Lung cancer: New evidence - new realities - new challenges

The past years have yielded a wealth of new data on how to improve the outcome for patients with lung cancer, in particular with non-small cell lung cancer.

Past achievements were largely based on the recognition that the delivery of optimal therapy mandates the involvement of a dedicated multidisciplinary team. Now, the major new advances are the suggestion that screening for patients with a high risk for lung cancer can be beneficial, that new radiotherapy techniques allow potentially curative treatment in early localized disease, and that the molecular analysis of tumor tissue allows to provide effective therapy beyond the standard chemotherapy to selected subsets of patients whose tumors harbor specific molecular features.

With new evidence gained from clinical studies, the reality of clinical practice has changed substantially. Patients today will ask their physicians about incidental lung-cancer screenings. As outlined in the article by Mark and colleagues, the questions on the feasibility of screening programs remain unresolved, in particular because of the large proportion of false positive CT scans, uncertainties about the target populations and the still unknown cost effectiveness of the implementation of screening programs. Notwithstanding the lack of randomizing screening studies in Switzerland, we feel that it is in the interest of the people at risk that they get access to quality-controlled CT screening at dedicated locations employing multidisciplinary teams, which include specialized thoracic surgeons.

The advances in radio-therapeutic techniques are manifold, and include the optimization of radiotherapy planning by FDG-PET as outlined in the article by Schmuecking and his team. These results also relate to the delivery of curative-intent radiotherapy, which today is restricted to patients not amenable to surgery: ongoing Phase III trials are, however, evaluating this modality also in patients with operable stage-I cancer. While these advances have been based on improvements in technology, the clinical studies have been driven by dedicated radio-oncologists focusing on the treatment of lung-cancer patients. The challenge will be to introduce these results into the community, as this will require a certain specialization also within radio-oncologists.

The composition of the multidisciplinary lung-tumor board has changed. With the advent of molecular targeted therapy, the pathologist has not only become a key person in helping to elaborate lung cancer diagnosis and staging, but also in providing information about biomarker testing, in particular for patients beyond the early stages of the disease. EGFR-mutation testing has become an integral part of the work-up for the determination of first-line therapy for patients with advanced non-squamous cell lung cancer. With the Swissmedic registration of crizotinib the determination of the ALK status for decision making in second or further line of therapies is becoming routine. It is very likely that additional treatment options will soon become routinely available for a small subset of patients with molecularly defined non-small cell lung cancer. The challenge then will be to provide a maximum of information on a limited amount of tumor tissue in a timely fashion and at reasonable costs.

Chemotherapy has improved the outcome of patients with non-small cell lung cancer, as we can be observed in the prolonged survival rates in advanced disease and higher cure rates for combinations with surgery or radiotherapy for earlier stages of disease. With the exception of maintenance therapy, the most recent advances have been achieved in selected, molecularly defined subgroups of patients. While the proportion of patients with adenocarcinoma and activating EGFR mutations in our environment is about 12%, the proportion of patients with the more recently identified oncogenic driver mutations is even smaller (1-5%). The rarity of these subsets of the disease is prompting a change in the way clinical trials are conceived, as larger-scale molecular testing needs to be per-

formed to identify patients amenable to molecularly driven treatments. This is a challenge, in particular in a small country with a fragmented health system. One approach taken to solve the problem was the creation of the European Thoracic Oncology Platform which, supported by investigators from Switzerland, provides a network for collaborative translational and clinical studies between study groups and dedicated centers within Europe.

Available information suggests that for patients affected by a tumor with activating EGFR mutation the integration of gefitinib or erlotinib in a treatment of advanced disease is associated with a doubling of survival as compared to a treatment with chemotherapy alone – no doubt a clinically significant improvement. Still, the fact remains, that tumors eventually become resistant also to targeted therapies. Thus notwithstanding all advances, patients will continue to need support beyond antitumor treatment, including psychological support as outlined by Ackeret, as well as supportive care as outlined by Serena. Indirectly, the second article also provides some stimulus to remember the fact that nursing is an integral part of the multidisciplinary approach and to appreciate the challenges the nursing profession is facing regarding specialization.

Individualized care for patients with lung cancer within an integrated system of care providers has become a reality within a few years and offers patients today a chance for a better outcome. We will continue to face challenges, including the adoption of internationally accepted regulatory decisions, which are better adapted to the new reality of cancer therapy. Notably, in the palliative setting, patients' access to efficient targeted agents must be ensured. For example, impressive response rates to a specific agent in the context of limited alternative options should be considered a sufficient argument for a provisional approval pending further and more definitive outcome data. How to deal with new the opportunities and how to move from standardized medicine to personalized medicine must become political priorities. And, last but not least, we must consider the question of whether and how society can deal with the related costs. This topic has been extensively dealt with in the last issue of this journal.

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