

SUPPLEMENTARY MATERIAL

Supplementary table 1. Number of genes differentially expressed between subgroups based on objective response (n=46), MCPyV status (assessed by IHC [n=48] or PCR [n=36]), PD-L1 status (n=48), and CD8⁺ T-cell density at the IM (n=45) and TC (n=47)

Comparison	p≤.001	p≤.001 up	p≤.001 down	p≤.001 up/ FC	p≤.001 down/ FC	Adjusted p, 1% FDR	Adjusted p, 1% FDR				Adjusted p, 10% FDR	Adjusted p, 10% FDR			
							Up	Down	Up/FC	Down/FC		Up	Down	Up/FC	Down/FC
Response	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
MCPyV status by IHC	1470	741	729	578	641	1316	657	659	527	587	4179	2119	2060	1183	1510
MCPyV status by PCR	974	490	484	452	473	643	323	320	310	318	2847	1435	1412	1041	1226
PD-L1 status	5	4	1	3	1	0	0	0	0	0	0	0	0	0	0
CD8 ⁺ T-cell density at IM	25	19	6	19	4	0	0	0	0	0	0	0	0	0	0
CD8 ⁺ T-cell density at TC	517	483	34	476	10	250	247	3	247	1	995	797	198	745	47

Values given are the number of genes with a p value ≤.001 for each criterion.

Abbreviations: FC, ±1.5-fold change; FDR, false discovery rate; IHC, immunohistochemistry; IM, invasive margin; MCPyV, Merkel cell polyomavirus; PCR, polymerase chain reaction; PD-L1, programmed death ligand 1; TC, tumor center.

Supplementary table 2. Differentially expressed gene sets between responders and nonresponders

Pathway	p value	Adjusted p value	Enrichment score	Normalized enrichment score
REACTOME_INTERFERON_ALPHA_BETA_SIGNALING	.000202	.012231	0.612175	2.382347
REACTOME_INTERFERON_SIGNALING	.000202	.012231	0.491436	2.30819
REACTOME_INTERFERON_GAMMA_SIGNALING	.000405	.021896	0.514191	2.057354
KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION	.000611	.029934	0.484083	1.97057
REACTOME_ANTIVIRAL_MECHANISM_BY_IFN_STIMULATE D_GENES	.000809	.036154	0.465642	1.910754
NABA_ECM_GLYCOPROTEINS	.000199	.012231	-0.39276	-1.91453
NABA_COLLAGENS	.000397	.021896	-0.52791	-2.00587
REACTOME_INFLUENZA_LIFE_CYCLE	.000198	.012231	-0.43146	-2.01752
REACTOME_CHOLESTEROL_BIOSYNTHESIS	.000202	.012231	-0.65408	-2.03496
NABA_CORE_MATRISOME	.000199	.012231	-0.41566	-2.11868
REACTOME_FORMATION_OF_THE_TERNARY_COMPLEX_AND SUBSEQUENTLY THE 43S COMPLEX	.000198	.012231	-0.5622	-2.1641
REACTOME_ACTIVATION_OF_THE_MRNA_UPON_BINDING_OF_THE_CAP_BINDING_COMPLEX_AND_EIFS_AND_SUBSEQUENT BINDING TO 43S	.000198	.012231	-0.55359	-2.19292
REACTOME_TRANSLATION	.000198	.012231	-0.46702	-2.20515
REACTOME_SRP_DEPENDENT_COTRANSLATIONAL_PROTEIN TARGETING TO MEMBRANE	.0002	.012231	-0.51419	-2.31943
REACTOME_NONSENSE_MEDIATED_DECAY_ENHANCED_BY_THE_EXON_JUNCTION_COMPLEX	.000199	.012231	-0.54923	-2.46874
REACTOME_INFLUENZA_VIRAL_RNA_TRANSCRIPTION_AND REPLICATION	.0002	.012231	-0.56359	-2.50749
KEGG_RIBOSOME	.000199	.012231	-0.61976	-2.68182
REACTOME_3_UTR_MEDIATED_TRANSLATIONAL_REGULATION	.000199	.012231	-0.59995	-2.6849
REACTOME_PEPTIDE_CHAIN_ELONGATION	.000199	.012231	-0.63264	-2.7338

Adjusted p values were calculated using the Benjamin-Hochberg method. A positive enrichment score identifies gene sets enriched in responders (PR/CR), a negative enrichment score identifies gene sets enriched in nonresponders (SD/PD).

Abbreviations: CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

Supplementary table 3. Correlation between MHC class I gene expression and immune gene signatures

Signature	Spearman's ρ
HLA-C	0.892
HLA-F	0.861
HLA-B	0.847
MHCI	0.804
HLA-A	0.799
MHC	0.784
HLA-H	0.772
human_immune_stimulatory_checkpoint	0.766
Guinney2015.crc.TGFB2	0.765
msd.asco.2016.TcellExhaustion	0.761
msd.asco.2016.TcellAndNK	0.755
human_immune_inhibitory_checkpoint	0.731
HLA-DPB1	0.724
angelova2015.Th1	0.724
IMvigor210.APM	0.724
HLA-DRA	0.722
MHCII	0.720
Lehmann.2011.IM.up.refined	0.718
CongGroup3_IFN	0.717
MSD_Cristescu_2018_tcell_inflamed	0.714
HLA-DMA	0.711
Chaussabel2008_M3.4_ifn.sig	0.709
HLA-DMB	0.705
IMvigor210.Immune_Checkpoint	0.705
Hu2018Glucocorticoid.down	0.705
Chaussabel2008_M5.12_ifn.sig	0.704
HLA-DPA1	0.704
CongGroup1_IFN	0.701
kardos_2016_immune_supression	0.699
angelova2015.T.cells	0.696
angelova2015.Cytotoxic.cells	0.695
angelova2015.DC	0.694
bindea2013.pDC	0.694
bindea2013.BloodVessel	0.692
IFN_signature	0.684
msd.asco.2015.TCR	0.680
msd.asco.2015.Immune	0.674
HLA-L	0.669

angelova2015.Treg	0.668
S5_NK_cells_plus_Monocytes	0.667
HLA-DQB2	0.667
xcell.Macrophages M1	0.658
xcell.Macrophages	0.657
CD141.Geok.8genes	0.657
HLA-DOA	0.656
Sharma2017.Ifng.Urothelial	0.651
S1_NK_cells	0.650
DDR_NER	-0.653
IMvigor210.Nucleotide_excision_repair	-0.686
IMvigor210.Fanconi	-0.700
EC	-0.712
IMvigor210.DDR	-0.723

Abbreviations: MHC, major histocompatibility complex.

Supplementary table 4. Differentially expressed gene sets between patients with PD-L1+ and PD-L1- tumors

