Non-Hodgkin Lymphoma				
Characteristics	Total N= 137 (100%)	No P-I-M antibiotic exposure n= 116 (84.7%)	P-I-M antibiotic exposure n= 21 (15.3%)	p-value
Gender				
Male	93 (67.9)	79 (68.1)	14 (66.7)	0.897
Female	44 (32.1)	37 (31.9)	7 (33.3)	
Age – median [IQR]	61 [51-69]	60 [52-68]	63 [46-70]	0.843
Center				
MSK	72 (52.6)	54 (46.6)	18 (85.7)	*0.001*
Penn	65 (47.4)	62 (53.4)	3 (14.3)	
Performance status (ECOG)				
0-1	120 (87.6)	107 (93.9)	13 (72.2)	*0.003*
≥2	12 (8.8)	7 (6.1)	5 (27.8)	
Missing	5 (3.6)			
Previous lines of therapy				
≤4	77 (56.2)	69 (59.5)	8 (38.1)	0.069
>4	60 (43.8)	47 (40.5)	13 (61.9)	
Disease status at infusion				
Complete response	4 (2.9)	4 (3.4)	0 (0.0)	0.388
Persistent disease	133 (97.1)	112 (96.6)	21 (100.0)	
Costimulatory domain				
CD28	72 (52.6)	58 (50.0)	14 (66.7)	0.159
4-1BB	65 (47.4)	58 (50.0)	7 (33.3)	
Toxicity				
No	33 (24.1)	32 (27.8)	1 (4.8)	*0.023*
Yes	103 (75.2)	83 (72.2)	20 (95.2)	
Missing	1 (0.7)			
CRS				
No	37 (27.0)	34 (29.3)	3 (14.3)	0.154
Yes	100 (73.0)	82 (70.7)	18 (85.7)	
ICANS/ Neurotoxicity				
No	91 (66.4)	83 (72.8)	8 (38.1)	*0.002*
Yes	44 (32.1)	31 (27.2)	13 (61.9)	
Missing	2 (1.5)			
Complete response, Day 100				
Yes	62 (45.3)	55 (47.4)	7 (33.3)	0.340
No	75 (54.7)	61 (52.6)	14 (66.7)	
Vital status				
Alive	88 (64.2)	82 (70.7)	6 (28.6)	
Dead	49 (35.8)	34 (29.3)	15 (71.4)	

Supplementary Table 1. Antibiotic cohort: non-Hodgkin lymphoma patient characteristics by exposure to piperacillin-tazobactam, imipenem-cilastatin, or meropenem (P-I-M). Non-Hodgkin lymphoma patients from Memorial Sloan Kettering Cancer Center (MSK) and the University of Pennsylvania (Penn) who received anti-CD19 CAR T immunotherapy (N= 137) were

assessed based upon exposure to piperacillin-tazobactam, imipenem-cilastatin, or meropenem (P-I-M) antibiotics in the 30 days before CAR T infusion and evaluated for clinical characteristics and outcomes. The baseline and clinical characteristics of the patients in each of these group was compared to assess for variables that are associated with exposure to these antibiotics. Vital status is noted within 24 months of follow-up after CAR T cell infusion.

Wilcoxon rank-sum tests were used to compare the pairwise association between continuous variables and a binary outcome, while Fisher's exact test was used to compare two categorical variables. Two-tailed P values less than 0.05 were considered statistically significant across all tests. All tests were two-sided and there was no adjustment for multiple comparisons.

Abbreviations: No P-I-M antibiotic exposure: patients exposed to non-P-I-M plus patients who did not receive any antibiotics within the 4 weeks before CD19 CAR T cell infusion; IQR: inter-quartile range; NHL: non-Hodgkin lymphoma; ECOG: Eastern Cooperative Oncology Group; CRS: cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome

