

The International Association for the Study of Lung Cancer Pleural Mesothelioma Staging Project: Expanded Database to Inform Revisions in the Ninth Edition of the TNM Classification of Pleural Mesothelioma

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ABSTRACT

The International Association for the Study of Lung Cancer collaborated with the International Mesothelioma Interest Group to propose the first TNM stage classification system for diffuse pleural mesothelioma in 1995, accepted by the Union for International Cancer Control and the American Joint Committee on Cancer for the sixth and seventh edition stage classification manuals. The International Association for the Study of Lung Cancer Staging and Prognostic Factors Committee Mesothelioma Domain developed and analyzed an international registry of patients with pleural mesothelioma and updated TNM descriptors for the eighth edition of the stage classification system. To inform revisions for the forthcoming ninth edition of the TNM stage classification system, data submission was solicited for patients diagnosed between 2013 and 2022 with expanded data elements on the basis of the first project's exploratory analyses, including pleural thickness measurements, updated surgical

nomenclature, and molecular markers. The resulting database consisted of a total of 3598 analyzable cases from Europe, Australia, Asia, North America, and South America, with a median age of 71 years (range: 18–99 y), 2775 (77.1%) of whom were men. With only 1310 patients (36.4%) undergoing curative-intent operations, this iteration

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of the database includes far more patients treated non-surgically compared with prior. Four separate manuscripts on T, N, M, and stage groupings submitted to this journal will summarize analyses of these data and will serve collectively as the primary source of the proposed changes to the upcoming ninth edition of the pleural mesothelioma stage classification system.

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Keywords: Mesothelioma; Mesothelioma databases; Staging; TNM classification; Pleurectomy/decortication; Extrapleural pneumonectomy

Introduction

As part of the International Association for the Study of Lung Cancer (IASLC) Staging Project to inform revisions to the TNM stage classification systems for thoracic malignancies, the Mesothelioma Domain of the Staging and Prognostic Factors Committee developed and analyzed a global multicenter database of diffuse pleural mesothelioma cases. This geographically diverse database included patients with pleural mesothelioma irrespective of treatment, pathologic subtype, and stage. The most recent iteration was used to develop evidence-based recommendations for revision of the current (eighth edition) stage classification system for the ninth edition of the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC) stage classification system.

Early Pleural Mesothelioma Staging Systems

As described by Pass et al.,¹ several early stage classification systems for pleural mesothelioma were proposed, beginning with Butchart's system published in 1976,² derived from a small series of patients undergoing extrapleural pneumonectomy. Other systems were subsequently proposed.³⁻⁵ Nevertheless, these were based on small, single-institution series, mostly included tumor stage without TNM descriptors, and were not widely applicable to clinical and pathologic stage classification.

In 1994, the IASLC and International Mesothelioma Interest Group (IMIG) co-sponsored a workshop during which pleural mesothelioma investigators analyzed available surgical and clinical trial data sets to create a TNM-based stage classification system, often known as the "IMIG staging system." This collaboration yielded a system that was accepted by the AJCC and UICC for the

sixth and seventh editions of their stage classification systems.⁶ Although subsequently validated by analysis of two surgical series,^{7,8} this stage classification system was not accurate for clinical stage classification in patients who were managed nonsurgically. Later, Richards et al.⁹ analyzed a large series of patients who underwent extrapleural pneumonectomy and recommended updates for the pathologic stage classification of pleural mesothelioma, highlighting the possibility that patients not undergoing extrapleural pneumonectomy and those with nonepithelioid histologic subtype might require different staging descriptors. From all this published experience, it was clear that a large international database was needed to inform revisions of the stage classification system in this rare disease.

