

## Supplemental Online Content

Anscher MS, Arora S, Weinstock C, et al. Association of radiation therapy with risk of adverse events in patients receiving immunotherapy: a pooled analysis of trials in the US Food and Drug Administration database. *JAMA Oncol*. Published online January 6, 2022.  
doi:10.1001/jamaoncol.2021.6439

**eMethods.** Statistical Analysis Details

**eTable 1.** List of Trials Included in Analysis

**eTable 2.** Grouping of Adverse Event Terms

**eTable 3.** Analysis of AE Rates for the Matched Patients Who Received RT Within 90 Days Before Initiating an ICI vs the Corresponding Matched Patients Who Did Not Receive RT Adjusted for the Length of Time Each Patient Was on Study

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

## **eMethods. Statistical Analysis Details**

Patients with missing performance status and prior lines of therapy data were assigned an “unknown” category to enable matching. For the propensity score analysis, performance status assigned score was grouped as 0-1, 2+, or unknown; prior lines of therapy were grouped as 0-1 vs 2+ or unknown, tumor type was considered as melanoma, renal, lung, bladder, head and neck, or other and type of ICI-based therapy was categorized as anti-CTLA-4, anti-PD-1, anti-PD-L1, anti-PD-1 plus anti-CTLA-4, anti-PD-1 plus tyrosine kinase inhibitor and anti-PD-1 plus chemotherapy.

To maintain a conservative approach, differences between groups of  $\geq 1\%$  for higher incidence groups or ratios of AE occurrence of  $\geq 2$  for lower incidence groups were considered potentially clinically meaningful. Higher incidence groups and lower incidence groups were identified based on observing  $\geq 1\%$  and  $< 1\%$  incidence of an AE prior to matching, respectively.

<b>eTable 1. List of Trials Included in Analysis</b>	
<b>ClinicalTrials.gov NCT Identification number</b>	
1.	NCT01772004
2.	NCT01943461
3.	NCT02155647
4.	NCT01295827
5.	NCT01704287
6.	NCT01866319
7.	NCT01905657
8.	NCT01848834
9.	NCT01953692
10.	NCT01876511
11.	NCT02039674
12.	NCT02142738
13.	NCT02054806
14.	NCT02220894
15.	NCT02256436
16.	NCT02335424
17.	NCT02362594
18.	NCT02255097
19.	NCT02335411
20.	NCT02453594
21.	NCT02628067
22.	NCT02460198
23.	NCT02576990
24.	NCT02564263
25.	NCT02578680
26.	NCT02702414
27.	NCT02775435
28.	NCT02195479
29.	NCT02684006
30.	NCT00730639
31.	NCT01024231
32.	NCT01358721
33.	NCT01472081
34.	NCT01642004
35.	NCT01668784
36.	NCT01928394
37.	NCT01721746
38.	NCT01592370
39.	NCT01658878

40. NCT01673867
41. NCT01721772
42. NCT01844505
43. NCT01927419
44. NCT02105636
45. NCT02060188
46. NCT02066636
47. NCT02181738
48. NCT02231749
49. NCT02388906
50. NCT02387996
51. NCT02713867
52. NCT02714218
53. NCT01693562
54. NCT02453282
55. NCT02125461
56. NCT02087423
57. NCT02207530
58. NCT01846416
59. NCT01903993
60. NCT02031458
61. NCT02366143
62. NCT02763579
63. NCT00057889
64. NCT02267343
65. NCT01375842
66. NCT02425891
67. NCT02853331
68. NCT02501096

<b>eTable 2. Grouping of Adverse Event Terms</b>	
Neurologic AEs of interest	Meningitis, encephalitis, myelitis, demyelination, myasthenic syndrome, myasthenia gravis, Guillain-Barré syndrome, nerve palsy, autoimmune neuropathy
Skin (Stevens-Johnson; Toxic Epidermal Necrolysis)	Erythema multiforme, Stevens-Johnson syndrome; Toxic epidermal necrolysis
Renal AEs of interest	Autoimmune nephritis, Glomerulonephritis, Glomerulonephritis acute, Nephritic syndrome, Nephrotic syndrome, Tubulointerstitial nephritis, Renal tubular necrosis, Immune-mediated nephritis, Nephritis radiation, Nephritis haemorrhagic
Endocrine AEs of interest	new onset diabetes mellitus, hyperglycemia, Adrenal insufficiency, diabetes, hyperthyroidism, hypothyroidism, Diabetic Ketoacidosis, type 1 diabetes mellitus
Fatigue	Asthenia, Fatigue, Malaise, Lethargy, decreased activity
Neutropenia	Autoimmune neutropenia, Febrile neutropenia, neutropenia, Chemotherapy induced neutropenia
Thrombocytopenia	Thrombocytopenia
Pneumonitis	Pneumonitis, Interstitial Lung Disease, Pulmonary Fibrosis, Acute Interstitial Pneumonitis, Alveolitis Necrotising, Alveolitis, Hypersensitivity Pneumonitis, Organizing Pneumonia
Diarrhoea and related AEs of interest	autoimmune colitis, colitis, colitis microspscopic, enterocolitis, frequent bowel movements, diarrhea, diarrhea hemorrhagic, enteritis, gastroenteritis, Diarrhoea, Diarrhoea haemorrhagic
Hepatitis	Autoimmune hepatitis, hepatitis, hepatitis acute
Myocarditis	Autoimmune myocarditis, eosinophilic myocarditis, myocarditis
Musculoskeletal and Connective Tissue AEs of interest	Myositis, polymyositis, rhabdomyolysis, arthritis, polymyalgia rheumatica

**eTable 3. Analysis of AE Rates for the Matched Patients Who Received RT Within 90 Days Before Initiating an ICI vs the Corresponding Matched Patients Who Did Not Receive RT Adjusted for the Length of Time Each Patient Was on Study**

	<b>Rates per 100 person-years (1:1 Propensity Score Matched set)</b>	
<b>AE</b>	<b>No RT (n=1662)</b>	<b>RT (n=1662)</b>
neutropenia	4.05	4.02
thrombocytopenia	4.45	5.46
pneumonitis	6.59	11.31
colitis	5.78	4.69
hepatitis	1.79	1.63
myocarditis	0.14	0.10
neurologic	0.39	0.38
skin	0.35	0.19
renal	0.47	0.67
endocrine	23.08	24.53
fatigue	78.27	88.24
diarrhea	46.53	45.03
muscular	2.49	2.40