

IASLC Lung Cancer Staging Project: The New Database to Inform Revisions in the Ninth Edition of the TNM Classification of Lung Cancer



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ABSTRACT

In the past 20 years, the International Association for the Study of Lung Cancer (IASLC) has been working on a global project to revise the TNM classification of lung cancer. The first and second phases of the staging projects proposed recommendations for revision of the TNM classification, which were adopted by the Union for International Cancer Control and the American Joint Committee on Cancer as their seventh and eighth editions of the TNM classifications of lung cancer. For the third phase of the IASLC Staging Project, a new database of lung cancer cases diagnosed between January 2011 and December 2019 has been established. The Staging and Prognostic Factors Committee of the IASLC is in charge of the process of proposing new recommendations. The newly established database consisted of 124,581 cases. The data were obtained from Asia and Australia (56.0%), Europe (24.7%), North America (15.7%), South/Central America (3.4%), and Africa and the Middle East (0.1%). After cases with incomplete data are excluded, 87,043 cases were enrolled in the analysis, of which 52,069 (59.8%) were invasive adenocarcinoma and 15,872 (18.2%) were

squamous cell carcinoma. Both clinical and pathologic stages were available in 44,831 (51.5%) cases. Analyses of this database are expected to provide proposals for changing the TNM classification toward the ninth edition, which is scheduled to be in use in January 2024. This newly established global database on lung cancer is described to provide fundamental elements for revisions of the TNM rules for staging lung cancer.

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Keywords: Lung cancer; Lung cancer databases; Staging; Non-small cell lung cancer; Small cell lung cancer; TNM classification

History of the IASLC International Staging Project

The Staging Project of the International Association for the Study of Lung Cancer (IASLC) is a global effort to

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Statistical consulting by Cancer Research And Biostatistics employees for data collection, analysis, and manuscript preparation in the Staging

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investigate and improve the TNM staging system for thoracic malignancies.

In 1997, the IASLC established a multidisciplinary International Staging Committee, now known as the Staging and Prognostic Factors Committee (SPFC), to start the first phase of the IASLC International Staging Project with the aim of revising and improving the TNM classification of lung cancer.^{1,2} The IASLC undertook this work as the only global organization dedicated to the study of lung cancer.

As the first phase of the IASLC International Staging Project, a global database of lung cancer cases was collected and managed in cooperation with Cancer Research And Biostatistics (CRAB). The data for 100,869 lung cancer cases from 45 sources in 20 countries in Europe, North America, Asia, and Australia that were diagnosed between 1990 and 2000 were submitted to the database at CRAB.³ Subcommittees of the SPFC analyzed this database to revise the TNM classification system. Recommendations for changes to the TNM classification of lung cancer were developed^{4–7} and submitted to the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC). All these recommendations were adopted by the UICC and AJCC as their seventh edition of the staging classifications for lung cancer, which were enacted in 2010.^{8,9} These recommendations were also published in the first edition of the IASLC Staging Manual in Thoracic Oncology and the IASLC Staging Handbook in Thoracic Oncology.^{10,11}

Because the globally uniform assessment of nodal status is a pivotal element of the IASLC International Staging Project, a new lymph node map for lung cancer was proposed in 2009 as part of the activity of the IASLC SPFC. This new IASLC lymph node map was created to reconcile differences among maps that had been used at that time and to provide precise anatomical definitions for all lymph node stations.¹²

The second phase of the IASLC International Staging Project began in 2009 and resulted in a new database of 94,708 cases of lung cancer diagnosed between 1999 and 2010.¹³ The data were obtained from 35 sources in 16 countries in Europe, Asia, North America, Australia, and South America. Different subcommittees conducted a detailed analysis of the data from the database and proposed recommendations for revision of the TNM classification,^{14–18} which were adopted by the UICC and AJCC as their eighth edition of the TNM classification for lung cancer.^{19,20} The changes from the seventh edition to the eighth edition were characterized by segmentation of the T categories and emphasis on the size of the solid component on computed tomography and on the invasive component on pathologic examination (Supplementary Table 1).^{14,17} The M descriptor was also

subdivided to create the new M1c category to designate multiple extrathoracic metastases, and the seventh edition M1b was redefined to code single extrathoracic metastasis.¹⁶ The eighth edition of the TNM classification has been implemented since 2017 worldwide, except in North America, where it was delayed until 2018. Simultaneously, the IASLC produced the second editions of the Staging Handbook in Thoracic Oncology and the Staging Manual in Thoracic Oncology, which included the TNM classifications for lung cancer, pleural mesothelioma, thymic malignancies, and carcinoma of the esophagus and the esophagogastric junction.^{21,22}

For the second phase of the IASLC International Staging Project, in addition to the descriptors of the TNM classification, nonanatomical elements were included in the data dictionary to prepare for the development of prognostic groups. The combination of the TNM classification with nonanatomical prognostic factors would help to personalize evaluation of the prognosis in patients with lung cancer.