The Initial IASLC Pleural Mesothelioma Database

The IASLC Staging Project in pleural mesothelioma was initiated at the 2009 IASLC Workshop on Advances in Mesothelioma¹ and led to the creation of the mesothelioma domain as part of the IASLC Staging and Prognostic Factors Committee. The IASLC and IMIG collaborated to form an international registry of institutional data sets of pleural mesothelioma cases diagnosed between 1995 and 2009. Limited or deidentified data were collected by the Cancer Research And Biostatistics (Seattle, WA) and reviewed to establish common data elements. The resulting database included 3101 patients from 15 centers across five continents. Surgical procedures were dichotomized according to intention: palliative or curative. Palliative-intent operations included exploration without resection and partial pleurectomy. Curative-intent operations, including pleurectomy/decortication with resection of all gross disease, pleurectomy/decortication with anatomical lung resection other than pneumonectomy, and extrapleural pneumonectomy, were performed in 64.5% of patients, half of whom underwent extrapleural pneumonectomy. In accordance with AJCC and UICC guidelines, clinical and pathologic stage classifications were combined as "best stage," with pathologic stage used for patients in whom both were available and clinical stage used in patients lacking pathologic stage classification.¹⁰ Analysis of this registry confirmed overall survival differences found in the original IMIG stage classification system but also identified the need for additional data to refine T and N descriptors.¹⁰

In parallel with the analysis of this initial IASLC pleural mesothelioma database, the mesothelioma domain developed a white paper to standardize the terminology used to describe parenchyma-sparing surgical procedures.¹¹ Using a web-based survey of 62

experienced pleural mesothelioma thoracic surgeons from 39 medical centers in 14 countries, the white paper recommended that pleurectomy/decortication be used to describe resection of all gross pleural diseases and extended pleurectomy/decortication be used to describe macroscopic complete resection of pleural disease in conjunction with resection of the diaphragm, pericardium, or both.

Supplementary clinical and demographic variables from this first IASLC database, including exposure to carcinogens, symptoms, performance status, selected laboratory results, and use of adjuvant treatment, were also analyzed. The mesothelioma domain developed three prognostic models to improve the ability to predict prognosis of patients either at initial diagnosis or after completion of initial treatment including information available from surgical resection.¹²

The Second IASLC Pleural Mesothelioma Database

In 2011, the Mesothelioma Domain revised the database to inform the eighth edition of the pleural mesothelioma stage classification system, adding an electronic data capture (EDC) system developed by the Cancer Research And Biostatistics for prospective data entry. The submission of cases diagnosed between 1995 and 2013 from additional investigators was solicited, expanding the database to include more patients managed nonsurgically. The resulting data set included 3519 patients (2460 eligible for analysis) from 29 centers spanning four continents, 52.7% of whom had undergone curative-intent operations. Ultimately, the committee recommended no changes to the T descriptors, but an exploratory analysis suggested that a systematic method of measuring pleural thickness at three levels improved the prognostication of overall survival.¹³ The previous N descriptors were revised, moving from the system used for lung cancer to one that discriminated overall survival better for pleural mesothelioma. N1 was changed to designate involvement of any ipsilateral intrathoracic nodes, and N2 was redefined as involvement of contralateral intrathoracic or any supraclavicular lymph nodes.¹⁴ The updated analysis supported maintenance of the distinction between M0 and M1, and when combined with T and updated N stage classification, the results supported major revisions to the stage groupings as follows: stage IA (T1N0), stage IB (T2-3N0), stage II (T1-2N1), stage IIIA (T3N1), stage IIIB (T1-3N2 or any T4), and stage IV (any M1).¹⁵

After publication of the eighth edition of the pleural mesothelioma stage classification system, the Mesothelioma Domain performed an updated analysis of prognostic factors. To evaluate the models generated by analysis of the first version of the IASLC database,¹² the original

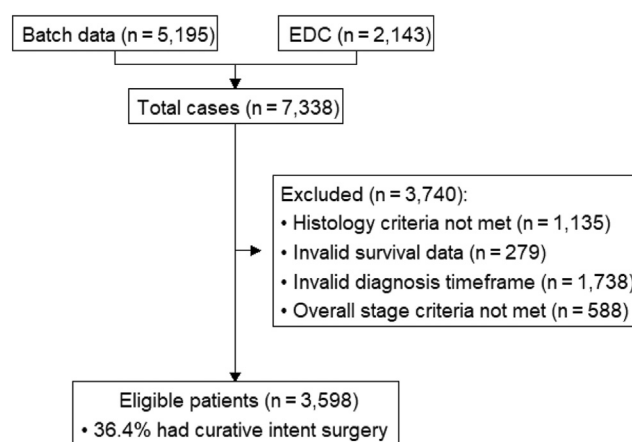


Figure 1. International Association for the Study of Lung Cancer pleural mesothelioma database to inform the ninth edition of the AJCC and UICC staging system. AJCC, American Joint Committee on Cancer; EDC, electronic data capture; UICC, Union for International Cancer Control.