Pathway	p value	Adjusted p value	Enrichment score	Normalized enrichment score
KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION	.000168492	.009508658	0.57857323	2.293500381
REACTOME_LIGAND_GATED_ION_CHANNEL_TRANSPORT	.000541028	.012434531	0.681315369	2.018538526
REACTOME_INTERFERON_ALPHA_BETA_SIGNALING	.000683878	.014065429	0.506477849	1.912381697
BIOCARTA_NO2IL12_PATHWAY	.001268346	.01962806	0.653175528	1.903797359
KEGG_AUTOIMMUNE_THYROID_DISEASE	.00123348	.019507963	0.558789179	1.901785443
BIOCARTA_RHO_PATHWAY	.001163332	.018686017	-0.527669616	-1.902799265
REACTOME_ACTIVATION_OF_NF_KAPPAB_IN_B_CELLS	.000245881	.009508658	-0.457092608	-1.908408539
REACTOME_LAGGING_STRAND_SYNTHESIS	.001570563	.02172596	-0.623544051	-1.934655425
KEGG_RIBOSOME	.000249439	.009508658	-0.435802259	-1.935386139
REACTOME_FORMATION_OF_THE_TERNARY_COMPLEX_AND_SUBSEQUENTLY_THE_43S_COMPLEX	.000237982	.009508658	-0.493783597	-1.937914031
REACTOME_MUSCLE_CONTRACTION	.000238209	.009508658	-0.497393127	-1.940678339
BIOCARTA_CDMAC_PATHWAY	.00132626	.01962806	-0.661435744	-1.942488533
BIOCARTA_IL1R_PATHWAY	.000924428	.016239421	-0.545258323	-1.951131695
REACTOME_CDT1_ASSOCIATION_WITH_THE_CDC6_ORC_ORIGIN_COMPLEX	.000240906	.009508658	-0.483376853	-1.955281434
REACTOME_SYNTHESIS_OF_DNA	.000253807	.009508658	-0.441423123	-1.970524787
REACTOME_RESPONSE_TO_ELEVATED_PLATELET_CYTOSOLIC_CA2	.000247586	.009508658	-0.456329169	-1.985005887
BIOCARTA_CD40_PATHWAY	.000884173	.016230896	-0.676046897	-1.985398215
KEGG_SPLICEOSOME	.000265745	.009508658	-0.421301449	-1.993398366
REACTOME_TRANSLATION	.00026824	.009508658	-0.418046104	-2.028284805
PID_INTEGRIN2_PATHWAY	.000460511	.012427842	-0.602029417	-2.038942389
PID_UPA_UPAR_PATHWAY	.000709555	.014065429	-0.545811742	-2.042871423
REACTOME_3_UTR_MEDIATED_TRANSLATIONAL_REGULATION	.000258198	.009508658	-0.448856599	-2.066056493
KEGG_DRUG_METABOLISM_OTHER_ENZYMES	.000460511	.012427842	-0.594416509	-2.094096712
REACTOME_METABOLISM_OF_NUCLEOTIDES	.000246792	.009508658	-0.497317747	-2.09866367
PID_INTEGRIN3_PATHWAY	.000236407	.009508658	-0.555802022	-2.10013685
REACTOME_SMOOTH_MUSCLE_CONTRACTION	.000227324	.009508658	-0.641231315	-2.130502372

REACTOME_METABOLISM_OF_NON_CODING_RNA	.000239234	.009508658	-0.540872064	-2.133036624
PID_INTEGRIN_A9B1_PATHWAY	.000227324	.009508658	-0.647054336	-2.14984946
PID_FRA_PATHWAY	.000232288	.009508658	-0.58518954	-2.167712328
PID_INTEGRIN1_PATHWAY	.000246245	.009508658	-0.518915041	-2.175362112
BIOCARTA_PROTEASOME_PATHWAY	.000230894	.009508658	-0.629372138	-2.195175656
REACTOME_CHONDROITIN_SULFATE_BIOSYNTHESIS	.000224165	.009508658	-0.710721201	-2.241121085
PID_AVB3_OPN_PATHWAY	.000231107	.009508658	-0.651099487	-2.329869703

Adjusted p values were calculated using the Benjamin-Hochberg method. A positive enrichment score identifies gene sets enriched in patients with PD-L1+ tumors, a negative enrichment score identifies gene sets enriched in patients with PD-L1- tumors.

Abbreviations: PD-L1, programmed death ligand 1.

Supplementary table 5. Differentially expressed gene sets between patients with median or higher CD8⁺ T-cell density and less than median CD8⁺ T-cell density at the invasive margin

Pathway	p value	Adjusted p value	Enrichment score	Normalized enrichment score
KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION	.000161	.007722	0.655323	2.613255
REACTOME_IMMUNOREGULATORY_INTERACTIONS_BETWEEN_A_LYMPHOID_AND_A_NON_LYMPHOID_CELL	.000161	.007722	0.652793	2.576579
REACTOME_INTERFERON_ALPHA_BETA_SIGNALING	.000164	.007722	0.671745	2.55499
KEGG_GRAFT_VERSUS_HOST_DISEASE	.000169	.007722	0.716776	2.492694
REACTOME_INTERFERON_GAMMA_SIGNALING	.000163	.007722	0.622885	2.430537
PID_IL12_2PATHWAY	.000161	.007722	0.596681	2.360936
REACTOME_INTERFERON_SIGNALING	.000151	.007722	0.512755	2.343
REACTOME_ACTIVATION_OF_THE_PRE_REPLICATIVE_COMPLEX	.00017	.007722	0.618365	2.08321
BIOCARTA_NO2IL12_PATHWAY	.000522	.008795	0.700537	2.065272
REACTOME_TRNA_AMINOACYLATION	.000167	.007722	0.548292	2.012495
KEGG_AUTOIMMUNE_THYROID_DISEASE	.000508	.008787	0.586966	2.010615
KEGG_SYSTEMIC_LUPUS_ERYTHEMATOSUS	.000152	.007722	0.442031	1.985548
KEGG_ALLOGRAFT_REJECTION	.00051	.008787	0.582329	1.97917
REACTOME_STRIATED_MUSCLE_CONTRACTION	.001028	.011998	0.589409	1.952887
KEGG_AMINOACYL_TRNA_BIOSYNTHESIS	.000166	.007722	0.522264	1.910956
BIOCARTA_HDAC_PATHWAY	.0012	.013398	-0.53716	-1.90303
PID_AR_NONGENOMIC_PATHWAY	.001464	.014804	-0.51843	-1.90361
PID_ERBB1_DOWNSTREAM_PATHWAY	.000568	.009157	-0.40359	-1.90997
BIOCARTA_MTOR_PATHWAY	.002385	.018975	-0.57036	-1.9115
BIOCARTA_FMLP_PATHWAY	.000994	.011849	-0.50355	-1.9146
PID_TGFBR_PATHWAY	.001553	.014804	-0.45742	-1.9149
KEGG_NEUROTROPHIN_SIGNALING_PATHWAY	.000296	.007722	-0.39211	-1.9158
SIG_IL4RECEPTOR_IN_B_LYPHOCYTES	.0012	.013398	-0.54185	-1.91964
REACTOME_THROMBOXANE_SIGNALLING_THROUGH_TP_RECEPTOR	.002378	.018975	-0.5666	-1.9236

REACTOME_ACTIVATED_NOTCH1_TRANSMITS_SIGNAL_TO_THE_NUCLEUS	.002639	.019636	-0.5548	-1.92387
SIG_CHEMOTAXIS	.001004	.011849	-0.47987	-1.92422
PID_NOTCH_PATHWAY	.001553	.014804	-0.46106	-1.93014
REACTOME_MAP_KINASE_ACTIVATION_IN_TLR_CASCADE	.000513	.008787	-0.47323	-1.9312
REACTOME_MAPK_TARGETS_NUCLEAR_EVENTS_MEDIATED_BY_MAP_KINASES	.000971	.011811	-0.53079	-1.93286
REACTOME_SIGNALING_BY_EGFR_IN_CANCER	.000571	.009157	-0.41261	-1.94727
REACTOME_RESPIRATORY_ELECTRON_TRANSPORT_ATP_SYNTHESIS_BY_CHEMIOSMOTIC_COUPLING_AND_HEAT_PRODUCTION_BY_UNCOUPLING_PROTEINS	.000273	.007722	-0.43357	-1.95503
KEGG_ERBB_SIGNALING_PATHWAY	.000277	.007722	-0.427	-1.95515
BIOCARTA_ERK_PATHWAY	.000727	.01092	-0.54892	-1.95798
PID_AVB3_OPN_PATHWAY	.000488	.008787	-0.53457	-1.96284
PID_TRKR_PATHWAY	.000263	.007722	-0.4603	-1.9716
SA_TRKA_RECEPTOR	.001644	.015226	-0.63455	-1.97434
REACTOME_SIGNALLING_BY_NGF	.000338	.008063	-0.37621	-1.98322
PID_MAPK_TRK_PATHWAY	.000734	.01092	-0.53334	-1.9863
BIOCARTA_IGF1MTOR_PATHWAY	.001426	.014655	-0.61103	-1.99336
REACTOME_RESPIRATORY_ELECTRON_TRANSPORT	.000266	.007722	-0.46094	-1.99359
PID_INSULIN_PATHWAY	.00025	.007722	-0.50336	-2.00542
BIOCARTA_AT1R_PATHWAY	.00049	.008787	-0.5443	-2.01057
SA_PTEN_PATHWAY	.000939	.011763	-0.64951	-2.02088
PID_S1P_S1P3_PATHWAY	.000485	.008787	-0.56317	-2.03072
REACTOME_NUCLEAR_EVENTS_KINASE_AND_TRANSCRIPTION_FACTOR_ACTIVATION	.000477	.008787	-0.59445	-2.04031
PID_MET_PATHWAY	.000274	.007722	-0.45321	-2.04404
BIOCARTA_BCR_PATHWAY	.000494	.008787	-0.54535	-2.04705
PID_IGF1_PATHWAY	.000486	.008787	-0.56539	-2.05888
BIOCARTA_NDKDYNAMIN_PATHWAY	.00047	.008787	-0.66397	-2.06587
PID_ER_NONGENOMIC_PATHWAY	.000252	.007722	-0.53167	-2.0776
PID_PRL_SIGNALING_EVENTS_PATHWAY	.000713	.01092	-0.61284	-2.08061
PID_VEGFR1_PATHWAY	.000478	.008787	-0.59481	-2.08704