Acute Lymphoblastic Leukemia				
Characteristics	Total N= 91 (100%)	No P-I-M antibiotic exposure n= 65 (71.4%)	P-I-M antibiotic exposure n= 26 (28.6%)	p-value
Gender				
Male	66 (72.5)	49 (75.4)	17 (65.4)	0.334
Female	25 (27.5)	16 (24.6)	9 (34.6)	
Age - median [IQR]	43 [28-59]	44 [30-60]	40 [28-58]	0.849
Center				
MSK	55 (60.4)	33 (50.8)	22 (84.6)	*0.004*
Penn	36 (39.6)	32 (49.2)	4 (15.4)	
Performance status (ECOG)				
0-1	85 (93.4)	62 (96.9)	23 (95.8)	0.863
≥2	3 (3.3)	2 (3.1)	1 (4.2)	
Missing	3 (3.3)			
Previous lines of therapy				
≤4	54 (59.3)	41 (63.1)	13 (50.0)	0.251
>4	37 (40.7)	24 (36.9)	13 (50.0)	
Disease status at infusion				
Complete response	22 (24.2)	16 (24.6)	6 (23.1)	0.877
Persistent disease	69 (75.8)	49 (75.4)	20 (76.9)	
Costimulatory domain				
CD28	55 (60.4)	33 (50.8)	22 (84.6)	*0.003*
4-1BB	36 (39.6)	32 (49.2)	4 (15.4)	
Toxicity				
No	7 (7.7)	5 (7.8)	2 (7.7)	0.985
Yes	83 (91.2)	59 (92.2)	24 (92.3)	
Missing	1 (1.1)			
CRS				
No	10 (11.0)	8 (12.3)	2 (7.7)	0.525
Yes	81 (89.0)	57 (87.7)	24 (92.3)	
Neurotoxicity				
No	27 (29.7)	15 (32.6)	12 (46.2)	0.254
Yes	45 (49.4)	31 (67.4)	14 (53.8)	
Missing	19 (20.9)			
Complete response, Day 100				
Yes	55 (60.4)	44 (67.7)	11 (42.3)	0.046
No	36 (39.6)	21 (32.3)	15 (57.7)	
Vital status				
Alive	38 (41.8)	33 (50.8)	5 (19.2)	
Dead	53 (58.2)	32 (49.2)	21 (80.8)	