The Third Phase of the IASLC International Staging Project

After the publication of the eighth edition of the TNM classification, the IASLC launched the third phase of its International Staging Project.²³ The SPFC of the IASLC has been restructured (Appendices 1 and 2) and has started gathering data on lung cancer cases from around the world. For this phase of the project, molecular information has been collected to evaluate both its prognostic value and the feasibility of incorporating this information into the TNM classification. In addition, for the purpose of making the TNM classification available where detailed clinical or pathologic information is not complete, an Essential TNM system has been considered on the basis of a proposal from the UICC.²⁴

Data Components of the New IASLC Database

For the third phase of the IASLC International Staging Project, a new database of lung cancer cases diagnosed between January 2011 and December 2019 was established. The deadline for updating the follow-up data of the cases was the end of December 2021. The data sets were submitted to CRAB either by means of batch data sets or by electronic data capture (EDC). This EDC system allows contributors to submit data online and retrieve their own data for their own studies at any time.

The EDC system provided by CRAB contains data set elements including T, N, and M descriptors with detailed specific reasons for categorizing them in both clinical and pathologic settings. The non-TNM elements included in the database to inform the ninth edition are listed in

Supplementary Table 2. The status of residual disease has also been a focal point, and its accuracy and availability will be essential to further validate the IASLC definitions of completeness of lung cancer resection. Nevertheless, data that were not submitted by means of the EDC system often lacked some of the essential elements due to the nature of the data set.

Details of the Accumulated Data

The newly formed database consisted of 124,581 cases, of which 101,033 (81.1%) were submitted as batch data sets and 23,548 (18.9%) were submitted by means of the EDC. The data came from 25 countries and 75 unique sites. They came from Asia and Australia (69,749 cases, 56.0%), Europe (30,827 cases, 24.7%), North America (19,608 cases, 15.7%), South/Central America (4225 cases, 3.4%), and Africa and the Middle East (172 cases, 0.1%) (Fig. 1). Data sources are found in **Supplementary Table 3**.

The submitted data were mapped to a data dictionary and checked to verify whether they included a valid histologic type, survival time, date of diagnosis window, and clinical and pathologic stages (Fig. 2). Finally, 87,043 cases were enrolled in the analysis. The most dominant source of data was the Japanese Joint Lung Cancer Registry (Japan, 23,663 cases), followed by the University Hospital Heidelberg (Germany, 8840 cases), West China Hospital, Sichuan University (China, 7345 cases), Korean Association for Lung Cancer (Republic of Korea, 4022 cases), and Samsung Medical Center (Republic of Korea, 3645 cases). The number of eligible cases

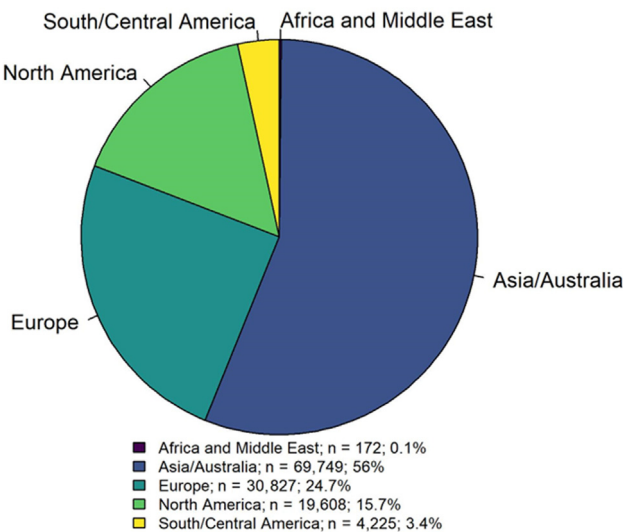


Figure 1. Number of cases submitted, classified by region. The data were obtained from Asia and Australia (69,749 cases, 56.0%), Europe (30,827 cases, 24.7%), North America (19,608 cases, 15.7%), South/Central America (4225 cases, 3.4%), and Africa and the Middle East (172 cases, 0.1%).

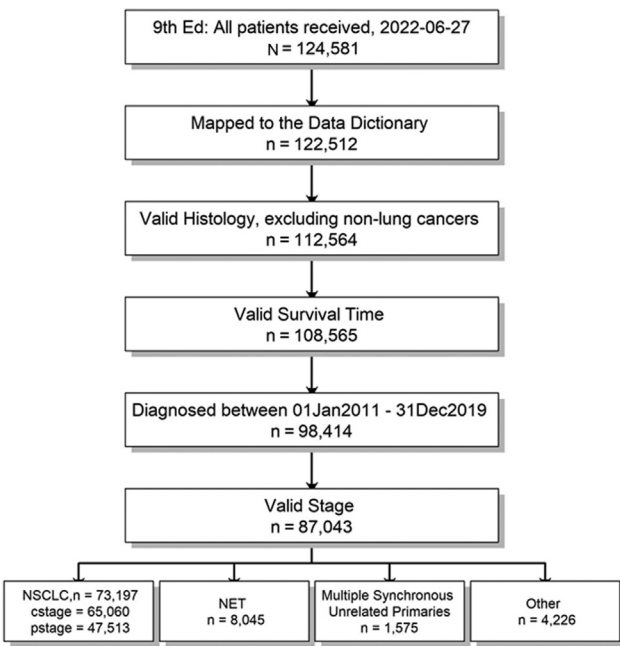


Figure 2. Case selection. The submitted data were mapped to a data dictionary and checked to verify whether they included a valid histologic type, survival time, date of diagnosis window, and clinical and pathologic stages. NET, neuroendocrine tumor.

submitted by each participating institution is found in **Appendix 3**.

