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Lung Cancer: New Therapeutic Approaches

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Non-small cell lung cancer (NSCLC) is responsible for roughly 27% of all cancer-related fatalities globally, making it a serious public health issue. Healing needs full, indefinitely-lasting tumour removal (usually by surgery or radiation [RT]), although substantial shrinking (typically by systemic therapies) might result in long-term disease management. More realistically, in the absence of treatments, host-tumor interactions, which are major determinants in the natural history of diseases, will have a significant impact on disease progression, with treatments primarily aimed at causing the host-tumor balance to tip toward improvement or, if possible, healing. As a result, full tumoral excision of the original tumour (and, if possible, oligometastatic illness) is still regarded the optimum treatment, with the hope that the host-immune response can eliminate microscopic residual disease, potentially with the aid of systemic adjuvant therapies. The majority of patients, however, are not candidates for surgery and have been treated for decades with standard chemotherapy (cisplatin-based regimens) and/or radiation. Targeted treatments (namely Tyrosine Kinase Inhibitors, TKIs) and immunotherapies may provide exceptional results in select subgroups.

The benefit of targeting immune cells (that is, restoring their physiologic function that has been altered by the presence of tumour) has changed the therapeutic paradigm, which now aims to target the interface host-tumor, i.e., the tumour microenvironment (TME), as well as host-related factors, which have a strong impact on tumour development and response to therapies.

As a result, the best approaches available today are probably adopting highly effective tumor-targeted approaches (ablation by surgery or RT, or precision systemic treatments, especially against driver mutations) and preserving or improving patient fitness to allow the immune response to be maintained or even improved.

Obviously, care should be multidisciplinary, with the goal of optimising tumour phenotyping, assessing treatment resistance, evaluating and improving patient fitness, optimising the timing of multiple methods, especially in patients with locally advanced cancer, and avoiding toxicities.

Toxicity is still an issue with surgery, particularly pneumonectomy. ARDS, whose aetiology is often unknown and unrelated to infection, is commonly associated to mortality following pneumonectomy. Pulmonary hypertension might also be a factor. On the basis of the hypothesis that pulmonary artery diameter was a sign of subclinical pulmonary hypertension, this parameter was measured on a CT scan at the bifurcation level and standardised to body surface area.

In patients with locally resectable III A, i.e., non-bulky, discrete, or single-level N2 involvement that can be treated with multimodality, major lung resection is indicated. IIIA-N2 NSCLC, on the other hand, has a wide spectrum of clinical and pathological heterogeneity, with a lack of precise pretreatment staging. It might be challenging to choose the appropriate treatment approach in this situation.

Retrospective analysis, in particular, did not take into account the rapid rise of various treatment choices, as noted in the review by Brascia et al. , and only provided results of standard chemo and radiation methods (based on TNM extent) (more and more based on the biological nature of the tumor, i.e., targeted therapies and immunotherapies). This review is quite useful in guiding complicated treatment decisions in this varied group of stage IIIA patients.