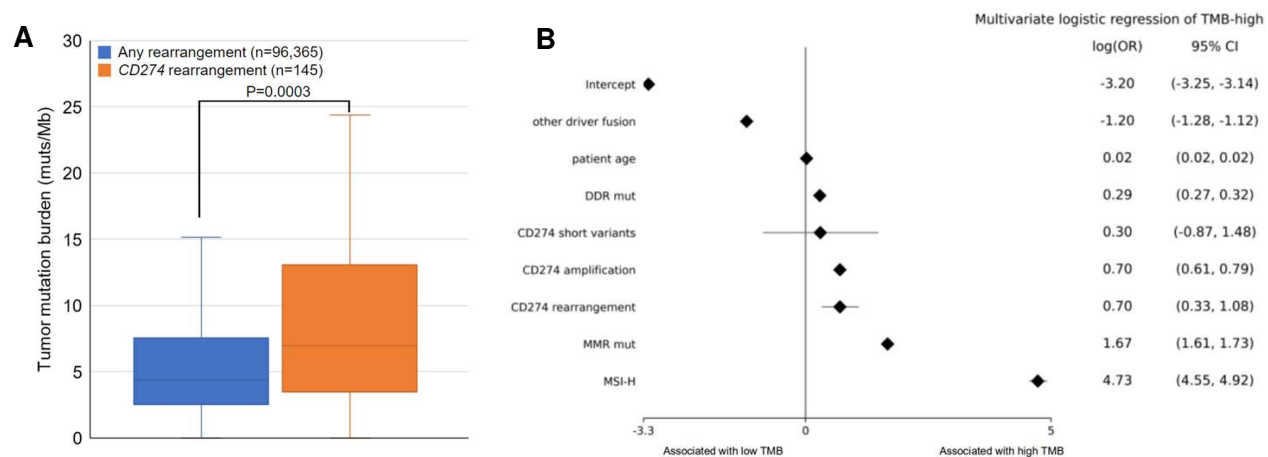
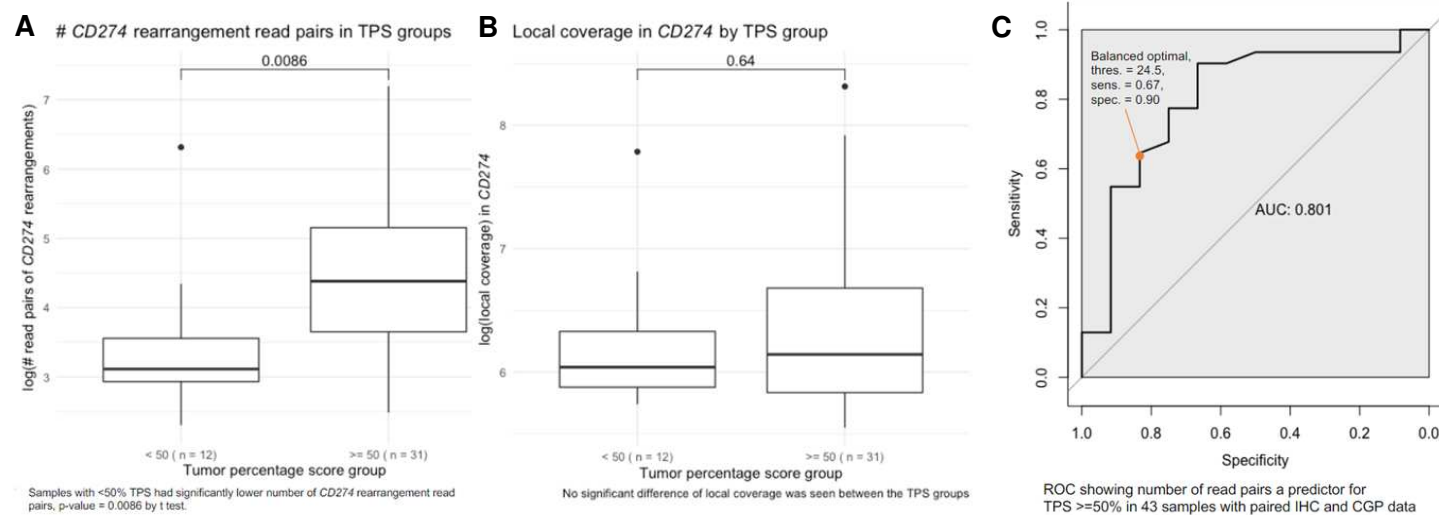


Supplementary Figure 1. Distribution of alteration types in *CD274* altered tumors.



