Non-small-cell lung cancer: should histology guide chemotherapy treatment?

Tan et al. [1] reported a phase III trial, Glob3, comparing vinorelbine to docetaxel, each combined with cisplatin, for the treatment of advanced non-small-cell lung cancer (NSCLC). Apart from the use of an oral chemotherapy, it assessed retrospectively the outcome of treatment in patients with adenocarcinoma and patients with squamous cell carcinoma. In the two arms, survival was close to 2 months longer in patients with adenocarcinomas (11.73 months in the vinorelbine arm and 11.60 months in the docetaxel arm) compared with patients with squamous cell carcinoma (8.87 months in the vinorelbine arm and 9.82 months in the docetaxel arm).

Histology is gaining prominence in scientific communications on NSCLC but good decision making requires a growing number of criteria. A study by Scagliotti et al. [2] compared cisplatin plus gemcitabine with cisplatin plus pemetrexed. Using a non-inferiority design, the primary objective was achieved with median overall survival (OS) of 10.3 months in each arm. More significant, this study highlighted the differences in survival according to histological type showing that pemetrexed–cisplatin seems to be more
effective in patients with adenocarcinomas compared with patients with squamous cell carcinomas. In adenocarcinoma subgroup, OS was improved in the pemetrexed arm compared with the gemcitabine arm (12.6 versus 10.9 months; hazard ratio 0.84; 95% confidence interval 0.71–0.99; \( P = 0.03 \)). Conversely, gemcitabine was more effective in patients with squamous cell carcinomas. It is important to point out that patients were not stratified according to histology, it was a prespecified subset analysis. In the same way, other agents seem to be more effective in nonsquamous cell carcinomas, particularly cisplatin-based chemotherapy rather than carboplatin-based chemotherapy as showed in the meta-analysis published by Ardizzoni et al. [3]. In the FLEX study, a higher chemosensitivity of nonsquamous cell carcinomas is indicated by the results, with an OS of 12 months for patients with adenocarcinoma versus 10.3 months for patients with squamous cell carcinoma in the vinorelbine–cisplatin plus cetuximab arm [4]. However, other factors, correlated to histological type, may also influence survival, such as duration of treatment and the number of lines of chemotherapy received. Because adenocarcinomas are more chemosensitive, more lines can be considered, particularly as an increasing number of new agents become available. This, combined with the growing proportion of patients with adenocarcinoma, could explain the constant improvement of survival witnessed over the past decade.

Hence, histological type should be added to other already known favourable prognostic factors (female, Asian, never smoker, good performance status, and stage IIIb) and biological factors (genomics and proteomics). However, histological diagnosis is far from being certain, particularly with peripheral and deep tumours, which are often adenocarcinomas but also mixed tumours with a squamous component.

Given the reported difficulty in making a definitive histological diagnosis and the alternative interpretations of these results, it may be premature, without further research, to change our current recommendations for first-line treatment of NSCLC.

Several chemotherapies are more active on adenocarcinomas and more comparative trials must validate this. In this way, the authors of Glob3 create the opportunity of a more open paradigm.

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references


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