**TABLE 1.** Frequently Asked Question and Answer[1]

| | |
|---|---|
| Question | Clinical classification suggested that our patient had a T2 N2 M0 NSCLC. Preoperative biopsy of ipsilateral mediastinal nodes confirmed N2 disease, and a thoracotomy was not undertaken. Should this case be classified as cN2 or pN2? Should this case now be assigned a pathologic stage? |
| Answer | Microscopic confirmation of the nodal disease would allow this to be classified as pN2. However, to be designated a pathologic stage, the primary tumor must also have been confirmed on biopsy to establish the pT category. |

ative Group of the Spanish Society of Pneumology and Thoracic Surgery.

To classify as pathologic (p) N2 a tumor that has not been resected, even if there is pathologic confirmation of the metastatic nature of the lymph nodes by means of any preoperative endoscopy (transbronchial needle aspiration, ultrasonography-assisted bronchoscopy, or oesophagoscopy with fine needle aspiration), percutaneous needle aspiration, or surgical exploration (mediastinoscopy, mediastinotomy, extended cervical mediastinoscopy, or thoracoscopy) goes against general rule 2 of the tumor (T), node (N), metastasis (M) classification of malignant tumors, which says "Clinical classification (. . .) is based on evidence acquired before treatment. Such evidence arises from physical examination, imaging, endoscopy, biopsy, surgical exploration, and other relevant examinations."[2] "Pathologic classification (. . .) is based on the evidence acquired before treatment, supplemented or modified by the additional evidence acquired from surgery and from pathologic examination (. . .)" and "entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category (. . .)" and "the removal of nodes (. . .)." "An excisional biopsy alone of a lymph node without pathologic assessment of the primary is insufficient to fully evaluate the pN category and is a clinical classification (. . .)."[2]

Back, at least, to the early 1990s, some chest physicians and oncologists, mainly in North America, started to think that pathologic confirmation of tumor extent in the pretreatment assessment of lung cancer entitled them to assign a pathologic classification to these tumors. This is an evident misinterpretation of the word "pathologic" in the context of the TNM classification and a violation of the general rule 2. This misinterpretation eventually found its way into medical writing, as we pointed out in 2004.[3] Now, 5 years later, this schismatic use of the "p" prefix seems to be explicitly sanctioned by the International Association for the Study of Lung Cancer.

There are important implications associated with this misunderstanding that go beyond mere taxonomy. According to the general rules, even if a cytohistologically diagnosed tumor has pathologic evidence of nodal disease, its classification will still be clinical by definition, because the tumor has not been resected. If we assign "p" status to tumors that have not been resected, we will be mixing tumors with very different prognosis, i.e., tumors with pathologic confirmation of their anatomic extent but that do not undergo resection and tumors that have been resected and have a proper pathologic classification. The Certainty Factor[4] offers the possibility to code in a different way those nodes considered involved by imaging methods and by pathologic confirmation in the clinical phase of the tumor classification without relying to the "p" prefix, which should be reserved for pathologic classification, only.

In conclusion, assigning "p" status to unresected tumors that have pathologic confirmation of their nodal extent goes against general rule 2 of the TNM classification; it produces a mixture of cases of different prognosis that undermines the prognostic capacity of the TNM classification for lung cancer gained by the revisions that lead to its 7th edition, and therefore, it should be avoided.

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***In Response:***

We are grateful to the editor for an opportunity to respond to this question, which it is proposed to publish in the *Journal of Thoracic Oncology*. We should emphasize that the chapters in the *IASLC Manual on Thoracic Staging*[1] to which the comments are addressed, and many other chapters in this book, and the companion *IASLC Handbook of Staging in Thoracic Oncology*,[2] were reproduced with the permission of the International Union Against Cancer from publications to be published later this year: the *TNM Classification of Malignant Tumors* 7th edition and the *TNM Supplement: A Commentary on Uniform Use* 4th edition. Fuller explanatory notes will be available in these publications.