Supplementary Figure 2. Multivariate analysis associating TMB-high with *CD274* rearrangements. A) Comparison between tumor mutational burden between samples with *CD274* rearrangement and other rearrangement. B) Multivariate analysis showing the effect of *CD274* rearrangement on TMB-high. Effect of *CD274* rearrangement on TMB was statistically independent of microsatellite status, mismatch repair mutations, DNA damage response gene mutations, other pathogenic gene fusions, other *CD274* alterations, and patient age. DDR mut = DNA damage repair mutation; MMR mut = mismatch repair mutation; MSI-H microsatellite instability high.



Supplementary Figure 3. Lower sequencing read pairs for *CD274* rearrangements associated with lower TPS scores. A) Comparison of supporting sequencing read pairs between cases with TPS<50% versus TPS≥50% for PD-L1. B) Comparison of sequencing coverage of *CD274* between cases with TPS<50% versus TPS≥50% for PD-L1. C) Receiver operating characteristic analysis for prediction of TPS≥50% with *CD274* rearrangement read pairs.

Supplementary Table 1. Demographic characteristics of CD274 rearrangement patient cohort.

		CD274 RE (N=145)	CD274 RE WT (N= 282905)	P Value
Sex: Males (%)		47.6	44.7	0.5
Median age (IQR; years)		64.5 (56.0-73.0)	63.0 (54.0-71.0)	0.2
Genomic ancestry (%)	AFR	7.5	9.6	0.5
	AMR	14.5	8.6	0.02
	EAS	2.1	3.7	0.4
	EUR	75.9	77.0	0.8
	SAS	0.0	1.0	0.4
Metastatic (%)		44.2 (50/113)	45.1 (103451/229399)	0.9

Supplementary Table 2. Association of CD274 rearranged status of the patient and the ancestry, tumor type of the patients, across the whole dataset (N=283,050). An estimate value greater than 0 denotes an association with CD274 rearrangement and an estimate lesser than 0 denotes an association with CD274 not rearranged. A binomial logistic regression model was used to derive the estimate and P value.

	Estimate	Standard Error	Z Value	P Value
(Intercept)	-22.844572	19615.98383	-0.0011646	0.99907079
AMR	0.71818308	0.373676561	1.92193773	0.05461359
EAS	-0.4334252	0.65261582	-0.6641353	0.50660373
EUR	0.20757952	0.318031551	0.65270103	0.51394904
SAS	-14.699074	856.1137088	-0.0171695	0.98630137
adenoid cystic carcinoma	0.08038488	19664.72774	4.09E-06	0.99999674
adrenal gland	16.3696599	19615.98385	0.00083451	0.99933416
angiosarcoma	0.06709009	20607.02408	3.26E-06	0.9999974
anus	0.04331561	19678.22174	2.20E-06	0.99999824
appendix	0.07546715	19659.04197	3.84E-06	0.99999694
b-cell neoplasm	0.07092389	52035.13194	1.36E-06	0.99999891
benign	0.00244464	22023.18595	1.11E-07	0.99999991
biliary	14.5672326	19615.98385	0.00074262	0.99940748
bladder	15.0753741	19615.98384	0.00076853	0.99938681
bone sarcoma	0.02528458	19855.7308	1.27E-06	0.99999898
breast	14.7236597	19615.98383	0.0007506	0.99940111
carcinoid	0.06714659	19691.43814	3.41E-06	0.99999728
central nervous system (cns) underspecified	0.1364988	34033.23084	4.01E-06	0.9999968
cervix	16.1869952	19615.98383	0.00082519	0.99934159
cholangiocarcinoma	14.0175297	19615.98385	0.0007146	0.99942983
chondrosarcoma	0.0118228	21902.64275	5.40E-07	0.99999957
cns non-glioma	0.02140883	19648.92654	1.09E-06	0.99999913
cns sarcoma	-0.0419915	21143.31844	-1.99E-06	0.99999842
colorectal (crc)	14.9890505	19615.98383	0.00076412	0.99939032

