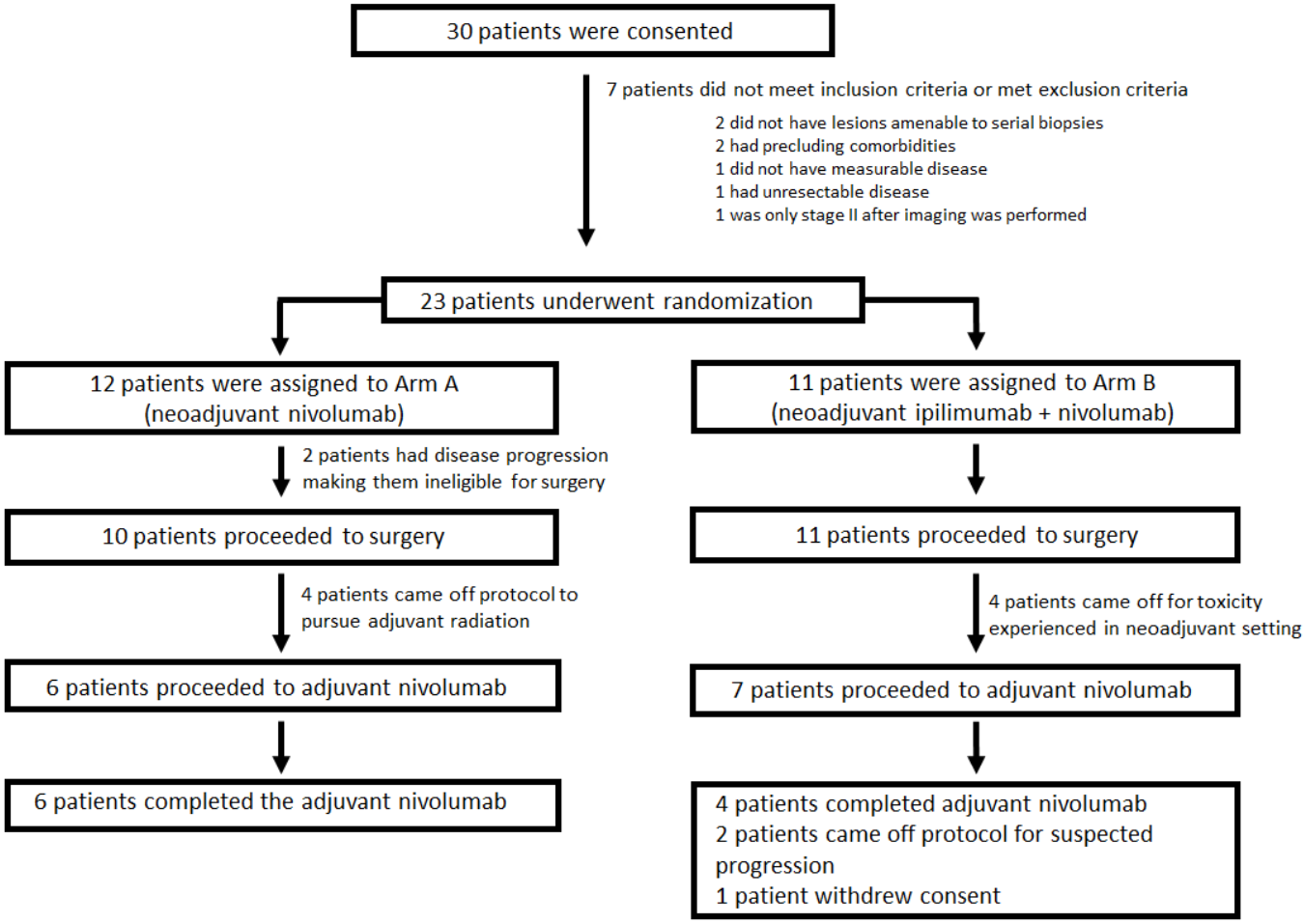
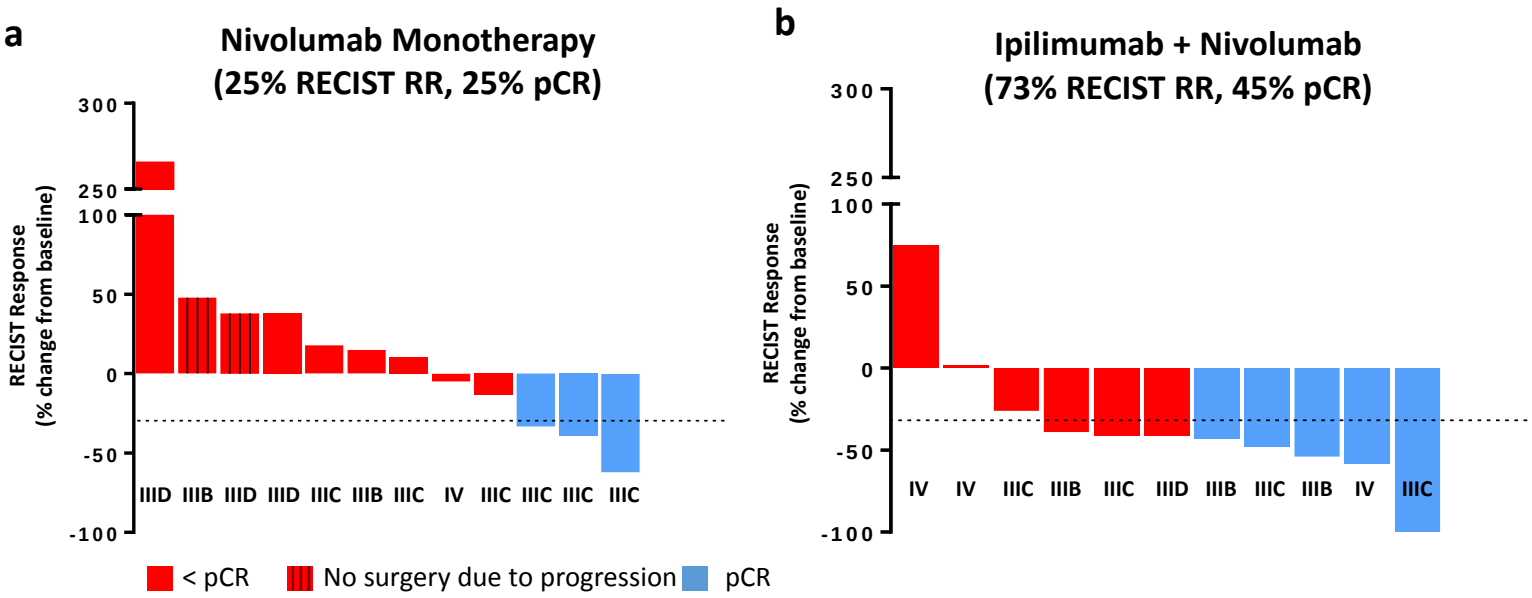
Supplementary Fig. 1



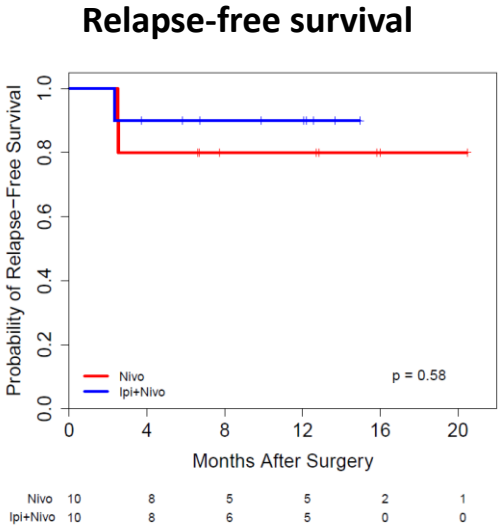
CONSORT diagram. Flow diagram of the progress through the phases of the non-comparative randomized trial of neodjuvant nivolumab (Arm A) and ipilimumab with nivolumab (Arm B) followed by surgical resection and adjuvant nivolumab.

Supplementary Fig. 2



Radiographic and pathologic responses to neoadjuvant nivolumab (n=12) and combination ipilimumab with nivolumab (n=11) as broken down by AJCC 8th Edition staging system.

