

Supplementary Online Content

Witt RG, Cass SH, Tran T, et al. Gut microbiome in patients with early-stage and late-stage melanoma. *JAMA Dermatol*. Published online August 30, 2023.
doi:10.1001/jamadermatol.2023.2955

eTable 1. Permutational Multivariate Analysis of Variance (PERMANOVA) Results for All Relevant Covariates per Cohorts Tested

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Permutational Multivariate Analysis of Variance (PERMANOVA) Results for All Relevant Covariates per Cohorts Tested

Melanoma vs. Controls					
Covariates	Df	SumOfSqs	R2	F	Pr(>F)
Age	1	0.809	0.011	2.459	<2e-16
Sex	1	0.405	0.005	1.229	0.145
BMI	1	0.503	0.007	1.527	0.028
PPI/H2 Blocker	1	0.384	0.005	1.167	0.208
Melanoma vs Control	1	1.126	0.015	3.42	<2e-16
Corticosteroid	1	0.311	0.004	0.945	0.546
Statin	1	0.251	0.003	0.762	0.867
Antibiotic Use	1	0.359	0.005	1.091	0.294
Residual	218	71.775	0.945	NA	NA
Total	226	75.923	1	NA	NA

Early-Stage vs Late-Stage Melanoma					
Covariates	Df	SumOfSqs	R2	F	Pr(>F)
Age	1	0.58	0.01	1.745	0.01
Sex	1	0.344	0.006	1.037	0.388
BMI	1	0.364	0.006	1.097	0.295
PPI/H2 Blocker	1	0.392	0.007	1.179	0.198
Early vs Late-Stage	1	0.504	0.009	1.519	0.032
Corticosteroid	1	0.324	0.005	0.975	0.485
Statin	1	0.23	0.004	0.692	0.938
Antibiotic Use	1	0.393	0.007	1.183	0.193
Residual	169	56.117	0.947	NA	NA
Total	177	59.247	1	NA	NA

Recurrence vs No Recurrence					
Covariates	Df	SumOfSqs	R2	F	Pr(>F)
Age	1	0.496	0.023	1.531	0.037
Sex	1	0.287	0.013	0.887	0.632
BMI	1	0.387	0.018	1.193	0.192
PPI/H2 Blocker	1	0.441	0.02	1.362	0.088
Recurrence	1	0.351	0.016	1.084	0.317
Corticosteroid	1	0.375	0.017	1.159	0.223
Statin	1	0.45	0.021	1.389	0.078
Antibiotic use	1	0.393	0.018	1.212	0.182
Residual	57	18.468	0.853	NA	NA
Total	65	21.649	1	NA	NA

eTable 2. Characteristics of Patients With Melanoma Who Received Adjuvant Treatment After Excision

	No Recurrence n=46¹	Recurrence n=20¹	p-value
Age	60 (28-81)	51 (21-90)	0.26
Sex			0.79
Female	19 (41.3%)	9 (45%)	
Male	27 (58.7%)	11 (55%)	
BMI	30.6* (23.9-48.9)	31.4 (23.6–50.2)	0.90
Race			1.0
White	45 (97.8%)	20 (100%)	
Asian	1 (2.2%)	0 (0%)	
Stage			0.19
IIIA	10 (21.7%)	1 (5.0%)	
IIIB	13 (26.1%)	5 (20.0%)	
IIIC	21 (45.7%)	11 (55.0%)	
IIID	2 (4.4%)	3 (15.0%)	
Adjuvant Therapies			0.80
Anti-PD-1	39 (84.8%)	16 (80.0%)	
Anti-CTLA-4	4 (8.7%)	3 (15.0%)	
Targeted	2 (4.3%)	1 (5.0%)	
Other	1** (2.2%)	0 (0%)	
Medications (within 30 days)			
Antibiotic Use	9 (19.6%)	5 (25%)	0.62
PPI/H2 Blocker	16 (34.8%)	3 (15.0%)	0.14
Metformin	6 (13.0%)	1 (5.0%)	0.67
Statin	14 (30.4%)	3 (15.0%)	0.23
Corticosteroids	5 (10.9%)	1 (5.0%)	0.66