Of the 87,043 cases enrolled in the analysis, 52,069 (59.8%) were invasive adenocarcinoma, 15,872 (18.2%) were squamous cell carcinoma, 1142 (1.3%) were adenocarcinoma in situ, 1100 (1.3%) were adenosquamous cell carcinoma, 1057 (1.2%) were large-cell carcinoma, 5530 (6.4%) were SCLC, and 689 (0.8%) were large-cell neuroendocrine carcinoma (Table 1). Of the 87,043 cases, both clinical and pathologic stages were available in 44,831 (51.5%). In 33,268 (38.2%)/8944 (10.3%) cases, only the clinical/pathologic stage was available (Fig. 3).

Approximately 67% of the cases underwent surgical treatment, with or without chemotherapy or radiotherapy (Table 1). Of the 77,811 cases in which clinical staging was available, the most dominant clinical stage according to the eighth edition of the TNM classification was stage IA2 (10,402 cases, 13.4%), followed by stage IVB (9236 cases, 11.9%) and stage IA3 (7357 cases, 9.4%) (Supplementary Table 4). Of the 54,248 cases in which pathologic staging was available, 22,206 cases (40.9%) were stage IA, 9021 cases (16.6%) were stage IB, 8246 (15.2%) were stage IIIA, and 7625 (14.1%) were stage IIB according to the eighth edition of the TNM classification (Supplementary Table 5). Numbers of cases in each stage group categorized by geographic regions are found in **Supplementary Figure 1**. Of the 47,933 surgical cases in which data were available,

Table 1. Numbers of Cases Categorized by Histology and Resection Status

Histology				Resection Status							
				Total		Surgical		Nonsurgical		Unknown	
				N	%	N	%	n	%	n	%
Total		87,043	100	58,440	100	26,099	100	2504	100		
NSCLC	Adenocarcinoma	52,069	59.8	37,252	63.7	13,590	52.1	1227	49.0		
	Squamous	15,872	18.2	11,262	19.3	3813	14.6	797	31.8		
	NSCLC NOS	1957	2.2	336	0.6	1542	5.9	79	3.2		
	AIS	1142	1.3	1078	1.8	60	0.2	4	0.2		
	Adenosquamous	1100	1.3	919	1.6	172	0.7	9	0.4		
	Large cell	1057	1.2	679	1.2	362	1.4	16	0.6		
NET	SCLC	5530	6.4	716	1.2	4500	17.2	314	12.5		
	Typical carcinoid	1215	1.4	1076	1.8	121	0.5	18	0.7		
	LCNEC	689	0.8	634	1.1	50	0.2	5	0.2		
	Atypical carcinoid	369	0.4	280	0.5	88	0.3	1	0.0		
	Mixed SCLC/NSCLC	173	0.2	155	0.3	16	0.1	2	0.1		
	Carcinoid, NOS	54	0.1	43	0.1	11	0.0	.	.		
	NET-DIN	15	0.0	9	0.0	6	0.0	.	.		
Other	Other	3465	4.0	1753	3.0	1701	6.5	11	0.4		
	Sarcomatoid	615	0.7	595	1.0	16	0.1	4	0.2		
	Salivary type	146	0.2	140	0.2	6	0.0	.	.		
	Multiple synchronous primary tumor	1575	1.8	1513	2.6	45	0.2	17	0.7		

AIS, adenocarcinoma in situ; DIN, diffuse idiopathic pulmonary neuroendocrine cell hyperplasia; LCNEC, large-cell neuroendocrine carcinoma; NET, neuroendocrine tumor; NOS, not otherwise specified.

R0 resection was achieved in 42,623 (88.9%) (Supplementary Table 6). A comparison of stage distribution and treatment modality between the EDC and batch data is presented in Supplementary Table 7. A

similar case distribution was observed regardless of the data source.

Information on EGFR mutation and anaplastic large-cell lymphoma kinase rearrangement status, among

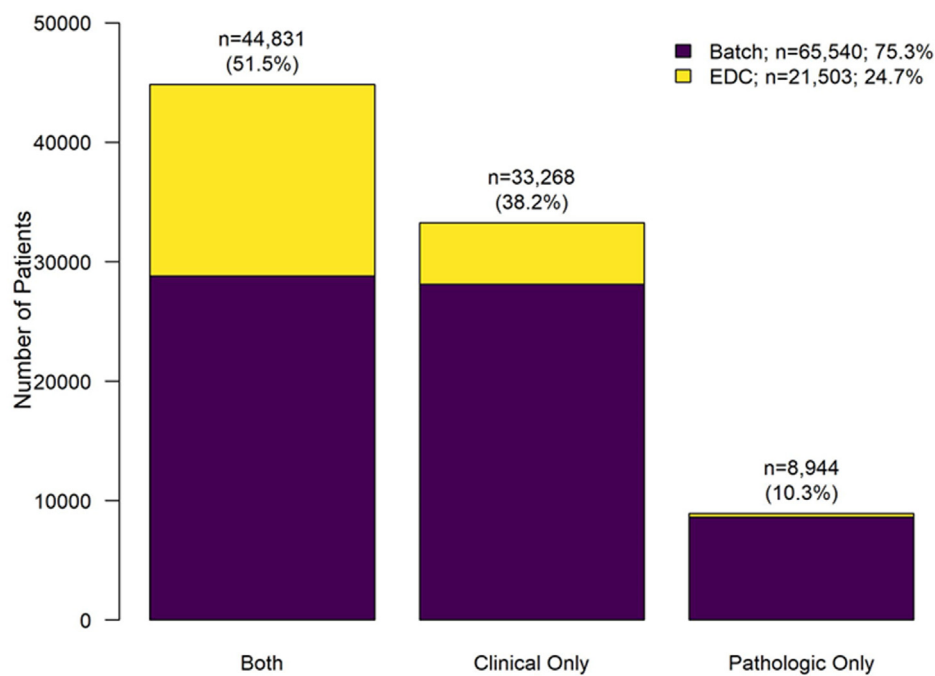


Figure 3. Numbers of cases categorized by data status. Of the 87,043 cases, both clinical and pathologic stages were available in 44,831 (51.5%). Only the clinical/pathologic stage was available in 33,268 (38.2%)/8944 (10.3%) cases.

