**Fig. S1.** Association between antibiotics administered 30 days before (pre-ICI 30-days) first dose of ICI therapies and irAE risks in all cancer patients.

Magenta indicates that irAEs are more likely to occur in antibiotic users; cyan indicates that irAEs are more likely to occur in non-antibiotic users; shade of the dot indicates FDR-adjusted p value. Dot size from large to small respectively indicates FDR-adjusted p < 0.001, 0.001 < FDR-adjusted p < 0.1, and FDR-adjusted p >=0.1. ATB: antibiotics.
Fig. S2

<table>
<thead>
<tr>
<th>Cancer types</th>
<th>log2(OR 95%CI)</th>
<th>OR (95%CI)</th>
<th>Total</th>
<th>With ATB</th>
<th>Without ATB</th>
<th>FDR-adjusted p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal cancer</td>
<td></td>
<td>1.62(0.30–8.75)</td>
<td>63</td>
<td>15</td>
<td>48</td>
<td>0.67</td>
</tr>
<tr>
<td>Liver cancer</td>
<td></td>
<td>2.32(0.36–15.11)</td>
<td>107</td>
<td>14</td>
<td>93</td>
<td>0.53</td>
</tr>
<tr>
<td>Lung cancer</td>
<td></td>
<td>2.68(1.32–5.44)</td>
<td>340</td>
<td>57</td>
<td>283</td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>Head and neck cancer</td>
<td></td>
<td>3.36(0.38–29.63)</td>
<td>59</td>
<td>7</td>
<td>52</td>
<td>0.48</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td></td>
<td>6.53(0.56–76.68)</td>
<td>37</td>
<td>6</td>
<td>31</td>
<td>0.32</td>
</tr>
<tr>
<td>PanCan</td>
<td></td>
<td>2.13(1.38–3.30)</td>
<td>767</td>
<td>133</td>
<td>634</td>
<td><strong>4.75×10^{-2}</strong></td>
</tr>
</tbody>
</table>

Fig. 2. Analysis of irAEs in antibiotic and non-antibiotic users among patients with different cancer types receiving anti-PD-1/PD-L1 by adding duration of treatment as covariates.

Magenta indicates that irAEs are more likely to occur in antibiotic users; cyan indicates that irAEs are more likely to occur in non-antibiotic users; shade of the dot indicates FDR-adjusted p value. Dot size from large to small respectively indicates FDR-adjusted p < 0.001, 0.001 < FDR-adjusted p < 0.1, and FDR-adjusted p >=0.1, as shown. ATB: antibiotics.
Fig. S3

A

Specified irAEs | log2(OR 95%CI) | OR (95%CI) | Total | With ATB Total irAE | Without ATB Total irAE | FDR-adjusted p
--- | --- | --- | --- | --- | --- | ---
Hematologic irAEs | | | | | | 
Rash | | | | | | 
Hepatic irAEs | | | | | | 
Gastrointestinal irAEs | | | | | | 
Thyroid irAEs | | | | | | 
Vascular irAEs | | | | | | 
Pneumonitis | | | | | | 

B

grade of irAEs | log2(OR 95%CI) | OR (95%CI) | Total | With ATB Total irAE | Without ATB Total irAE | FDR-adjusted p
--- | --- | --- | --- | --- | --- | ---
grade 1-2 irAEs | | | | | | 
grade 3-5 irAEs | | | | | | 

Fig S3. Multivariable logistic regression analysis on in-house cohort for association between antibiotic use and different irAE subgroups.


Magenta indicates that irAEs are more likely to occur in antibiotic users; cyan indicates that irAEs are more likely to occur in non-antibiotic users; shade of the dot indicates FDR-adjusted p value. Dot size from large to small respectively indicates FDR-adjusted p < 0.001, 0.001 < FDR-adjusted p < 0.1, and FDR-adjusted p >=0.1. ATB: antibiotics.
Fig. S4

Spearman correlation between microbial diversity and irAE related factors

Fig S4. Spearman correlation between irAE related factors/signatures and microbial diversity across 25 cancer types. Inverse Simpson index was used to evaluate microbial diversity. Red indicates positive correlation; blue indicates negative correlation; shade of the square indicates spearman R (Rs); size of the dots indicate significance; Dot size from large to small respectively indicates FDR-adjusted p < 0.001, and 0.001 < FDR-adjusted p < 0.05.

LUSC, lung squamous cell carcinoma; BRCA, breast invasive carcinoma; SARC, sarcoma; BLCA, bladder urothelial carcinoma; LUAD, lung adenocarcinoma; HNSC, head and neck squamous cell carcinoma; LGG, brain lower grade glioma; TGCT, testicular germ cell tumors; LIHC, liver hepatocellular carcinoma; THYM, Thymoma; CESC, cervical squamous cell carcinoma and endocervical adenocarcinoma; ESCA, esophageal carcinoma; GBM, glioblastoma multiforme; KIRC, kidney renal clear cell carcinoma; KIRP, kidney renal papillary cell carcinoma; OV, ovarian serous cystadenocarcinoma; PAAD, pancreatic adenocarcinoma; PCCG, pheochromocytoma and paraganglioma; READ, rectum adenocarcinoma; SKCM, skin cutaneous melanoma; STAD, stomach adenocarcinoma; THCA, thyroid carcinoma; UCEC, uterine corpus endometrial carcinoma; PRAD, prostate adenocarcinoma; COAD, colon adenocarcinoma.