Published in final edited form as:

JAMA Oncol. 2016 November 01; 2(11): 1507–1508. doi:10.1001/jamaoncol.2016.2238.

Prevalence of Autoimmune Disease Among Patients With Lung Cancer: Implications for Immunotherapy Treatment Options

Saad A. Khan, MD, Sandi L. Pruitt, PhD, Lei Xuan, PhD, and David E. Gerber, MD

Division of Hematology and Oncology, University of Texas Southwestern Medical Center, Dallas (Khan, Gerber); Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas (Khan, Pruitt, Gerber); Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas (Pruitt, Xuan)

The emergence of immune checkpoint inhibitors targeting either the programmed death 1 (PD1) or cytotoxic T lymphocyte antigen 4 (CTLA4) axis represents a major therapeutic advance in treating lung cancer and other malignant diseases. These new treatments also convey risks for unpredictable, possibly severe, and potentially irreversible autoimmune toxic events that can have an effect on diverse organ systems. With combination immunotherapy regimens, rates of these events may exceed 50%.¹

To limit risk of immune-related adverse events, clinical trials of immune checkpoint inhibitors have routinely excluded patients with preexisting autoimmune disease, a population estimated to include 20 to 50 million individuals in the United States.² To determine the impact of this practice on patient eligibility for immunotherapy, we calculated the prevalence of autoimmune disease among patients diagnosed with lung cancer using a large, representative, population-based data set.

Corresponding Author: David E. Gerber, MD, Division of Hematology and Oncology, Harold C. Simmons Comprehensive Cancer Center, 5323 Harry Hines Blvd, Mail Code 8852, Dallas, TX 75390-8852 (David.Gerber@UTsouthwestern.edu).

Author Contributions: Dr Gerber had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Khan, Pruitt, and Gerber contributed equally to this work.

Study concept and design: Khan, Pruitt, Gerber.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Khan, Pruitt, Gerber.

Critical revision of the manuscript for important intellectual content: Pruitt, Xuan, Gerber.

Statistical analysis: Khan, Pruitt, Xuan.

Obtained funding: Pruitt, Gerber.

Administrative, technical, or material support: Khan, Pruitt, Gerber.

Study supervision: Khan, Pruitt, Gerber.

Conflict of Interest Disclosures: None reported.

Disclaimer: Contents of this article are solely the responsibility of the authors and do not necessarily represent the official view of the NIH.

Previous Presentation: This study was presented in abstract form at the 52nd annual meeting of the American Society of Clinical Oncology; Chicago, Illinois; June 4, 2016.

Additional Contributions: The authors thank Helen Mayo, MLS, from the University of Texas Southwestern Medical Library, for assistance with literature searches and Dru Gray, BA, Division of Hematology-Oncology, Harold C. Simmons Comprehensive Cancer, University of Texas Southwestern Medical Center for assistance with manuscript preparation. They were not compensated for their contributions. The authors also acknowledge the efforts of the Applied Research Program, NCI; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

Methods

This study was reviewed and approved by the institutional review board of the University of Texas Southwestern Medical Center (STU 082012-040) and a waiver of participant consent was granted. We identified lung cancer patients aged 65 years or older using Medicare data from 1991 to 2011 that was linked between 1992 and 2009 in the Surveillance, Epidemiology, and End Results (SEER) database. We identified patients with autoimmune disease diagnosed at any time before or after their lung cancer diagnosis using *ICD-9* codes for 7 systemic and 36 organ-specific autoimmune diseases modified from a prior study. We determined the prevalence of autoimmune disease using 2 approaches: (1) individuals with 1 or more inpatient claims or 2 or more outpatient claims at least 30 days apart (claim “rule-out” approach), and (2) a more liberal approach, individuals with 1 or more claims of any type. Autoimmune diseases not routinely excluded from cancer immunotherapy (eg, type 1 diabetes, hypothyroidism) were not included. We report the prevalence of autoimmune diseases occurring before and after lung cancer diagnoses because immunotherapy is used for patients with progressive metastatic disease. Therefore, incident autoimmune diagnoses occurring after initial lung cancer diagnoses are still relevant to treatment considerations. Characteristics of patients with and without autoimmune diseases were compared using χ^2 tests.

Results

We identified 210 509 patients with lung cancer, of whom 28 453 (13.5%) also had autoimmune disease. Characteristics of patients are listed in Table 1. Patients with autoimmune disease were more likely to be female, older, have greater comorbidity burden, and to have earlier-stage lung cancer (all $P < .001$). The most common autoimmune diseases in this patient group were rheumatoid arthritis (5.9%), psoriasis (2.8%), and polymyalgia rheumatic (1.8%) (Table 2). Using the alternative definition of an autoimmune disease appearing on 1 or more claims of any type, the prevalence was 24.6%.