Table 2. Characteristics of the IASLC Databases

Element	Database for the Seventh Edition	Database for the Eighth Edition	Database for the Ninth Edition
Period of diagnosis	1990-2000	1999-2010	2011-2019
Total patients submitted	100,869	94,708	124,581
Geographic origin, n (%)			
Europe	58,701 (58)	46,560 (49)	30,827 (25)
North America	21,130 (21)	4660 (5)	19,608 (16)
Asia/Australia	21,038 (21)	43,298 (46)	69,749 (56)
South/Central America	0	190 (0.3)	4225 (3)
Africa/Middle East	0	0	172 (0.1)
Patients excluded, n (%)	19,374 (19)	17,552 (18)	37,583 (30)
Patients included	81,495	77,154	87,043
NSCLC, n (%)	68,463 (84)	70,967 (92)	73,197 (84)
SCLC, n (%)	13,032 (16)	6189 (8)	5530 (6)
Other, n (%)			8316 (10)
Treatment modalities, %			
Surgery alone	41	58	47
Radiotherapy + surgery	5	2	2
Chemotherapy + surgery	4	21	13
Chemotherapy alone	23	9	11
Radiotherapy alone	11	2	3
Chemotherapy + radiotherapy	12	5	6
Trimodality	3	4	13

IASLC, International Association for the Study of Lung Cancer.

other biomarkers, was collected as well. The impact of molecular markers on the prognosis will be analyzed using the collected data.

Table 2 provides the basic characteristics of the IASLC databases used to inform the seventh, eighth, and ninth editions of the TNM classification of lung cancer. In the latter, although more patients were collected in comparison with the other two databases, more patients had to be excluded. This is due to the fact that, for this edition, international participants contributed more batch databases. These often lacked some of the essential elements needed for revision of the TNM classification and, therefore, patients had to be excluded. This emphasizes the importance of submitting data through the EDC online system, because these data are often more complete and accurate.

Contributions from Asia/Australia have replaced Europe as the leading geographic region participating in this project, mainly because of the huge contribution from Japan. It is also important to note that the number of cases from South/Central America has increased from a mere, almost symbolic, 0.3% (190 patients) in the eighth edition to 3.4% (4225 patients) in the ninth, which is a very substantial increase. For the first time, the IASLC database has data from Africa/Middle East, 172 (0.1%) patients, which we hope will increase in future editions of the IASLC International Staging Project.

The number of cases with NSCLC is about the same, but that of SCLC is slightly lower. Nevertheless, among

the 8357 cancers classified as “other,” there are typical and atypical carcinoids, large-cell neuroendocrine carcinomas, and 1577 multiple synchronous primary tumors. These will be very useful for validating the classification of lung cancers presenting with multiple lesions proposed in the eighth edition of the TNM classification.²⁵

Multifaceted analyses of the database will be performed on the basis of the strategic method designed by the validation and methodology subcommittee of the SPFC.²⁶ This analysis of the database should provide findings that will be reflected in the proposals to change the TNM classification system. The main proposals will be published in the *Journal of Thoracic Oncology* in 2023. They will be submitted to the UICC and AJCC as recommendations for the ninth edition TNM staging system, which is scheduled to be in use in 2024.

The IASLC SPFC will continue its activities to improve the staging systems and refine the prognostic information of thoracic malignancies, while constantly building an up-to-date and comprehensive database. The database is also expected to be a resource for additional research studies on further detailed or focused issues.

CRediT Authorship Contribution Statement

Hisao Asamura: Conceptualization, Methodology, Writing—original draft, Project administration.

Katherine K. Nishimura, Dorothy J. Giroux, Kari Chansky, Antje Hoering: Formal analysis, Investigation, Resources, Data curation.

Valerie Rusch, Ramón Rami-Porta: Conceptualization, Methodology, Writing—review and editing.

Appendix 1

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Appendix 2

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Lung Cancer Domain Lepidic and GGO Subcommittee. William Travis (chair), Philippe Joubert (co-chair), Hisao Asamura, Frank Detterbeck, Giuseppe Cardillo, Wendy Cooper, Ritu R. Gill, Jin Mo Goo, Young Tae Kim, Ho Yun Lee, Heber MacMahon, Edith M. Marom, David Naidich, Andrew Nicholson, Mizuki Nishino, Helmut Prosch, Ramón Rami-Porta, Valerie Rusch, Shuji Sakai, Yasushi Yatabe, Shun-ichi Watanabe.