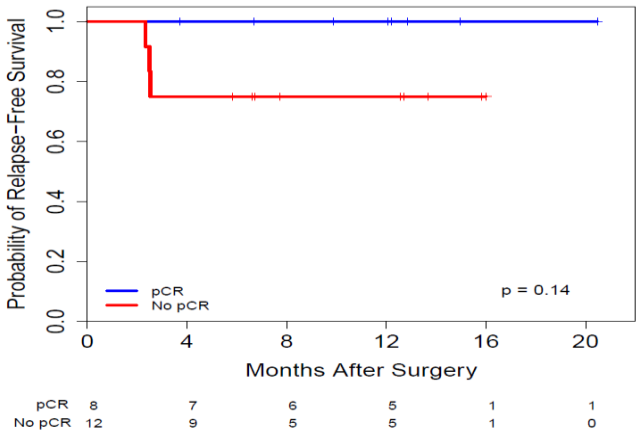
Supplementary Fig. 3



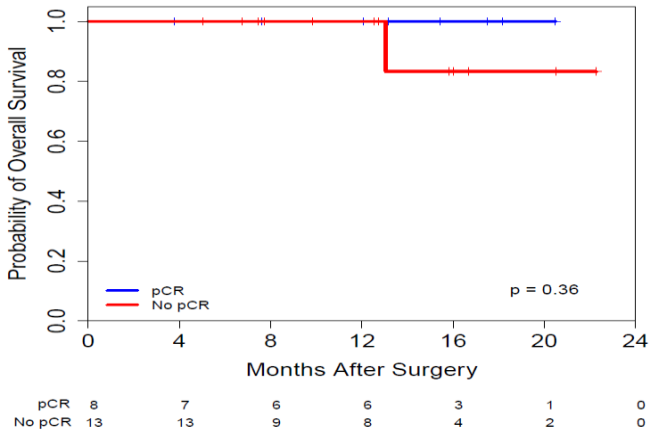
Relapse-free survival by Treatment Arm. Kaplan-Meier estimate of relapse-free survival by treatment group by two-sided log-rank test. Survival rates were 90% (95% CI 47-99%) at 14.9 months with ipilimumab with nivolumab (n=10) versus 80% (41-95%) at 20.5 months with nivolumab monotherapy (n=10), *p*=0.58. The two patients who developed metastatic disease prior to surgery are not included in these survival curves.

Supplementary Fig. 4

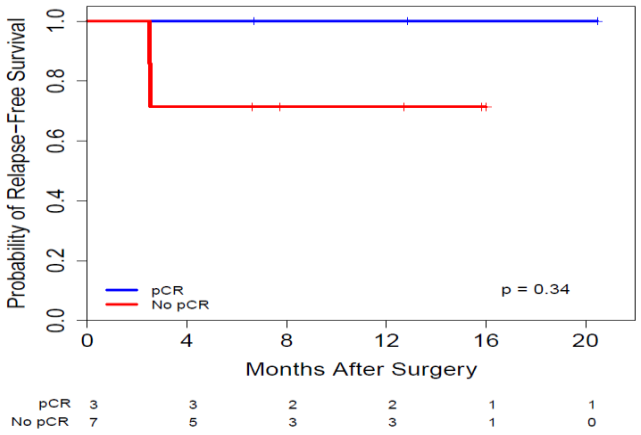
a RFS combined treatment arms



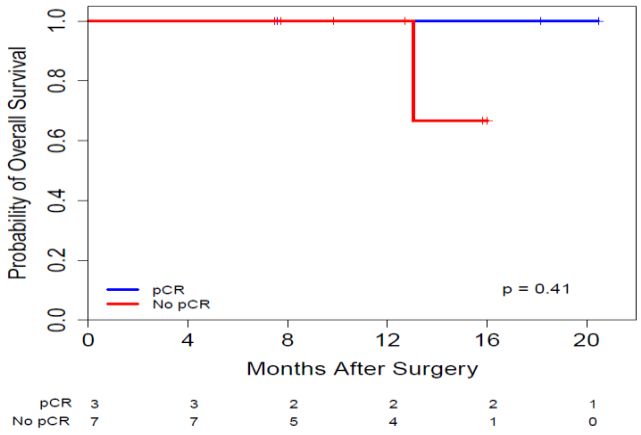
b OS combined treatment arms



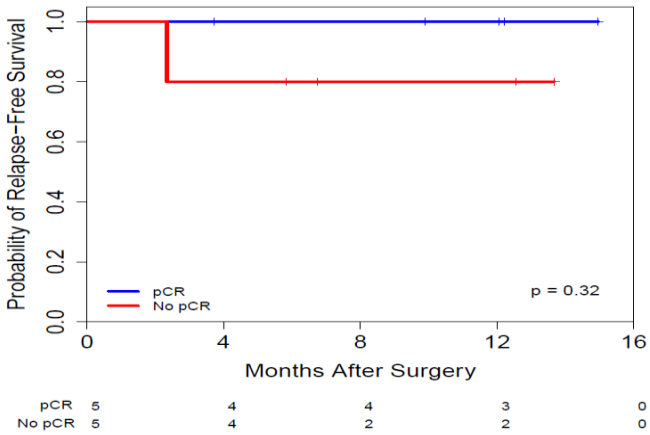
c RFS nivolumab arm only



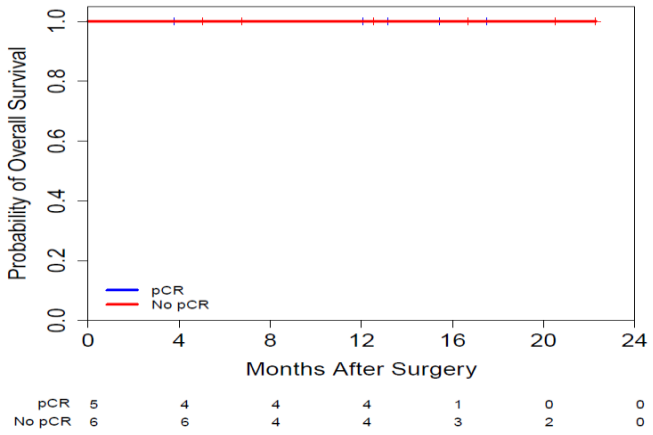
d OS nivolumab arm only



e RFS ipilimumab+nivolumab arm only



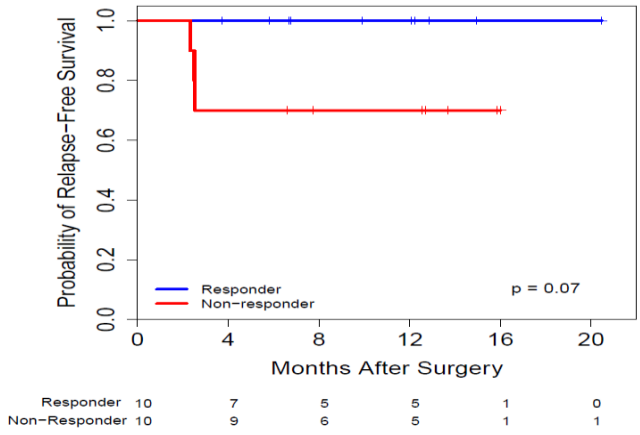
f OS ipilimumab + nivolumab arm only



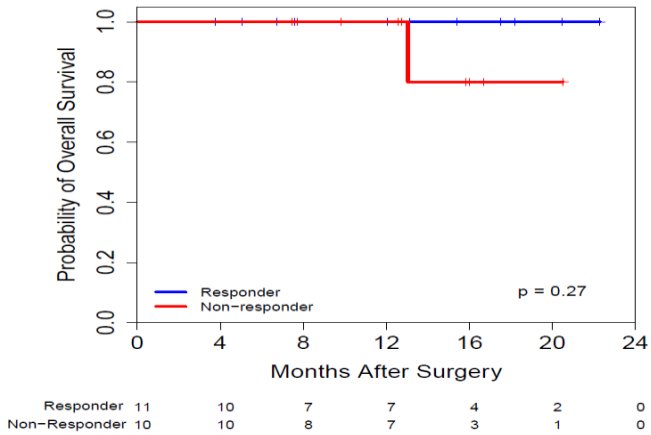
Survival outcomes by pathologic complete response. a,b, Kaplan-Meier estimates of relapse-free survival (RFS) and overall survival (OS) by pathologic complete response (pCR) status for combined treatment arms. For RFS, survival rates of 100% (95% CI 100-100%) at 20.5 months (mo) with pCR (n=8) vs 75% (41-91%) at 16.0 mo with non-pCR (n=12), *p*=0.14. For OS, rates of 100% (100-100%) at 20.5 mo with pCR (n=8) vs 83% (27-97%) at 22.3 months with non-pCR (n=13), *p*=0.36. c,d, Kaplan-Meier estimates of RFS and OS by pCR status for nivolumab arm only. For RFS, rates of 100% (100-100%) at 20.5 mo with pCR (n=3) vs 71% (26-92%) at 16.0 mo with non-pCR (n=7), *p*=0.34. For OS, rates of 100% (100-100%) at 20.5 mo with pCR (n=3) vs 67% (5-95%) at 16.0 mo with non-pCR (n=7), *p*=0.41. e,f, Kaplan-Meier estimates of RFS and OS by pCR status for ipilimumab with nivolumab arm only. For RFS, rates of 100% (100-100%) at 14.9 mo with pCR (n=5) vs 80% (20-97%) at 13.7 mo with non-pCR (n=5), *p*=0.32. For OS, rates of 100% (100-100%) at 17.5 mo with pCR (n=5) vs 100% (100-100%) at 22.3 mo with non-pCR (n=6). The two patients who developed metastatic disease prior to surgery are not included in these survival curves. Of note, all relapses were distant. Survival estimates were computed by two-sided log rank tests.