diffuse large b-cell lymphoma (dlbcl)	-0.0074586	22812.21055	-3.27E-07	0.99999974
endocrine-neuro	0.05807583	19658.33809	2.95E-06	0.99999764
endometrial	14.2518019	19615.98384	0.00072654	0.99942031
esophagus	15.8625269	19615.98383	0.00080865	0.99935479
ewing sarcoma	0.01464707	22208.24085	6.60E-07	0.99999947
eye	19.3095054	19615.98385	0.00098438	0.99921458
fallopian tube	15.895678	19615.98384	0.00081034	0.99935344
female genital	17.1565621	19615.98384	0.00087462	0.99930215
female-neuro	0.03405666	19810.16944	1.72E-06	0.99999863
germ cell	-0.0279679	19736.18409	-1.42E-06	0.99999887
gi-neuro	0.07709831	19687.63542	3.92E-06	0.99999688
gist	15.4795901	19615.98385	0.00078913	0.99937036
glioma	13.3762916	19615.98385	0.00068191	0.99945592
glomus	-0.0094818	25300.45907	-3.75E-07	0.9999997
head and neck	16.1186579	19615.98383	0.00082171	0.99934437
head and neck-neuro	0.03352533	19909.66426	1.68E-06	0.99999866
heart sarcoma	0.07092388	34045.20845	2.08E-06	0.99999834
histiocytosis	-0.0260804	21543.954	-1.21E-06	0.99999903
kaposi sarcoma	0.1705633	39303.91454	4.34E-06	0.99999654
kidney	16.1347882	19615.98383	0.00082253	0.99934371
kidney sarcoma	0.0709239	52035.13191	1.36E-06	0.99999891
leiomyosarcoma	0.03628814	19891.31511	1.82E-06	0.99999854
liver	15.2460849	19615.98385	0.00077723	0.99937986
liver sarcoma	0.07092388	52035.13194	1.36E-06	0.99999891
lung non-small cell lung carcinoma (nscic)	15.1483019	19615.98383	0.00077224	0.99938384
lung salivary gland-type	0.04795509	21934.55505	2.19E-06	0.99999826
lung sarcoma	-0.0033065	22453.72322	-1.47E-07	0.99999988
lung underspecified	0.0709239	52035.13189	1.36E-06	0.99999891
lymphoproliferative disease	-0.4396796	52035.13057	-8.45E-06	0.99999326

male genital	0.00318063	19862.8832	1.60E-07	0.99999987
male-neuro	0.07511625	19770.67602	3.80E-06	0.99999697
melanoma	14.9722734	19615.98383	0.00076327	0.999391
mesothelioma	0.03617251	19662.86029	1.84E-06	0.99999853
myelodysplastic syndrome (mds)	0.0709239	31072.5579	2.28E-06	0.99999818
myeloproliferative neoplasm (mpn)	0.0709239	39322.0161	1.80E-06	0.99999856
nk t-cell neoplasm	0.07092403	52035.12818	1.36E-06	0.99999891
non-hodgkin lymphoma	0.00304631	25337.13554	1.20E-07	0.9999999
ovary	15.182924	19615.98383	0.00077401	0.99938243
pancreas	12.8598608	19615.98385	0.00065558	0.99947692
peripheral nervous system (pns)	0.02927592	19725.09624	1.48E-06	0.99999882
peritoneum	15.7427678	19615.98385	0.00080255	0.99935966
pineal gland	-0.0305643	21547.45289	-1.42E-06	0.99999887
pituitary gland	-0.0033436	20772.9131	-1.61E-07	0.99999987
placenta	0.01546104	21166.02012	7.30E-07	0.99999942
plasma cell neoplasm	-0.0664083	27709.0188	-2.40E-06	0.99999809
prostate	14.480598	19615.98384	0.0007382	0.999411
rhabdomyosarcoma	-0.0409108	21834.15097	-1.87E-06	0.99999851
salivary gland	0.07731737	19661.54055	3.93E-06	0.99999686
skin	0.06117512	19659.70682	3.11E-06	0.99999752
skin sarcoma	0.0709239	23020.99215	3.08E-06	0.99999754
skin-neuro	0.02876567	19762.96957	1.46E-06	0.99999884
small cell	14.4507765	19615.98385	0.00073668	0.99941221
small intestine	0.08573107	19657.39659	4.36E-06	0.99999652
soft tissue sarcoma	0.03488294	19689.63792	1.77E-06	0.99999859
solitary fibrous tumor	0.09081953	21599.13737	4.20E-06	0.99999665
stomach	16.2180815	19615.98383	0.00082678	0.99934033
t-cell neoplasm	0.1500177	29134.60089	5.15E-06	0.99999589
testis	0.0510746	21687.9466	2.35E-06	0.99999812