Lung Cancer Domain Neuroendocrine Tumors Subcommittee. Ming Tsao (chair), Andrew G. Nicholson, (co-chair), Ricardo Beyruti, Frank Detterbeck, Wilfried Eberhardt, Pier Luigi Filosso, Yolande Lievens, Eric Lim, Geoffrey Liu, José-María Matilla, Natasha Rekhtman, William Travis, Jeffrey Yang, Yasushi Yatabe.

Lung Cancer Domain Stage. Hisao Asamura (chair), Giuseppe Cardillo, Frank Detterbeck, John Edwards,

Kwun Fong, Meredith Giuliani, James Huang, Kemp Kernstine, Edith M. Marom, Andrew G. Nicholson, Ramón Rami-Porta, William Travis, Ming Tsao, Paul Van Schil, Shun-ichi Watanabe.

Lung Cancer Domain Lymph Node Chart Subcommittee. Shun-ichi Watanabe (chair), Jin Mo Goo (co-chair), Hisao Asamura, Hans Hoffman, James Huang, Kemp Kernstine, Yolanda Lievens, Raymond U. Osarogiagbon, Paul Martin Putora, Ramón Rami-Porta, Valerie Rusch, Paul Van Schil, Jeffrey Yang.

Lung Cancer Domain Validation and Methodology Subcommittee. Frank Detterbeck (chair), Alyson Mahar (co-chair), Hisao Asamura, Meredith Giuliani, Mirella Marino, Raymond U. Osarogiagbon, Valerie Rusch.

Lung Cancer Domain Prognostic Factors Subcommittee. Frank Detterbeck (chair), Raymond U. Osarogiagbon (co-chair), Alex Brunelli, Kwun Fong, James Huang, Young Tae Kim, Mark Krasnik, Hui Liu, Jan van Meerbeeck, Luis M. Montuenga, Andrew G. Nicholson, Valerie Rusch, Robert Samstein, Navneet Singh, Martin Tammemägi, Ricardo Terra, Ming Tsao, Akif Turna, Terence Williams.

Lung Cancer Domain R Factor Subcommittee. John Edwards (chair), Marcin Ostrowski (co-chair), Souheil Boubia, Jessica Donington, Hans Hoffman, Maurizio Infante, Mirella Marino, Edith M. Marom, Jun Nakajima, Andrew G. Nicholson, Paul Van Schil, William Travis, Ming Tsao, Yasushi Yatabe.

Lung Cancer Domain Imaging Subcommittee. Jim Mo Goo (chair), Ritu R. Gill (co-chair), Helmut Prosch (co-chair), Samuel Armato, Hui Liu, Heber MacMahon, Edith M. Marom, David Naidich, Charles Powell, Paul Van Schil, William Travis.

Lung Cancer Domain Multiple Pulmonary Nodules Subcommittee. Frank Detterbeck (chair), Alyson Mahar (co-chair), Sarit Appel, Jason Chang, Keneng Chen, Nicolas Girard, Jin Mo Goo, Young Tae Kim, Heber MacMahon, Andrew G. Nicholson, Paul Martin Putora, Natasha Rekhtman, M. Patricia Rivera, Lynn Tanoue, Ricardo M. Terra, William Travis, Paula Ugalde.

Lung Cancer Domain Molecular Subcommittee. David Carbone (co-chair), Fred Hirsch (co-chair), Luiz Henrique Araujo, Hisao Asamura, Elisabeth Brambilla, Jason Chang, Frank Detterbeck, Oliver Gautschi, Nagla Karim, Keith Kerr, Peter Kneuert, Eric Lim, Philip Mack, José-María Matilla, Luis M. Montuenga, Andrew G. Nicholson,

Raymond U. Osarogiagbon, Harvey Pass, Carolyn J. Presley, Ramón Rami-Porta, Natasha Rekhtman, Harry Ren, Robert Samstein, Kenichi Suda, Ricardo M. Terra, William Travis, Ming Tsao, Terence Williams, Ignacio Wistuba, Dawei Yang, Yasushi Yatabe.

Lung Cancer Domain Database Subcommittee. Paula Ugalde (chair), Pietro Bertoglio (co-chair), Sarit Appel, Philippe Joubert, Catherine Labbe, Hongxu Liu, Gustavo Lyons, José-María Matilla, Robert Samstein, Ricardo Terra, María Teresa Ruiz Tzukazan, Benny Weksler.

Cancer Research And Biostatistics. Vanessa Cilento, Daniel Dibaba, Dorothy Giroux, Antje Hoering, Katie Nishimura, Adam Rosenthal.

Epithelial Thymic Tumors Domain

Enrico Ruffini (chair), James Huang (co-chair), Usman Ahmad, Sarit Appel, Andrea Billè, Souheil Boubia, Cecilia Brambilla, A. K. Cangir, Frank Detterbeck, Conrad Falkson, Wentao Fang, Pier Luigi Filosso, Giuseppe Giaccone, Nicholas Girard, Francesco Guerrera, Maurizio Infante, Hong Kwan Kim, Marco Lucchi, Mirella Marino, Edith M. Marom, Andrew Nicholson, Meinoshin Okumura, Andreas Rimner, Charles B. Simone II.

Thymic Domain T descriptor Subcommittee. Andrew Nicholson (chair), Cecilia Brambilla, A. K. Cangir, Maurizio Infante, Mirella Marino, Edith M. Marom, Meinoshin Okumura.

Thymic Domain N descriptor Subcommittee. Wentao Fang (chair), Frank Detterbeck, Pier Luigi Filosso, Marco Lucchi, Edith M. Marom, Charles B. Simone II.