The International Association for the Study of Lung Cancer was accorded the privilege of publishing these chapters ahead of the source material because of its central role in formulating the proposals for the 7th edition and delays in the publishing schedules of the International Union Against Cancer and the American Joint Committee on Cancer, the two bodies that administer the tumor, node, metastasis (TNM) classification worldwide. In no sense was it the

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intention of the International Association for the Study of Lung Cancer to presume to "sanction" the authority of these publications.

The central question raised in the letter by Lopez-Encuentra et al. asks whether it is ever appropriate to use the "p" descriptor in association with (a) a TNM classification or stage or (b) a T, N, or M category, in cases in which resection has not been performed. They accurately quote General Rule 2, and in practice, a pTNM classification or pStage is most commonly applied when describing the extent of disease after surgical resection and pathologic examination e.g. pT3 N2 M0, pStage IIIA. Although in this situation the "pT" category will have been assigned on the basis of a high level of certainty, C4, and it is usual to afford the same level of certainty to the "pN" category, the "M0" category is always assumed on the basis of the clinical classification, with a Certainty factor of C1 or C2. Some would further question whether it is appropriate to assign a "pN" category after resection in cases in which the N3 nodes have not been thoroughly evaluated or in which the assessment of pN0 has been based on a casual assessment of the ipsilateral nodes in N1 and/or N2 locations. In this edition of TNM, we have sought to address the latter by reinstating a minimum number of lymph nodes expected to assure pN0 and have suggested that an "R1(un)" classification be trialed for cases, which are designated pN0 on less robust evidence.

There are circumstances in which surgical treatment is inappropriate and yet a higher Certainty factor, C3, has been achieved in the pathologic confirmation of the T, N, or M category. Surgical procedures such a mediastinoscopy have traditionally been accorded a specificity of 100%. We are fortunate that an expanding armamentarium is now available in thoracic oncology, which allows us to assess nodal status by less invasive procedures, such as endobronchial ultrasound and endoscopic ultrasound, with a similarly high specificity. It is therefore not illogical to assign a pN category in such circumstances.

Although General Rules must remain inviolable, it is surely appropriate that their interpretation evolves as the science of oncology improves. Indeed, in the *TNM Supplement: A commentary on Uniform Use*,[3] on page 97, the Site specific Recommendations for pT and pN in Lung and Pleural Tumors requires only the "Microscopic confirmation of metastasis" when assigning a pN category.

We accept that the N2 case illustrated in the Frequently Asked Questions in Chapter 12[1] will have a different prognosis to one in which a pN2 category is assigned after surgical resection, usually in cases in which a cN0 or cN1 category had been assigned prior to thoracotomy. However, this could be related to the different treatments appropriate in these scenaria or the reduced performance status that could weigh against surgery in some situations. Although the anatomic extent of disease, as described by the TNM classification, remains the single most important prognostic factor, the surest way to ensure homogeneity within any study population is to collect data on as many prognostic factors as possible.

We hope that this clarifies the situation.

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# The Mesothelioma and Radical Surgery Feasibility Study

***To the Editor:***

As Chair of the Trial Steering Committee for the mesothelioma and radical surgery trial, I was pleased to see the preliminary results of this study published in the *Journal of Thoracic Oncology*,[1] with the positive aspects of the trial emphasized in an accompanying editorial by Dr. Rusch.[2] However, one should note that the original trial design required the randomization of 50 cases in 1 year, and not the 3 plus years that proved necessary to achieve this accrual. Given the high incidence of malignant pleural mesothelioma in the United Kingdom and the organizational advantages in this county, emphasized in the editorial, this does suggest that those who expressed concern as to the feasibility of this randomization, mentioned in the Discussion, were not completely wrong! I raise this issue, as it must have a profound impact on the question to be posed in any follow-up study, an issue on which the authors of the article, and the editorial seem to hold differing opinions.

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