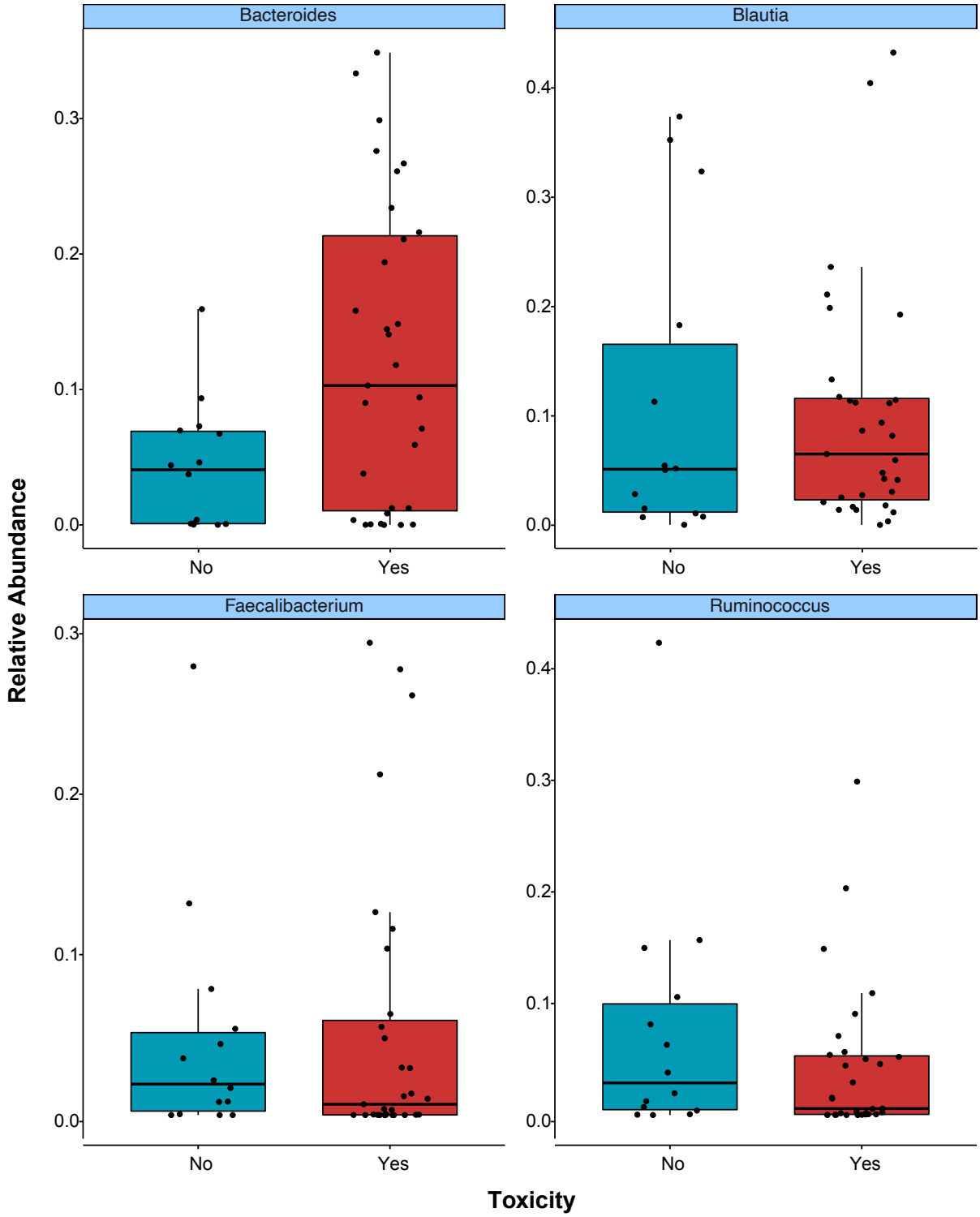
Supplementary Table 2. Antibiotic cohort: acute lymphoblastic leukemia patient characteristics by exposure to piperacillin-tazobactam, imipenem-cilastatin, or meropenem (P-I-M). Acute lymphoblastic leukemia (ALL) patients from Memorial Sloan Kettering Cancer Center (MSK) and the University of Pennsylvania (Penn) who received anti-CD19 CAR T cell immunotherapy (N= 91) were assessed based upon exposure to piperacillin-tazobactam, imipenem-cilastatin, or meropenem (P-I-M) antibiotics in the 30 days before CAR T infusion and evaluated for clinical characteristics and outcomes. The baseline and clinical characteristics of

the patients in each of these group was compared to assess for variables that are associated with exposure to these antibiotics. Vital status is noted within 24 months of follow-up after CAR T cell infusion.

Wilcoxon rank-sum tests were used to compare the pairwise association between continuous variables and a binary outcome, while Fisher's exact test was used to compare two categorical variables. Two-tailed P values less than 0.05 were considered statistically significant across all tests. All tests were two-sided and there was no adjustment for multiple comparisons.

Abbreviations: IQR: inter-quartile range; ALL: acute lymphoblastic leukemia; ECOG: Eastern Cooperative Oncology Group; CRS: cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome; No P-I-M antibiotic exposure: patients exposed to non-P-I-M plus patients who did not receive any antibiotics within the 4 weeks before CD19 CAR T cell infusion