cohort of 3101 patients was treated as a training data set and the models' performance was validated in predicting overall survival with data available in the second version of the IASLC database.¹⁶ Additional variables were added in an attempt to improve the original prognostic models. For the prognostic model at initial diagnosis, non-epithelioid tumor histologic subtype, anemia, high platelet count, high mesothelin level, and older patient age were all independently predictive of worse overall survival. For the multivariable model that included treatment and final tumor stage information, non-epithelioid histologic subtype, anemia, high platelet count, no adjuvant therapy, and higher tumor stage were all independent predictors of worse overall survival. In the future, the addition of molecular data will be tested to see whether it improves these prognostic models.

The Third IASLC Pleural Mesothelioma Database

To inform potential revisions for the upcoming ninth edition of the AJCC and UICC pleural mesothelioma stage classification system, the mesothelioma domain solicited data submission by both EDC (preferred) or transfer of institutional "batch" data for patients diagnosed between 2013 and 2022. The committee sought broad geographic representation, aiming to include patients with all disease stages and treatment approaches. As for the previous iterations of the database, participating institutions were required to obtain institutional review board approval and to sign a Data Use Agreement to submit limited or deidentified data. Demographic information, extent of disease by clinical and pathologic findings, methods of disease assessment, treatment, and overall survival data were collected ([Supplementary Materials 1, Protocol, and 2,](#)

Table 1. Patient and Tumor Characteristics in the International Association for the Study of Lung Cancer Pleural Mesothelioma Database to Inform the Ninth Edition American Joint Committee on Cancer and Union for International Cancer Control Staging System (N = 3598)

Characteristic	Value
Age at diagnosis (n = 3462)	
Mean (SD)	69.9 (10.20)
Median (range)	71.0 (18.4-99.0)
Sex, n (%)	
Female	822 (22.8)
Male	2775 (77.1)
No data	1 (0.0)
Eighth edition clinical stage, n (%)	
IA	892 (24.8)
IB	1129 (31.4)
II	246 (6.8)
IIIA	222 (6.2)
IIIB	519 (14.4)
IV	228 (6.3)
No data	362 (10.1)
Histology type/subtype, n (%)	
Epithelioid	2799 (77.8)
Biphasic	470 (13.1)
Sarcomatoid	290 (8.1)
Desmoplastic	39 (1.1)
Most definitive pleural procedure, n (%)	
None	821 (22.8)
Surgical pleural biopsy (VATS or thoracotomy)	506 (14.1)
Exploration, no resection	461 (12.8)
Partial pleurectomy	179 (5.0)
Pleurectomy/decortication	522 (14.5)
Extended pleurectomy/decortication	529 (14.7)
Extrapleural pneumonectomy	259 (7.2)
No data	321 (8.9)
WHO performance status, n (%)	
0 - Fully active	1627 (45.2)
1 - Restricted	1276 (35.5)
2 - No work, ambulatory	219 (6.1)
3 - Limited self-care	58 (1.6)
4 - Completely disabled	14 (0.4)
No data	404 (11.2)
Asbestos exposure, n (%)	
Definite	1606 (44.6)
Probable	251 (7.0)
Possible	304 (8.4)
No known exposure	738 (20.5)
No data	699 (19.4)

VATS, video-assisted thoracoscopic surgery.

