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10th International Workshop on Surgical Exploration of the Mediastinum and Systematic Nodal Dissection



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3rd Joint Meeting of the Spanish Society of Thoracic Surgery (SECT)



30th Congress of the "Asociación Iberoamericana de Cirugía Torácica" AIAC



THE ROLE OF MOLECULAR BIOLOGY AS A COMPLEMENT TO THE ANATOMIC CLASSIFICATION

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The purpose of staging is to communicate our best understanding of the likely future behavior of a cancer and, secondarily, provide guidance on treatment options likely to yield the best possible outcomes based on existing knowledge. The lung cancer staging system currently achieves this solely by describing the anatomic extent of disease by categorizing descriptors of the Tumor, Node, Metastasis components. As our knowledge of cancer biology expands apace, our staging system has to adapt to stay relevant. For example, there are now at least 12 biomarker-delineated subsets of lung cancer: ALK, BRAF, EGFR, ERBB2, KRAS, MET, NTRK, RET, ROS-1, Program Death-Ligand 1 Tumor Proportion Score high (>50%), mis-match repair deficient/MSI-high, and non-categorized non-small cell lung cancer, with more likely to come. Although these biomarker-delineated subsets currently mostly used to predict the likelihood of responsiveness to specific treatments, some of them also independently predict patterns of disease behavior, including greater or lesser metastatic potential, a proclivity for metastasis to certain organs (e.g. brain metastasis) and a greater likelihood of recurrence after definitive treatment (such as curative-intent surgery) for seemingly early-stage disease.

Characterizing and understanding these specific patterns of behavior among biomarker-delineated subsets is an important direction in the development of distinct prognostic subsets of lung cancer, as well as the evolution of treatment, leading to better outcomes. Along with the 3rd phase of the International Staging Project leading to the 9th edition of the TNM Staging system, the International Association for the Study of Lung Cancer's Staging and Prognostic Factors Group constructed the Global Molecular Database which collected data on molecular characteristics of lung cancer with testing across multiple platforms in use at institutions across the globe. The results from the initial analysis of that dataset are forthcoming, but will be limited to the evaluation of canonical (del exon 19, L858R, T790M) and non-canonical (all other) EGFR mutations, ALK mutations, and Kras (G12C and other) mutations. In addition, using lessons learned from this initial effort, the construction of the next iteration of the Global Molecular Database, for use towards the 10th edition of the TNM classification, will focus on the prospective collection of mostly next-generation sequencing data from institutions able to

provide reliable, high-quality data. There is also consideration of collecting data on circulating tumor DNA (ct-DNA) which is likely to be prognostic.

In my discussion of this topic, I will cover the rationale for augmenting the TNM staging system with a complementary molecular biology approach, review emerging evidence for the prognostic value of this approach, and explore the possible different ways in which such a system might be developed and used.