thymus	0.0852529	19791.05743	4.31E-06	0.99999656
thymus thymoma	0.1090053	19955.25393	5.46E-06	0.99999564
thymus-neuro	0.08105214	22230.54825	3.65E-06	0.99999709
thyroid	0.03174045	19641.39564	1.62E-06	0.99999871
underspecified	0.45385565	27382.32316	1.66E-05	0.99998678
unknown primary carcinoma (cup)	15.4792489	19615.98383	0.00078911	0.99937038
unknown primary underspecified	0.05618103	19697.47271	2.85E-06	0.99999772
unknown primary-neuro	15.066761	19615.98385	0.00076809	0.99938716
urinary	0.08513147	19707.07987	4.32E-06	0.99999655
urinary-neuro	0.05137022	20288.63317	2.53E-06	0.99999798
uterus	0.09537073	19658.35048	4.85E-06	0.99999613
uterus sarcoma	0.02988947	20551.43002	1.45E-06	0.99999884

Supplementary Table 3. Characteristics of CD274 rearrangements with PD-L1 IHC scores.

Specimen ID	Age	Sex	Tumor type	Gene	Rearrangement partner gene	Gene co-ordinates	Partner gene co-ordinates	Rearrangement type	PD-L1 test	PD-L1 test score	PD-L1 test platform
1	71	Male	adrenal gland cortical carcinoma	CD274	N/A	chr9:5466758-5466912	chr9:7819480-7819610	rearrangement	Tumor Stain	0	DAKO
2	70	Female	lung small cell undifferentiated carcinoma	CD274	CFAP52	chr9:5466613-5466970	chr17:9496835-9497088	rearrangement	Tumor Stain	0	DAKO
3	48	Female	breast invasive ductal carcinoma (idc)	CD274	N/A	chr9:5467780-5467988	chr9:6511502-6511679	rearrangement	Tumor Stain	0	DAKO
4	86	Female	lung adenocarcinoma	CD274	N/A	chr9:5467646-5467904	chr9:5447459-5447604	rearrangement	Tumor Stain	0	DAKO
5	62	Male	colon adenocarcinoma (crc)	CD274	MYLK	chr9:5465373-5465731	chr3:123592212-123592310	rearrangement	Tumor Stain	1	DAKO
6	75	Male	colon adenocarcinoma (crc)	CD274	N/A	chr9:5467655-5467913	chr9:5489388-5489533	rearrangement	Tumor Stain	5	DAKO
7	40	Male	colon adenocarcinoma (crc)	CD274	N/A	chr9:5466698-5466964	chr9:5582855-5583098	rearrangement	Tumor Stain	10	DAKO
8	65	Female	lung non-small cell lung carcinoma (nsccl) (nos)	CD274	N/A	chr9:5467714-5467907	chr18:28214456-28214689	rearrangement	Tumor Stain	10	DAKO
9	76	Female	unknown primary melanoma	CD274	PTPRD	chr9:5467743-5467994	chr9:9745527-9745899	rearrangement	Tumor Stain	20	DAKO
10	81	Male	lung squamous cell carcinoma (scc)	CD274	RIC1	chr9:5466596-5466853	chr9:5731619-5731896	rearrangement	Tumor Stain	30	DAKO
11	59	Male	lung adenocarcinoma	CD274	N/A	chr9:5466689-5466956	chr9:6676528-6676754	rearrangement	Tumor Stain	30	DAKO
12	76	Male	eye lacrimal duct carcinoma	CD274	HIPK2	chr9:5466598-5467002	chr7:139280432-139281022	rearrangement	Tumor Stain	30	DAKO
13	40	Male	prostate acinar adenocarcinoma	CD274	N/A	chr9:5467714-5467957	chr9:4316216-4316474	rearrangement	Tumor Stain	50	DAKO
14	80	Male	lung adenocarcinoma	CD274	N/A	chr9:5467678-5467931	chr9:3590897-3591102	rearrangement	Tumor Stain	50	DAKO
15	69	Male	unknown primary adenocarcinoma	CD274	PLGRKT	chr9:5465378-5465661	chr9:5428506-5428752	rearrangement	Tumor Stain	60	DAKO
16	74	Male	lung non-small cell lung carcinoma (nsccl) (nos)	CD274	N/A	chr9:5465440-5465671	chr9:5479019-5479384	rearrangement	Tumor Stain	60	DAKO