Data Elements). The collection of a prespecified list of molecular alterations from two institutions was piloted. On the basis of the exploratory analyses performed for the T descriptors in the eighth edition, measurements of pleural thickness at three prespecified levels on computed tomography were requested,¹³ along with pleural thickness measurements at the fissure and diaphragm. Data on the T descriptors defined in the eighth editions were also submitted. Information regarding

involvement of lymph nodes defined as N1 or N2 in the eighth edition and the individual lymph node stations sampled were also collected. For patients found to have metastatic (M1) disease at diagnosis, investigators were asked to document the presence or absence of distant metastases in eight organ systems, including the number of lesions, if present. In accordance with the 2011 white paper recommendations for surgical terminology,¹¹ the descriptors for the types of surgical procedures were categorized as surgical biopsy, exploration without resection, partial pleurectomy, pleurectomy/decortication, extended pleurectomy/decortication, and extrapleural pneumonectomy.

A total of 7338 cases were contributed to this third version of the pleural mesothelioma database, with 3598 patients from 38 data sources eligible for analysis, of whom 36.4% underwent curative-intent surgical procedures (Fig. 1). Data for analysis of radiation and systemic therapy were available for 1535 of these patients whose information was submitted through EDC. Of these, 266 (17.3%) received radiation and 1193 (77.7%) systemic therapy as some component of their treatment. Characteristics of the entire cohort of 3598 analyzable patients are found in Table 1. This geographically diverse cohort included patients from Europe, Australia, Asia, North America, and South America (Fig. 2). Relative to previous iterations, the current database includes more patients treated nonsurgically and reflects a shift in the practice of surgery from extrapleural pneumonectomy to predominantly extended pleurectomy/decortication. The distribution of patient sex and tumor histologic subtype is similar to historical patterns (Table 2). This data set was analyzed to evaluate eighth edition staging parameters and tumor thickness measurements. The results of T, N, M, and stage grouping analyses, detailed in separate manuscripts, serve as the primary sources to support changes to the ninth edition of the pleural mesothelioma stage classification system.

In the fifth edition of the WHO Classification of Tumours, mesothelioma in situ is recognized as a rare but distinct entity characterized by a preinvasive single-layer surface proliferation of neoplastic mesothelial cells.¹⁷ As such, it would potentially qualify for designation as a carcinoma in situ or Tis. Few cases have been reported worldwide, and the third version of the IASLC database was not designed to evaluate this entity. Nevertheless, additional data may be collected for a future 10th edition of the pleural mesothelioma stage classification to determine whether mesothelioma in situ should be included in the staging system as Tis.

Limitations of the project include missing data and variability in reporting details with regard to surgery, imaging, and pathologic findings, such as the location and number of nodes sampled and the presence and location

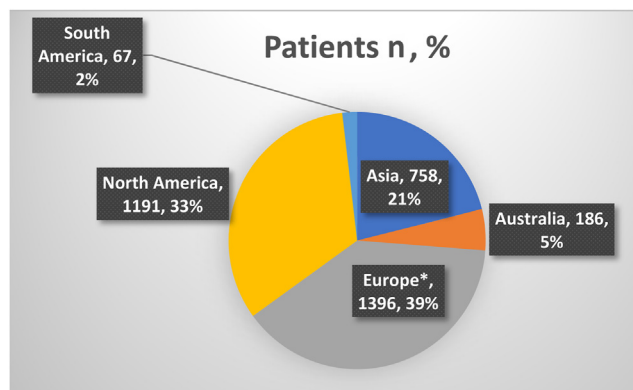


Figure 2. Distribution of patients by region in the International Association for the Study of Lung Cancer pleural mesothelioma database to inform the ninth edition American Joint Committee on Cancer and Union for International Cancer Control Staging System (N = 3598).

of metastases. Tumor and serum biomarkers, such as programmed death-ligand 1 expression, BAP-1 staining, and mesothelin, are not currently solicited for all patients. Details of systemic therapy, such as chemotherapy, checkpoint inhibitors, and/or targeted therapies, are likewise not currently included. The benefit of comprehensive data collected in a large multicenter registry must be weighed against the resources required to complete entry (and the risk of overwhelming investigators with prohibitively extensive data requested), and thus, there is a balance required to optimize participation and analysis. As noted, data collection for a prespecified list of

molecular alterations was piloted at two institutions as part of the third version of the pleural mesothelioma database. Correlation of molecular alterations with clinical and pathologic features will be the subject of a future report. This initial experience will guide further collection of data for the 10th edition of the stage classification system. Expanding this and insuring comprehensive streamlined data collection from participants are among the future goals of the IASLC Staging and Prognostic Factors Committee Mesothelioma Domain.