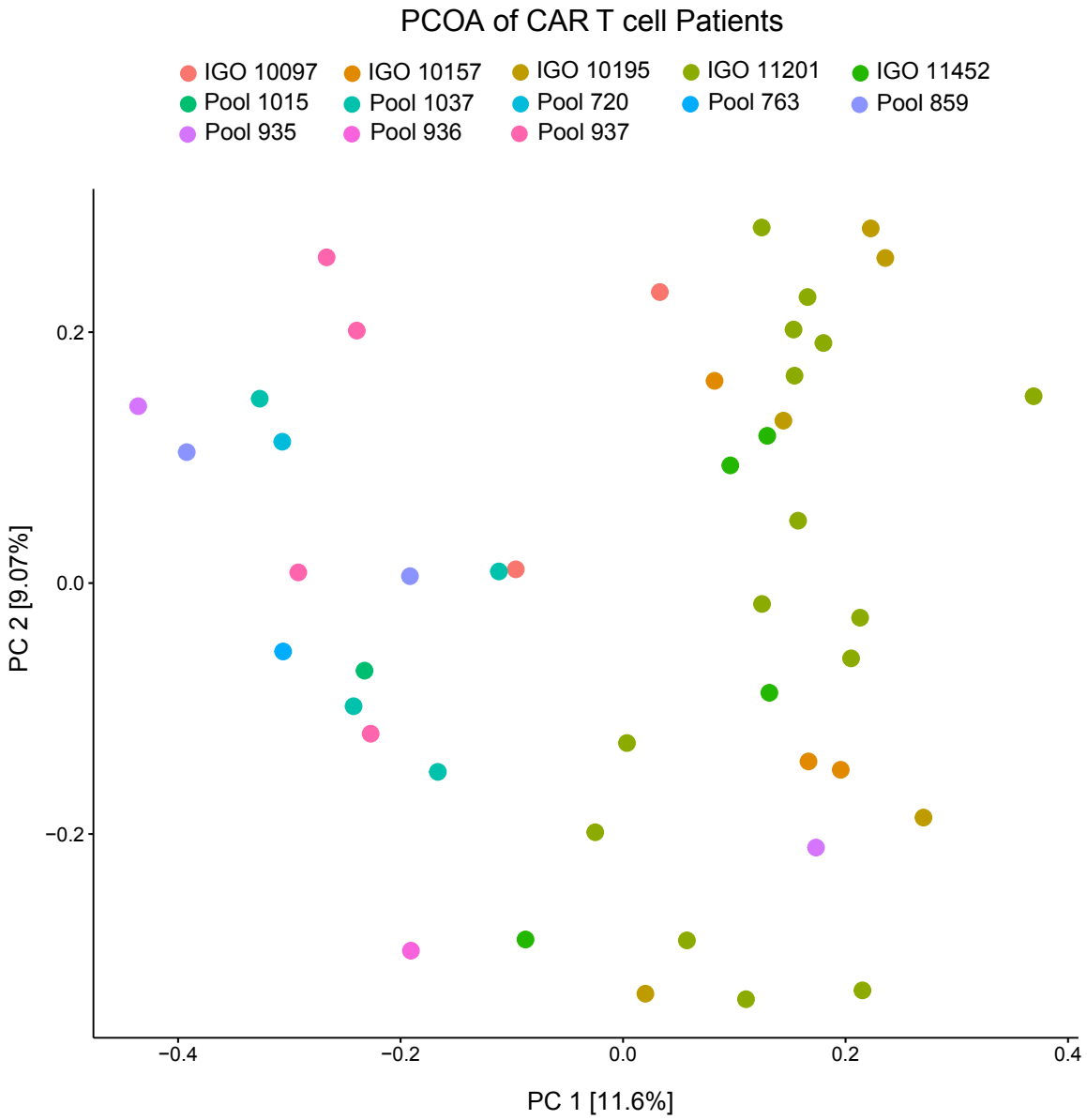
Supplementary Figure 1



Supplementary Figure 1. Boxplots of the relative abundance of selected taxa from LEfSe of toxicity. All data reported in this figure is based on 16S rRNA gene sequencing data from patients (n= 45). The relative abundance of *Bacteroides*, *Blautia*, *Faecalibacterium*, and