PID_RAS_PATHWAY	.000486	.008787	-0.57519	-2.09456
KEGG_B_CELL_RECEPTOR_SIGNALING_PATHWAY	.000272	.007722	-0.47311	-2.10723
PID_BCR_5PATHWAY	.000267	.007722	-0.48644	-2.11018
PID_P75_NTR_PATHWAY	.000268	.007722	-0.48212	-2.11066
REACTOME_NGF_SIGNALLING_VIA_TRKA_FROM_THE_PLASMA_MEMBRANE	.000298	.007722	-0.43129	-2.12376
ST_ERK1_ERK2_MAPK_PATHWAY	.000488	.008787	-0.58296	-2.14055
BIOCARTA_EIF4_PATHWAY	.000476	.008787	-0.63195	-2.14548
PID_EPHB_FWD_PATHWAY	.000249	.007722	-0.55124	-2.15119
BIOCARTA_FCER1_PATHWAY	.000248	.007722	-0.56271	-2.1707
BIOCARTA_RAS_PATHWAY	.000238	.007722	-0.64387	-2.18593
BIOCARTA_CDC42RAC_PATHWAY	.000466	.008787	-0.72132	-2.19682
BIOCARTA_PTDINS_PATHWAY	.000238	.007722	-0.66605	-2.26123
KEGG_RENAL_CELL_CARCINOMA	.000267	.007722	-0.51547	-2.27391
PID_RET_PATHWAY	.000249	.007722	-0.60001	-2.32758

Adjusted p values were calculated using the Benjamin-Hochberg method. A positive enrichment score identifies gene sets enriched in patients with median or higher CD8⁺ T-cell density, a negative enrichment score identifies gene sets enriched in patients with less than median CD8⁺ T-cell density.

Supplementary table 6. Differentially expressed gene sets between patients with median or higher CD8⁺ T-cell density and less than median CD8⁺ T-cell density at the tumor center

Pathway	p value	Adjusted p value	Enrichment score	Normalized enrichment score
REACTOME_IMMUNOREGULATORY_INTERACTIONS_BETWEEN_A_LYMPHOID_AND_A_NON_LYMPHOID_CELL	.00015	.001675	0.856952	3.173176
PID_IL12_2PATHWAY	.000149	.001675	0.841314	3.123603
KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION	.000147	.001675	0.823942	3.082774
REACTOME_INTERFERON_ALPHA_BETA_SIGNALING	.000153	.001675	0.831254	2.964752
KEGG_GRAFT_VERSUS_HOST_DISEASE	.000159	.001675	0.905795	2.961281
REACTOME_INTERFERON_GAMMA_SIGNALING	.00015	.001675	0.800318	2.934554
KEGG_AUTOIMMUNE_THYROID_DISEASE	.00016	.001675	0.897599	2.893335
KEGG_ALLOGRAFT_REJECTION	.00016	.001675	0.901104	2.88632
KEGG_NATURAL_KILLER_CELL_MEDIATED_CYTOTOXICITY	.000137	.001675	0.696815	2.867681
KEGG_HEMATOPOIETIC_CELL_LINEAGE	.000145	.001675	0.735707	2.841351
KEGG_CYTOKINE_CYTOKINE_RECEPTOR_INTERACTION	.000122	.001675	0.63147	2.832642
REACTOME_INTERFERON_SIGNALING	.000132	.001675	0.663376	2.80889
KEGG_PRIMARY_IMMUNODEFICIENCY	.000158	.001675	0.850474	2.798013
KEGG_TYPE_I_DIABETES_MELLITUS	.000157	.001675	0.832317	2.792732
REACTOME_CYTOKINE_SIGNALING_IN_IMMUNE_SYSTEM	.000121	.001675	0.612212	2.766562
KEGG_LEISHMANIA_INFECTION	.000147	.001675	0.726645	2.752867
KEGG_INTESTINAL_IMMUNE_NETWORK_FOR_IGA_PRODUCTION	.000156	.001675	0.796224	2.71923
KEGG_CELL_ADHESION_MOLECULES_CAMS	.000134	.001675	0.64779	2.707281
PID_CD8_TCR_DOWNSTREAM_PATHWAY	.000151	.001675	0.722738	2.612611
BIOCARTA_NKT_PATHWAY	.000163	.001675	0.849519	2.610758
KEGG_COMPLEMENT_AND_COAGULATION_CASCADES	.000151	.001675	0.706279	2.569821
KEGG_VIRAL_MYOCARDITIS	.000148	.001675	0.681356	2.561212
BIOCARTA_NO2IL12_PATHWAY	.000169	.001675	0.921162	2.557357
PID_IL27_PATHWAY	.000163	.001675	0.838487	2.55111
PID_IL23_PATHWAY	.000158	.001675	0.768823	2.529385

REACTOME_CHEMOKINE_RECEPTORS_BIND_CHEMOKINE_S	.000152	.001675	0.709527	2.521599
PID_CD8_TCR_PATHWAY	.000151	.001675	0.691579	2.506494
REACTOME_INNATE_IMMUNE_SYSTEM	.000123	.001675	0.5625	2.504591
PID_IL12_STAT4_PATHWAY	.00016	.001675	0.772804	2.491071
KEGG_TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY	.000141	.001675	0.62386	2.473224
PID_TCR_PATHWAY	.000147	.001675	0.651784	2.456745
KEGG_JAK_STAT_SIGNALING_PATHWAY	.000134	.001675	0.5832	2.437343
REACTOME_PD1_SIGNALING	.00017	.001675	0.897798	2.420485
BIOCARTA_IL10_PATHWAY	.000169	.001675	0.870374	2.416357
REACTOME_GENERATION_OF_SECOND_MESSENGER_MOLECULES	.000163	.001675	0.792432	2.410985
BIOCARTA_CTLA4_PATHWAY	.000169	.001675	0.864716	2.40065
BIOCARTA_IL12_PATHWAY	.000165	.001675	0.811644	2.391073
BIOCARTA_TH1TH2_PATHWAY	.000169	.001675	0.871373	2.386851
REACTOME_IL_3_5_AND_GM-CSF_SIGNALING	.000157	.001675	0.703983	2.385936
REACTOME_THE_ROLE_OF_NEF_IN_HIV1_REPLICATION_AND_DISEASE_PATHOGENESIS	.000161	.001675	0.762485	2.382704
REACTOME_ADAPTIVE_IMMUNE_SYSTEM	.00011	.001675	0.494256	2.373253
KEGG_LYSOSOME	.000135	.001675	0.569393	2.359652
KEGG_ASTHMA	.000166	.001675	0.813597	2.359057
REACTOME_TCR_SIGNALING	.000153	.001675	0.660841	2.356958
PID_INTEGRIN2_PATHWAY	.000163	.001675	0.764953	2.350868
REACTOME_SIGNALING_BY_ILS	.000138	.001675	0.578285	2.348734
ST_T_CELL_SIGNAL_TRANSDUCTION	.000154	.001675	0.669371	2.34614
BIOCARTA_DC_PATHWAY	.000169	.001675	0.855622	2.343704
REACTOME_COSTIMULATION_BY_THE_CD28_FAMILY	.00015	.001675	0.629857	2.332273
BIOCARTA_COMP_PATHWAY	.000169	.001675	0.85028	2.329073
BIOCARTA_NKCELLS_PATHWAY	.000166	.001675	0.802803	2.327757
REACTOME_COMPLEMENT_CASCADE	.000164	.001675	0.777248	2.315421
KEGG_T_CELL_RECEPTOR_SIGNALING_PATHWAY	.000137	.001675	0.567459	2.310716
BIOCARTA_IL22BP_PATHWAY	.00017	.001675	0.856906	2.310239

