INDUCTION THERAPY FOLLOWED BY SURGERY IN NSCLC

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Induction (neoadjuvant) therapy before surgery in operable stage III NSCLC has theoretical advantages: in vivo assessment of response to chemotherapy; early treatment of micrometastatic disease; a reduction in drug resistance due to early exposure to treatment; and downstaging, with improved resectability, becomes possible.

The group of patients with stage IIIA N2 NSCLC is heterogeneous and their treatment should be discussed in a multidisciplinary committee. For most patients with clinically evident N2 disease, the approach is concurrent chemoradiotherapy, using platinum-based chemotherapy plus full-dose radiation therapy (RT). However, in a highly selected subset of patients, induction chemotherapy or chemoradiotherapy followed by surgery may be appropriate options.

A study in patients with resectable stage III NSCLC showed a benefit for induction chemotherapy in terms of the pathological response, and also an improvement of the mediastinal stage, with no differences in survival rates. A meta-analysis showed that the addition of radiotherapy to induction therapy does not increase survival.

In the Intergroup 0139 trial, including over 400 patients with stage IIIA NSCLC due to N2 disease receiving chemoradiotherapy, the use of surgery was not associated with an improvement in overall survival (five-year OS, 27% vs. 20%).

The EORTC 08941 trial also suggested that there was no OS difference after induction chemotherapy for those receiving surgery versus RT. The two groups also experienced similar PFS.

Although no prospective randomized data exist to define the subset who would benefit from surgery, factors that lead some experts to offer it include single-station N2 disease that was <3 cm prior to induction therapy, disease that can be resected via lobectomy rather than

pneumonectomy, and disease that responded to induction therapy, as evidenced by clearance of mediastinal lymph nodes.

Contraindications to surgical resection include poor or borderline performance status, poor pulmonary function, active heart disease, progressive disease with induction therapy, extracapsular nodal extension, T4 disease, and multistation N2 disease.

In the future the possible way could be neoadjuvant chemoimunotherapy. NADIM Study (CA209-547) was a phase II, multicenter study aimed to assess the feasibility, safety, and efficacy of combined neoadjuvant chemotherapy and immunotherapy. At the time of data cutoff (Jan 31, 2020), the median duration of follow-up was 24,0 months and 35 of 41 patients who had tumour resection were progression free. At 24 months, progression-free survival was 77,1%.

Neoadjuvant chemoimmunotherapy could change the perception of locally advanced lung cancer as a potentially lethal disease to one that is curable.

Conclusion

Concurrent chemoradiotherapy is recommended for pts with inoperable stage II (node positive) and stage III. Neoadjuvant concurrent chemotherapy/RT is an option for pts with resectable IIIA (min. N2) and for resectable sulcus superior tumor. If patients are not well-able for surgery (as originally planned), RT should be completed into a radical dose without interruption. Preoperative chemotherapy and postoperative RT are an alternative for pts with resectable stage IIIA.