Discussion

Among patients diagnosed with lung cancer, approximately 14% to 25% have autoimmune disease. These patients are more likely to be women and to be older. Potential explanations for the relatively high rate of autoimmune diseases among patients with lung cancer include advanced age at diagnosis and smoking history, which has been linked to risk of certain autoimmune diseases.³

Limitations include the reliability of clinical diagnoses of autoimmune disease, which incorporate combinations of clinical, serologic, and histologic data. In addition, it is not known what proportion of these cases required systemic immune suppression—the threshold for patient exclusion from cancer immunotherapy clinical trials. Because patients with lung cancer may be older and have greater smoking histories, these findings cannot be generalized to other cancer populations.

A considerable proportion of patients diagnosed with lung cancer may also have autoimmune disease. Although prior series have suggested that administering immune

therapy to patients with autoimmune disease may be feasible, doing so conveys risk of disease exacerbation and requires careful monitoring.⁴ Given the widespread and expanding use of cancer immunotherapy, examining the prescribing patterns, effectiveness, and toxicity of these promising treatments among patients with autoimmune diseases will be critical.

Acknowledgments

Funding/Support: This work was supported by the National Cancer Institute (NCI) (1R03CA191875-01A1; to Dr Gerber, Dr Pruitt), a National Institutes of Health (NIH) Midcareer Investigator Award in Patient-Oriented Research (K24CA201543-01) (to Dr Gerber), Cancer Prevention and Research Institute of Texas (CPRIT) R1208 (to Dr Pruitt), the UT Southwestern Center for Patient-Centered Outcomes Research (PCOR), Agency for Healthcare Research and Quality (1R24HS022418-01) (to Dr Pruitt, Dr Xuan) and the National Center for Advancing Translational Sciences UT Southwestern Center for Translational Medicine (U54 RFA-TR-12-006) (to Dr Pruitt).

Role of the Funder/Sponsor: The funders/sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

References

1. Postow MA, Chesney J, Pavlick AC, et al. Nivolumab and ipilimumab versus ipilimumab in untreated melanoma. *N Engl J Med*. 2015; 372(21):2006–2017. [PubMed: 25891304]
2. February 11th, 2016; Available from: <http://www.aarda.org/autoimmune-information/autoimmune-statistics>.
3. Anderson LA, Pfeiffer RM, Landgren O, Gadalla S, Berndt SI, Engels EA. Risks of myeloid malignancies in patients with autoimmune conditions. *Br J Cancer*. 2009; 100(5):822–828. [PubMed: 19259097]
4. Johnson DB, Sullivan RJ, Ott PA, et al. Ipilimumab Therapy in Patients With Advanced Melanoma and Preexisting Autoimmune Disorders. *JAMA Oncol*. 2016; 2(2):234–240. [PubMed: 26633184]

Table 1

Characteristics of Lung Cancer Patients With Autoimmune Disease

Patient Characteristics	All Patients, No.	With Autoimmune Disease, No. (%)	<i>P</i> Value ^a
Total	210 509	28 453 (13.5)	
Age			
<75	94 804	11 664 (12.3)	<.001
75 to <85	92 045	13 529 (14.7)	<.001
85	23 660	3260 (13.8)	<.001
Sex			
Female	97 494	16 374 (16.8)	<.001
Male	113 015	12 079 (10.7)	<.001
Stage (AJCC)			
I	36 152	6331 (17.5)	<.001
II	6758	1028 (15.2)	<.001
III	51 542	6692 (13)	<.001
IV	77 833	9302 (12)	<.001
Other	38 224	5100 (13.3)	<.001

Abbreviation: AJCC, American Joint Committee on Cancer.

^aTwo-sided *P* values were calculated from logistic model Wald χ^2 .

Table 2

Prevalence of the 10 Most Common Individual Autoimmune Diseases Among 210 509 Patients With Lung Cancer

Autoimmune Disease	Prevalence, %
Rheumatoid arthritis	5.9
Psoriasis	2.8
Polymyalgia rheumatic	1.8
Addison disease	1.0
Systemic lupus erythematosus	0.9
Ulcerative colitis	0.8
Giant cell arteritis	0.8
Sicca syndrome	0.6
Regional enteritis	0.5
Ménière disease, unspecified	0.5
Total (any autoimmune disease)	13.5