Supplementary Fig. 5

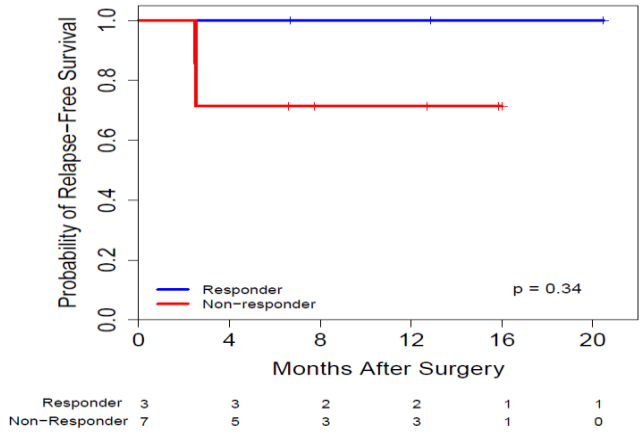
a RFS combined treatment arms



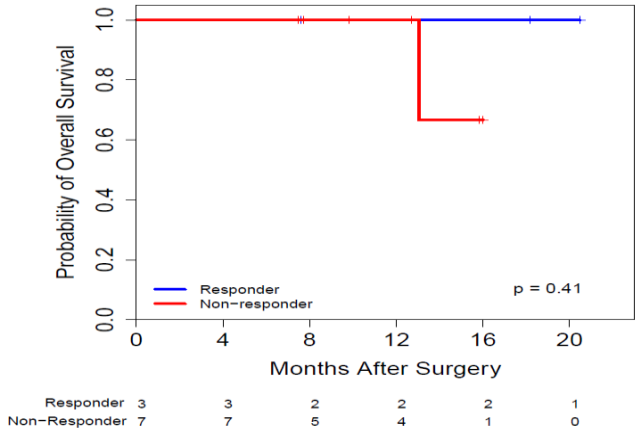
b OS combined treatment arms



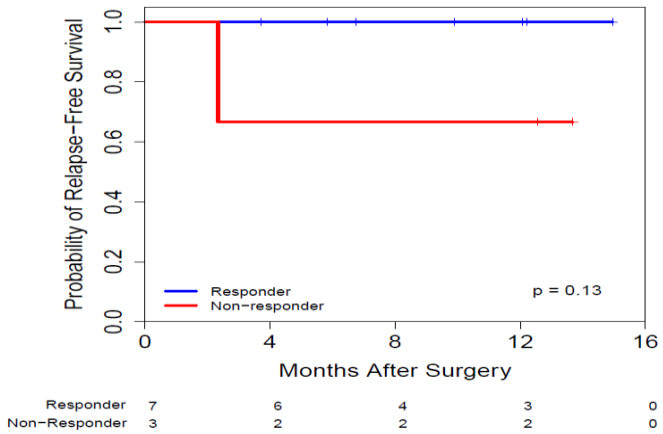
c RFS nivolumab arm only



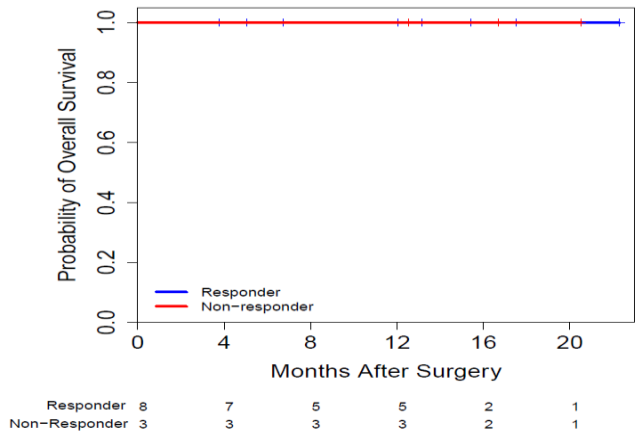
d OS nivolumab arm only



e RFS ipilimumab+nivolumab arm only

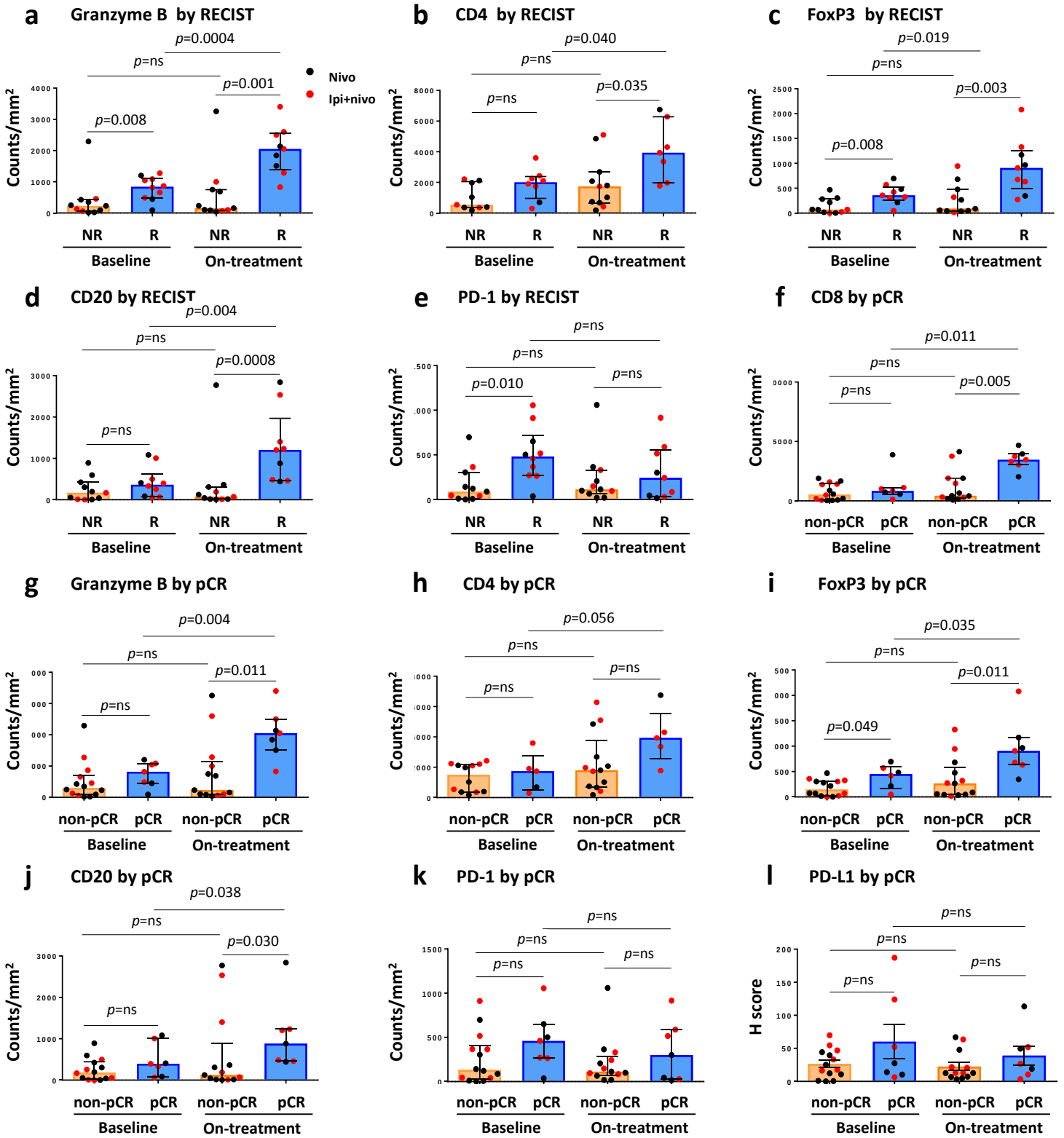


f OS ipilimumab + nivolumab arm only



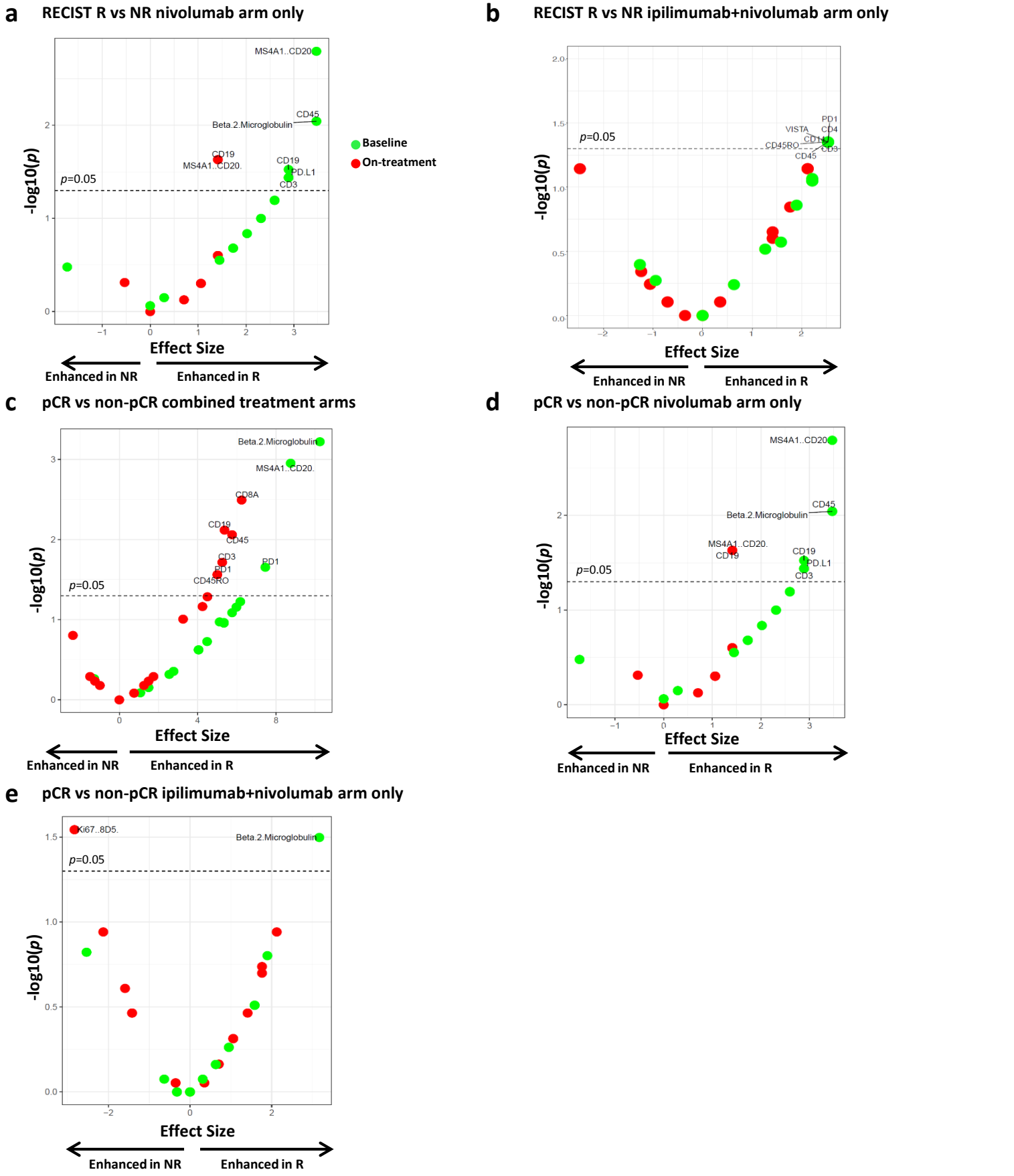
Survival outcomes by radiographic response. a,b, Kaplan-Meier estimates of relapse-free survival (RFS) and overall survival (OS) by radiographic response for combined treatment arms, with responders (R) defined as having a complete or partial response by RECIST 1.1 prior to surgery. For RFS, survival rates of 100% (95% CI 100-100%) at 20.5 months (mo) with R (n=10) vs 70% (33-89%) at 16.0 mo with NR (n=10), *p*=0.07. For OS, rates of 100% (100-100%) at 22.3 mo with R (n=11) vs 80% (20-97%) at 20.5 mo with NR (n=10), *p*=0.27. c,d, Kaplan-Meier estimates of RFS and OS by radiographic response for nivolumab arm only. For RFS, rates of 100% (100-100%) at 20.5 mo with R (n=3) vs 71% (26-92%) at 16.0 mo with NR (n=7), *p*=0.34. For OS, rates of 100% (100-100%) at 20.5 mo with R (n=3) vs 67% (5-95%) at 16.0 mo with NR (n=7), *p*=0.41. e,f, Kaplan-Meier estimates of RFS and OS by radiographic response for ipilimumab with nivolumab arm only. For RFS, rates of 100% (100-100%) at 14.9 mo with R (n=7) vs 67% (5-95%) at 13.7 mo with NR (n=3), *p*=0.13. For OS, rates of 100% (100-100%) at 22.3 mo with R (n=8) vs 100% (100-100%) at 20.5 mo with NR (n=3). The two patients who developed metastatic disease prior to surgery are not included in these survival curves. Of note, all relapses were distant. Survival estimates were computed by two-sided log rank tests.

