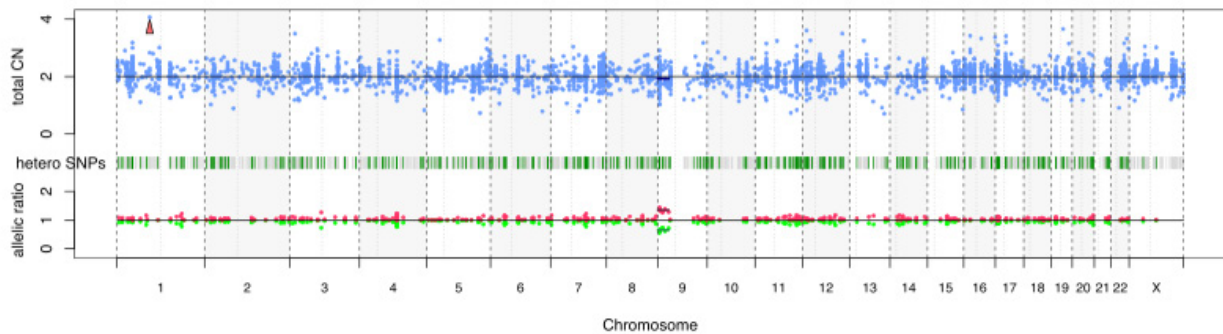
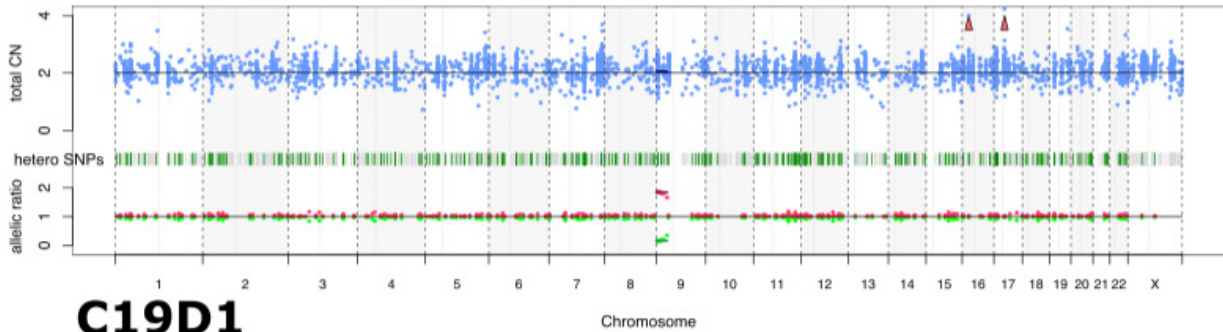


Supplementary Figure 1: An example of cnLOH, detected by CNACS algorithm. The plots show the CNACS copy number and allelic ratio output of patient for baseline (top panel) and cycle 19, day 1 after idasanutlin therapy (bottom panel) samples. As seen in both figures, in 9p region we observe a total copy number of 2, whereas a clear deviation of the alleles is observed in the allelic ratio panel of the figures. These indicate these samples harbor a cnLOH of 9p locus that includes the JAK2 gene.

Patient 1 - Baseline

9p cnLOH (JAK2)



