Switch Maintenance versus Second-Line Treatment in Non-small Cell Lung Cancer

To the Editor:

Three randomized phase III trials[1–3] evaluated the role of "switch maintenance" or "early second-line treatment," i.e., continuing treatment with a non–cross-resistant drug, in patients with advanced non-small cell lung cancer who did not progress after four cycles of platinum-based doublets.[4] In two of these three studies, patients randomized in the placebo arm could receive at progression any second-line therapy,[1,2] whereas in the third trial,[3] patients randomized in both arms, immediately or at progression, were treated with the same drug, i.e., docetaxel. In the control arm of these three trials, only 67%,[1] 72%,[2] and 63%[3] of enrolled patients received a second-line therapy at progression, respectively (Table 1). So, more than one-third of patients did not receive a second-line therapy due mainly to the worsening of their general conditions. This consideration reinforced the goal of the switch maintenance approach which is to recover all possible patients, who do not progress during induction therapy, to a second-line treatment.

Although data on dropout rates were not reported in the three studies, they can be derived from the survival curves: the finding is that in the experimental arms there was approximately one-third of withdrawn patients. This is of great interest because it means that there is a portion of patients who do not benefit anyway from second-line treatment and to whom a further possible toxicity, related to the switch maintenance treatment, could be avoided. This consideration is reinforced by the survival rate reported in the patients who effectively received docetaxel in the delayed arm of the study by of the Fidias et al., which was identical to that registered in the immediate docetaxel arm.[3] This led to the question regarding the survival rate of the patients who effectively received an active treatment in the control arm after progression during placebo administration of the other two studies.[1,2] Unfortunately, these data are lacking. Moreover, in these two studies, the percentage of patients randomized in the placebo arm and who actually received pemetrexed[1] or an epidermal growth factor tyrosine kinase inhibitor (erlotinib or gefitinib)[2] was only 18% and 21%, respectively. To date, pemetrexed and erlotinib are licensed for switch maintenance approach based on the evidence that they improve survival outcomes, but the need of investigating the real role of switch maintenance versus second-line treatment at progression using the same drug in the experimental and control arm remains unmatched. Regulatory agencies requested such type of trial, and for erlotinib this kind of trial is going to start. This is the only way to confirm whether this approach is able to rescue the percentage of patients otherwise lost to second-line therapy also getting information to select patients who could really benefit from a further therapy.

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Classification of Large Cell Neuroendocrine Carcinoma

At the Cross Roads of Small and Non-small Cell Lung Cancer

To the Editor:

The European Respiratory Society, American Thoracic Society, and the International Association for Study of Lung Cancer need to be complimented for undertaking the much needed task of reclassifying adenocarcinoma. The consensus document has now been published in a recent issue of *Journal of Thoracic Oncology*.[1] I have a comment related to the section that discusses the distinction of adenocarcinoma from neuroendocrine carcinomas (NECs). It has been stated that because neither the prognosis nor treatment of non-small cell lung cancer (NSCLC) is affected by the presence of neuroendocrine markers, routine immunohistochemistry (IHC) and staining with these markers should be avoided in the absence of histological features suggestive of large cell NEC (LC-NEC). However, it is becoming increasingly evident that LC-NEC, as an entity, tends to share some, if not all, of

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