17	61	Male	lung squamous cell carcinoma (scc)	CD274	N/A	chr9:5465342-5465658	chr9:5270435-5270947	rearrangement	Tumor Stain	70	DAKO
18	49	Male	head and neck squamous cell carcinoma (hnscc)	CD274	N/A	chr9:5467863-5468050	chr9:5500043-5500268	rearrangement	Tumor Stain	70	DAKO
19	32	Male	bladder carcinoma (nos)	CD274	CD274	chr9:5467755-5467993	chr9:5470492-5470836	rearrangement	Tumor Stain	70	DAKO
20	69	Male	lung non-small cell lung carcinoma (nsccl) (nos)	CD274	PTPRD	chr9:5467715-5467879	chr9:8809122-8809281	rearrangement	Tumor Stain	70	DAKO
21	82	Female	skin melanoma	CD274	PLGRKT	chr9:5466638-5466892	chr9:5399714-5400057	rearrangement	Tumor Stain	80	DAKO
22	58	Female	cervix adenocarcinoma	CD274	PLGRKT	chr9:5465459-5465671	chr9:5421268-5421464	rearrangement	Tumor Stain	80	DAKO
23	69	Female	ovary epithelial carcinoma	CD274	N/A	chr9:5467659-5467922	chr2:157519407-157519682	rearrangement	Tumor Stain	80	DAKO
24	55	Female	lung non-small cell lung carcinoma (nsccl) (nos)	CD274	N/A	chr9:5467787-5468003	chr9:5471671-5471863	rearrangement	Tumor Stain	80	DAKO
25	47	Female	ovary clear cell carcinoma	CD274	PLGRKT	chr9:5467683-5468029	chr9:5426435-5426627	rearrangement	Tumor Stain	80	DAKO
26	42	Female	cervix squamous cell carcinoma (scc)	CD274	PDCD1LG2	chr9:5466586-5466770	chr9:5543484-5543698	rearrangement	Tumor Stain	90	DAKO
27	89	Female	ovary serous carcinoma	CD274	N/A	chr9:5467642-5467900	chr6:94722507-94722813	rearrangement	Tumor Stain	90	DAKO
28	86	Female	colon adenocarcinoma (crc)	CD274	ERMP1	chr9:5467653-5467891	chr9:5789739-5790086	rearrangement	Tumor Stain	90	DAKO
29	72	Female	lung adenocarcinoma	CD274	CHMP5	chr9:5465378-5465756	chr9:33281589-33281786	rearrangement	Tumor Stain	90	DAKO
30	61	Female	lung adenocarcinoma	CD274	N/A	chr9:5467648-5467991	chr18:27844666-27844942	rearrangement	Tumor Stain	95	DAKO
31	66	Male	lung adenocarcinoma	CD274	PTPRB	chr9:5467734-5467932	chr12:70937973-70938263	rearrangement	Tumor Stain	95	DAKO
32	76	Female	lung adenocarcinoma	CD274	PLGRKT	chr9:5467639-5467873	chr9:5420662-5421059	rearrangement	Tumor Stain	95	DAKO
33	67	Female	liver hepatocellular carcinoma (hcc)	CD274	N/A	chr9:5466585-5466876	chr9:5201780-5202054	rearrangement	Tumor Stain	95	DAKO
34	78	Female	lung non-small cell lung carcinoma (nsccl) (nos)	CD274	N/A	chr9:5467638-5467928	chr9:5441513-5441883	duplication	Tumor Stain	95	DAKO
35	53	Female	ovary serous carcinoma	CD274	N/A	chr9:5467681-5467968	chr9:5198653-5198919	rearrangement	Tumor Stain	99	DAKO
36	46	Female	vagina squamous cell carcinoma (scc)	CD274	JAK2	chr9:5467855-5467998	chr9:5005621-5005795	rearrangement	Tumor Stain	99	DAKO
37	89	Female	unknown primary carcinoma (cup) (nos)	CD274	PLGRKT	chr9:5467709-5467965	chr9:5429881-5430057	rearrangement	Tumor Stain	100	DAKO
38	53	Male	esophagus adenocarcinoma	CD274	N/A	chr9:5466590-5466996	chr9:5149992-5150287	duplication	Tumor Stain	100	DAKO
39	71	Male	unknown primary adenocarcinoma	CD274	PLGRKT	chr9:5467661-5467911	chr9:5424930-5425336	rearrangement	Tumor Stain	100	DAKO
40	57	Male	kidney renal cell carcinoma	CD274	PLGRKT	chr9:5467674-5467950	chr9:5425490-5425913	rearrangement	Tumor Stain	100	DAKO