Supplementary Table 1

Patient	Therapy TimeLine	Gene	Protein Change	VAF	Depth	Sequencing Center
Patient 1	Baseline	DNMT3A	p.P700L	7.79%	1592	MSKCC, TGD Panel (IWG)
Patient 1	C7D1	DNMT3A	p.P700L	19.90%	1533	MSKCC, TGD Panel (IWG)
Patient 1	C19D1	DNMT3A	p.P700L	27.56%	1005	MSKCC, TGD Panel (IWG)
Patient 1	Baseline	JAK2-V617F	p.V617F	83.04%	1038	MSKCC, TGD Panel (IWG)
Patient 1	C7D1	JAK2-V617F	p.V617F	55.74%	949	MSKCC, TGD Panel (IWG)
Patient 1	C19D1	JAK2-V617F	p.V617F	31.18%	417	MSKCC, TGD Panel (IWG)
Patient 1	7m_PostCessation	JAK2-V617F	p.V617F	65.43%	512	Genoptix, TGD Panel
Patient 1	Baseline	SH2B3	p.?	4.18%	1580	MSKCC, TGD Panel (IWG)
Patient 1	C7D1	SH2B3	p.?	1.81%	1604	MSKCC, TGD Panel (IWG)
Patient 1	C19D1	SH2B3	p.?	1.41%	922	MSKCC, TGD Panel (IWG)
Patient 1	Baseline	TP53	p.R248Q	0.09%	1174	MSKCC, TGD Panel (IWG)
Patient 1	C7D1	TP53	p.R248Q	1.31%	1217	MSKCC, TGD Panel (IWG)
Patient 1	C19D1	TP53	p.R248Q	2.03%	690	MSKCC, TGD Panel (IWG)
Patient 1	7m_PostCessation	TP53	p.R248Q	3.17%	978	Genoptix, TGD Panel
Patient 2	Baseline	EZH2	p.N693K	39.94%	1868	MSKCC, TGD Panel (IWG)
Patient 2	C7D1	EZH2	p.N693K	37.74%	1370	MSKCC, TGD Panel (IWG)
Patient 2	C33D1	EZH2	p.N693K	21.67%	1043	MSKCC, TGD Panel (IWG)
Patient 2	Baseline	JAK2-V617F	p.V617F	99.88%	867	MSKCC, TGD Panel (IWG)
Patient 2	C7D1	JAK2-V617F	p.V617F	98.87%	706	MSKCC, TGD Panel (IWG)
Patient 2	C33D1	JAK2-V617F	p.V617F	64.40%	545	MSKCC, TGD Panel (IWG)
Patient 2	3m-postCessation	JAK2-V617F	p.V617F	93.00%	NA	Saint-Louis Hospital, TGD Panel
Patient 2	6m-postCessation	JAK2-V617F	p.V617F	95.00%	NA	Saint-Louis Hospital, TGD Panel
Patient 2	9m-postCessation	JAK2-V617F	p.V617F	95.00%	NA	Saint-Louis Hospital, TGD Panel
Patient 2	Baseline	TP53	p.G245S	0.00%	1295	MSKCC, TGD Panel (IWG)
Patient 2	C7D1	TP53	p.G245S	0.39%	1038	MSKCC, TGD Panel (IWG)
Patient 2	C33D1	TP53	p.G245S	12.18%	944	MSKCC, TGD Panel (IWG)
Patient 2	3m-postCessation	TP53	p.G245S	12.10%	3864	Saint-Louis Hospital, TGD Panel
Patient 2	6m-postCessation	TP53	p.G245S	5.30%	2697	Saint-Louis Hospital, TGD Panel
Patient 2	9m-postCessation	TP53	p.G245S	2.00%	3466	Saint-Louis Hospital, TGD Panel
Patient 2	Baseline	TP53	p.R175H	0.20%	1517	MSKCC, TGD Panel (IWG)
Patient 2	C7D1	TP53	p.R175H	0.43%	1161	MSKCC, TGD Panel (IWG)
Patient 2	C33D1	TP53	p.R175H	6.93%	1083	MSKCC, TGD Panel (IWG)
Patient 2	Baseline	TP53	p.R248Q	0.16%	1282	MSKCC, TGD Panel (IWG)
Patient 2	C7D1	TP53	p.R248Q	0.38%	1042	MSKCC, TGD Panel (IWG)
Patient 2	C33D1	TP53	p.R248Q	1.68%	950	MSKCC, TGD Panel (IWG)
Patient 2	3m-postCessation	TP53	p.R248Q	1.20%	4033	Saint-Louis Hospital, TGD Panel
Patient 2	6m-postCessation	TP53	p.R248Q	0.80%	2826	Saint-Louis Hospital, TGD Panel
Patient 2	9m-postCessation	TP53	p.R248Q	0.00%	3637	Saint-Louis Hospital, TGD Panel
Patient 2	Baseline	TP53	p.R248W	0.00%	1279	MSKCC, TGD Panel (IWG)
Patient 2	C7D1	TP53	p.R248W	0.10%	1043	MSKCC, TGD Panel (IWG)
Patient 2	C33D1	TP53	p.R248W	2.00%	951	MSKCC, TGD Panel (IWG)
Patient 2	3m-postCessation	TP53	p.R248W	1.90%	4023	Saint-Louis Hospital, TGD Panel
Patient 2	6m-postCessation	TP53	p.R248W	1.20%	2809	Saint-Louis Hospital, TGD Panel
Patient 2	9m-postCessation	TP53	p.R248W	0.00%	3640	Saint-Louis Hospital, TGD Panel
Patient 2	Baseline	TP53	p.V172D	0.13%	1529	MSKCC, TGD Panel (IWG)