KEGG_CHEMOKINE_SIGNALING_PATHWAY	0.000126	.001675	0.525937	2.305414
PID_NFAT_TFPATHWAY	.000156	.001675	0.66873	2.295864
PID_IL4_2PATHWAY	.00015	.001675	0.615357	2.278584
REACTOME_IL_RECEPTOR_SHC_SIGNALING	.000163	.001675	0.754892	2.270147
REACTOME_RIG_I_MDA5_MEDIATED_INDUCION_OF_IFN_ALPHA_BETA_PATHWAYS	.00015	.001675	0.614599	2.267089
REACTOME_ANTIGEN_PRESENTATION_FOLDING_ASSEMBLY_AND_PEPTIDE_LOADING_OF_CLASS_I_MHC	.000166	.001675	0.781377	2.265633
KEGG_CYTOSOLIC_DNA_SENSING_PATHWAY	.000156	.001675	0.653425	2.243322
BIOCARTA_IL7_PATHWAY	.000169	.001675	0.806483	2.238983
PID_CXCR4_PATHWAY	.000138	.001675	0.547744	2.217357
PID_IL2_STAT5_PATHWAY	.000161	.001675	0.701352	2.210264
REACTOME_NEF_MEDIATES_DOWN_MODULATION_OF_CELL_SURFACE_RECEPTORS_BY_RECRUITING_THEM_TO_CLATHRIN_ADAPTERS	.000166	.001675	0.760419	2.204866
NABA_ECM_REGULATORS	.000125	.001675	0.499433	2.203032
REACTOME_INTEGRIN_CELL_SURFACE_INTERACTIONS	.000144	.001675	0.568437	2.201686
REACTOME_NEGATIVE_REGULATORS_OF_RIG_I_MDA5_SIGNALING	.00016	.001675	0.68516	2.194632
SA_MMP_CYTOKINE_CONNECTION	.00017	.001675	0.813581	2.193434
BIOCARTA_CSK_PATHWAY	.000166	.001675	0.755081	2.189388
REACTOME_DOWNSTREAM_TCR_SIGNALING	.000159	.001675	0.672913	2.186522
PID_PI3KCI_PATHWAY	.000153	.001675	0.612945	2.186132
BIOCARTA_LAIR_PATHWAY	.00017	.001675	0.81037	2.184777
KEGG_SYSTEMIC_LUPUS_ERYTHEMATOSUS	.000134	.001675	0.522735	2.176884
REACTOME_ANTIGEN_PROCESSING_CROSS_PRESENTATION	.000146	.001675	0.566807	2.170943
BIOCARTA_IL2RB_PATHWAY	.000157	.001675	0.643649	2.169162
PID_INTEGRIN_CS_PATHWAY	.000162	.001675	0.694644	2.150206
REACTOME_CLASS_A1_RHODOPSIN_LIKE_RECEPTORS	.000121	.001675	0.475414	2.145455
KEGG_B_CELL_RECEPTOR_SIGNALING_PATHWAY	.000145	.001675	0.556249	2.144445
BIOCARTA_INFLAM_PATHWAY	.000166	.001675	0.732899	2.125069
KEGG_RIG_I_LIKE_RECEPTOR_SIGNALING_PATHWAY	.000151	.001675	0.579982	2.10203

REACTOME_IL_2_SIGNALING	.000157	.001675	0.625209	2.097808
SA_CASPASE_CASCADE	.000168	.001675	0.721868	2.063028
REACTOME_TRAF6_MEDIATED_IRF7_ACTIVATION	.000169	.001675	0.741853	2.059555
SIG_PIP3_SIGNALING_IN_B_LYMPHOCYTES	.000157	.001675	0.615142	2.054797
REACTOME_CELL_SURFACE_INTERACTIONS_AT_THE_VASCULAR_WALL	.000142	.001675	0.519953	2.045993
BIOCARTA_CASPASE_PATHWAY	.000163	.001675	0.674864	2.029484
SIG_BCR_SIGNALING_PATHWAY	.000154	.001675	0.576658	2.028847
REACTOME_SIGNALING_BY_RHO_GTPASES	.000137	.001675	0.492745	2.02532
REACTOME_GPVI_MEDIATED_ACTIVATION_CASCADE	.00016	.001675	0.62831	2.025306
PID_TXA2PATHWAY	.00015	.001675	0.542387	1.988789
PID_PTP1B_PATHWAY	.000152	.001675	0.555124	1.988189
PID_AMB2_NEUTROPHILS_PATHWAY	.000156	.001675	0.578179	1.974571
REACTOME_GPCR_LIGAND_BINDING	.000116	.001675	0.422479	1.96325
REACTOME_PEPTIDE_LIGAND_BINDING_RECEPTORS	.000131	.001675	0.457857	1.952069
BIOCARTA_TOB1_PATHWAY	.000339	.002553	0.7016	1.947802
REACTOME_GLYCOSPHINGOLIPID_METABOLISM	.000158	.001675	0.589777	1.940334
BIOCARTA_STATHMIN_PATHWAY	.000168	.001675	0.686821	1.937238
KEGG_NOD_LIKE_RECEPTOR_SIGNALING_PATHWAY	.000298	.002447	0.52	1.930638
PID_IL6_7_PATHWAY	.000308	.002447	0.549981	1.927678
ST_B_CELL_ANTIGEN_RECEPTOR	.000314	.002454	0.568009	1.925096
PID_BCR_5PATHWAY	.000147	.001675	0.509788	1.921523
KEGG_LEUKOCYTE_TRANSENDOTHELIAL_MIGRATION	.000274	.002447	0.468669	1.920253
PID_IL2_1PATHWAY	.000302	.002447	0.525267	1.911203
NABA_ECM_AFFILIATED	.000131	.001675	0.449359	1.911192
PID_FCER1_PATHWAY	.000298	.002447	0.514685	1.910906
PID_EPO_PATHWAY	.000476	.00315	0.583588	1.907901
REACTOME_GPCR_DOWNSTREAM_SIGNALING	.000112	.001675	0.400254	1.907766
REACTOME_ER_PHAGOSOME_PATHWAY	.0003	.002447	0.517875	1.905251
REACTOME_NUCLEOTIDE_LIKE_PURINERGIC_RECEPTORS	.00051	.003308	0.706361	1.904365
BIOCARTA_IL2_PATHWAY	.000329	.00252	0.645293	1.90101

