ND	ND	ND	ND	ND	ND								
	TP53 Y234C	NA	NA	ND	NA	NA	ND	ND	ND	ND	0.71%	ND	0.55%								
7							Day 49														
	TP53 K351*	NA	NA	NA	NA	NA	0.22%														
8				**Day 41**			**Day 98**	**Day 132**	**Day 223**	**Day 419**	**Day 538**	**Day 727**	**Day 909**								
	None identified	NA	NA	ND	NA	NA	ND	ND	ND	ND	ND	ND	ND								
9		Day 2		Day 34			Day 84	Day 125	Day 217	Day 692	Day 784										
	RB1 frameshift	28.59%	NA	ND	NA	NA	ND	ND	ND	ND	ND										
	TP53 E204*	26.08%	NA	ND	NA	NA	ND	ND	ND	ND	ND										
	NOTCH2 V1987A	20.35%	NA	ND	NA	NA	ND	ND	ND	ND	ND										
	TP53 F134V	17.08%	NA	ND	NA	NA	ND	ND	ND	ND	ND										
	RB1 G304*	13.43%	NA	ND	NA	NA	ND	ND	ND	ND	ND										
	PIK3CA amplification	4.01	NA	ND	NA	NA	ND	ND	ND	ND	ND										
	RB1 amplification	3.53	NA	ND	NA	NA	ND	ND	ND	ND	ND										
	PTEN deletion	ND	NA	ND	NA	NA	ND	ND	ND	ND	ND										
10		**Day 30**					**Day 99**	**Day 121**	**Day 170**	**Day 231**	**Day 294**	**Day 329**									
	RB1 Frameshift	3.65%	NA	NA	NA	NA	ND	ND	ND	ND	ND	ND									
	TP53 E258K	2.10%	NA	NA	NA	NA	ND	ND	ND	ND	ND	ND									
11		**Day 11**		**Day 60**			**Day 109**	**Day 165**	**Day 221**	**Day 249**	**Day 270**	**Day 313**	**Day 334**	**Day 363**	**Day 396**						
	PIK3CA E542K	ND	NA	ND	NA	NA	ND	ND	ND	ND	ND	ND	ND	ND	0.24%						
12		**Day 40**		**Day 82**			**Day 144**														
	TP53 V272L	3.51%	NA	0.40%	NA	NA	2.29%														
	NOTCH1 S1708L	0.19%	NA	0.20%	NA	NA	ND														
	NOTCH3 E668K	0.15%	NA	ND	NA	NA	ND														
	NOTCH3 D1481N	0.06%	NA	0.16%	NA	NA	ND														
	BRAF GAGAA30A	ND	NA	0.38%	NA	NA	ND														
	NOTCH2 S763L	ND	NA	0.18%	NA	NA	ND														
	NOTCH3 D527N	ND	NA	0.28%	NA	NA	ND														
	NOTCH E187K	ND	NA	0.14%	NA	NA	ND														
13		**Day 21**	**Day 34**	**Day 61**	**Day 89**		**Day 146**	**Day 173**	**Day 236**	**Day 453**	**Day 516**	**Day 565**	**Day 754**								
	None identified	ND	ND	ND	ND	NA	ND	ND	ND	ND	ND	ND	ND								
14		**Day 18**					**Day 49**	**Day 95**	**Day 116**	**Day 179**	**Day 214**	**Day 235**	**Day 286**	**Day 321**							
	TP53 E298*	44.40%	NA	NA	NA	NA	0.96%	ND	0.26%	8.63%	17.74%	45.28%	40.05%	56.55%							
	RB1 E313*	40.86%	NA	NA	NA	NA	0.96%	ND	0.17%	8.17%	17.33%	45.88%	43.12%	59.27%							
	PIK3CA E726K	13.05%	NA	NA	NA	NA	0.40%	ND	0.11%	3.06%	5.97%	12.20%	12.58%	16.51%							
	KIT N655H	2.36%	NA	NA	NA	NA	0.15%	ND	ND	ND	ND	ND	ND	ND							
	NOTCH4 C205*	ND	NA	NA	NA	NA	ND	ND	ND	ND	ND	0.24%	ND	ND							
	NOTCH1 P711P?	ND	NA	NA	NA	NA	ND	ND	ND	ND	ND	0.05%	0.27%	1.05%							
	PIK3CA amplification	3.56%	NA	NA	NA	NA	ND	ND	ND	ND	ND	3.66	3.67	3.52							
	PTEN deletion	Detected	NA	NA	NA	NA	ND	ND	ND	ND	Detected	Detected	Detected	Detected							
