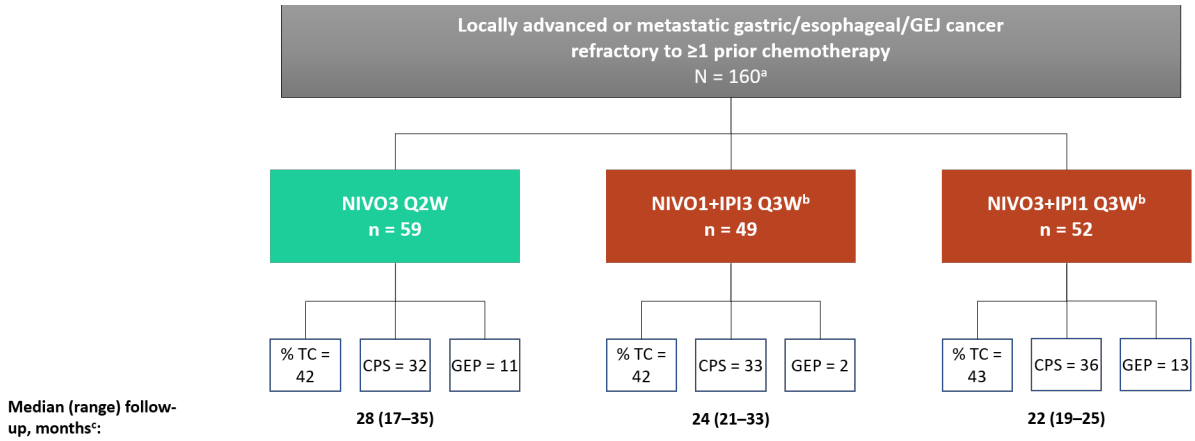
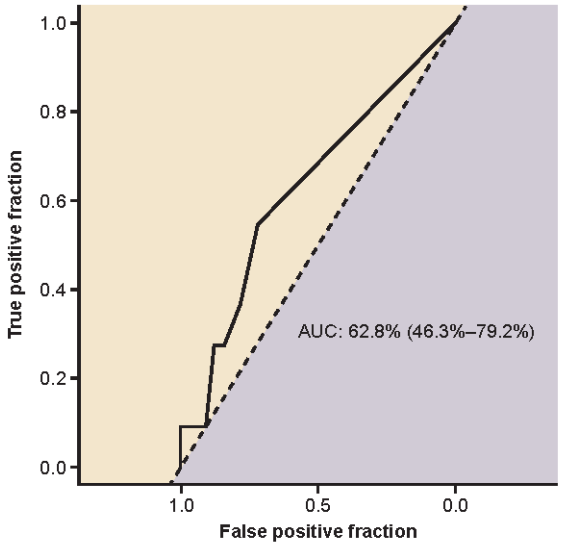
Supplementary Material

Supplementary Figure 1. CheckMate 032 GC/GEJC cohort study design and biomarker-evaluable patients. [a]Three patients who were treated with NIVO1+IPI1 Q3W in the dose-escalation phase were also included in the analyses if data were available. [b]NIVO+IPI administered for 4 cycles followed by NIVO3 Q2W. [c]Time from first dose to data cutoff; follow-up was shorter for patients who died prior to data cutoff. CPS, combined positive score; GEP, gene expression profiling; GEJ, gastroesophageal junction; IPI1, ipilimumab 1 mg/kg; IPI3, ipilimumab 3 mg/kg; NIVO1, nivolumab 1 mg/kg ; NIVO3, nivolumab 3 mg/kg; Q2W, every 2 weeks; Q3W, every 3 weeks; TC, tumor cell.