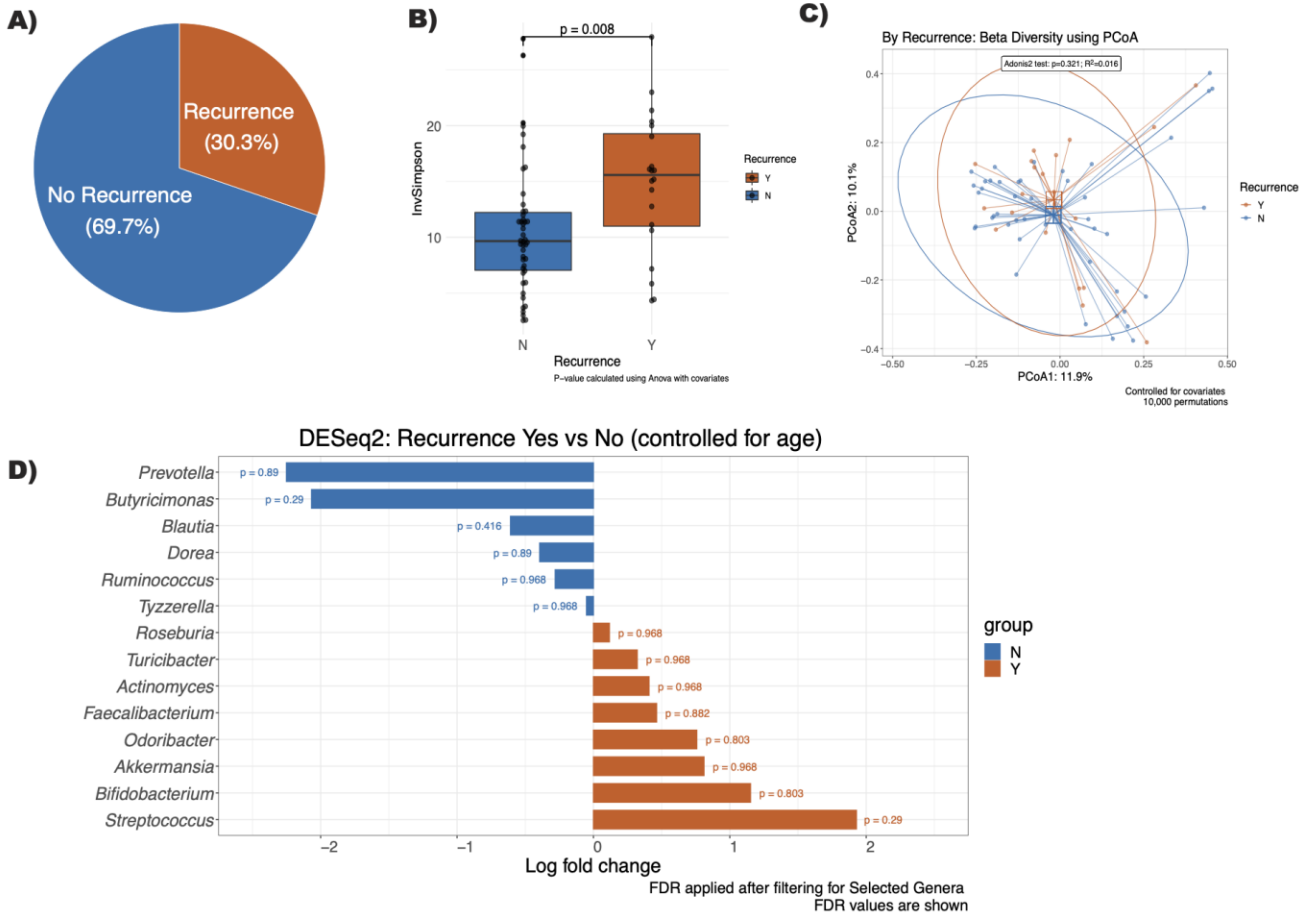
BMI – Body Mass Index, PPI – Proton Pump Inhibitor

¹Median (Range); n (%)

* missing BMI value for a single patient who did not develop recurrence (n=1)

** Other therapy received by one patient who did not develop recurrence (n=1) was adjuvant interferon alfa-2b

eFigure. Comparison of the Gut Microbiome of Patients With Stage III With Disease Recurrence Following Adjuvant Immune Checkpoint Inhibition



A) Recurrence occurred in 30.3% of all included stage III patients who underwent adjuvant therapy. Significant differences were seen in those that did and did not recur with regard to B) α -diversity ($p=0.008$) but not with C) β -diversity. D) DESeq2 analysis of known bacterial genus that impact response to immunotherapy was performed with no statistically significant differences on adjusted analysis.