Patient 2	C7D1	TP53	p.V172D	0.25%	1200	MSKCC, TGD Panel (IWG)
Patient 2	C33D1	TP53	p.V172D	1.11%	1080	MSKCC, TGD Panel (IWG)
Patient 2	3m-postCessation	TP53	p.V172D	0.80%	4378	Saint-Louis Hospital, TGD Panel
Patient 2	6m-postCessation	TP53	p.V172D	0.00%	2981	Saint-Louis Hospital, TGD Panel
Patient 2	9m-postCessation	TP53	p.V172D	0.00%	3974	Saint-Louis Hospital, TGD Panel
Patient 3	Baseline	JAK2-V617F	p.V617F	4.30%	1023	MSKCC, TGD Panel (IWG)
Patient 3	C7D1	JAK2-V617F	p.V617F	4.47%	515	MSKCC, TGD Panel (IWG)
Patient 3	C14D1	JAK2-V617F	p.V617F	1.37%	364	MSKCC, TGD Panel (IWG)
Patient 3	14m_PostCessation	JAK2-V617F	p.V617F	20.74%	593	Genoptix, TGD Panel
Patient 3	Baseline	TP53	p.G262D	0.13%	1558	MSKCC, TGD Panel (IWG)
Patient 3	C7D1	TP53	p.G262D	2.00%	1298	MSKCC, TGD Panel (IWG)
Patient 3	C14D1	TP53	p.G262D	8.35%	1054	MSKCC, TGD Panel (IWG)
Patient 3	14m_PostCessation	TP53	p.G262D	0.00%	1	Genoptix, TGD Panel
Patient 4	Baseline	DNMT3A	p.R366H	5.39%	1503	MSKCC, TGD Panel (IWG)
Patient 4	C7D1	DNMT3A	p.R366H	4.53%	1413	MSKCC, TGD Panel (IWG)
Patient 4	C12D1	DNMT3A	p.R366H	5.62%	1744	MSKCC, TGD Panel (IWG)
Patient 4	Baseline	JAK2-V617F	p.V617F	69.21%	916	MSKCC, TGD Panel (IWG)
Patient 4	C7D1	JAK2-V617F	p.V617F	17.78%	478	MSKCC, TGD Panel (IWG)
Patient 4	C12D1	JAK2-V617F	p.V617F	12.97%	617	MSKCC, TGD Panel (IWG)
Patient 4	Baseline	TET2	p.L1398_N1403del	4.60%	1138	MSKCC, TGD Panel (IWG)
Patient 4	C7D1	TET2	p.L1398_N1403del	0.61%	1322	MSKCC, TGD Panel (IWG)
Patient 4	C12D1	TET2	p.L1398_N1403del	1.01%	1689	MSKCC, TGD Panel (IWG)
Patient 4	Baseline	TP53	p.H193Y	0.18%	1706	MSKCC, TGD Panel (IWG)
Patient 4	C7D1	TP53	p.H193Y	3.78%	1456	MSKCC, TGD Panel (IWG)
Patient 4	C12D1	TP53	p.H193Y	3.66%	1967	MSKCC, TGD Panel (IWG)
Patient 4	Baseline	TP53	p.V143M	0.29%	1715	MSKCC, TGD Panel (IWG)
Patient 4	C7D1	TP53	p.V143M	6.96%	1551	MSKCC, TGD Panel (IWG)
Patient 4	C12D1	TP53	p.V143M	8.72%	2007	MSKCC, TGD Panel (IWG)
Patient 4	Baseline	TP53	p.V203M	0.26%	1914	MSKCC, TGD Panel (IWG)
Patient 4	C7D1	TP53	p.V203M	2.43%	1608	MSKCC, TGD Panel (IWG)
Patient 4	C12D1	TP53	p.V203M	2.82%	2164	MSKCC, TGD Panel (IWG)
Patient 5	Baseline	ASXL1	p.C594fs*25	18.45%	944	MSKCC, TGD Panel (IWG)
Patient 5	C7D1	ASXL1	p.C594fs*25	2.02%	1288	MSKCC, TGD Panel (IWG)
Patient 5	Baseline	GNAS	p.R844H	17.26%	1900	MSKCC, TGD Panel (IWG)
Patient 5	C7D1	GNAS	p.R844H	46.11%	1759	MSKCC, TGD Panel (IWG)
Patient 5	Baseline	IRF1	p.W246*	1.78%	1519	MSKCC, TGD Panel (IWG)
Patient 5	C7D1	IRF1	p.W246*	0.52%	1353	MSKCC, TGD Panel (IWG)
Patient 5	Baseline	JAK2-other	p.G301W	2.21%	1808	MSKCC, TGD Panel (IWG)
Patient 5	C7D1	JAK2-other	p.G301W	0.73%	1368	MSKCC, TGD Panel (IWG)
Patient 5	Baseline	JAK2-V617F	p.V617F	82.73%	880	MSKCC, TGD Panel (IWG)
Patient 5	C7D1	JAK2-V617F	p.V617F	98.55%	619	MSKCC, TGD Panel (IWG)
Patient 5	20m_PostCessation	JAK2-V617F	p.V617F	89.94%	537	Genoptix, TGD Panel
Patient 5	Baseline	TP53	p.R248Q	1.14%	963	MSKCC, TGD Panel (IWG)
Patient 5	C7D1	TP53	p.R248Q	7.40%	932	MSKCC, TGD Panel (IWG)
Patient 5	20m_PostCessation	TP53	p.R248Q	0.21%	954	Genoptix, TGD Panel
Patient 5	Baseline	TP53	p.R248W	5.50%	964	MSKCC, TGD Panel (IWG)
Patient 5	C7D1	TP53	p.R248W	36.73%	931	MSKCC, TGD Panel (IWG)
Patient 5	20m_PostCessation	TP53	p.R248W	4.99%	621	Genoptix, TGD Panel