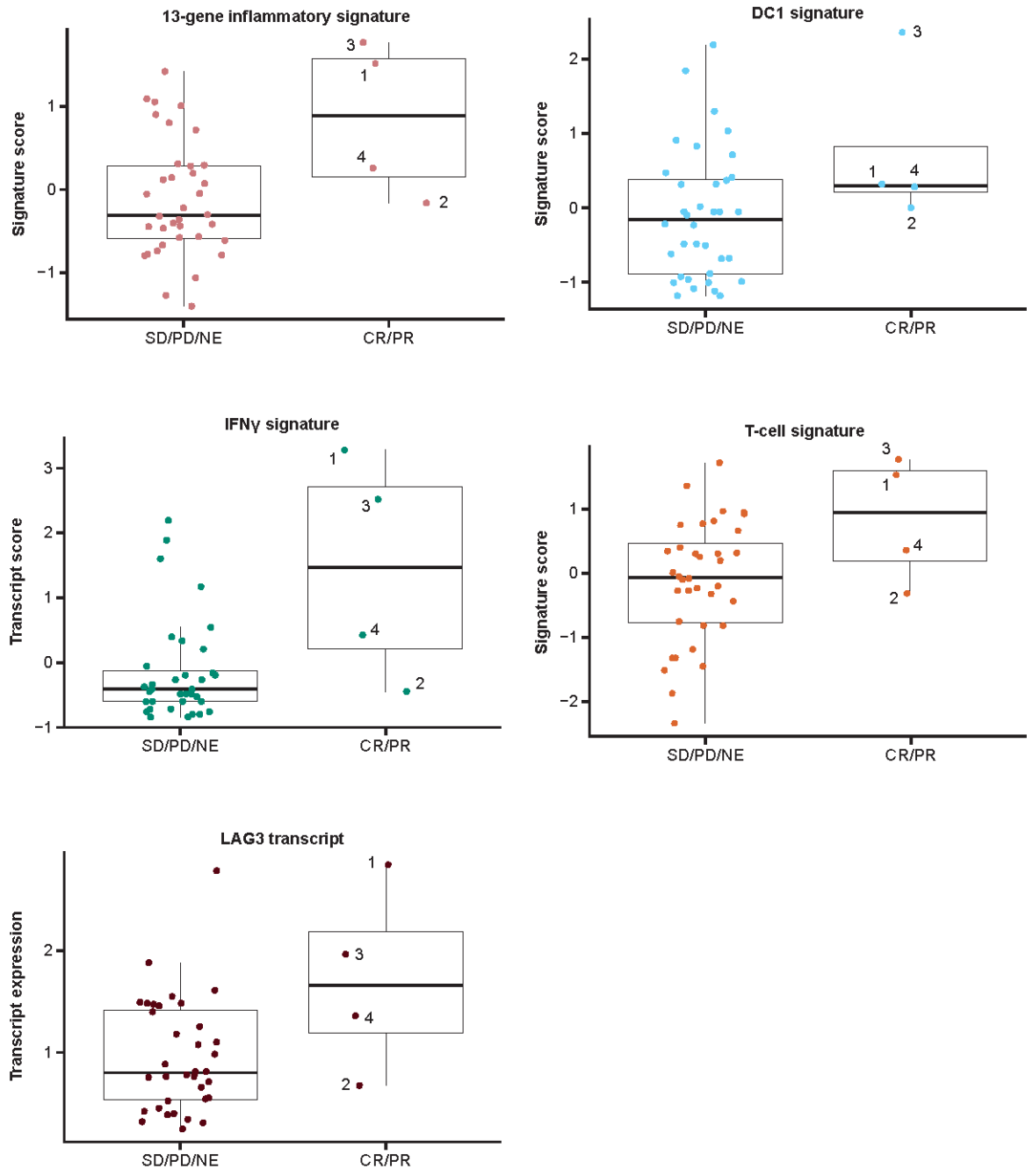


Supplementary Figure 2. ROC analysis on the association of PD-L1 expression as assessed by % TC with objective response in patients with both CPS and % TC data available (n = 104)