Supplementary Fig. 6



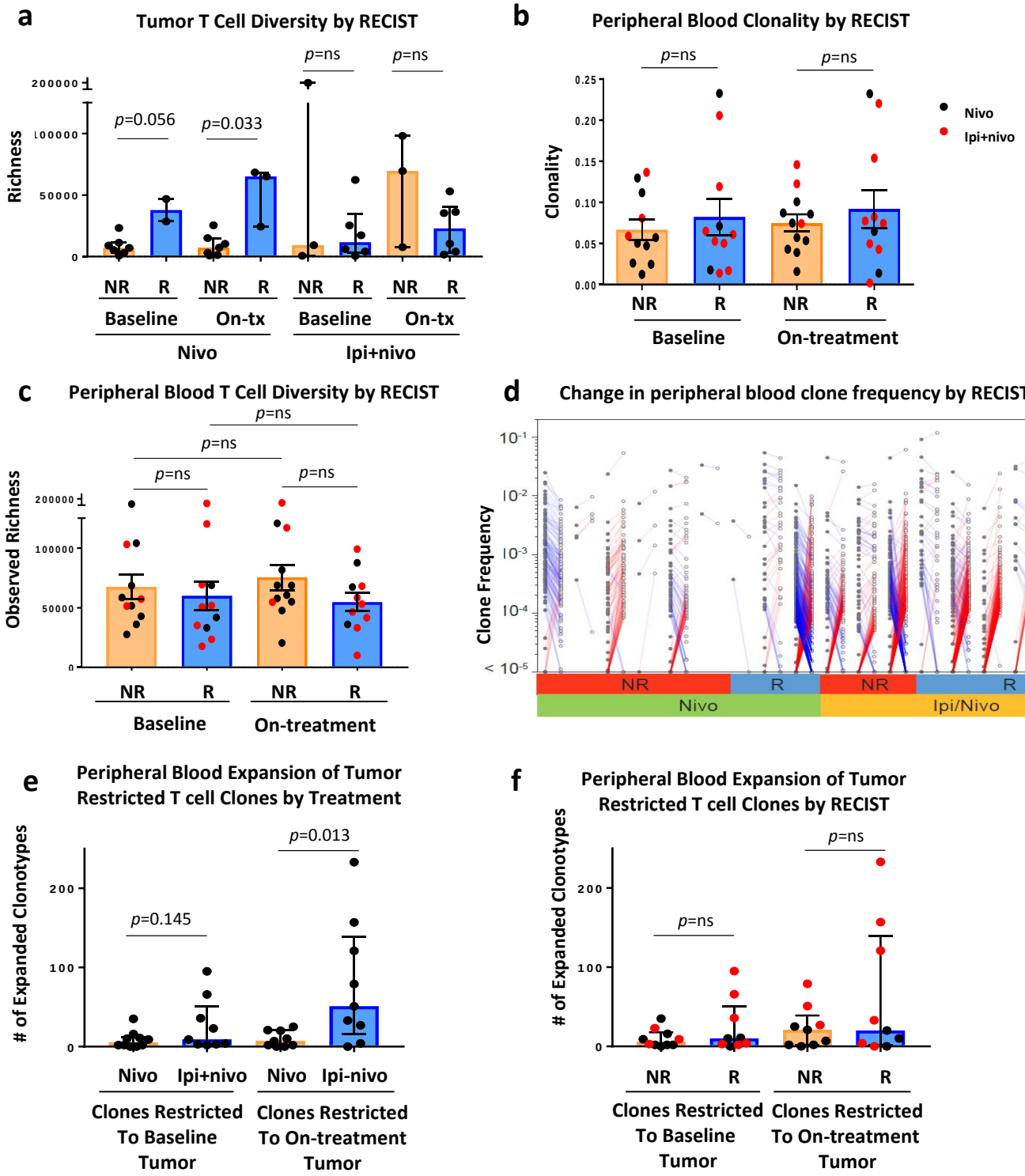
Immune infiltration per singlet immunohistochemistry (IHC) by response to neoadjuvant immune checkpoint blockade. a-e, Quantification by IHC of non-responders (NR) versus responders (R) at baseline (b/l) and on-treatment (on-tx), with R being defined as patients achieving a complete or partial response by RECIST 1.1. Shown are of quantifications of Granzyme B (n=11 NR and 10 R at b/l, n=11 NR and 9 R on-tx), CD4 (n=9 NR and 8 R at b/l, n=11 NR and 7 R on-tx), FoxP3 (n=11 NR and 9 R at b/l, n= 11 NR and 9 R on-tx), CD20 (n=11 NR and 10 R at b/l, n=11 NR and 9 R on-tx), and PD-1 (n=11 NR and 10 R at b/l, n=11 NR and 9 R on-tx). f-l, Quantification by IHC of NR versus R, with R being defined as patients achieving a pathologic complete response (pCR). Shown are quantifications of CD8 (n=14 NR and 7 R at b/l, n=13 NR and 7 R on-tx), Granzyme B (n=14 NR and 7 R at b/l, n=13 NR and 7 R on-tx), CD4 (n=12 NR and 5 R at b/l, n=13 NR and 5 R on-tx), FoxP3 (n=14 NR and 6 R at b/l, n=13 NR and 7 R on-tx), CD20 (n=14 NR and 7 R at b/l, n=13 NR and 7 R on-tx), PD-1 (n=14 NR and 7 R at b/l, n=13 NR and 7 R on-tx), and PD-L1 (n=14 NR and 7 R at b/l, n=13 NR and 7 R on-tx). Black dots indicate patients on nivolumab monotherapy arm and red dots patients on combination ipilimumab with nivolumab arm. Bar heights indicate median values of cell count density (for all markers except PD-L1 which is displayed as H score), and interquartile ranges are presented in addition to individual data points. All comparisons were made using Mann-Whitney U tests with two-sided analyses.