REACTOME_RESPIRATORY_ELECTRON_TRANSPORT_ATP_SYNTHESIS_BY_CHEMIOSMOTIC_COUPLING_AND_HEAT_PRODUCTION_BY_UNCOUPLING_PROTEINS	.000329	.00252	-0.43015	-1.90544
KEGG_OOCYTE_MEIOSIS	.000373	.002598	-0.40821	-1.90848
REACTOME_MITOTIC_G1_G1_S_PHASES	.000403	.002753	-0.3981	-1.91703
REACTOME_TRANSCRIPTION	.000503	.003284	-0.38115	-1.94656
REACTOME_G1_S_SPECIFIC_TRANSCRIPTION	.002197	.012106	-0.63917	-1.94934
REACTOME_DEPOSITION_OF_NEW_CENPA_CONTAINING_NUCLEOSOMES_AT_THE_CENTROMERE	.000305	.002447	-0.46741	-1.95185
REACTOME_DNA_REPAIR	.000369	.002598	-0.42144	-1.95652
REACTOME_G0_AND_EARLY_G1	.00129	.007348	-0.59565	-1.97164
REACTOME_KINESINS	.00129	.007348	-0.60062	-1.98811
REACTOME_RNA_POL_II_PRE_TRANSCRIPTION_EVENTS	.000295	.002447	-0.48719	-1.98898
REACTOME_CLEAVAGE_OF_GROWING_TRANSCRIPT_IN_THE_TERMINATION_REGION	.000563	.003606	-0.51803	-1.99411
REACTOME_CHROMOSOME_MAINTENANCE	.000372	.002598	-0.42726	-2.0165
KEGG_SPLICEOSOME	.000391	.00271	-0.42395	-2.0216
REACTOME_CYCLIN_A_B1_ASSOCIATED_EVENTS_DURIN_G2_M_TRANSITION	.000729	.004445	-0.6987	-2.04576
REACTOME_MRNA_SPLICING	.000369	.002598	-0.44595	-2.07031
REACTOME_LATE_PHASE_OF_HIV_LIFE_CYCLE	.000352	.002598	-0.45251	-2.08021
REACTOME_MRNA_PROCESSING	.000446	.003009	-0.42277	-2.08392
REACTOME_ACTIVATION_OF_THE_PRE_REPLICATIVE_COMPLEX	.000265	.002447	-0.59353	-2.08407
REACTOME_RNA_POL_II_TRANSCRIPTION_PRE_INITIATION_AND_PROMOTER_OPENING	.000276	.002447	-0.55816	-2.11087
REACTOME_PROCESSING_OF_CAPPED_INTRON_CONTAINING_PRE_MRNA	.000411	.00279	-0.43734	-2.11805
REACTOME_CHOLESTEROL_BIOSYNTHESIS	.000251	.002445	-0.67892	-2.16463
PID_AURORA_B_PATHWAY	.000276	.002447	-0.57318	-2.1677
PID_FANCONI_PATHWAY	.000287	.002447	-0.55295	-2.17978
REACTOME_RECRUITMENT_OF_MITOTIC_CENTROSOME_PROTEINS_AND_COMPLEXES	.00031	.002447	-0.52731	-2.21354
KEGG_CELL_CYCLE	.000394	.002713	-0.46382	-2.21439

REACTOME_ACTIVATION_OF_ATR_IN_RESPONSE_TO_REPLICATION_STRESS	.000274	.002447	-0.61329	-2.25731
PID_PLK1_PATHWAY	.000281	.002447	-0.57841	-2.26151
REACTOME_E2F_MEDIATED_REGULATION_OF_DNA_REPLICATION	.000269	.002447	-0.63119	-2.27583
KEGG_BASAL_TRANSCRIPTION_FACTORS	.000269	.002447	-0.63484	-2.289
REACTOME_RNA_POL_II_TRANSCRIPTION	.000352	.002598	-0.4989	-2.29347
REACTOME_G2_M_CHECKPOINTS	.000279	.002447	-0.60646	-2.3237
REACTOME_LOSS_OF_NLP_FROM_MITOTIC_CENTROSOMES	.000297	.002447	-0.56824	-2.3255
REACTOME_MITOTIC_M_M_G1_PHASES	.000452	.003029	-0.48754	-2.42408
REACTOME_MITOTIC_G2_G2_M_PHASES	.000325	.00252	-0.55661	-2.45021
REACTOME_DNA_REPLICATION	.000479	.00315	-0.48528	-2.45461
REACTOME_CELL_CYCLE	.000848	.005025	-0.4501	-2.4821
REACTOME_CELL_CYCLE_MITOTIC	.000672	.004172	-0.47804	-2.56776
REACTOME_MITOTIC_PROMETAPHASE	.000332	.002524	-0.61104	-2.71735

Adjusted p values were calculated using the Benjamin–Hochberg method. A positive enrichment score identifies gene sets enriched in patients with median or higher CD8⁺ T-cell density, a negative enrichment score identifies gene sets enriched in patients with less than median CD8⁺ T-cell density.

Supplementary table 7. Genomic changes in MHC class I HLA genes from evaluable patients (n=52)

Patient index	Copy number	LOH p value ^a	HLA-A CPM	Response
1	0	.03916	4.868469	PD
2	3	.31531	9.497004	PD
3	2	.521523	26.80647	PD
4	2	.367322	28.56273	CR
5	3	1.48E-14	29.3798	PR
6	0	.426004	38.31475	PR
7	4	.180245	38.60858	SD
8	2	.00332	43.1118	CR
9	2	.745383	46.26426	PR
10	2	.027803	47.46753	CR
11	2	3.19E-05	48.14221	PD
12	2	.628389	55.58881	PD
13	2	.258372	56.24426	PD
14	2	NA	60.98662	CR
15	3	.000117	61.18176	PR
16	2	.373787	63.09015	PD
17	2	.486616	64.89194	PD
18	3	1.45E-05	67.00792	CR
19	3	NA	70.2086	PR
20	3	9.13E-05	73.11615	PR
21	2	.074355	90.63647	PD
22	2	.898439	90.993	PR
23	2	.056999	91.27235	PD
24	2	.206808	95.88008	PD
25	4	NA	99.93093	NE
26	2	.767739	101.437	NE
27	2	.215022	105.4922	PD
	13	.215022	105.4922	PD
	2	.215022	105.4922	PD

28	6	.360161	106.4498	CR
29	2	.001388	111.1427	SD
30	3	1.4E-21	128.4024	PD
31	11	.964307	136.0562	PD
32	2	.05865	138.9101	NE
33	4	.531189	141.7456	SD
34	3	5.04E-12	148.949	PD
35	2	.779579	154.931	PR
36	2	NA	155.1063	PR
37	3	3.86E-06	158.5355	PR
38	2	.125364	169.9979	PD
39	5	4.23E-08	195.1644	PD
40	2	.015731	195.6263	PR
41	2	.148086	197.9184	PR
42	2	.114746	212.1019	SD
43	8	.856964	233.8113	PD
44	3	.000365	234.2959	CR
45	3	.027023	239.721	NE
46	5	.074121	262.0522	CR
47	2	.242573	277.4213	PD
48	2	.0017	368.4451	PD
49	2	.122983	620.7722	CR
50	4	.967667	943.726	PD
51	2	.465484	NA	PR
52	2	.001743	NA	PR

Abbreviations: CPM, counts per million; CR, complete response; LOH, loss of heterozygosity; MHC, major histocompatibility complex; NA, not available; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

^aRaw values.

