

Supplemental Tables for:
Cumulative antibiotic use significantly decreases efficacy of checkpoint inhibitors in patients with advanced cancer
Nadina Tinsley et al.

Table S1. Characteristics of patients treated with antibiotics

Metric	Categories	N	Percentage
ICI treatment	Pembrolizumab	42	45.7%
	Nivolumab	46	50.0%
	Ipilimumab	13	14.1%
	Combination ¹	11	12.0%
	Avelumab	2	2.2%
	Atezolizumab	0	0.0%
	Antibiotic administration route ²	Oral	77
Intravenous		26	28.3%
Infection ²	Respiratory	37	40.2%
	Skin	10	10.9%
	Sepsis	8	8.7%
	Genitourinary	7	7.6%
	Unknown	6	6.5%
	Mixed	5	5.4%
	URTI	3	3.3%
	CNS	2	2.2%
Time elapsed ³	Other	14	15.2%
	2 weeks before	19	20.7%
	6 weeks after	75	81.5%

	Overlap	2	2.2%
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ICI: immune checkpoint inhibitor; RCC: renal cell carcinoma; NSCLC: non-small cell lung cancer.

1. Combination therapy consists of treatment with 4 cycles of nivolumab and ipilimumab, followed by single agent nivolumab.
2. Some patients experienced >1 route of antibiotic therapy or >1 infection type.
3. Some patients will have received antibiotics 2 weeks before and 6 weeks after, with overlap.

Table S2. Association between clinical factors and antibiotics use. The association between antibiotics use and other clinical factors were examined using chi-square tests.

Clinical factors	Association with antibiotics
Gender	0.297
Age	0.540
Number of previous treatments	0.852
Cancer type	0.251
Participate in trials	0.853
Number of metastatic sites	0.776
ECOG performance status	0.026*
Comorbidities	0.954

*statistically significant

Table S3a. Impact of cumulative use of antibiotics on PFS

Name of covariates	Category	p-values	Hazard ratio	95% CI
ECOG performance status	1 vs. 0	0.198	1.270	0.883-1.829
	2+ vs. 0	0.0006	3.141	1.638-6.025
Comorbidities	yes. Vs. no	0.022	1.425	1.052-1.930
Cumulative use of ABX	Single course vs. no	0.279	1.324	0.796-2.200
	cumulative courses vs. no	0.026	2.625	1.245-6.127
Interaction of ECOG PS and use of ABX	PS=1 & single ABX	0.856	0.929	0.420-2.057
	PS=2+ & single ABX	0.385	0.599	0.188-1.905
	PS=1 & cumulative ABX	0.937	0.959	0.341-2.698
	PS=2+ & cumulative ABX	0.021	0.225	0.063-0.798

ECOG: Eastern Cooperative Oncology Group PS: Performance Status ABX: antibiotics

Table S3b. Impact of cumulative use of antibiotics on OS

Name of covariates	Category	p-values	Hazard ratio	95% CI
Participate in trials	Yes vs. no	0.002	0.559	0.384-0.812
Number of metastatic sites	2 vs. 0/1	0.697	1.120	0.633-1.983
	3+ vs. 0/1	0.004	2.289	1.304-4.019
ECOG performance status	1 vs. 0	0.002	1.812	1.238-2.651
	2+ vs. 0	0.00003	3.027	1.801-5.090
Comorbidities	Yes vs. no	0.020	1.523	1.069-2.169
Use of antibiotics	Single course vs. no	0.294	1.259	0.819-1.934
	cumulative courses vs. no	0.009	1.904	1.178-2.078

ECOG: Eastern Cooperative Oncology Group