Supplementary Fig. 7



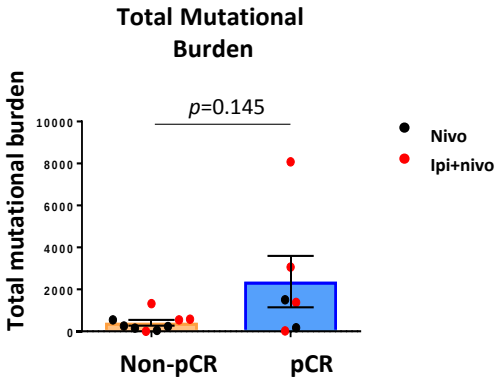
Immune infiltration per multiplex immunohistochemistry (IHC) by response to neoadjuvant checkpoint blockade. a-e, Volcano plots of pairwise two-sided Mann-Whitney comparisons of multiplex IHC marker expression between non-responders (NR) and responders (R) at baseline (b/l, green) and on-treatment (on-tx, red) samples. Immune marker expression was assessed on CD45 positive cells and quantified as expression per area of assayed tissue. a, b, comparisons of NR and R by RECIST 1.1 for nivolumab arm only (n=9 NR and 3 R at b/l, n=7 NR and 1 R on-tx) and ipilimumab with nivolumab arm only (n=2 NR and 8 R at b/l, n=3 NR and 5 R on-tx). c-e, Volcano plots of NR versus R by pathologic complete response (pCR) for combined arms (n=14 NR and 8 R at b/l, n=11 NR and 5 R on-tx), nivolumab arm only (n=9 NR and 3 R at b/l, n=7 NR and 1 R on-tx), and ipilimumab with nivolumab arm only (n=5 NR and 5 R at b/l, n=4 NR and 4 R on-tx).

Supplementary Fig. 8



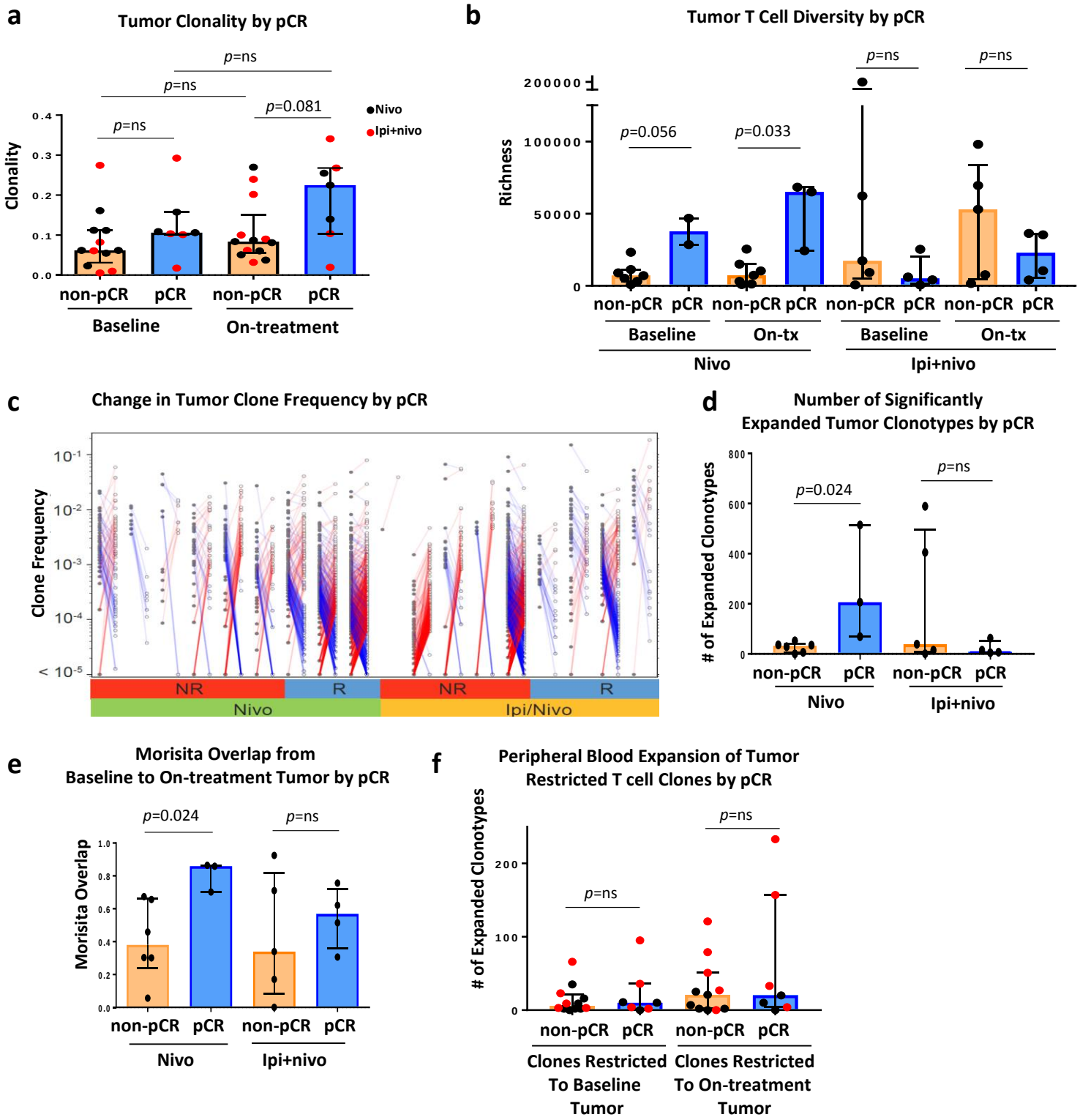
T cell repertoire analysis of tumor and peripheral blood by RECIST response. a, Tumor T cell richness scores between non-responders (NR) and responders (R) to nivolumab monotherapy (N) and ipilimumab with nivolumab combination (I+N), with response defined as having a complete or partial response by RECIST 1.1. Scores shown at baseline (b/l) (n=7 NR and 2 R for N, n=3 NR and 6 R for I+N) and on-treatment (on-tx) (n=7 NR and 3 R for N, n=3 NR and 6 R for I+N). b,c Peripheral blood clonality (n=11 NR and 11 R at b/l, n=12 NR and 11 R on-tx) and richness scores (n=11 NR and 11 R at b/l, n=12 NR and 11 R on-tx), respectively. d, Analysis of change in T cell repertoire in peripheral blood was performed using differential abundance analysis with significantly expanded and contracted clones shown. Differential abundance of clonotypes was assessed using a modification of the DESeq R package. e, Number of significantly expanded tumor restricted clonotypes in the peripheral blood shown by treatment type (n= 10 for N and 9 for I+N for b/l tumor restricted clones, and n=9 for N and 9 for I+N for on-tx tumor restricted clones). f, Depiction of data from (e) by response, n=10 NR and 9 R for b/l tumor restricted clones and n=9 NR and 9 R for on-tx tumor restricted clones. For b, c, f, Black dots indicate patients on N arm and red dots patients on I+N arm. For a-c, e, f, Bar heights indicate median values, and interquartile ranges are presented in addition to individual data points. Comparisons were made using Mann-Whitney U tests with two-sided testing.