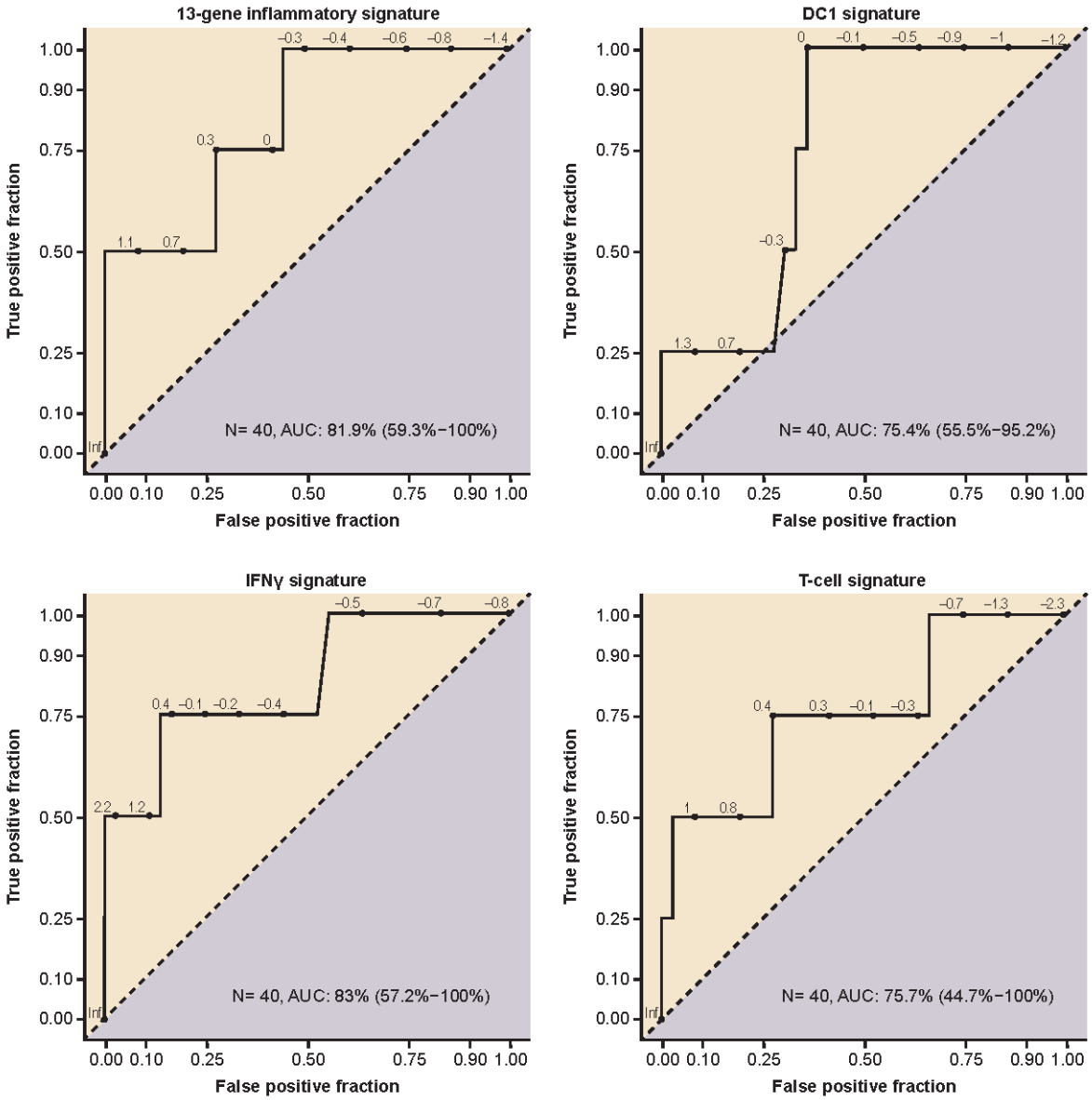


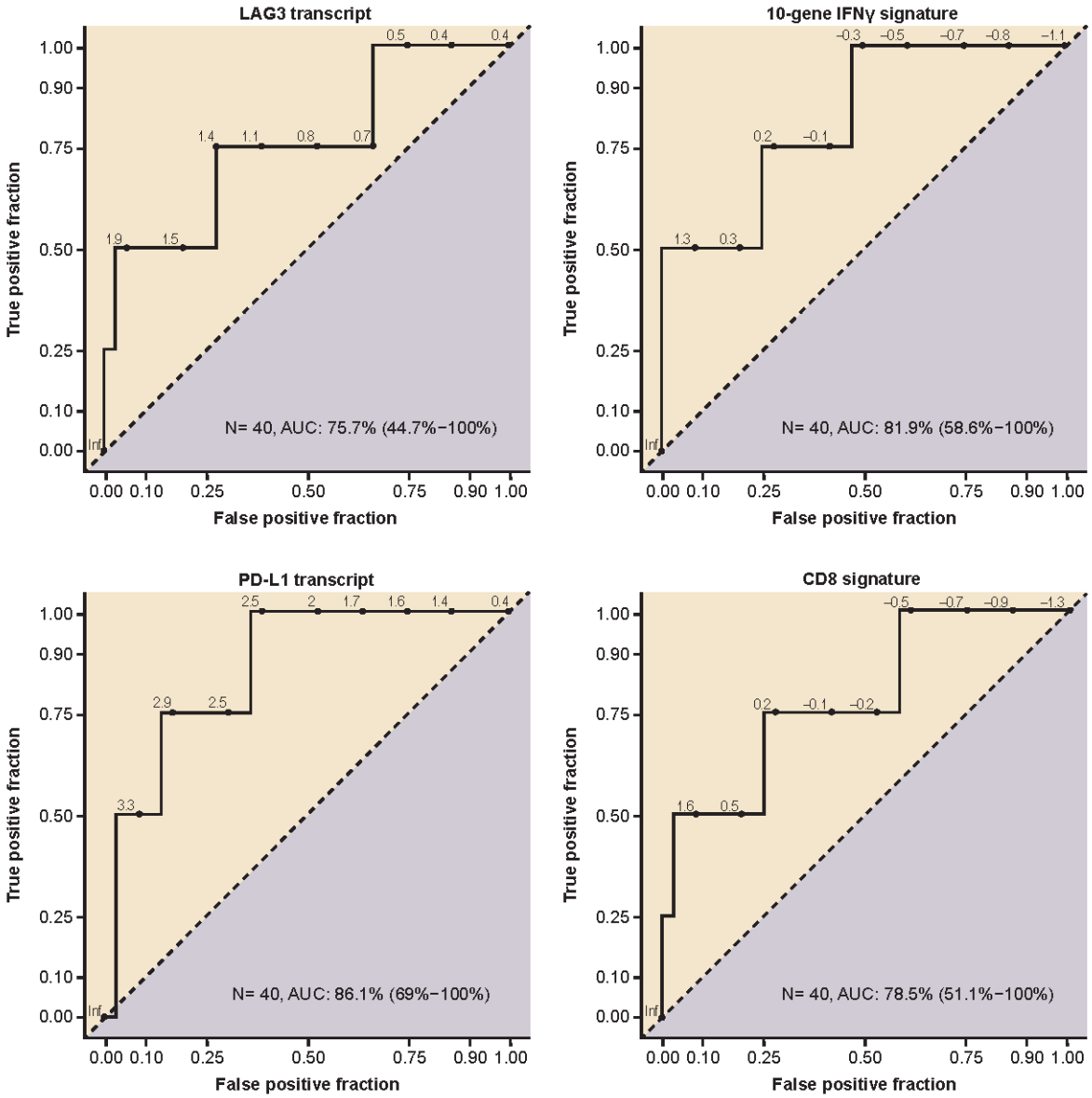
Supplementary Figure 3. (A) Association of gene expression signatures or individual transcripts with objective response to nivolumab ± ipilimumab. Individual patients with objective response (CR/PR) are labelled 1–4. **(B)** ROC analysis.