In summary, robust international collaboration through the IASLC has repeatedly yielded worldwide data about this rare disease and has enabled serial refinements of the pleural mesothelioma stage classification system. Each iteration of the pleural mesothelioma data set has been informed by lessons learned from the previous versions with consistent improvement in the data elements collected. Increasing case eligibility through greater use of the EDC rather than batch imported data sets will be a focus of quality improvement for work on the 10th edition database, which will also seek to answer questions and close gaps identified by analyses for the ninth edition stage classification system.

CRediT Authorship Contribution Statement

Andrea S. Wolf: Conceptualization, Investigation, Writing—original draft, Writing—review and editing, Visualization.

Table 2. Overview of Iterations of the IASLC Databases to Inform the Seventh, Eighth, and Ninth Editions of the AJCC and UICC Pleural Mesothelioma Staging Systems

Features	Edition of the AJCC and UICC Pleural Mesothelioma Staging System		
	Seventh	Eighth	Ninth
Total available cohort	3101	3519	7338
Total eligible cases	2316	2450	3598
Period of diagnosis	1995-2009	2000-2013	2013-2022
Geographic origin, n (%)			
Europe ^a	1049 (45.3)	1173 (47.9)	1396 (38.8)
North America	1048 (45.3)	817 (33.3)	1191 (33.1)
Asia	150 (6.5)	233 (9.5)	758 (21.0)
Australia	69 (3.0)	227 (9.3)	186 (5.2)
South America			67 (1.9)
Histology of included patients, n (%)			
Epithelioid	1596 (68.9)	1784 (72.8)	2799 (77.8)
Nonepithelioid	685 (29.6)	666 (27.2)	799 (22.2)
No data	35 (1.5)	0 (0.0)	0 (0.0)
Surgical procedures performed, n (%)			
Surgery-palliative	729 (31.5)	692 (28.2)	1146 (31.9)
Surgery-curative	1494 (64.5)	1291 (52.7)	1310 (36.4)
No surgery	70 (3.0)	458 (18.7)	821 (22.8)
No data	23 (1.0)	9 (0.4)	321 (8.9)

^aEurope includes United Kingdom and Turkey.

AJCC, American Joint Committee on Cancer; IASLC, International Association for the Study of Lung Cancer; UICC, Union for International Cancer Control.

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Harvey I. Pass: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data curation, Writing—original draft, Writing—review and editing, Visualization, Supervision.

Valerie W. Rusch: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data curation, Writing—original draft, Writing—review, and editing, Visualization, Supervision, Project administration, Funding acquisition.

Disclosure

Dr. Hasegawa received an endowed course from Kubota Corporation. Dr. Opitz has relationships with Roche (institutional grant and speakers bureau), AstraZeneca (advisory board and speakers bureau), Merck Sharp & Dohme (advisory board), Bristol-Myers Squibb (advisory board), Medtronic (institutional grant), and Intuitive (proctorship). Dr. Pass has relationships with Roche (steering committee and speakers bureau) and AstraZeneca (advisory board). Dr. Ripley receives institutional clinical trial funding from AstraZeneca and serves on the speakers bureau of Merck. Dr. Rusch receives institutional clinical trial funding from Genentech; receives meeting prep and travel reimbursement from NIH/NCI Thoracic Malignancy Steering Committee; is an unpaid member of DSMC Committee and MARS II Trial (Cancer Research UK). The remaining authors declare no conflict of interest.

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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.2024.01.018>.