Supplementary Fig. 9



Total mutational burden of tumor by pathologic response. Bar heights represent median sum of non-synonymous exonic mutations, and interquartile ranges are presented in addition to individual data points. Comparisons were made using two-sided Mann-Whitney U tests by response, with response defined as having a pathologic complete response (pCR) (n=9 non-pCR and 6 pCR). Black dots indicate patients on nivolumab monotherapy arm and red dots patients on combination ipilimumab with nivolumab arm.

Supplementary Fig. 10



T cell repertoire analysis of tumor and peripheral blood by pathologic response. a, T cell clonality scores between non-responders (NR) and responders (R) at baseline (b/l) (n=12 NR and 7 R) and on-treatment (on-tx) (n=13 NR and 7 R), with R defined as those having a complete pathologic response (pCR) and NR as those who had less than a pCR (non-pCR). b, T cell richness scores between NR and R to nivolumab monotherapy (N) and ipilimumab with nivolumab combination (I+N). Scores shown at b/l (n= 7 NR and 2 R for N, n= 5 NR and 4 R for I+N) and on-tx (n= 7 NR and 3 R for N, n= 5 NR and 4 R for I+N). c, Analysis of change in tumor T cell repertoire was performed using differential abundance analysis with significantly expanded and contracted clones. Differential abundance of tumor clonotypes was assessed using a modification of the DESeq R package. d, e, Change in T cell repertoire was assessed for number of significantly expanded clonotypes (n=6 NR and 3 R for N, n=5 NR and 4 R for I+N) and Morisita Overlap index (n=6 NR and 3 R for N, n=5 NR and 4 R for I+N). f, Numbers of significantly expanded tumor restricted clonotypes in the peripheral blood are shown by pathologic response, n= 12 NR and 7 R for b/l tumor restricted clones and n= 11 NR and 7 R for on-tx tumor restricted clones. For a,b, d-f, Bar heights indicate median values, and interquartile ranges are presented in addition to individual data points. For a, f, Black dots indicate patients treated with N and red dots patients treated with I+N. All comparisons were made using Mann-Whitney U tests with two-sided testing.

Supplementary Table 1. Patient and Clinical Characteristics.		
Characteristic	**Nivolumab (n=12)**	**Ipilimumab + Nivolumab (n=11)**
Age (years), median (range)	55 (34 – 73)	49 (29 – 74)
Gender, n (%)		
Male	9 (75)	10 (91)
Female	3 (25)	1 (9)
ECOG PS, n (%)		
0	12 (100)	11 (100)
AJCC 7th Edition Clinical Stage, n (%)		
IIIB	6 (50)	3 (27)
IIIC	5 (42)	5 (45)
IV	1 (8)	3 (27)
AJCC 8th Edition Clinical Stage, n (%)		
IIIB	2 (17)	3 (27)
IIIC	6 (50)	4 (36)
IIID	3 (25)	1 (9)
IV	1 (8)	3 (27)
LDH (U/L) [α], n (%)		
≤ ULN	10 (83)	11 (100)
> ULN	2 (17)	0
Sum of Lesion Diameters (mm), median (range)	28.5 (11.0 – 82.0)	31.0 (12.0 – 61.0)
Primary Tumor Type - no (%)		
Superficial Spreading	5 (42)	2 (18)
Nodular	1 (8)	4 (36)
Lentigo maligna	1 (8)	0 (0)
Acral Lentiginous	0 (0)	0 (0)
Unclassified	2 (17)	1 (9)
Unknown Primary	3 (25)	4 (36)
PD-L1, n (%)		

Positive (≥1%)	8 (67)	7 (64)
Negative (<1%)	4 (33)	4 (36)
Mutation Status, n (%)		
BRAF mutated[β]	7 (58)	4 (36)
NRAS mutated	1 (8)	3 (27)
CKIT mutated	0	0
Prior Therapy, n (%)		
Treatment Naïve	7 (58)	4 (36)
Surgery	4 (33)	4 (36)
Surgery and Systemic Therapy	0	3 (27) [¥]
Surgery, Radiation, and Systemic Therapy	1 (8) *	0

Note: All p-values ≥ 0.19 and were calculated used two-sided Fisher's exact tests.

[α]All samples measured in common lab, with upper limit of normal being 618 U/L.

[β]All V600E except one tumor that was V600R.

[¥] 2 patients received adjuvant interferon (one only 6 weeks), another peginterferon after prior surgical resection.

*1 patient received neoadjuvant dabrafenib + trametinib for 2 months followed by surgery, and then adjuvant radiation as well as biochemotherapy with dacarbazine, vinblastine, interferon, and IL-2.

Supplementary Table 2. Adverse Events During Neoadjuvant Treatment*.								
	Nivolumab (n=12)				**Ipilimumab + Nivolumab (n=11)**			
	Any Grade (n)	%	Grade 3 (n)	%	Any Grade (n)	%	Grade 3 (n)	%
Any Adverse Event	11	(92)	1	(8)	10	(91)	8	(73)
Fatigue	8	(67)	0	(0)	6	(55)	0	(0)
Headache	5	(42)	0	(0)	3	(27)	0	(0)
Pruritus	4	(33)	0	(0)	3	(27)	0	(0)
Tumor Pain	3	(25)	1	(8)	3	(27)	0	(0)
Rash (acneiform, maculopapular)	2	(17)	0	(0)	8	(73)	0	(0)
Diarrhea	2	(17)	0	(0)	7	(64)	0	(0)
Transaminitis	2	(17)	0	(0)	7	(64)	3	(27)
Vomiting	2	(17)	0	(0)	4	(36)	0	(0)
Weight loss/ Anorexia	2	(17)	0	(0)	3	(27)	0	(0)
Arthralgia	2	(17)	0	(0)	4	(36)	1	(9)
Fever/Chills/Flu like Symptoms	1	(8)	0	(0)	7	(64)	0	(0)
Cough	1	(8)	0	(0)	4	(36)	0	(0)
Hyperthyroidism/ thyrotoxicosis	1	(8)	0	(0)	3	(27)	1	(9)
Anemia	1	(8)	0	(0)	3	(27)	0	(0)
Nasal congestion	1	(8)	0	(0)	3	(27)	0	(0)
Night sweats	1	(8)	0	(0)	2	(18)	0	(0)
New skin lesions	1	(8)	0	(0)	2	(18)	0	(0)
Pneumonia	1	(8)	0	(0)	2	(18)	2	(18)
Myositis/myalgia	1	(8)	0	(0)	2	(18)	1	(9)
Hypomagnesemia	1	(8)	0	(0)	2	(18)	0	(0)
Hypothyroidism	0	(0)	0	(0)	4	(36)	0	(0)
Dyspnea	0	(0)	0	(0)	3	(27)	0	(0)
Colitis	0	(0)	0	(0)	2	(18)	2	(18)

Dehydration	0	(0)	0	(0)	2	(18)	2	(18)
Fall	0	(0)	0	(0)	1	(9)	1	(9)
Hyperglycemia	0	(0)	0	(0)	1	(9)	1	(9)
Hypokalemia	0	(0)	0	(0)	1	(9)	1	(9)
Hyponatremia	0	(0)	0	(0)	2	(18)	2	(18)
Sinus tachycardia	0	(0)	0	(0)	1	(9)	1	(9)

*Includes all treated related adverse events (AEs) present in ≥10% of cases in addition to all grade 3 AEs.

*Several grade 3 trAEs co-occurred such as thyrotoxicosis, sinus tachycardia, and fall in one patient; myositis and pneumonia in one patient; dehydration, hyponatremia, hypokalemia, and transaminitis in one patient, and colitis, dehydration, hyponatremia, hyperglycemia, and arthralgia in one patient.

Supplementary Table 3. Adverse Events During Post-Surgical and Adjuvant Treatment*.

	Nivolumab (n=10)		Ipilimumab + Nivolumab (n=11)	
	Any Grade, n (%)	Grade 3-4, n (%)	Any Grade, n (%)	Grade 3-4, n (%)
Any Adverse Event	6 (60)	2 (20)	9 (82)	2 (18)
Transaminitis	2 (20)	0 (0)	3 (27)	0 (0)
Weight loss/Anorexia	2 (20)	0 (0)	2 (18)	0 (0)
Fever/Chills/Flu-like Symptoms	1 (10)	0 (0)	2 (18)	0 (0)
Hypothyroidism	4 (40)	0 (0)	0 (0)	0 (0)
Myositis	0 (0)	0 (0)	3 (27)	0 (0)
Rash	2 (20)	0 (0)	1 (9)	0 (0)
Skin hypopigmentation	2 (20)	0 (0)	1 (9)	0 (0)
Hypophysitis	0 (0)	0 (0)	1 (9)	1 (9)
Diabetic Ketoacidosis	1 (10)	1 (10)	0 (0)	0 (0)
Hypoalbuminemia	1 (10)	0 (0)	1 (9)	1 (9)
Colitis	1 (10)	1 (10)	0 (0)	0 (0)

*Includes all treatment related adverse events (AEs) present in ≥10% of cases in addition to all grade 3-4 AEs in the patients who received surgical resection.