41	66Male	esophagus squamous cell carcinoma (scc)	CD274N/A	chr9:5467660-5467942chr9:5479655-5479937	rearrangement	Tumor Stain	100DAKO
42	62Male	bladder urothelial (transitional cell) carcinoma	CD274N/A	chr9:5465343-5465699chr9:8143594-8144044	rearrangement	Tumor Stain	100DAKO
43	66Female	cervix squamous cell carcinoma (scc)	CD274N/A	chr9:5467637-5467886chr9:5484662-5485082	rearrangement	Tumor Stain	100DAKO

Supplementary Table 4. Real-world patient treatment course in CD274 rearrangement positive tumors.

Patient	Age at diagnosis	Sex	Diagnosis	Stage at diagnosis	Diagnosis date	FMI test	Specimen collection date	CD274 rearrangement description	Other functional genomic alterations	TMB (mutations/Mb)	MSI status	Comments	PDL1 specimen collected date	PDL1 STATUS	Therapy	Line number	Start of therapy	Duration of therapy (days)	Event	Real-world response
1	75	M	Lung non-squamous cell lung adenocarcinoma	Stage IV B	Dec-19	Blood test	Jan-20	chr9 duplication fragment: CD274 (NM_014143): 5' rearrangement breakpoint exon 7	ATM V2951F, PIK3CA E545K, PTEN Y155C, TP53 G266V, RB1 K8*, ATM S1601fs*4, MAP2K1 F53C,	NA	UNKNOWN	NA	Jan-20	High Positive (DAKO 22C3), 50%-59%	Carboplatin, Pembrolizumab, Pemetrexed	1	Feb-20	219	Censored	PR (May 2020), PD (Aug 2020), SD (September 2020)

