The Oncologist
The official journal of the Society for Translational Oncology

Supplemental Tables for:
Antibacterial use is associated with an increased risk of hematologic and gastrointestinal adverse events in patients treated with gemcitabine for stage IV pancreatic cancer
Robert Wallace Corty et al.

Supplementary Information

Adverse Event	Number of Patients	Number of Events	Total Duration (days)	Incidence rate (events per 1000 patient-days)
ae_any	264 (61%)	537	5108	11.5
aeclass_hem	131 (30%)	268	2547	5.8
aecode_Neutropenia	81 (19%)	155	1403	3.3
aeclass_gi	39 (9%)	48	279	1
aecode_Thrombocytopenia	29 (7%)	45	354	1
aecode_Anaemia	30 (7%)	44	459	0.9
aeclass_const	28 (7%)	33	354	0.7
aecode_Neutrophil count decreased	16 (4%)	30	270	0.6
aecode_Abdominal pain	20 (5%)	26	131	0.6
aecode_Fatigue	19 (4%)	23	271	0.5
aeclass_hep	18 (4%)	21	251	0.5
aecode_Leukopenia	13 (3%)	21	198	0.5
aecode_Platelet count decreased	7 (2%)	15	121	0.3
aecode_Alanine aminotransferase increased	13 (3%)	15	149	0.3
aecode_Aspartate aminotransferase increased	12 (3%)	14	160	0.3
aecode_Vomiting	12 (3%)	12	69	0.3
aecode_Asthenia	8 (2%)	10	77	0.2
aecode_Nausea	8 (2%)	8	94	0.2
aeclass_pulm	5 (1%)	6	30	0.1
aecode_Constipation	6 (1%)	6	28	0.1
aecode_Dyspnoea	5 (1%)	6	30	0.1
aecode_Diarrhoea	4 (1%)	5	25	0.1
aecode_Pyrexia	4 (1%)	4	21	0.1
aecode_Oedema peripheral	3 (1%)	3	58	0.1
aecode_Decreased	1 (0%)	1	13	0

appetite				
aecode_Chills	0 (0%)	0	0	0

Table S 1: Expanded version of Table 2, showing all adverse events considered. In contrast, Table 2 shows only those adverse events that met our thresholds for analysis.