*The patients that developed ≥grade 3 hypophysitis, diabetic ketoacidosis, and colitis did not have ≥grade 3 trAEs in the neoadjuvant period.

Supplementary Table 4. Immune Markers Plotted in Volcano Plot (Combined Treatment Arms by RECIST response).			
Marker	**p value**	**Effect Size**	**Timepoint**
PD-1	0.00162	10.02043	Baseline
β2-Microglobulin	0.00245	9.16763	Baseline
CD20	0.00255	7.88843	Baseline
CD8A	0.01509	7.67523	Baseline
CD45RO	0.01577	7.46203	Baseline
GZMB	0.01577	7.46203	Baseline
CD19	0.01905	7.03562	Baseline
CD3	0.01923	7.24882	Baseline
Ki67	0.02807	6.82242	Baseline
VISTA	0.03360	6.60922	Baseline
CD4	0.03998	6.39602	Baseline
CD45	0.10142	5.11682	Baseline
PD-L1	0.10142	5.11682	Baseline
CD68	0.23456	3.62441	Baseline
CD14	0.29999	3.19801	Baseline
CD44	0.60632	1.49241	Baseline
FoxP3	0.69935	1.06600	Baseline
CD56	0.72058	-1.27920	Baseline
B7-H3	0.79694	-1.27920	Baseline
CD45	0.00050	7.25000	On-treatment
CD3	0.00175	6.75000	On-treatment
CD8A	0.00175	6.75000	On-treatment
CD45RO	0.00300	6.50000	On-treatment
CD19	0.00415	5.87500	On-treatment
PD1	0.01598	5.50000	On-treatment
CD20	0.04095	4.00000	On-treatment
GZMB	0.05594	4.50000	On-treatment

CD56	0.10128	-3.00000	On-treatment
Beta-2-Microglobulin	0.11788	3.75000	On-treatment
B7.H3	0.26349	-2.75000	On-treatment
CD14	0.31319	-2.50000	On-treatment
PD.L1	0.36763	2.25000	On-treatment
CD4	0.42782	2.00000	On-treatment
VISTA	0.71279	1.00000	On-treatment
FoxP3	0.87038	0.50000	On-treatment
Ki67	0.87488	-0.50000	On-treatment
CD68	0.95672	-0.25000	On-treatment
CD44	1.00000	0.00000	On-treatment
Two-sided comparisons between non-responders (NR) and responders (R) at baseline (n=11 NR and 11 R) and on-treatment (n=10 NR and 6 R) were made using the Mann-Whitney U test.			

Supplementary Table 5. Immune Markers Plotted in Volcano Plot (Ipilimumab+Nivolumab by RECIST response).			
Marker	**p value**	**Effect Size**	**Timepoint**
CD14	0.04444	2.52982	Baseline
CD3	0.04444	2.52982	Baseline
CD4	0.04444	2.52982	Baseline
CD45	0.04444	2.52982	Baseline
CD45RO	0.04444	2.52982	Baseline
PD1	0.04444	2.52982	Baseline
VISTA	0.04444	2.52982	Baseline
CD68	0.08576	2.21359	Baseline
β2-Microglobulin	0.08889	2.21359	Baseline
CD8A	0.08889	2.21359	Baseline
GZMB	0.08889	2.21359	Baseline
Ki67	0.08889	2.21359	Baseline
CD19	0.13841	1.89737	Baseline
PD.L1	0.26667	1.58114	Baseline
CD20	0.30319	1.26491	Baseline
FoxP3	0.40000	-1.26491	Baseline
B7.H3	0.53333	-0.94868	Baseline
CD56	0.57615	0.63246	Baseline
CD44	1.00000	0.00000	Baseline
CD45	0.07143	2.12132	On-treatment
CD45RO	0.07143	2.12132	On-treatment
CD8A	0.07143	2.12132	On-treatment
Ki67	0.07143	-2.47487	On-treatment
PD1	0.14286	1.76777	On-treatment
CD19	0.22170	1.41421	On-treatment
CD3	0.25000	1.41421	On-treatment

FoxP3	0.45336	-1.23744	On-treatment
B7.H3	0.57143	-1.06066	On-treatment
CD4	0.57143	-1.06066	On-treatment
PD.L1	0.57143	-1.06066	On-treatment
β2-Microglobulin	0.78571	0.35355	On-treatment
CD14	0.78571	-0.70711	On-treatment
CD68	0.78571	-0.70711	On-treatment
GZMB	0.78571	0.35355	On-treatment
CD44	1.00000	-0.35355	On-treatment
CD20	1.00000	0.00000	On-treatment
VISTA	1.00000	0.00000	On-treatment
Two-sided comparisons between non-responders (NR) and responders (R) at baseline (n=2 NR and 8 R) and on-treatment (n=3 NR and 5 R) were made using the Mann-Whitney U test.			

Supplementary Table 6. Immune Markers Plotted in Volcano Plot (Nivolumab by RECIST response).			
Marker	**p value**	**Effect Size**	**Timepoint**
CD20	0.00160	3.46410	Baseline
β2-Microglobulin	0.00909	3.46410	Baseline
CD45	0.00909	3.46410	Baseline
CD19	0.02993	2.88675	Baseline
CD3	0.03636	2.88675	Baseline
PD.L1	0.03636	2.88675	Baseline
CD4	0.06364	2.59808	Baseline
PD-1	0.06399	2.59808	Baseline
CD8A	0.10000	2.30940	Baseline
FoxP3	0.10000	2.30940	Baseline
VISTA	0.14545	2.02073	Baseline
CD44	0.20909	1.73205	Baseline
CD45RO	0.20909	1.73205	Baseline
GZMB	0.20909	1.73205	Baseline
Ki67	0.20909	1.73205	Baseline
CD14	0.28182	1.44338	Baseline
CD56	0.33165	-1.73205	Baseline
CD68	0.71105	0.28868	Baseline
B7.H3	0.86364	0.00000	Baseline
CD19	0.02334	1.41421	On-treatment
CD20	0.02334	1.41421	On-treatment
β2-Microglobulin	0.25000	1.41421	On-treatment
CD3	0.25000	1.41421	On-treatment
CD4	0.25000	1.41421	On-treatment
CD45	0.25000	1.41421	On-treatment
CD45RO	0.25000	1.41421	On-treatment

CD8A	0.25000	1.41421	On-treatment
GZMB	0.25000	1.41421	On-treatment
PD-1	0.25000	1.41421	On-treatment
PD.L1	0.25000	1.41421	On-treatment
CD56	0.48550	-0.53033	On-treatment
CD14	0.50000	1.06066	On-treatment
CD68	0.50000	1.06066	On-treatment
FoxP3	0.50000	1.06066	On-treatment
Ki67	0.50000	1.06066	On-treatment
VISTA	0.50000	1.06066	On-treatment
CD44	0.75000	0.70711	On-treatment
B7.H3	1.00000	0.00000	On-treatment
Two-sided comparisons between non-responders (NR) and responders (R) at baseline (n=9 NR and 3 R) and on-treatment (n=7 NR and 1 R) were made using the Mann-Whitney U test.			

Supplementary Table 7. Immune Markers Plotted in Volcano Plot (Combined Treatment Arms by pathologic response).			
Marker	**p value**	**Effect Size**	**Timepoint**
β2-Microglobulin	0.00060	10.23363	Baseline
CD20	0.00111	8.74123	Baseline
PD-1	0.02219	7.46203	Baseline
GZMB	0.05937	6.18282	Baseline
CD45RO	0.06983	5.96962	Baseline
VISTA	0.06983	5.96962	Baseline
CD45	0.08170	5.75642	Baseline
CD19	0.10682	5.11682	Baseline
CD8A	0.10863	5.33002	Baseline
CD4	0.10998	5.33002	Baseline
CD3	0.18760	4.47722	Baseline
CD44	0.23824	4.05081	Baseline
Ki67	0.23824	4.05081	Baseline
PD.L1	0.23824	4.05081	Baseline
CD14	0.44114	2.77161	Baseline
B7.H3	0.48217	2.55841	Baseline
CD56	0.54575	-1.27920	Baseline
CD68	0.70578	1.49241	Baseline
FoxP3	0.81540	1.06600	Baseline
CD8A	0.00321	6.25000	On-treatment
CD19	0.00762	5.37500	On-treatment
CD45	0.00870	5.75000	On-treatment
CD3	0.01923	5.25000	On-treatment
CD45RO	0.02747	5.00000	On-treatment
PD-1	0.02747	5.00000	On-treatment
GZMB	0.05174	4.50000	On-treatment

β2-Microglobulin	0.06868	4.25000	On-treatment
CD20	0.09836	3.25000	On-treatment
CD56	0.15740	-2.37500	On-treatment
B7.H3	0.50962	-1.50000	On-treatment
PD.L1	0.50962	1.75000	On-treatment
CD44	0.58333	1.50000	On-treatment
Ki67	0.58333	-1.25000	On-treatment
CD14	0.66117	-1.00000	On-treatment
CD4	0.66117	1.25000	On-treatment
CD68	0.82062	0.75000	On-treatment
VISTA	0.82692	0.75000	On-treatment
FoxP3	1.00000	0.00000	On-treatment

Two-sided comparisons between non-responders (NR) and responders (R) at baseline (n=14 NR and 8 R) and on-treatment (n=11 NR and 5 R) were made using the Mann-Whitney U test.

