

# A closer look at the safety and effectiveness of modern PORT in stage III-N2 non-small cell lung cancer

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We appreciate the interest of Dr. Fiorica in our study (1). The optimal treatment of patients with stage III locally advanced non-small-cell lung cancer (NSCLC) is still debatable. Regarding the high incidences and poor treatment outcomes (2), there is gaining interest in an optimization of the multimodality treatment for these patients.

In selected patients with IIIA-N2 disease, arguments remain to perform surgical resection after induction therapy after three large prospective randomized trials (2-4). Nevertheless, a benefit in overall survival (OS) compared with curative radiation alone was never demonstrated, although the progression-free survival (PFS) was longer in the surgical arm of the Lung Intergroup Trial (3).

In regard to the recent published comment of F. Fiorica, “radiotherapy is an ideal complement to systemic therapy for controlling the eradication of microscopic residual disease and/or gross tumor” (5). In this context, the importance of achieving an R0 resection and thus of proper patient selection for surgical multimodality treatment has to be emphasized. We earlier demonstrated lower OS and higher local recurrence (LR) rates after an incomplete resection in stage III-N2 NSCLC patients treated with surgery after induction chemotherapy (1). Complete resection was also a significant prognostic factor for OS, as already demonstrated in other studies (6). In regard of the poor OS in all NSCLC patients, most long-term survivors are patients having had a complete surgical resection. The recent improvements in diagnostic

imaging [fluorodeoxyglucose F 18 positron emission tomography (FDG-PET)/computed tomography (CT) scans and brain imaging] and invasive staging techniques [endobronchial ultrasound (EBUS) or endoscopic ultrasound (EUS)] are helpful for a better patient selection.

The issue of postoperative radiotherapy (PORT) in patients with completely resected NSCLC remains controversial. As the results of the prospective randomized Lung ART study are awaited (7), we performed a retrospective research project concerning PORT in stage III-N2 patients with persistent mediastinal involvement (ypN2) and/or incomplete resection (R1/2 resection) after induction chemotherapy and surgery. PORT seemed effective and safe in stage III NSCLC patients with the current more modern treatment and staging strategies in contrast with older, suboptimal techniques. We optimized the target volume delineation (8) and demonstrated the feasibility of these radiation plans. According to F. Fiorica (5), we want to emphasize the advances in radiation techniques, leading to more conformal radiation delivery with an improved therapeutic ratio. In contrary, the recent revision of the PORT meta-analysis by the Cochrane group (9), demonstrating the detrimental effect of PORT, used trials starting from 1966 to 1998.

Besides this, no information is available about the non-radiation related toxicity in patients in this group, who often suffer from other comorbidities that possibly predispose them to cardiac and pulmonary toxicity. Although in our study, the PORT group received an additional treatment

compared to the non-PORT group, no clear difference in toxicity was seen (1). The upfront cardiac and pulmonary comorbidity, present in both subgroups, can probably explain the cardiac and pulmonary events during follow up mainly.

Also no significant difference in non-cancer-related deaths was seen between both subgroups (57% in the PORT group *vs.* 44% in the non-PORT group), therefore we could state that the toxicity profile of PORT is acceptable.

As an improvement in local tumor control can result in an increase in OS (10), we believe in a tailored postoperative radiation treatment in selected patients (ypN2 and/or R1/2 resection).

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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