Supplementary table 8. Gini index ranking of relevant genes to classify MCPyV+ tumors

Gene name	Gini index
ZSCAN1	0.122285714
SEMA6C	0.121714286
ATF7IP2	0.120857143
NOA1	0.119714286
FRY	0.119142857
AMIGO2	0.106857143
TTC12	0.104285714
NPHS1	0.098571429
GCNT2	0.096571429
EIF3M	0.095428571
GH2	0.094857143
SLC4A8	0.094857143
LINC00577	0.094285714
RUNDC3A	0.090285714
LOC100996342	0.09
SVILP1	0.09
LONRF2	0.087428571
ABCG8	0.087428571
ZNF778	0.083428571
RFXAP	0.081428571
NEUROD2	0.08
KCNIP3	0.077714286
TRIM17	0.077142857
CHST9	0.076857143
RPL5	0.071428571
LRP1B	0.069428571
LOC100996634	0.069142857
RTN4RL1	0.068285714
CCDC151	0.068
ATP8B3	0.066
CCDC162P	0.066
ZNF835	0.065428571
RNF183	0.065428571
AQP10	0.065142857
C2orf61	0.064857143
SHISA9	0.064857143
CCNA1	0.063714286
SYTL3	0.063142857
SLC25A19	0.063142857
TAAR6	0.062857143

COL8A1	0.059142857
ARHGEF28	0.056
CD47	0.055428571
RFC3	0.055428571
RNF128	0.054571429
SLC29A1	0.054285714
DLEU1	0.053142857
ECHDC3	0.052857143
TMEM2	0.052285714
MAS1	0.052285714
CA9	0.052285714
HHIP	0.052285714
IL1RAPL1	0.052
ADAMTS19	0.051714286
TEX14	0.051714286
SPIB	0.051714286
MIR604	0.051142857
PRODH2	0.050857143
SRSF8	0.05
LINC00173	0.048857143
FAM184B	0.048857143
RPL39L	0.047714286
TAAR8	0.046571429
LINC00663	0.045142857
SLC7A4	0.044857143
RANBP17	0.041714286
CD248	0.041428571
NT5DC3	0.041428571
NUFIP1	0.041428571
PRDM5	0.041428571
ITGA6	0.041428571
EIF4B	0.040571429
NBEA	0.040285714
NPR2	0.040285714
PLCH1	0.040285714
TRPM2	0.039428571
C1orf95	0.039428571
RABEPK	0.039428571
RAP1GAP	0.039428571
SCN2A	0.039428571
MBLAC2	0.038857143
EEF1B2	0.038857143
RBP1	0.038857143

ZNF667	0.038
PLEKHF2	0.038
MYRF	0.037428571
TEAD2	0.037142857
LIN28B	0.037142857
SCG5	0.036857143
KBTBD6	0.036857143
STIL	0.033428571
FAM195A	0.032857143
TM7SF3	0.027714286
APC2	0.027714286
CREM	0.027714286
FOLR1	0.027714286
LOC101929303	0.027428571
ABCA2	0.026857143
PROK2	0.026571429
ABCG5	0.025714286
KIRREL2	0.025714286
TPRXL	0.025428571
EPHA4	0.025428571
SCGB2A1	0.025428571
ARHGEF10	0.025142857
NANP	0.024285714
USH1C	0.023428571
PALM2	0.023428571
CHST15	0.022857143
MET	0.020571429
PHLDA1	0.019714286
LOC101059957	0.014
SVIL	0.014
EML6	0.014
CSDC2	0.013714286
PCDH19	0.013714286
FBXW12	0.013714286
RD3	0.013714286
LOC101929726	0.012857143
SNX32	0.012857143
ABCB9	0.012857143
ZAN	0.012857143
EDA2R	0.012857143
PPP2R3A	0.012857143
SALL1	0.012857143
LOC101928664	0.011428571

<i>SYCP2</i>	0.011428571
<i>TG</i>	0.011428571
<i>XKR9</i>	0.011428571
<i>CACNA1E</i>	0.009428571
<i>SLC35D3</i>	0.009428571
<i>GPBAR1</i>	0.006857143
<i>LOC101929658</i>	0
<i>MF12-AS1</i>	0
<i>ZNF667-AS1</i>	0
<i>BMF</i>	0
<i>BMPER</i>	0
<i>MLK7-AS1</i>	0
<i>CDKN2B</i>	0
<i>GOT2</i>	0
<i>GRIK4</i>	0
<i>KALRN</i>	0

A high Gini index indicates more relevant genes.

Abbreviations: MCPyV, Merkel cell polyomavirus.

Supplementary table 9. Treatment-related adverse events (any grade in $\geq 10\%$ of patients or grade ≥ 3 in any patient)

Treatment-related adverse event (N=116)	Any grade	Grade ≥ 3
Any treatment-related adverse event, n (%)	94 (81.0)	21 (18.1)
Fatigue	24 (20.7)	1 (0.9)
Asthenia	16 (13.8)	0
Pruritus	15 (12.9)	1 (0.9)
IRR ^a	13 (11.2)	1 (0.9)
Chills	12 (10.3)	0
Lipase increased	6 (5.2)	4 (3.4)
Decreased appetite	6 (5.2)	1 (0.9)
ALT increased	5 (4.3)	1 (0.9)
Amylase increased	3 (2.6)	3 (2.6)
AST increased	2 (1.7)	1 (0.9)
Autoimmune nephritis	1 (0.9)	1 (0.9)
Autoimmune neuropathy	1 (0.9)	1 (0.9)
Cholangitis	1 (0.9)	1 (0.9)
Colitis	1 (0.9)	1 (0.9)
Dehydration	1 (0.9)	1 (0.9)
Dermatitis psoriasiform	1 (0.9)	1 (0.9)
Gait disturbance	1 (0.9)	1 (0.9)
Liver function test increased	1 (0.9)	1 (0.9)
Paraneoplastic encephalomyelitis	1 (0.9)	1 (0.9)
Paraneoplastic syndrome	1 (0.9)	1 (0.9)
Polyneuropathy in malignant disease	1 (0.9)	1 (0.9)
Troponin increased	1 (0.9)	1 (0.9)
Tumor lysis syndrome	1 (0.9)	1 (0.9)
Any IRR^b	34 (29.3)	1 (0.9)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; IRR, infusion-related reaction.

^aTreatment-related IRRs based on the single Medical Dictionary for Regulatory Activities preferred term.

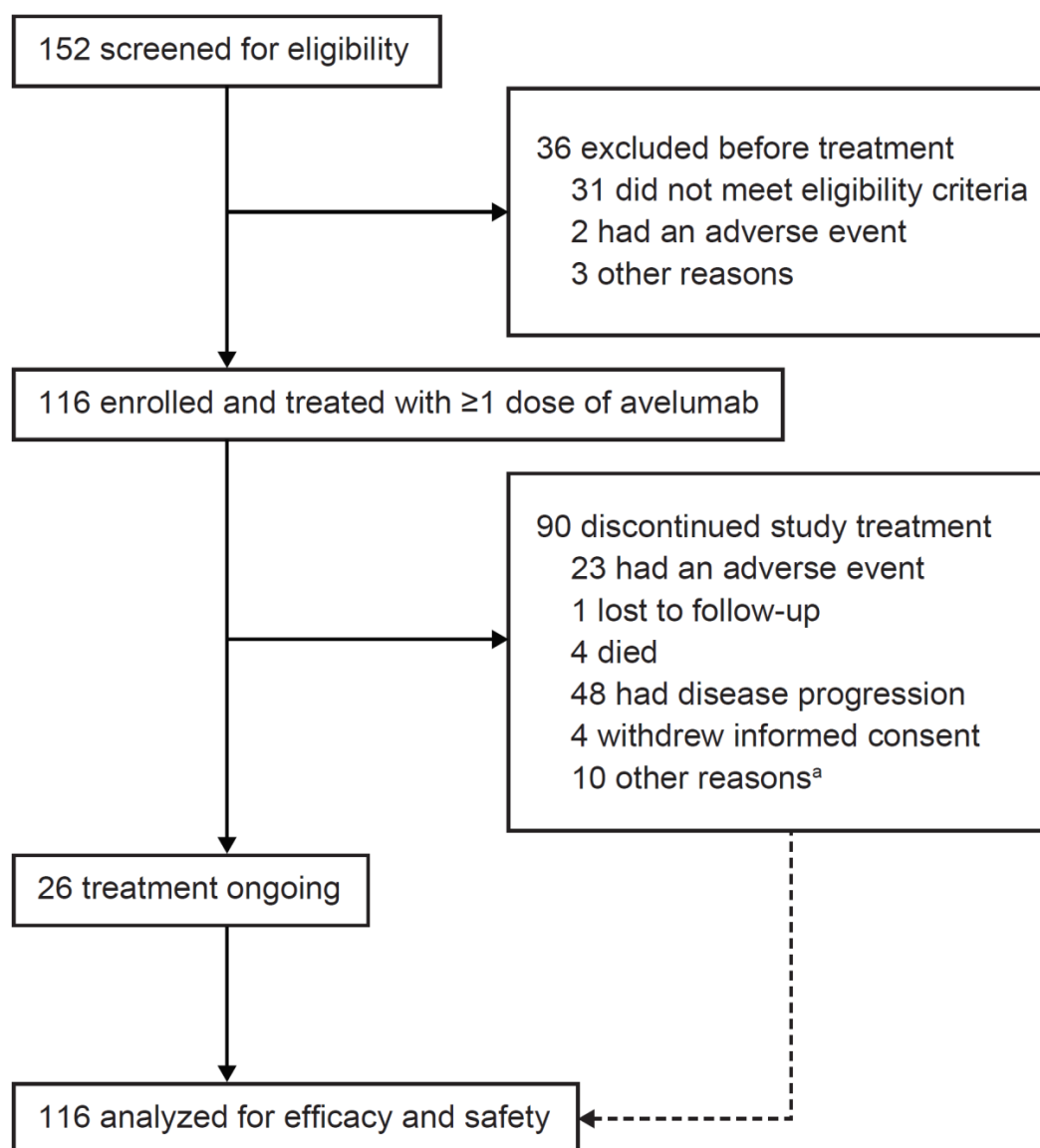
^bIncludes adverse events (irrespective of relatedness) categorized as IRR, drug hypersensitivity, or hypersensitivity reaction that occurred on the day of or the day after infusion, in addition to signs/symptoms of IRR that occurred on day of infusion (during or after the infusion) that resolved on the day of onset or the next day.

