



Figure S1 Study design and structural timeline of cohort.

Table S1 Claims-based definitions of radiation therapy and immune checkpoint inhibition

Exposure	Current Procedural Terminology (CPT)/Healthcare Common Procedure Coding System (HCPCS) Codes
Radiation therapy	77401, 77402, 77403, 77404, 77406, 77407, 77408, 77409, 77411, 77412, 77413, 77414, 77416, G6003, G6004, G6005, G6006, G6007, G6008, G6009, G6010, G6011, G6012, G6013, G6014, 77418, 0073T, 0197T, 77385, 77386, G6015, G6016, G6017, 77387, 77421, G6001, G6002, G6017, 77520, 77521, 77522, 77523, 77524, 77525, 77422, 77423, 77373, 32701
Immune checkpoint inhibition	
Atezolizumab	J9022, C9483
Durvalumab	J9173, C9492
Ipilimumab	J9228, C9284
Pembrolizumab	J9271, C9027
Nivolumab	J9299, C9453

Table S2 Claims-based definitions of pneumonitis

Algorithm	International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)-based Definition of Pneumonitis
Algorithm B (Primary analysis)	J700, J701, J702, J703, J704, J708, J709, J84111, J84113, J84114, 5080, 5081, 5088, 5089, 51630, 51632, 51633, 51635
Algorithm A	J679, J700, J701, J702, J703, J704, J708, J709, J8401, J8402, J8403, J8409, J8410, J84111, J84112, J84113, J84114, J84115, J84116, J84117, J842, J8489, J849, 4959, 5080, 5081, 5088, 5089, 51630, 51631, 51632, 51633, 51634, 51636, 51637, 51635, 515, 5168, 5169
Algorithm B with Steroid Prescriptions	Algorithm B and an outpatient steroid prescription within 7 days of inpatient discharge or outpatient encounter
Algorithm A with Steroid Prescriptions	Algorithm A and an outpatient steroid prescription within 7 days of inpatient discharge or outpatient encounter
Steroids	CORTISONE ACETATE, HYDROCORTISONE, HYDROCORTISONE ACETATE, HYDROCORTISONE BUTYRATE, HYDROCORTISONE SOD SUCCINATE, PREDNISONE, PREDNISOLONE, PREDNISOLONE SOD PHOSPHATE, PREDNISOLONE SODIUM PHOSPHATE, DEXAMETHASONE, DEXAMETHASONE SOD PHOSPHATE, DEXAMETHASONE SODIUM PHOSP/PF, METHYLPREDNISOLONE, METHYLPREDNISOLONE ACETATE, METHYLPREDNISOLONE SOD SUCCINATE, METHYLPREDNISOLONE SOD SUCC/PF

Table S3 Claims-based definitions of covariates and Surveillance Epidemiology and End Results Selection Criteria

Diagnosis	Definition
Non-small cell lung cancer histology (ICD-O-3)	8010, 8012, 8014, 8015, 8020, 8021, 8022, 8030, 8031, 8035, 8310, 8046, 8050, 8051, 8052, 8053, 8060, 8070, 8071, 8072, 8073, 8074, 8075, 8076, 8077, 8078, 8083, 8084, 8140, 8211, 8230, 8231, 8250, 8251, 8252, 8253, 8254, 8255, 8260, 8323, 8480, 8481, 8490, 8550, 8551, 8552, 8560, 8570, 8571, 8673, 8574, 8575, 8576
COPD (ICD-10-CM and ICD-9-CM)	J40, J410, J411, J418, J42, J430, J431, J432, J438, J439, J440, J441, J449, J470, J471, J479, J43, J982, J983, P25, P250, P258, J43, J430, J431, J432, J438, J439, J982, J983, P25, P250, P258, 490, 4910, 4911, 49120, 49121, 49122, 4918, 4919, 4920, 4928, 4940, 4941, 496

COPD, chronic obstructive pulmonary disease. ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification. ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification

Table S4 Sensitivity analyses

Primary Analysis	Control, aHR (95% CI)	RT, aHR (95% CI)	ICI, aHR (95% CI)	RT + ICI, aHR (95% CI)	RERI (95% CI), P value
	Reference	9.5 (6.4, 14.0)	6.2 (3.7, 10.2)	10.6 (5.9, 19.0)	-4.0 (-10.7, 1.5), P=0.90
Primary analysis (EAW = 12 months, DEW = 3 months, OAW = 6 months)					
Exposure Assessment Window (EAW) adjustments: time from diagnosis to first treatment					
EAW = 9 months	Reference	10.9 (7.3, 16.2)	8.0 (4.8, 13.4)	12.4 (6.8, 22.5)	-5.7 (-13.6, 1.1), P=0.94
EAW = 6 months	Reference	12.1 (8.1, 17.9)	10.8 (6.4, 18.2)	11.2 (5.8, 21.7)	-8.6 (-21.6, -1.72), P=0.97
EAW = 3 months	Reference	5.7 (4.3, 7.5)	5.2 (3.1, 8.9)	6.1 (3.3, 11.6)	-3.0 (-8.7, 0.8), P=0.95
Double Exposure Window (DEW) adjustments: time from first treatment to second treatment					
DEW = 21 Days	Reference	9.2 (6.3, 13.7)	5.6 (3.4, 9.2)	4.9 (1.5, 16.1)	-9.0 (-17.4, -2.2), P=0.99
DEW = 2 months	Reference	9.6 (6.5, 14.2)	6.0 (3.6, 9.9)	8.4 (4.2, 16.9)	-4.1 (-14.9, -0.6), P=0.88
DEW = 6 months	Reference	10.8 (7.1, 16.4)	6.8 (4.0, 11.5)	12.5 (7.5, 20.6)	-4.5 (-9.4, 0.4), P=0.96
Outcome Assessment Window (OAW) adjustments: time from treatment to event					
OAW = 3 months	Reference	8.7 (5.0, 15.3)	8.9 (4.5, 17.3)	12.1 (5.6, 26.3)	-5.9 (-17.6, 3.7), P=0.87
OAW = 9 months	Reference	9.0 (6.4, 12.6)	6.1 (3.9, 9.4)	10.2 (6.1, 17.0)	-3.8 (-9.3, 0.8), P=0.93
OAW = 12 months	Reference	7.8 (5.8, 10.5)	5.1 (3.4, 7.6)	8.3 (5.1, 13.5)	-3.0 (-7.6, 0.3), P=0.93
Time-varying exposure					
Time-varying exposure	Reference	9.6 (7.5, 12.4)	5.1 (3.5, 7.3)	12.9 (9.5, 17.6)	-0.8 (-3.9, 2.3), P=0.67
Claims-based exposure definitions for RT and ICI					
Thoracic RT (TRT)*	Reference	15.7 (11.3, 21.8)	7.2 (4.8, 10.8)	19.0 (9.6, 37.7)	-2.8 (-15.1, 11.4), P=0.66
TRT with Deletions**	Reference	16.9 (12.1, 23.6)	8.0 (5.3, 12.0)	20.5 (10.4, 40.7)	-3.4 (-18.5, 10.5), P=0.68
PD1 Inhibition Only	Reference	9.5 (6.4, 14.1)	6.4 (3.9, 10.6)	9.6 (5.2, 17.8)	-5.3 (-11.6, 0.4), P=0.96
RT + ICI (RT before ICI)	Reference	9.5 (6.4, 14.0)	6.2 (3.7, 10.2)	10.7 (5.6, 20.3)	-3.9 (-11.2, 3.3), P=0.86
RT + ICI (ICI before RT)	Reference	9.5 (6.4, 14.0)	6.2 (3.7, 10.2)	9.7 (3.7, 25.2)	-4.9 (-15.0, 5.8), P=0.82
Claims-based outcome definitions for pneumonitis					
Inpatient Pneumonitis	Reference	12.1 (6.8, 21.4)	9.8 (5.0, 19.4)	15.4 (7.1, 33.4)	-5.5 (-20.5, 4.7), P=0.81
20 ICD-10-CM Codes	Reference	1.3 (1.1, 1.5)	0.9 (0.7, 1.2)	1.4 (1.0, 2.1)	0.2 (-0.4, 0.8), P=0.21
11 Codes + Steroid Rx	Reference	15.7 (7.3, 34.0)	8.2 (3.2, 20.7)	16.6 (6.0, 46.0)	-6.3 (-28.5, 8.3), P=0.50
20 Codes + Steroid Rx	Reference	2.3 (1.7, 3.1)	1.9 (1.2, 3.0)	2.5 (1.3, 4.7)	-0.7 (-2.3, 1.2), P=0.76
Stage of disease					
Stage 3A-3C	Reference	36.5 (16.3, 81.7)	12.6 (4.0, 39.0)	50.2 (18.6, 135.9)	2.2 (-47.9, 49.5), P=0.50
Stage 4	Reference	11.6 (7.1, 18.9)	8.9 (5.0, 15.8)	12.7 (6.5, 25.0)	-6.7 (17.9, 1.0), P=0.92

*, Requiring a threshold number of fractions of RT: 15 for conventional, 5 for stereotactic body radiation therapy, 1 for intensity modulated radiation therapy, 1 for proton therapy; **, Deleting non-threshold exposures to RT. RT, radiation therapy; ICI, immune checkpoint inhibition; RERI, relative excess risk due to interaction; 95% CI, 95% confidence interval.