Thymic Domain M descriptor Subcommittee. Nicholas Girard (chair), Sarit Appel, Conrad Falkson, Wentao Fang, Giuseppe Giaccone, Hong Kwuan Kim, Edith M. Marom, Andreas Rimner.

Thymic Domain Database Subcommittee. Pier Luigi Filosso (chair), Usman Ahmad, Andrea Billè, Souheil Boubia, Frank Detterbeck, Wentao Fang, Nicholas Girard, Francesco Guerrera, James Huang, Hong Kwan Kim, Meinoshin Okumura, Enrico Ruffini.

Malignant Pleural Mesothelioma Domain

Valerie Rusch (chair), Anna Nowak (co-chair), Pietro Bertoglio, Andrea Billè, Dean Fennell, Françoise Galateau-Sallé, Ritu R. Gill, Seiki Hasegawa, Hong Kwan Kim, Hedy Kindler, Jan van Meerbeeck, Isabelle Opitz, Harvey Pass, Marc de Perrot, David Rice, Andreas Rimner, Jennifer Sauter, Ming Tsao, David Waller, Andrea Wolf, A. K. Cangir.

Esophageal Cancer Domain

Wentao Fang (chair), Xavier D'Journo (co-chair), Gail Darling, Jeremy Erasmus, Mark Ferguson, Wayne Hofstetter, Hong Kwan Kim, Donald Low, Paula Ugalde.

Appendix 3

Participating Institutions in the Third Phase of the IASLC Lung Cancer Staging Project

Participating institutions ordered by number of eligible cases submitted

I. Yoshino, Japanese Joint Lung Cancer Registry, Chiba, Japan (23,663 cases); T. Muley, University Hospital Heidelberg, Heidelberg, Germany (8887 cases); W. Li, CAALC: West China Hospital, Sichuan University, Chengdu, People's Republic of China (7345 cases); Y. Kim, Korean Association for Lung Cancer, Seoul, Republic of Korea (4622 cases); H. K. Kim, Samsung Medical Center, Seoul, Republic of Korea (4130 cases); F. Griesinger, CRISP*, Berlin, Germany (5482 cases); J. Huang, Memorial Sloan Kettering Cancer Center, New York, New York, USA (3146 cases); R. Osarogiagbon, Baptist Memorial Hospital, Memphis, USA (3021 cases); S. Park, Seoul National University Hospital, Seoul, Republic of Korea (2542 cases); G. Liu, Princess Margaret Cancer Center, Toronto, Canada (2280 cases); N. Singh, Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh, India (2060 cases); P. Ugalde Figueroa, IUCPQ—Université Laval, Quebec, Canada (2018 cases); P. Kneuert, The Ohio State University, Columbus, Ohio, USA (1819 cases); J. Shih, Taiwan Society of Pulmonary and Critical Care Medicine, Taipei, Taiwan (1481 cases); E. Lim, Royal Brompton & Harefield NHS Foundation Trust, London, United Kingdom (1434 cases); B. McCaughan, University of Sydney, Newtown, Australia (1368 cases); H. Liu, Liaoning Cancer Hospital, Shenyang, People's Republic of China (1161 cases); A. Cangir, Ankara University School of Medicine, Ankara-Sihhiye, Turkey (887 cases); A. Billè, Guy's Hospital, London, United Kingdom (882 cases); F. Leo, S. Luigi Hospital, University of Turin, Orbassano, Torino, Italy (840 cases); H. Liu, Sun Yat-sen University Cancer Center, Guangzhou, People's Republic of China (825 cases); M. Redman, SWOG-0819, Seattle, USA (782 cases); H. Pass, NYU-Langone Medical Center and Cancer Center, New York, New York, USA (762 cases); J. Sun,

* CRISP is an AIO study (project no. AIO TRK-0315) under the medical leadership of the Executive Committee (Prof. F. Griesinger (Oldenburg), Prof. M. Thomas (Heidelberg), Dr. M. Sebastián (Frankfurt), and Dr. W. Eberhardt (Essen)). CRISP is conducted by AIO-Studien-GmbH (sponsor) in cooperation with iOMEDICO (conception, project management, analysis). CRISP is supported by AstraZeneca GmbH, Boehringer Ingelheim Pharma GmbH & Co. KG, Bristol-Myers Squibb GmbH & Co. KGaA, Celgene GmbH, Lilly Deutschland GmbH, Merck Sharp & Dohme GmbH, Novartis Pharma GmbH, Pfizer Pharma GmbH, Roche Pharma AG, and Takeda Pharma Vertrieb GmbH & Co. KG. Nevertheless, these companies have no input into or influence in data analysis, data interpretation, or writing of the manuscript.