Supplementary table 10. Immune-related adverse events (any grade in $\geq 5\%$ of patients or grade ≥ 3 in any patient)

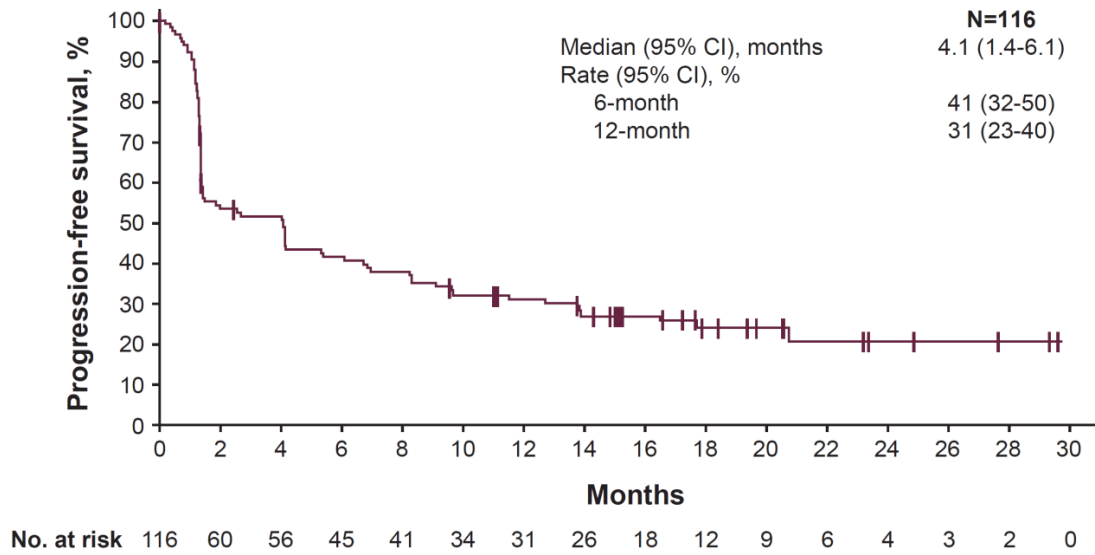
irAE (N=116)	Any grade	Grade ≥ 3
Any irAE, n (%)^a	35 (30.2)	7 (6.0)
Pruritus	9 (7.8)	1 (0.9)
Rash maculopapular	6 (5.2)	0
ALT increased	3 (2.6)	1 (0.9)
Autoimmune nephritis	1 (0.9)	1 (0.9)
Autoimmune neuropathy	1 (0.9)	1 (0.9)
Dermatitis psoriasiform	1 (0.9)	1 (0.9)
Diabetes mellitus	1 (0.9)	1 (0.9)
Liver function test increased	1 (0.9)	1 (0.9)

Abbreviations: ALT, alanine aminotransferase; irAE, immune-related adverse event.

^aBased on a prespecified list of Medical Dictionary for Regulatory Activities preferred terms followed by comprehensive medical review using predefined criteria.

Supplementary figure 1. Trial profile.

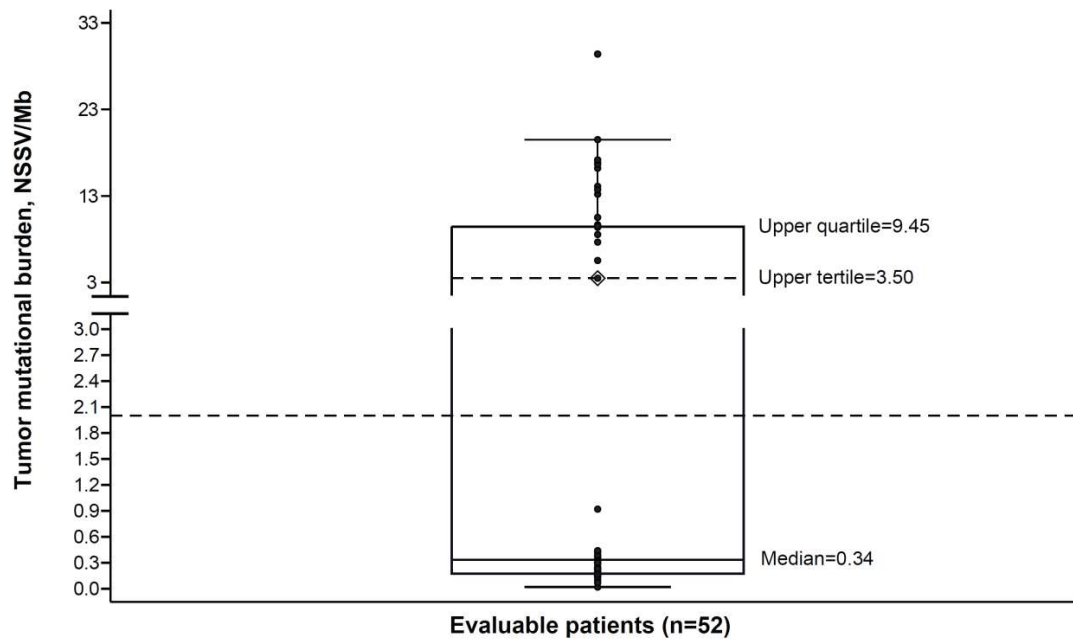
^aIncludes complete response (n=3), patient and investigator's decision (n=3), patient's decision (n=2), sponsor's decision (n=1), and travel logistics and convenience (n=1).