2	61	M	Lung squamous cell carcinoma	Stage IV	Oct-19	Tissue test	Oct-19	chr9 duplication fragment: CD274 (NM_014143); 5' rearrangement breakpoint intron 5	FGF19 CN amp, CDKN2B CN del, TP53 R290fs*55, CCND1 CN amp, FGF3 CN amp, MYC CN amp, MTAP CN del, FGF4 CN amp, RB1 CN del, PIK3CA E542K, CDKN2A CN del, BRIP1 K703fs*3X, MTD Q4284*, MTD S2834*	17.5	MSS	NA	Oct-19	High Positive (DAKO 22C3), 70%	Atezolizumab, Bevacizumab, Awwb, Carboplatin, Paclitaxel	1	Nov-19	0	Treatment discontinued due to death	NA
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3	73	F	Breast carcinoma	Stage IIB	Oct-16	Tissue test	Feb-20	chr9 inversion fragment: CD274 (NM_014143); 3' rearrangement breakpoint intron 6	TP53 E285K, FBXW7 Q242*, chr1 deletion fragment: 5'-CDC73(ex1-7 NM_024529)-CDC73(ex11-17 NM_024529) Breakpoints CDC73 exon 7, CDC73 intron 10	0	MSS	ER -ve, PR -ve, HER2 -ve	Feb-20	Positive (Ventana SP142), ICS 1%	Atezolizumab, Paclitaxel Protein-Bound	NA	Mar-20	183	Censored	NA
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4	55	F	Breast invasive ductal carcinoma (dc)	Stage IIIc	Jan-19	Blood test	Sep-19	chr9 deletion fragment: CD274 (NM_014143); 3' rearrangement breakpoint exon 7. Also seen Translocation: CD274 (NM_014143); 5' rearrangement breakpoint exon 7. Also seen chr9 deletion fragment: 5'-JAK2(ex1-4 NM_004972)-CD274(ex7-7 NM_014143)	PTEN splice site 634+1G>A, TP53 H296fs*10	NA	NA	ER -ve, PR -ve, HER2 -ve	NA	NA	Atezolizumab, Pembrolizumab, Protein-Bound	1	Aug-19	106	Censored	NA
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5	59	M	Stomach adenocarcinoma	Stage IIIc	Apr-17	Tissue test	Jul-17	chr9 duplication fragment: CD274 (NM_014143); 5' rearrangement breakpoint exon 7	PIK3CA E110del, BRCA1 K654fs*47, PBRM1 I279fs*4, ACVR1B K215fs*18, CREBBP Q97-KM12D H77fs*93, ARID1A D1850fs*33, ATRX R840fs*29, MLH1 Y684*, BRD4 P796fs*97	13.75	MSI-H	NA	NA	NA	Pembrolizumab	2	Jan-19	57	Treatment discontinued	NA
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6	44	F	Stomach adenocarcinoma	Stage IV	Nov-17	Tissue test	Dec-17	Translocation: CD274 (NM_014143): 5' rearrangement breakpoint exon 7	TP53 P278S, SMAD4 R515*, CTNNB1 G54R, PALB2 M723fs*21, CD273 M1fs*56, PIK3R1 T576fs*4	1.25	MSS	Positive for genomic Epstein Barr Virus (HRV-4)	NA	NA	Pembrolizumab	2	Jul-18	778	Censored	NA
7	77	F	Ovary serous carcinoma	Stage IIIc	Nov-12	Blood test	Apr-17	chr9 deletion fragment: CD274 (NM_014143): 3' deletion, breakpoint in exon 7 UTR	TP53 C176Y	NA	NA	NA	NA	NA	Nivolumab	NA	May-17	17	Treatment discontinued due to death	NA

8	84	F	Colon adenocarcinoma	Stage IVA	Nov-19	Tissue test	Nov-19	chr9 deletion fragment: CD274 (NM_014143); 3' rearrangement breakpoint exon 7	MVC amplification, CD274 amplification, PDCD11G2 amplification, JAK2 amplification, RAD21 amplification, PIK3R1 deletion, FBXW7 G437R, DNMT3A R882H, GATA6 E579K, CTCF E363fs*5, TP53 splice site 672+1G>T,	7.5	MSS	NA	Nov-19	High Positive (DAKO 22C3), 90%	Pembrolizumab	2	Jun-20	22	Censored	NA
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Supplementary Table 5. Genomic findings in CD274 rearrangement positive rectal adenocarcinoma.

Genomic findings based on FoundationOne CDx sequencing

Microsatellite stable

Tumor mutation burden - 16 Muts/Mb

CD274 (PD-L1) rearrangement exon 7

KRAS G12C

FBXW7 D600Y, E332*

PTEN loss exons 3-9

APC E1547*, E443*

CTNNA1 rearrangement exon 18

SMAD2 S460*

TP53 C176F
