

**Supplementary Table 1.** Baseline characteristics of the study participants

<b>Characteristic</b>	<b>N=15</b>
Age (years), median (range)	64 (41-78)
Sex, N (%)	
Male	10 (67)
Female	5 (33)
Race/Ethnicity, N (%)	
White, non-Hispanic	8 (53)
Hispanic	1 (7)
Black	5 (33)
Asian	1 (7)
Etiology, N (%)	
Hepatitis B	3 (20)
Hepatitis C	4 (27)
Non-viral	8 (53)
NASH/NAFLD	4 (27)
Alcohol	1 (7)
Other or unknown	3 (20)
AFP (ng/mL), N (%)	
<400	10 (67)
≥400	5 (33)
≥20,000	4 (27)
Child-Pugh Score, N (%)	
A5	13 (87)
A6	2 (13)
MELD Score, median (range)	7 (6-10)
Diameter of largest lesion (cm), N (%)	
<5	1 (7)
5-10	8 (53)
>10	6 (40)
Tumor features, N (%)	
Multinodular	6 (40)
Portal vein invasion	4 (27)
Infiltrative	9 (60)
Adenopathy	1 (7)

**Supplementary Table 2.** Number of individuals with treatment related AEs during the neoadjuvant treatment period. AEs are listed as the most severe treatment-related AE reached for each individual patient from the start of therapy up to 100 after the last dose of treatment.

<b>Toxicity</b>	<b>Grade 1/2</b>	<b>Grade 3/4</b>	<b>Total (N=15)</b>
Any	14	2	14
<b>Cardio-renal</b>			
Hypertension	2	0	2 (13.3%)
Creatinine, elevated	1	0	1 (6.7%)
<b>Constitutional</b>			
Fatigue	8	0	8 (53.3%)
Weight loss	1	0	1 (6.7%)
<b>Dermatologic</b>			
Palmar-plantar erythrodysesthesia syndrome	2	0	2 (13.3%)
Rash	2	0	2 (13.3%)
Skin hypopigmentation	1	0	1 (6.7%)
<b>Ears/Nose/Throat</b>			
Hoarseness	2	0	2 (13.3%)
<b>Gastrointestinal</b>			
Abdominal pain	1	0	1 (6.7%)
Anorexia	2	0	2 (13.3%)
Bloating	1	0	1 (6.7%)
Diarrhea	2	0	2 (13.3%)
Dry mouth	1	0	1 (6.7%)
Dysgeusia	1	0	1 (6.7%)
Nausea	5	0	5 (33.3%)
Oral dysesthesia	1	0	1 (6.7%)
Mucositis	1	0	1 (6.7%)
Vomiting	3	0	3 (20.0%)
ALT, elevated	1	0	1 (6.7%)
Autoimmune Hepatitis	0	1	1 (6.7%)
<b>Musculoskeletal</b>			
Myositis	1	0	1 (6.7%)
<b>Neurological and psychiatric</b>			
Insomnia	1	0	1 (6.7%)
Myasthenia gravis	0	1	1 (6.7%)

**Supplementary Table 3. Biospecimen Availability/Use**

	Timepoint	Baseline Week 0	Baseline Week 0	Baseline Week 0	Post-Cabo Week 2	Post-Cabo Week 2	Post-Cabo Week 2	Post-Nivo Week 8	Post-Nivo Week 8	Post-Nivo Week 8	Post-Nivo Week 8	Post-Nivo Week 8
	Specimen	Core biopsy	PBMC	Plasma	Core biopsy	PBMC	Plasma	FFPE	FFPE	TIL	PBMC	Plasma
	Assay	Nanostring	CyTOF	ELISA*	Nanostring	CyTOF	ELISA*	IMC	IHC	CyTOF	CyTOF	ELISA*
1	Patient 02	X	X		X	X	X	X	X	X	X	X
2	Patient 03			X			X					
3	Patient 04	X			X		X	X	X			X
4	Patient 05	X		X	X		X					
5	Patient 07	X	X	X	X	X	X	X	X		X	X
6	Patient 08		X	X		X	X	X	X	X	X	X
7	Patient 09		X	X		X	X	X	X	X	X	X
8	Patient 12		X	X		X	X	X	X	X	X	X
9	Patient 13		X			X	X	X	X	X	X	
10	Patient 14		X	X			X	X	X	X	X	X
11	Patient 15			X			X	X	X			
12	Patient 17			X			X	X	X			X
13	Patient 19		X	X			X				X	X
14	Patient 20			X			X	X	X			X
15	Patient 21			X			X	X	X			X