Shanghai Chest Hospital, Shanghai, People's Republic of China (634 cases); J. Sun, CAALC: Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, People's Republic of China (634 cases); K. Fong, The University of Queensland TPCB Thoracic Research Centre, Brisbane, Australia (577 cases); R. Terra, University of Sao Paulo Medical School, Sao Paulo, Brazil (555 cases); N. Wu, Second Department of Thoracic Surgery, Peking University Cancer, Beijing, People's Republic of China (455 cases); K. Chen, First Department of Thoracic Surgery, Peking University Cancer Hospital, Beijing, People's Republic of China (451 cases); A. Mohan, All India Institute of Medical Sciences, New Delhi, India (448 cases); P. Van Schil, University Hospital Antwerp, Edegem, Belgium (304 cases); P. Bertoglio, IRCCS Sacro Cuore-Don Calabria Hospital, Negrar, Italy (298 cases); C. Yang, Massachusetts General Hospital, Boston, Massachusetts, USA (295 cases); R. Moises, Hospital de Rehabilitación Respiratoria María Ferrer, Buenos Aires, Argentina (264 cases); A. Turna, Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Istanbul, Turkey (238 cases); A. Celik, Gazi University Faculty of Medicine, Ankara, Turkey (193 cases); M. Modesto Alapont, GCCB3: Consorcio Hospitalario Provincial de Castellón, Castellón, Spain (165 cases); L. Sánchez Moreno and M. Zabaleta Murguiondo, GCCB3: Hospital Universitario Marqués de Valdecilla, Santander, Spain (165 cases); C. Longo, Instituto COI, Rio de Janeiro, Brazil (150 cases); H. Zhou, Suining Central Hospital, Suining, People's Republic of China (147 cases); E. Pirondini, ASST San Gerardo, Monza, Italy (144 cases); G. Lyons, Hospital Británico de Buenos Aires, Buenos Aires, Argentina (143 cases); I. Gkiozos, Athens School of Medicine, Athens, Greece (133 cases); K. Kernstine, UT Southwestern Medical Center at Dallas, Dallas, Texas, USA (132 cases); M. Serra Mitjans and R. Costa, GCCB3: Hospital Universitari Mútua Terrassa, Terrassa, Spain (124 cases); M. Genovés Crespo and A. Nuñez Ares, GCCB3: Complejo Hospitalario Universitario of Albacete, Albacete, Spain (114 cases); C. Lee, Seoul National University Bundang Hospital, Seongnam, Republic of Korea (104 cases); Y. K. Pang, Malaysian Thoracic Society, Kuala Lumpur, Malaysia (99 cases); N. Evans, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania, USA (98 cases); F. Hirsch, Icahn School of Medicine at Mount Sinai, New York, New York, USA (84 cases); M. Ridai, University Hospital of Casablanca, Casablanca, Morocco (83 cases); C. Martínez Barenys and J. Sanz Santos, GCCB3: Hospital Universitari Germans Trias i Pujol, Badalona, Spain (77 cases); J. Sauleda Roig, Hospital Universitari Son Espases, Palma de Mallorca, Spain (76 cases); H. Hoffmann, University of Munich—Division of Thoracic Surgery, Munich, Germany (75 cases); M. A. Iñiguez-García, National Institute of Respiratory Diseases, Mexico City, Mexico (74 cases); L.H. de Lima Araujo, Brazilian National Cancer Institute (INCA), Rio de Janeiro, Brazil (72 cases); C. Grohé, Evangelische Lungenklinik Berlin—NET Registry, Berlin, Germany (71 cases); D. Ball, Peter MacCallum Cancer Institute, Melbourne, Australia (70 cases); N. Tarek, Ain Shams University Hospitals, Cairo, Egypt (64 cases); D. Yang, CAALC: Zhongshan Hospital Fudan University, Shanghai, People's Republic of China (63 cases); D. Sánchez, GCCB3: Hospital Clínic, Barcelona, Spain (62 cases); J. A. Gullón Blanco, GCCB3: Hospital Universitario San Agustín, Avilés, Asturias, Spain (61 cases); L. Montuenga, CIMA/Clínica Universidad de Navarra, Pamplona, Spain (55 cases); G. Galán Gil and R. Guijarro Jorge, GCCB3: Hospital Clínico Universitario de Valencia, Valencia, Spain (52 cases); C. García Rico and J. M. Matilla, GCCB3: Hospital Clínico Universitario de Valladolid, Valladolid, Spain (50 cases); A. Rodríguez Fuster and V. Curall, GCCB3: Hospital del Mar, Barcelona, Spain (50 cases); L. Miravet, GCCB3: Hospital La Plana, Castellón, Spain (49 cases); J. Abal Arca and I. Parente Lamelas, GCCB3: Complejo Hospitalario Universitario Ourense, Ourense, Spain (48 cases); E. Melis, IRCCS Regina Elena National Cancer Institute, Rome, Italy (41 cases); S. García Fuika, GCCB3: Hospital UA Txagorritxu, Vitoria-Gasteiz, Spain (34 cases); K. Tournoy, University Hospital Ghent, Ghent, Belgium (33 cases); M. T. Rosell Abós, GCCB3: Hospital Royo Vilanova, Zaragoza, Spain (31 cases); L. García Aranguena, GCCB3: Hospital Sierrallana, Torrelavega, Cantabria, Spain (28 cases); O. Arrieta, Instituto Nacional de Cancerología, Mexico City, Mexico (28 cases); M. G. Blum, Penrose Cancer Center, Colorado Springs, Colorado, USA (28 cases); D. Mishra, BP Koirala Institute of Health Sciences, Dharan, Nepal (25 cases); J.M. García Prim, Hospital Clínico Universitario de Santiago, Santiago de Compostela, Spain (25 cases); M. Mariñán Gorospe, Hospital San Pedro de Logroño, Logroño, Spain (24 cases); R. Stirling, The Alfred Hospital, Melbourne, Australia (23 cases); B. Steen, GCCB3: Hospital de Alcorcón, Madrid, Spain (23 cases); D. Chimondeguy, Hospital Universitario Austral, Buenos Aires, Argentina (22 cases); F. J. Montoro Zulueta, GCCB3: Hospital Universitario Infanta Sofía, San Sebastián de los Reyes, Spain (22 cases); M. Paradela de la Morena and A. Souto Alonso, GCCB3: Complejo Hospitalario Universitario de A Coruña, La Coruña, Spain (21 cases); R. Cordovilla and T. Gómez Hernández, GCCB3: Hospital Universitario de Salamanca, Salamanca, Spain (21 cases); C. Thomas, Mayo Clinic Rochester, Rochester, Minnesota, USA (20 cases); J. Hernández-Hernández, GCCB3: Complejo Asistencial de Ávila, Ávila, Spain (19 cases); I. Macía Vidueira and S. Padrones, GCCB3: Hospital de Bellvitge, Barcelona, Spain (16 cases); J. R. Jarabo Salcedo and B. Morales Chacón, GCCB3: Hospital Clínico San Carlos, Madrid, Spain (16 cases); Y. L. Wu, Guangdong General