Supplementary Table 8. Immune Markers Plotted in Volcano Plot (Ipilimumab+Nivolumab by pathologic response).			
Marker	**p value**	**Effect Size**	**Timepoint**
β2-Microglobulin	0.03175	3.16228	Baseline
FoxP3	0.15079	-2.52982	Baseline
CD20	0.15794	1.89737	Baseline
B7.H3	0.30952	1.58114	Baseline
CD45RO	0.30952	1.58114	Baseline
VISTA	0.30952	1.58114	Baseline
GZMB	0.54762	0.94868	Baseline
PD-1	0.54762	0.94868	Baseline
CD4	0.69048	0.63246	Baseline
CD44	0.69048	0.63246	Baseline
CD45	0.69048	0.63246	Baseline
CD8A	0.84127	0.31623	Baseline
PD.L1	0.84127	-0.63246	Baseline
CD14	1.00000	0.00000	Baseline
CD19	1.00000	0.00000	Baseline
CD3	1.00000	-0.31623	Baseline
CD56	1.00000	0.00000	Baseline
CD68	1.00000	-0.31623	Baseline
Ki67	1.00000	-0.31623	Baseline
Ki67	0.02857	2.82843	On-treatment
CD8A	0.11429	-2.12132	On-treatment
STAT3	0.11429	2.12132	On-treatment
CD19	0.18315	-1.76777	On-treatment
PD-1	0.20000	-1.76777	On-treatment
FoxP3	0.24538	1.59099	On-treatment
CD4	0.34286	1.41421	On-treatment

CD45RO	0.34286	-1.41421	On-treatment
PD.L1	0.34286	1.41421	On-treatment
β2-Microglobulin	0.48571	-1.06066	On-treatment
CD45	0.48571	-1.06066	On-treatment
GZMB	0.48571	-1.06066	On-treatment
CD44	0.68571	-0.70711	On-treatment
B7.H3	0.88571	0.35355	On-treatment
CD3	0.88571	-0.35355	On-treatment
VISTA	0.88571	0.35355	On-treatment
CD14	1.00000	0.00000	On-treatment
CD68	1.00000	0.00000	On-treatment
CD20	1.00000	0.00000	On-treatment

Two-sided comparisons between non-responders (NR) and responders (R) at baseline (n=5 NR and 5 R) and on-treatment (n=4 NR and 4 R) were made using the Mann-Whitney U test.

Supplementary Table 9. Immune Markers Plotted in Volcano Plot (Nivolumab by pathologic response).			
Marker	**p value**	**Effect Size**	**Timepoint**
CD20	0.00160	3.46410	Baseline
β2-Microglobulin	0.00909	3.46410	Baseline
CD45	0.00909	3.46410	Baseline
CD19	0.02993	2.88675	Baseline
CD3	0.03636	2.88675	Baseline
PD.L1	0.03636	2.88675	Baseline
CD4	0.06364	2.59808	Baseline
PD-1	0.06399	2.59808	Baseline
CD8A	0.10000	2.30940	Baseline
FoxP3	0.10000	2.30940	Baseline
VISTA	0.14545	2.02073	Baseline
CD44	0.20909	1.73205	Baseline
CD45RO	0.20909	1.73205	Baseline
GZMB	0.20909	1.73205	Baseline
Ki67	0.20909	1.73205	Baseline
CD14	0.28182	1.44338	Baseline
CD56	0.33165	-1.73205	Baseline
CD68	0.71105	0.28868	Baseline
B7.H3	0.86364	0.00000	Baseline
CD19	0.02334	1.41421	On-treatment
CD20	0.02334	1.41421	On-treatment
β2-Microglobulin	0.25000	1.41421	On-treatment
CD3	0.25000	1.41421	On-treatment
CD4	0.25000	1.41421	On-treatment
CD45	0.25000	1.41421	On-treatment
CD45RO	0.25000	1.41421	On-treatment

CD8A	0.25000	1.41421	On-treatment
GZMB	0.25000	1.41421	On-treatment
PD-1	0.25000	1.41421	On-treatment
PD.L1	0.25000	1.41421	On-treatment
CD56	0.48550	-0.53033	On-treatment
CD14	0.50000	1.06066	On-treatment
CD68	0.50000	1.06066	On-treatment
FoxP3	0.50000	1.06066	On-treatment
Ki67	0.50000	1.06066	On-treatment
VISTA	0.50000	1.06066	On-treatment
CD44	0.75000	0.70711	On-treatment
B7.H3	1.00000	0.00000	On-treatment
Two-sided comparisons between non-responders (NR) and responders (R) at baseline (n=9 NR and 3 R) and on-treatment (n=7 NR and 1 R) were made using the Mann-Whitney U test.			

Supplementary Table 10. Timing of On-treatment Sample Collection for Correlative Studies.

Treatment	Radiographic Response	Pathologic Response	IHC	Nanostring	TCR Seq Tumor	TCR Seq Blood for Expansion Analyses
Ipi+nivo	R	Non-pCR	Wk 4	n/a	Wk 4	Wk 4
Ipi+nivo	R	pCR	Wk 4	n/a	Wk 4	Wk 4
Ipi+nivo	R	pCR	Wk 4	Wk 4	Wk 4	Wk 4
Ipi+nivo	R	pCR	Wk 4	Wk 4	Wk 4	Wk 4
Ipi+nivo	R	pCR	Wk 4	Wk 4	Wk 4	Wk 4
Ipi+nivo	R	pCR	Wk 4	Wk 4	n/a	n/a
Ipi+nivo	R	Non-pCR	Wk 4	Wk 4	Wk 4	n/a
Ipi+nivo	R	Non-pCR	n/a	n/a	Wk 4	Wk 4
Ipi+nivo	NR	Non-pCR	Wk 4	Wk 4	Wk 4	Wk 4
Ipi+nivo	NR	Non-pCR	Wk 4	Wk 4	Wk 4	Wk 4
Ipi+nivo	NR	Non-pCR	Wk 4	Wk 4	Wk 4	Wk 4
Nivo	R	pCR	Wk 3	n/a	Wk 3	Wk 3
Nivo	R	pCR	Wk 3	n/a	Wk 3	Wk 3
Nivo	R	pCR	Wk 3	Wk 3	Wk 3	Wk 3
Nivo	NR	Non-pCR	Wk 3	Wk 3	Wk 3	Wk 3
Nivo	NR	Non-pCR	n/a	n/a	Wk 3	WK 3
Nivo	NR	Non-pCR	Wk 3	Wk 3	Wk 3	Wk 3
Nivo	NR	Non-pCR	Wk 5	Wk 3	Wk 5	Wk 3
Nivo	NR	Non-pCR	Wk 3	Wk 3	Wk 3	Wk 3
Nivo	NR	Non-pCR	Wk 3	Wk 3	n/a	n/a
Nivo	NR	Non-pCR	Wk 5	n/a	n/a	Wk 3
Nivo	NR	Non-pCR	Wk 3	Wk 3	Wk 3	Wk 3
Nivo	NR	Non-pCR	Wk 3	Wk 3	Wk 3	n/a

NR, non-responder; R, responder; Non-pCR, non-pathologic complete response; pCR, pathologic complete response; n/a, not available

Supplementary Table 11. Prior beta distributions.				
Number of patients in each treatment group	**Prior beta distribution**		**Posterior Probability of response**	
	Nivo	**Ipi+Nivo**	**RECIST**	**pCR**
1	(0.05, 0.95)	(0.15, 0.85)	0.99	0.86
10	(0.5, 9.5)	(1.5, 8.5)	0.99	0.89
20	**(1,19)**	**(3, 17)**	**0.99**	**0.92**
100	(5, 95)	(15, 85)	1.00	0.99
500	(25, 475)	(75, 425)	1.00	1.00