**Supplementary Table 4. CyTOF panel**

Mass	Metal	Antigen	Surface	Intracellular	Clone	Titration	Source	Custom
89	Y	CD45	x		HI30	1:50	Fluidigm	
113	In	CD45	x		HI30	1:100	Biolegend	x
115	In	CD45	x		HI30	1:100	Biolegend	x
141	Pr	CCR6	x		G034E3	1:66	Fluidigm	
142	Ce	CD19	x		HIB19	1:100	Fluidigm	
144	Nd	CCR5	x		NP-6G4	1:66	Fluidigm	
145	Nd	CD4	x		RPA-T4	1:200	Fluidigm	
146	Nd	CD8	x		RPA-T8	1:200	Fluidigm	
147	Sm	CD7	x		CD7-6B7	1:200	Fluidigm	
149	Sm	CD25	x		2A3	1:400	Fluidigm	
150	Nd	OX40	x		ACT35	1:100	Fluidigm	
151	Eu	CD2	x		TS1/8	1:400	Fluidigm	
152	Sm	TNFa		x	Mab11	1:200	Fluidigm	
153	Eu	TIM3	x		F38-2E2	1:100	Fluidigm	
155	Gd	PD1	x		EH12.2H7	1:200	Fluidigm	
158	Gd	IL2		x	MQ1-17H12	1:200	Fluidigm	
159	Tb	CCR7	x		G043H7	1:66	Fluidigm	
160	Gd	CD28	x		CD28.2	1:200	Fluidigm	
161	Dy	CTLA4	x	x	14D3	1:200 (S) 1:400 (I)	Fluidigm	
163	Dy	CXCR3	x		G025H7	1:66	Fluidigm	
165	Ho	CD45RO	x		UCHL1	1:100	Fluidigm	
167	Er	CD27	x		O323	1:200	Fluidigm	
168	Er	IFNg		x	B27	1:100	Fluidigm	
169	Tm	CD45RA	x		HI100	1:400	Fluidigm	
170	Er	CD3	x		UCHT1	1:200	Fluidigm	
171	Yb	GZMB		x	GB11	1:100	Fluidigm	
172	Yb	Ki67		x	B56	1:100	Fluidigm	
173	Yb	41BB	x		4B4-1	1:200	Fluidigm	
175	Lu	LAG3	x		11C3C65	1:100	Fluidigm	
176	Yb	CD127	x		A019D5	1:100	Fluidigm	
194	Pt	CD45	x		HI30	1:50	Biolegend	x
198	Pt	CD45	x		HI30	1:50	Biolegend	x

**Supplementary Table 5. IMC panel**

Mass	Metal	Antigen	Clone	Conc. ( $\mu\text{g/ml}$ )	Source	Custom
141	Pr	Smooth muscle actin	1A4	1.25	Fluidigm	
143	Nd	Vimentin	D21H3	1.67	Fluidigm	
146	Nd	CD16	EPR16784	5	Fluidigm	
147	Sm	CD163	EDHu-1	5	Fluidigm	
148	Nd	Pan-keratin	C11	2.5	Fluidigm	
149	Sm	CD15	W6D3	10	Fluidigm	
150	Nd	PD-L1	SP142	10	Fluidigm	
152	Sm	CD45	2B11	5	Fluidigm	
153	Eu	Lag3	D2G40	10	Fluidigm	
155	Gd	FoxP3	236A/E7	10	Fluidigm	
156	Gd	CD4	ERP6855	5	Fluidigm	
158	Gd	E-cadherin	24E10	5	Fluidigm	
159	Tb	CD68	KP1	10	Fluidigm	
160	Gd	CD28	EPR22076	10	Abcam	x
161	Dy	CD20	H1	5	Fluidigm	
162	Dy	CD8a	C8/144B	2.5	Fluidigm	
163	Dy	CCR6	Polyclonal	5	Fluidigm	
164	Dy	Arginase 1	D4E3M	10	Fluidigm	
167	Er	Granzyme B	EPR20129-17	5	Fluidigm	
168	Er	Ki-67	B56	2.5	Fluidigm	
169	Tm	Collagen type I	Polyclonal	1.25	Fluidigm	
170	Er	CD3	Polyclonal	5	Fluidigm	
172	Yb	Cl. Caspase 3	5A1E	10	Fluidigm	
173	Yb	CD45RO	UCHL1	2.5	Fluidigm	
174	Yb	HLADR	LN3	5	Fluidigm	
176	Yb	Histone H3	D1H2	1.25	Fluidigm	
191	Ir	DNA 1			Fluidigm	
193	Ir	DNA 2			Fluidigm	
195	Pt	Plasma Membrane 2			Fluidigm	
196	Pt	Plasma Membrane 3			Fluidigm	
198	Pt	Plasma Membrane 4			Fluidigm	

**Supplementary Table 6.** IHC Staining procedures for CD3, CD8, CD20, CD138, and IgA

Antibody	Clone	Source	Antigen retrieval condition	Antibody final concentration( $\mu\text{g/ml}$ )	Antibody incubation time
CD3	LN10	Cell Marque	Citrate buffer, pH 6.0	12.4	30min
CD8	4B11	Cell Marque	EDTA buffer, pH 9.0	19.2	15min
CD20	L26	LeicaBiosystems	EDTA buffer, pH 6.0	6.2	15min
CD138	MI15	Agilent	Citrate buffer, pH 6.0	0.1	30min
CD20	L26	LeicaBiosystems	Citrate buffer, pH6.0	0.38	30min
IgA	IgA-L-CE	LeicaBiosystems		0.046	30min