Hospital, Guangzhou, People's Republic of China (15 cases); E. Martínez Tellez and J. C. Trujillo, GCCB3: Hospital de la Santa Creu i Sant Pau, Barcelona, Spain (14 cases); L. Bai, CAALC: Xinqiao Hospital, No. 3 Army Medical University, Chongqing, People's Republic of China (14 cases); R. Magaroles and L. de Esteban Júlvez, Hospital Universitari Joan XXIII, Tarragona, Spain (14 cases); R. Melchor Íñiguez, Fundación Jiménez Díaz, Madrid, Spain (14 cases); R. Embun Flor and P. Teller Justes, GCCB3: Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain (13 cases); C. M. Ariza Prota, GCCB3: Hospital Universitario Asturias, Oviedo, Spain (13 cases); M. J. Pavón Fernández, Hospital Severo Ochoa, Leganés, Spain (13 cases); J. Menéndez, Hospital General de Agudos José M. Penna, Buenos Aires, Argentina (11 cases); S. Defranchi, Hospital Universitario-Fundación Favaloro, Buenos Aires, Argentina (11 cases); E. Martínez Tellez, Hospital de Terrassa, Terrassa, Spain (11 cases).

The Following Institutions Submitted Ten Eligible Cases or Less Listed Alphabetically

M. Curado, A.C. Camargo Cancer Center, Sao Paulo, Brazil; A. Badawy, Alexandria University, Alexandria, Egypt; X. Zhang, CAALC: Henan Provincial People's Hospital, Zhengzhou, People's Republic of China; Q. Wang, CAALC: The Second Hospital of Dalian Medical University, Dalian, People's Republic of China; S. Han, CAALC: Zhongda Hospital Affiliated to Southeast University, Nanjing, People's Republic of China; D. Levy Faber, Carmel Medical Center, Haifa, Israel; P. García Herreros, Clínica Cardiovid, Medellín, Antioquia, Colombia; F. Suárez, Clínica Santa María, Santiago de Chile, Chile; D. Subotic, Clinical Center of Serbia, Belgrade, Serbia; J. Abal Arca and I. Parente Lamelas, Complejo Hospitalario de Ourense, Ourense, Spain; T. Horvath, Czech Republic-Urazova Nemocnice Brno, BRNO, Czech Republic; M. Velásquez, Fundación Clínica Valle del Lili, Cali, Colombia; J. C. Peñalver Cuesta, GCCB3: Fundación Instituto Valenciano de Oncología, Valencia, Spain; S. García García, GCCB3: Complejo Asistencial Universitario de León, León, Spain; O. Bernadich Márquez, GCCB3: Hospital Althaia Red Asistencial Universidad de Manresa, Barcelona, Spain; J. García, GCCB3: Hospital Gregorio Marañón, Madrid, Spain; T. Ruiz Albi, GCCB3: Hospital Río Hortega, Valladolid, Spain; O. Castro Añón, GCCB3: Hospital Universitario Lucus Augusti, Lugo, Spain; M. Serraj, Hassan II University Hospital, Fez, Morocco; V. Baysungur, Health Science University Sureyyapasa Thoracic and Chest Disease, Istanbul, Turkey; M. Raíces, Hospital Italiano de Buenos Aires, Argentina; J. R. Hernández-Hernández, Hospital Nuestra Señora de Sonsoles, Ávila, Spain; Luis Berlanga, Hospital San Pedro

Alcántara, Cáceres, Spain; M. J. Pavón Fernández, GCCB3: Hospital Severo Ochoa, Leganés, Madrid, Spain; H. Hernández Rodríguez, Hospital Universitario de Canarias, Santa Cruz de Tenerife, Canary Islands, Spain; F. Abad Cavaco and E. Ansótegui Barrera, Hospital Universitario La Fe, Valencia, Spain; V. Cvijanovic, Military Medical Academy, Belgrade, Serbia; M. Zereu, Pavilhao Pereira Filho, Santa Casa de Porto Alegre, Brazil; W. Aguiar, SECITOR—Servico de Cirurgia Toracica de Recife, Recife, Brazil.

Supplementary Data

Note: To access the supplementary material accompanying this article, visit the online version of the *Journal of Thoracic Oncology* at www.jto.org and at <https://doi.org/10.1016/j.jtho.2023.01.088>

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