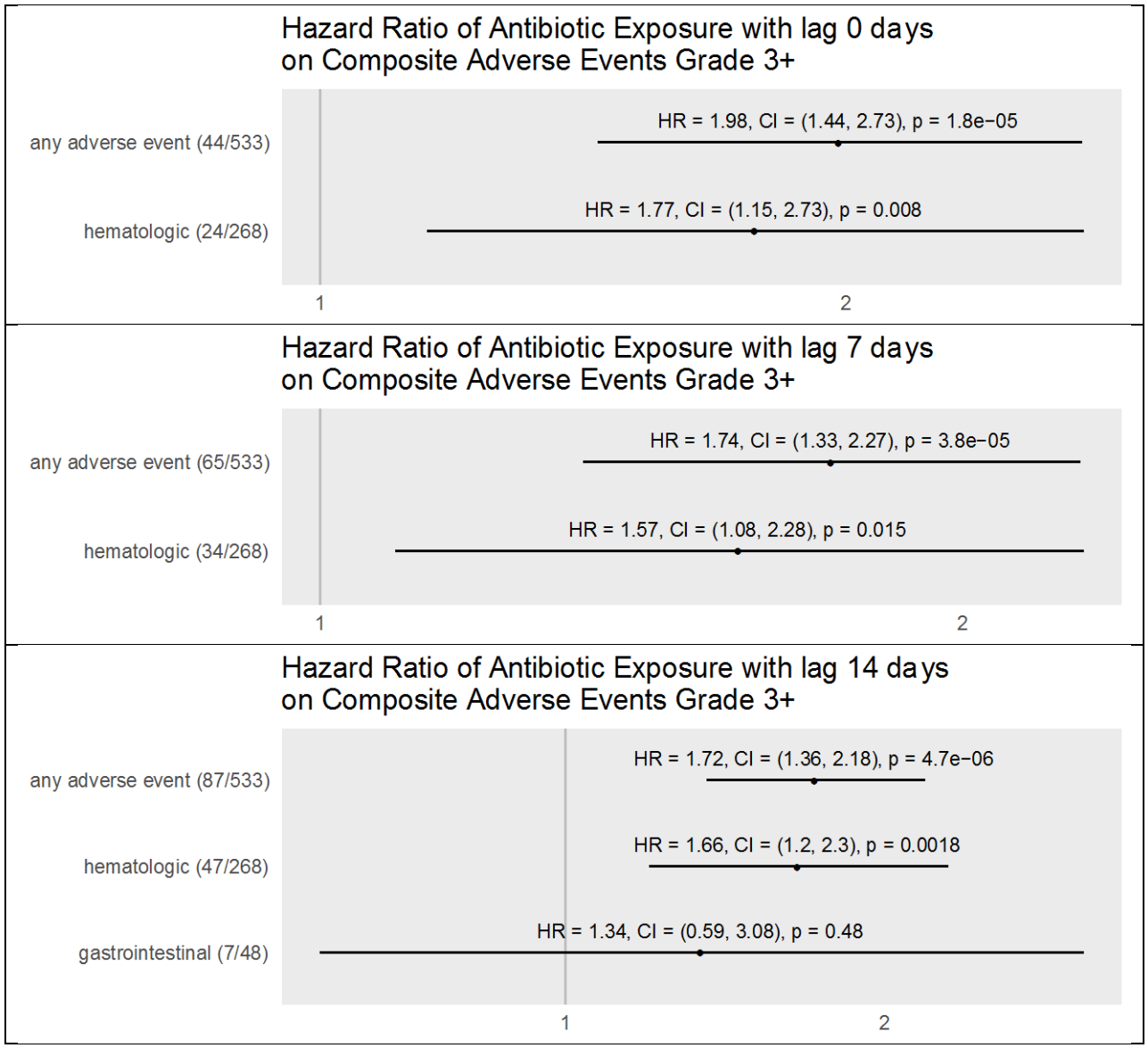

Table S 2: Sensitivity analysis – examining the sensitivity of the results presented in figure 1 to changing definition of "antibiotic exposure". In the main analysis, a patient is considered exposed from the first day of antibiotics until the day of study discontinuation. Here, the same analysis is conducted where patients are considered exposed to antibiotics only during an antibiotic prescription (top), during a prescription until 7 days after the end of the prescription (middle), and during a prescription until 14 days after the end of the prescription (bottom). The hazard ratio for "any adverse event" and "any hematologic adverse event" remain similar to those in the "permanent effect" analysis and statistically significant, though they are estimated less precisely due to a decrease in the number of adverse events that occur during the exposure period. The HR for "any gastrointestinal adverse event" is lower than in the "permanent effect" analysis and not statistically significant.

	Percent of patients with AE before AE on ABX
Any AE3+	35%
Hematologic 3+	27%
Gastrointestinal 3+	18%
Constitutional 3+	10%
Hepatologic 3+	0%

Table S 3: For each AE classification, the fraction of patients who experienced the AE after ABX exposure who also experienced the AE prior to ABX exposure.

	abx status	Number of days	Average day of study
Permanent exposure	off abx	31,702	89.3
	on abx	15,232	120.0
Temporary exposure	off abx	44,367	100.0
	on abx	2,588	82.1

Table S 4: In the permanent exposure framework, the average "on antibiotics" day occurred on day 89 of the study, while the average "off antibiotic" day occurred on day 120, permitting the possibility that the observed association between antibiotic exposure and increased risk of adverse events is due to cumulative chemotherapy exposure rather than antibiotic exposure itself. In the temporary exposure framework (with zero lag), the average "off antibiotic" day occurred on day 100 of the study, while the average "on antibiotic" day occurred on day 82, inconsistent with the possibility that the increased risk was mediated by cumulative chemotherapy exposure. That the hazard ratio of antibiotic exposure on hematologic adverse events was similar in both frameworks (1.64 vs 1.77) suggests that the effect is likely not mediated through cumulative chemotherapy exposure.