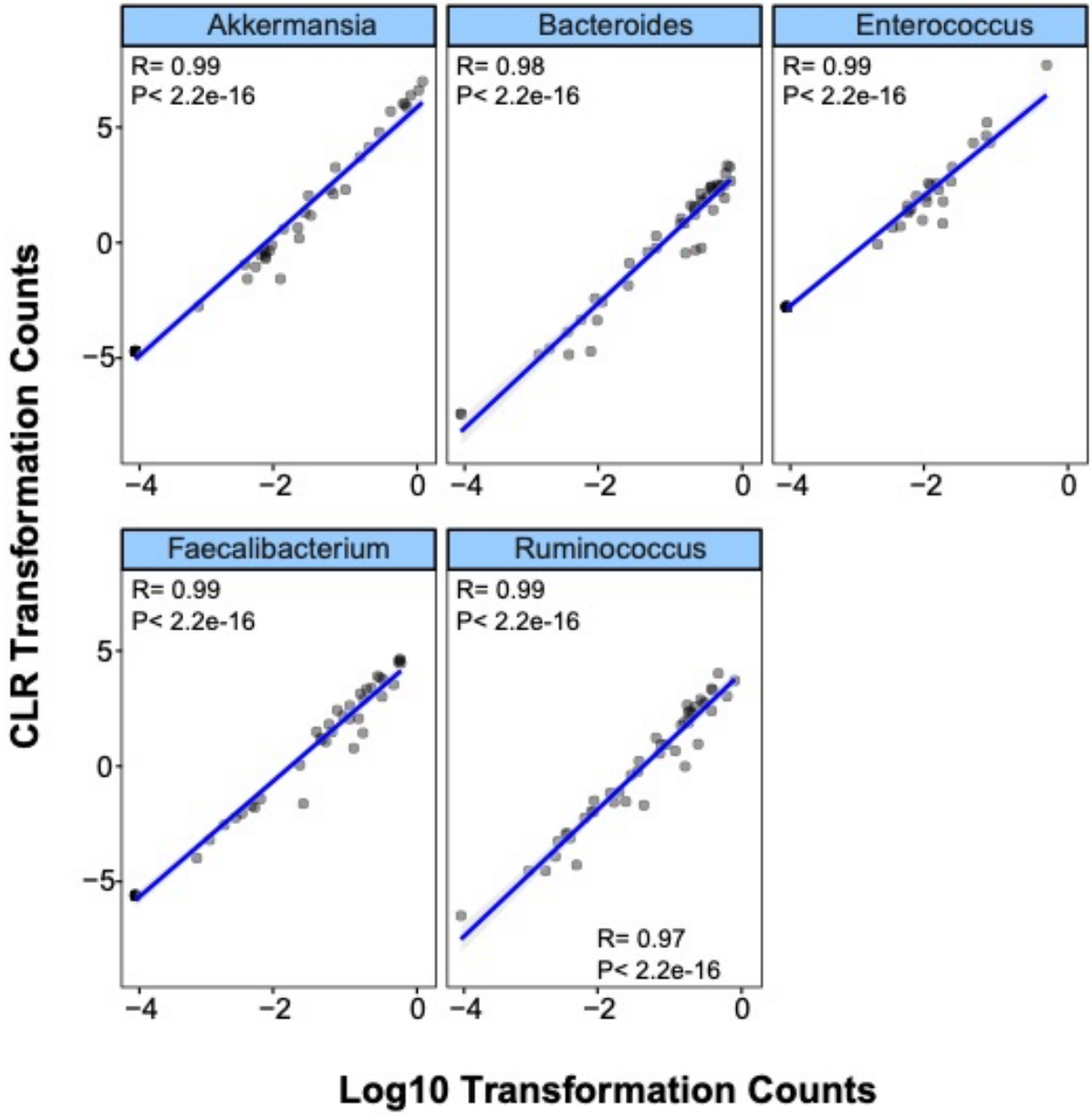
Ruminococcus are presented. Data is categorized by patients who did not experience toxicity (No), and patients who experienced toxicity (Yes). Dots indicate relative abundance of the baseline fecal sample from a CAR T cell patient. Two-sided Wilcoxon rank-sum test was used to calculate the p-values, and the p-values were adjusted for multiple hypothesis testing.

Supplementary Figure 2



Supplementary Figure 2. Principal Coordinates Analysis (PCoA) visualization of pools of 16S sequencing of baseline fecal samples from CAR T cell patients. Composition diversity of baseline patient samples (n= 45) is displayed according to principal coordinates analysis (PCoA). Dots are colored to indicate the sequencing pools (n= 13). All data reported in this figure is based on 16S rRNA gene sequencing data.

Supplementary Figure 3



Supplementary Figure 3. Correlation between the centered log-ratio and the log10 transformed counts for the five genera. Scatter plots show the Pearson correlation between the centered log-ratio and the log10 transformed counts for the five genera in the Bayesian model. All data reported in this figure are based on 16S rRNA gene sequencing data.

Abbreviations: CLR: centered log-ratio