15							**Day 89**	**Day 180**	**Day 205**	**Day 224**	**Day 252**	**Day 301**	**Day 328**	**Day 357**	**Day 392**	**Day 421**	**Day 443**	**Day 469**	**Day 495**		
	TP53 C176F	NA	NA	NA	NA	NA	ND	15.05%	32.23%	33.80%	26.35%	29.13%	55.33%	ND	64.08%	89.73%	ND	ND	ND		
	RB1 T497*	NA	NA	NA	NA	NA	ND	14.75%	26.49%	35.01%	23.57%	27.27%	49.83%	ND	58.43%	83.32%	ND	ND	ND		
	NOTCH1 R353C	NA	NA	NA	NA	NA	ND	13.51%	22.48%	24.96%	18.72%	22.13%	32.51%	ND	39.19%	47.95%	ND	ND	ND		
	PTEN K147*	NA	NA	NA	NA	NA	ND	ND	ND	ND	ND	ND	ND	ND	1.16%	1.10%	ND	ND	ND		
	RB1 deletion	NA	NA	NA	NA	NA	ND	Detected	Detected	Detected	Detected	Detected	Detected	ND	Detected	Detected	ND	ND	ND		
	PTEN deletion	NA	NA	NA	NA	NA	ND	ND	Detected	Detected	Detected	Detected	Detected	ND	Detected	Detected	ND	ND	ND		
	TP53 deletion	NA	NA	NA	NA	NA	ND	ND	ND	ND	ND	ND	Detected	ND	Detected	Detected	ND	ND	ND		
	MYC amplification	NA	NA	NA	NA	NA	ND	ND	ND	ND	ND	ND	3.27	ND	3.15	3	ND	ND	ND		
	NOTCH2 amplification	NA	NA	NA	NA	NA	ND	ND	ND	ND	ND	ND	ND	ND	2.41	2.35	ND	ND	ND		
	PIK3CA amplification	NA	NA	NA	NA	NA	ND	ND	3.97	4.8	3.65	4.16	4.06	ND	4.19	4.38	ND	ND	ND		
16				**Day 18**	**Day 25**		**Day 110**	**Day 243**													
	RB1 Q736*	NA	NA	3.18%	0.31%	NA	ND	0.29%													
	TP53 Y205S	NA	NA	2.63%	0.29%	NA	ND	0.24%													
17				Day 41			Day 86	Day 133	Day 201	Day 292	Day 364	Day 411									
	RB1 L779FL	NA	NA	49.04%	NA	NA	ND	1.28%	2.03%	1.11%	ND	0.77%									
	TP53 Frameshift	NA	NA	68.03%	NA	NA	0.39%	5.62%	6.08%	5.98%	0.68%	3.47%									
	NOTCH2 R2044C	NA	NA	ND	NA	NA	ND	ND	ND	0.64%	ND	ND									
18				**Day 45**	**Day 62**	**Day 83**	**Day 119**	**Day 167**	**Day 327**	**Day 481**											
	None detected	NA	NA	ND	ND	ND	ND	ND	ND	ND											
19							**Day 83**	**Day 89**	**Day 119**	**Day 197**	**Day 232**	**Day 257**	**Day 313**	**Day 369**	**Day 425**	**Day 481**	**Day 544**				
	NOTCH3 T272M	NA	NA	NA	NA	NA	0.08%	0.37%	ND	0.06%	ND	0.11%	ND	ND	ND	ND	ND				
20		**Day 9**		**Day 30**			**Day 72**	**Day 100**	**Day 171**	**Day 252**	**Day 322**										
	PIK3CA SPLICE	5.00%	NA	ND	NA	NA	ND	ND	ND	ND	0.57%										
	RB1 Q736Q?	8.73%	NA	ND	NA	NA	ND	ND	ND	ND	ND										
	TP53 G245C	19.89%	NA	0.52%	NA	NA	ND	ND	ND	ND	0.51%										
21		**Day 20**		**Day 49**			**Day 91**	**Day 126**													
	RB1 S76*	37.81%	NA	ND	NA	NA	ND	ND													
	TP53 Y234C	33.61%	NA	ND	NA	NA	ND	ND													
	NOTCH3 R969L	31.26%	NA	ND	NA	NA	ND	ND													
	NOTCH2 Y1680L?	21.01%	NA	ND	NA	NA	ND	ND													
	NOTCH3 D1628Y	12.72%	NA	ND	NA	NA	ND	ND													
	TPP53 R248W	ND	NA	ND	NA	NA	ND	0.15%													
22		**Day 20**		**Day 34**	**Day 68**		**Day 124**	**Day 231**													
	None identified	ND	NA	ND	ND	NA	ND	ND													
23		**Day 28**					**Day 35**														
	None identified	ND	NA	NA	NA	NA	ND														