Appendix 1

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Camilo Forlanini, Rome, Italy; Jason Chang, Memorial Sloan Kettering Cancer Center, New York, New York, USA; Keneng Chen, Peking University, Beijing Cancer Hospital, Beijing, People's Republic of China; Wendy Cooper, Royal Prince Alfred Hospital, NSW Health Pathology, Sydney, Australia; Pier Luigi Filosso, University of Torino, Torino, Italy; Liyan Jiang, Shanghai Chest Hospital, Shanghai, People's Republic of China; Nagla Karim, Inova Cancer Institute-University of Virginia, Virginia, USA; Peter Kneuert, The Ohio State University College of Medicine, Ohio, USA; Mark Krasnik, Gentofte University Hospital, Copenhagen, Denmark; Kaoru Kubota, Nippon Medical School Hospital, Tokyo, Japan; Catherine Labbe, Quebec Heart and Lung Institute, Quebec, Canada; Ho Yun Lee, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; Eric Lim, Imperial College and the Royal Brompton Hospital, London, United Kingdom; Geoffrey Liu, Princess Margaret Cancer Centre, University of Toronto, Toronto, Canada; Hongxu Liu, Cancer Hospital of China Medical University, Liaoning Cancer Hospital & Institute, Liaoning, People's Republic of China; Philip Mack, Mount Sinai, New York, New York, USA; David Naidich, NYU-Langone Medical Center, New York, New York, USA; Mizuki Nishino, Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, Massachusetts, USA; Marcin Ostrowski, Medical University of Gdańsk, Gdańsk, Poland; Charles Powell, Mount Sinai School of Medicine, New York, New York, USA; Carolyn Presley, The Ohio State University, Ohio, USA; Paul Martin Putora, Kantonsspital St. Gallen, St. Gallen, Switzerland; Natasha Rekhtman, Memorial Sloan Kettering Cancer Center, New York, New York, USA; Harry Ren, Shanghai Pulmonary Hospital, Shanghai, People's Republic of China; M. Patricia Rivera, Department of Medicine, University of North Carolina, Chapel Hill, North Carolina, USA; Gaetano Rocco, Memorial Sloan Kettering Cancer Center, New York, New York, USA; Maria Teresa Ruiz Tzukazan, Pontifical Catholic University of Rio Grande do Sul, PUCRS, Porto Alegre, Brazil; Robert Samstein, Mount Sinai, New York, New York, USA; Yu Yang Soon, National University Hospital, Harvard University Hospital, Singapore; Kenichi Suda, Kindai University Faculty of Medicine, Osaka, Japan; Martin Tammemägi, Department of Community Health Sciences, Ontario, Canada; Lynn Tanoue, Department of Medicine, Yale University, New Haven, Connecticut, USA; Akif Turna, Istanbul University, Cerrahpasa Medical School, Istanbul, Turkey; Benny Weksler, University of Tennessee Health Science Center, Tennessee, USA; Terence Williams, City of Hope Comprehensive Cancer Center, California, USA; Dawei Yang Zhongshan Hospital Fudan University, Shanghai, People's Republic of China; Jeff Yang, Massachusetts General Hospital/Harvard Medical

School, Massachusetts, USA; Masaya Yotsukura, Department of Thoracic Surgery, National Cancer Center Hospital, Tokyo, Japan.

Advisory Board to the Thymic Tumor Domain

Usman Ahmad, Cleveland Clinic, Cleveland, Ohio, USA, Thoracic Surgery, Heart, Vascular and Thoracic Institute, Cleveland Clinic and Cleveland Clinic Abu Dhabi, United Arab Emirates; Sarit Appel, Sheba Medical Center, Ramat Gan, Israel; Cecilia Brambilla, Royal Brompton and Harefield hospital, Guy's and St. Thomas NHS Foundation Trust, London, UK; Conrad B. Falkson, Queen's University, Kingston, Ontario, Canada; Pier Luigi Filosso, University of Torino, Torino, Italy; Giuseppe Giaccone, Weill-Cornell Medicine, New York, New York, USA; Francesco Guerrera, University of Torino, Torino, Italy; Maurizio Infante, University and Hospital Trust Azienda Ospedaliera Universitaria Integrata, Verona, Italy; Dong Kwan Kim, Asan Medical Center, Seoul, and University of Ulsan College of Medicine, Seoul, Republic of Korea; Marco Lucchi, Division of Thoracic Surgery, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; Anja Roden, Laboratory Medicine and Pathology, Mayo Clinic Rochester, Minnesota, USA; Charles B. Simone II, New York Proton Center and Memorial Sloan Kettering Cancer Center, New York, USA.