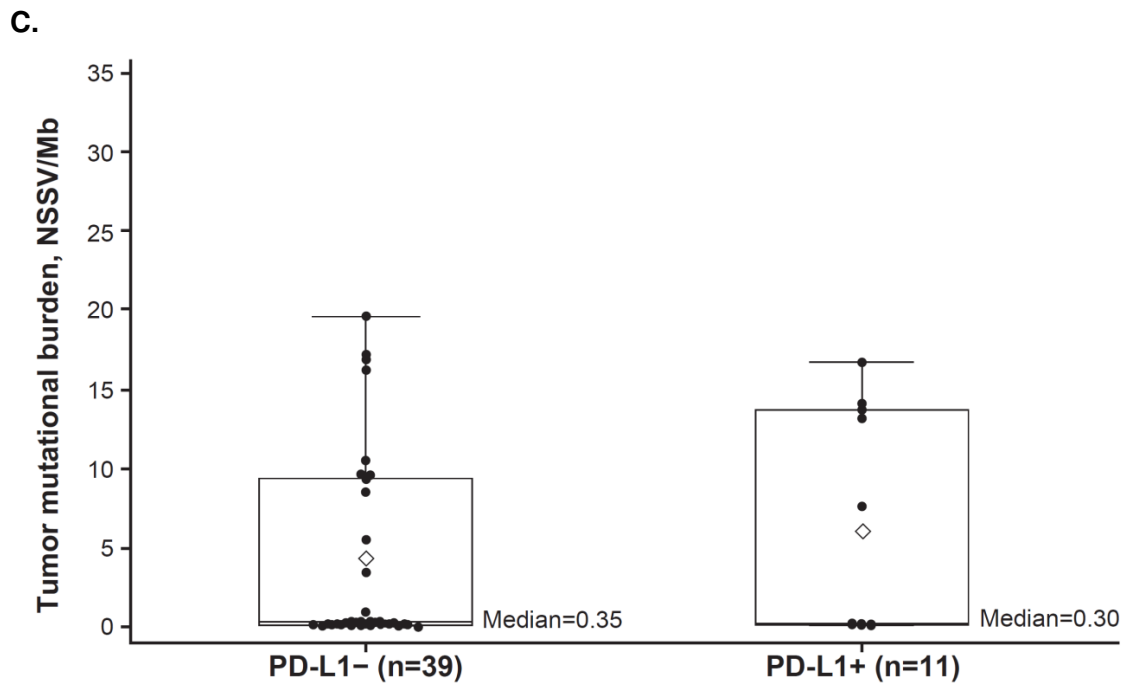
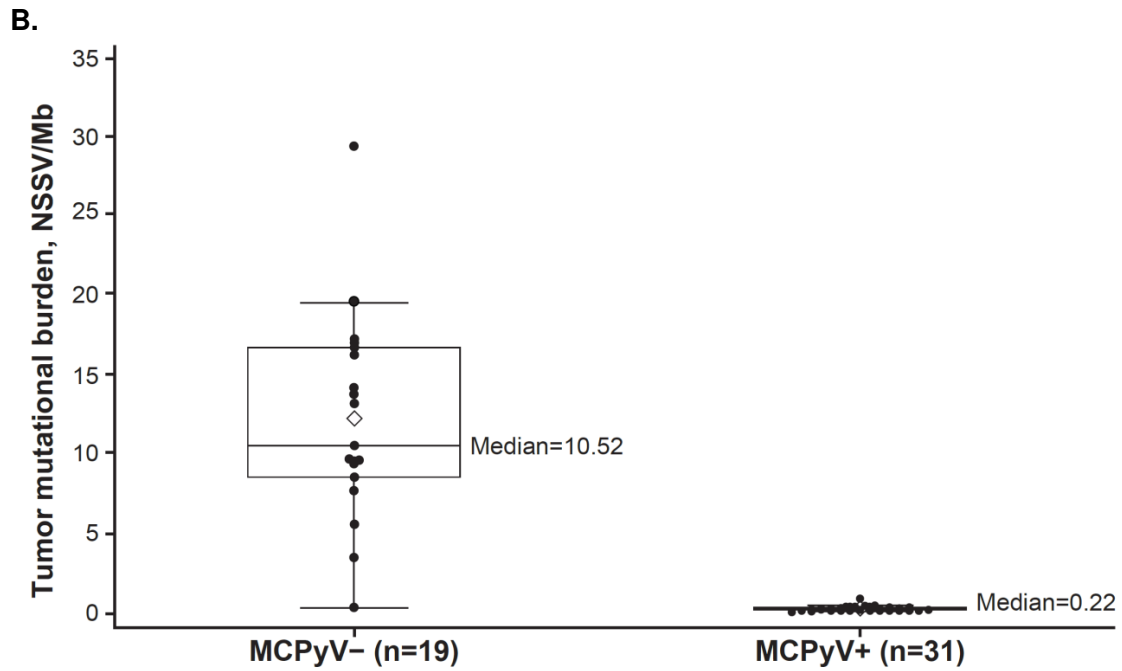
Supplementary figure 2. Kaplan-Meier estimate of progression-free survival (N=116).

Supplementary figure 3. (A) Distribution of TMB in evaluable patients (n=52).Association of TMB with (B) MCPyV status assessed by IHC, (C) PD-L1 status ($\geq 1\%$

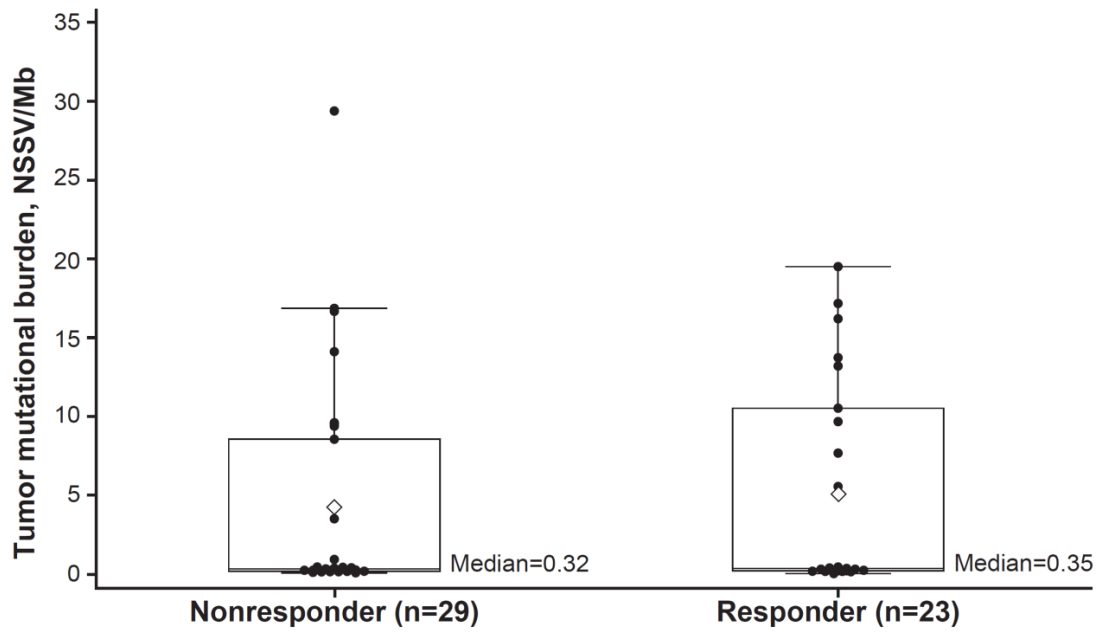
cutoff) in evaluable patients (n=50), and (D) response in evaluable patients (n=52).

Boxes represent interquartile range, diamonds denote the mean, lines within the boxes represent the median (upper tertile in A), and circles are observed values. IHC, immunohistochemistry; MCPyV, Merkel cell polyomavirus; NSSV/Mb, nonsynonymous somatic variants per megabase; PD-L1, programmed death ligand 1; TMB, tumor mutational burden.

A.



D.



Supplementary figure 4. Overall survival in the low TMB (<2 NSSV/Mb) and high TMB (≥ 2 NSSV/Mb) subgroups (n=52). HR, hazard ratio; NSSV/Mb, nonsynonymous somatic variants per megabase; TMB, tumor mutational burden.

