

Supplementary Table 1 Baseline characteristics of the patients

	Non-responder group (<i>n</i> = 3)	Responder group (<i>n</i> = 5)
Age, years	66 (58-68)	60 (56-65)
Etiology		
Alcohol	2 (66)	2 (44)
Hepatitis B	1 (33)	5 (100)
Child-Pugh class		
A	5 (100)	4 (80)
B	0 (0)	1 (20)
Modified UICC		
IV A	0 (0)	1 (20)
IV B	3 (100)	4 (80)
Macrovascular invasion	3 (100)	1 (20)
ANC, μ L	1310 (1170-3220)	2270 (1750-3610)
ANC/Lymphocyte ratio	1.28 (1-6.57)	2.54 (1.51-4.27)
Platelet count ($\times 10^3/\mu$ L)	69 (53-87)	115 (58-309)
Albumin, g/dL	3.9 (3.3-4.2)	3.6 (3-4.1)
AST, U/L	42 (39-53)	46 (44-54)
ALT, U/L	37 (14-37)	30 (23-57)
Total bilirubin, mg/dL	1.1 (0.98-1.06)	0.93 (0.5-2.05)
PT, INR	1.07 (1.04-1.17)	1.03 (1.01-1.12)
Creatinine	0.7 (0.5-1.06)	0.89 (0.61-1.05)
AFP, ng/mL	3647 (294-16600)	273.3 (2.5-16600)
PIVKA-II, mAU/mL	2098 (40-28446)	4268 (46-9612)
Number of prior therapies	3 (3-4)	4 (3-5)
Median follow-up duration, mo	3 (1-4)	15 (11-19)

Data are presented as median (range) or *n* (%). AFP: Alpha-fetoprotein; ALT: Alanine aminotransferase; ANC: Absolute neutrophil count; AST: Aspartate aminotransferase; INR: International normalized ratio; PIVKA-II: Protein-induced by vitamin K absence or antagonist-II; PT: Prothrombin time; UICC: Union for International Cancer Control.

Supplementary Table 2 Statistical values analyzed by PERMANOVA (Bray-Curtis)

Group 1	Group 2	Pseudo-f statistic	<i>P</i> value	<i>P</i> (Bonferroni)
Responder (T0)	Responder (T1)	0.71831	0.87302	1.0
Responder (T0)	Non-responder (T0)	1.48228	0.07143	0.42857
Responder (T1)	Non-responder (T0)	1.60242	0.03571	0.21429
Responder (T0)	Non-responder (T1)	1.52860	0.05357	0.32143
Responder (T1)	Non-responder (T1)	1.56850	0.03571	0.21429
Non-responder (T0)	Non-responder (T1)	1.01213	0.5	1.0

Gut microbiome data was obtained from fecal samples collected at two time points: before the first nivolumab injection (< 1 mo, T0) and at the 3-mo follow-up (T1).

Supplementary Figure 1 Composition of the gut microbiome is associated with response to nivolumab in hepatocellular carcinoma patients. Heatmap showing the abundance of operational taxonomic units in responders (yellow) and non-responders (blue), including the names of bacterial taxa.