Advisory Board to the Esophageal Cancer Domain

Mark Ferguson, The University of Chicago, Chicago, USA.

Advisory Board to the Mesothelioma Domain

J. Friedberg, Temple University, Philadelphia, Pennsylvania, USA; Jennifer Sauter, Memorial Sloan Kettering Cancer Center, New York, New York, USA; Andrea Wolf, Icahn School of Medicine at Mount Sinai, New York, New York, USA.

Appendix 2. Chairpersons and Members of the Subcommittees of the Lung Cancer, Thymic Epithelial Tumors, Pleural Mesothelioma and Esophageal Cancer Domains of the IASLC Staging and Prognostic Factors Committee

IASLC Staging and Prognostic Factors Committee Chair: Hisao Asamura.

Lung Cancer Domain

Lung Cancer Domain Chair: Paul Van Schil.

Lung Cancer Domain Vice Chair: Kemp H. Kernstine.

Lung Cancer Domain T Descriptors Subcommittee. Hisao Asamura (chair), Young Tae Kim (co-chair) Pietro Bertoglio, Ayten K. Cangir, Jessica Donington, Wentao Fang, Yolande Lievens, Hiu Liu, Gustavo Lyons, Shuji Sakai, William D. Travis, Paula Ugalde, Paul Van Schil, Jeff Yang, Masaya Yotsukura.

Lung Cancer Domain N Descriptors Subcommittee. James Huang (chair), Raymond U. Osarogiagbon (co-chair), Andrea Bille, Giuseppe Cardillo, Kemp H. Kernstine, Hong Kwan Kim, Kaoru Kubota, Yolande Lievens, Eric Lim, Edith M. Marom, Helmut Prosch, Paul Martin Putora, David Rice, Gaetano Rocco, Valerie Rusch, Paul Van Schil, Isabelle Opitz, Francisco Suárez, Jeff Yang, Shun-ichi Watanabe.

Lung Cancer Domain M Descriptors Subcommittee. Kwun Fong (chair), Wilfried Eberhardt (co-chair), Jeremy Erasmus, Yolande Lievens, Mirella Marino, Edith M. Marom, Paul Martin Putora, Navneet Singh, Francisco Suárez.

Lung Cancer Domain Lepidic & GGO Subcommittee. William D. 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 G. Nicholson, Mizuki Nishino, Helmut Prosch, Ramon Rami-Porta, Valerie Rusch, Shuji Sakai, Yasushi Yatabe, Shun-ichi Watanabe.

Lung Cancer Domain Neuroendocrine Tumors Subcommittee. Ming S. 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 Rekhman, William D. Travis, Jeff Yang, Yasushi Yatabe.

Lung Cancer Domain Stage Group Subcommittee. Hisao Asamura (chair), Giuseppe Cardillo, Frank Detterbeck, John Edwards, Kwun Fong, Meredith Giuliani, James Huang, Kemp H. Kernstine, Edith M. Marom, Andrew G. Nicholson, Ramón Rami-Porta, William D. Travis, Ming S. 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 H. Kernstine, Yolanda Lievens, Raymond U. Osarogiagbon, Paul Martin Putora, Ramón Rami-Porta, Valerie Rusch, Paul Van Schil, Jeff 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, Meredith Giuliani, James Huang, Young Tae Kim, Mark Krasnik, Hiu Liu, Jan van Meerbeeck, Luis M. Montuenga, Andrew G. Nicholson, Paul Martin Putora, Valerie Rusch, Robert Samstein, Navneet Singh, Martin Tammemägi, Ricardo Terra, Ming S. 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 D. Travis, Ming S. 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 D. Travis.