A)



B)


13-gene inflammatory signature
N= 40, AUC: 81.9% (59.3%−100%)
DC1 signature
N= 40, AUC: 75.4% (55.5%−95.2%)
IFNγ signature
N= 40, AUC: 83% (57.2%−100%)
T-cell signature
N= 40, AUC: 75.7% (44.7%−100%)
True positive fraction
False positive fraction
0.00 0.10 0.25 0.50 0.75 0.90 1.00
Inf


LAG3 transcript
N= 40, AUC: 75.7% (44.7%−100%)
10-gene IFNγ signature
N= 40, AUC: 81.9% (58.6%−100%)
PD-L1 transcript
N= 40, AUC: 86.1% (69%−100%)
CD8 signature
N= 40, AUC: 78.5% (51.1%−100%)
True positive fraction
False positive fraction
0.00
0.10
0.25
0.50
0.75
0.90
1.00
Inf

Supplementary Table 1. Additional details on CPS scoring done by Agilent-certified pathologists

Supplementary Table 2. Corresponding % TC and CPS with response and OS

In column C, “non-responder” refers to a response of SD/PD/NE, and “responder” refers to a response of CR/PR.

Supplementary Table 3. Gene expression levels by cohort

In column D, “non-responder” refers to a response of SD/PD/NE, and “responder” refers to a response of CR/PR.

Supplementary Table 4. Association of gene signatures or individual transcripts with ORR

Because of the small sample size and post hoc nature of the analysis, p values are not intended to demonstrate statistical significance.

Gene signatures/ transcripts	**Genes included in signature**	***p* value (CR/PR vs. SD/PD/NE)**
4-gene inflammatory signature (1)	*CD274* (PD-L1), *CD8A*, *LAG3*, *STAT1*	0.071
LAG3 transcript	*LAG3*	0.20
CD8 T-cell signature (1)	*CD8A*, *CD8B*	0.19
10-gene IFNγ signature (2)	*CCR5*, *CXCL9*, *CXCL10*, *CXCL11*, *GZMA*, *HLA-DRA*, *IDO1*, *IFNG*, *PRF1*, *STAT1*	0.14
IFNγ transcript	*IFNG*	0.16

PD-L1 transcript	*CD274*	0.032
13-gene inflammatory signature (3)	*CCL2*, *CCL3*, *CCL4*, *CD8A*, *CXCL9*, *CXCL10*, *GZMK*, *HLA-DMA*, *HLA-DMB*, *HLA-DOA*, *HLA-DOB*, *ICOS*, *IRF1*	0.13
T-cell signature (1)	*CD2*, *CD3D*, *CD3E*	0.14
DC1 signature	*CLEC9A*, *FLT3*, *XCR1*	0.22

1. Siemers NO, Holloway JL, Chang H, Chasalow SD, Ross-MacDonald PB, Voliva CF, et al. Genome-wide association analysis identifies genetic correlates of immune infiltrates in solid tumors. PLoS One 2017;12:e0179726.

2. Ayers M, Lunceford J, Nebozhyn M, Murphy E, Loboda A, Kaufman DR, et al. IFN-gamma-related mRNA profile predicts clinical response to PD-1 blockade. J Clin Invest 2017;127:2930–40.

3. Spranger S, Bao R, Gajewski TF. Melanoma-intrinsic beta-catenin signalling prevents anti-tumour immunity. Nature 2015;523:231–5.