Lung Cancer Domain Multiple Pulmonary Nodules Subcommittee. Frank Detterbeck (chair), Edith Marom (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 Rekhman, M. Patricia Rivera, Lynn Tanoue, Ricardo M. Terra, William D. Travis, Paula Ugalde, Yasushi Yatabe.

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 Rekhman, Harry Ren, Robert Samstein, Kenichi Suda, Ricardo M. Terra, William D. Travis, Ming S. Tsao, Terence Williams, Ignacio Wis-tuba, Dawei Yang, Yasushi Yatabe.

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

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

Thymic Epithelial Tumors Domain

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

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

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

Thymic Domain M descriptor: Nicolas Girard (chair), Usman Ahmad, Sarit Appel, Conrad Falkson, Wentao Fang, Giuseppe Giaccone, Dong Kwan Kim, Edith M. Marom, Andreas Rimner.

Thymic Domain Database subcommittee: Pier Luigi Filosso (chair), Usman Ahmad, Andrea Bille, Souheil Boubia, Frank Detterbeck, Wentao Fang, Nicolas Girard, Francesco Guerrera, James Huang, Dong Kwan Kim, Meinoshin Okumura, Enrico Ruffini.

Pleural Mesothelioma Domain

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

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 Mesothelioma Tumors Staging Project

Participating Institutions Listed in Alphabetical Order According to the Last Names of the PIs

K. Ando, Yokosuka Kyosai Hospital, Yokosuka, Japan; C. Atinkaya, Health Science, Hamidiye Medicine Faculty,

Istanbul, Turkey; H. Batirel, Marmara University, Department of Thoracic Surgery, Istanbul, Turkey; A. Bille, Guy's Hospital, Thoracic Surgery Department, London, UK; A. Bille, ESTS Registry, Exeter, UK; K.G. Blyth, School of Cancer Sciences, University of Glasgow, Glasgow, Scotland; A.J. Bograd, Swedish Cancer Institute, Seattle, Washington, USA; S. Call, Mutua Terrassa University Hospital, Terrassa, Barcelona, Spain; A.K. Cangir, Ankara University Faculty of Medicine, Ankara, Turkey; F.L. Cecere, IRCCS Regina Elena National Cancer Institute, Rome, Italy; S. Cedres, Vall d'Hebron University Hospital, Barcelona, Spain; H. Date, Japanese Joint Committee of Lung Cancer Registry, Tokyo, Japan; J. Friedberg, Temple University, Philadelphia, Pennsylvania, USA; M. de Perrot, UHN, Toronto General Hospital & Princess Margaret Hospital, Toronto, Canada; F. Galateau-Salle, MESOBANK, MESOPATH College Cancer Center Leon Berard, Lyon, France; M. Ginsberg, Memorial Sloan Kettering Cancer Center, New York, New York, USA; S. Hasegawa, Hyogo Medical University, Hyogo, Japan; K. Kernstine, University of Texas Southwestern Medical Center, Dallas, Texas, USA; H. Kindler, University of Chicago, Chicago, Illinois, USA; J. Luketich, University of Pittsburgh – Dept. of Cardiothoracic Surgery, Pittsburgh, Pennsylvania, USA; P. Martín-Martorell, Hospital Clínico Universitario de Valencia, Valencia, Spain; B. McCaughan and C. Kennedy, University of Sydney (SPH Campus), Sydney, Australia; A.K. Nowak, Sir Charles Gairdner Hospital, Nedlands, Australia; I. Opitz, University Hospital Zurich, Zurich, Switzerland; H. Pass, NYU-Langone Medical Center, New York, USA; D. Rice, The University of Texas MD Anderson Cancer Center, Texas, USA; R. T. Ripley, Baylor College of Medicine, Division of Thoracic Surgery, Houston, Texas, USA; K. Syrigos, University of Athens Oncology Unit, Athens, Greece; R. Terra, University of Sao Paulo Medical School, Sao Paulo, Brazil; A. Turna, Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Istanbul, Turkey; D. Waller, Barts Thorax Center, St Bartholomew's Hospital, London, UK; M. Zereu, Pavilhao Pereira Filho, ISCMPA, Porto Alegre, Brazil.

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