Lung

Imaging-based target volume reduction in chemoradiotherapy for locally advanced non-small-cell lung cancer (PET-Plan): a multicentre, open-label, randomised, controlled trial.

Nestle U, Schimek-Jasch T, Kremp S, Schaefer-Schuler A, Mix M, Küsters A, Tosch M, Hehr T, Eschmann SM, Bultel YP, Hass P, Fleckenstein J, Thieme A, Stockinger M, Dieckmann K, Miederer M, Holl G, Rischke HC, Gkika E, Adebahr S, König J, Grosu AL; PET-Plan study group.

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BACKGROUND:

With increasingly precise radiotherapy and advanced medical imaging, the concept of radiotherapy target volume planning might be redefined with the aim of improving outcomes. We aimed to investigate whether target volume reduction was feasible and effective compared with conventional planning in the context of radical chemoradiotherapy for patients with locally advanced non-small-cell lung cancer.

METHODS:

We did a multicentre, open-label, randomised, controlled trial (PET-Plan; ARO-2009-09) in 24 centres in Austria, Germany, and Switzerland. Previously untreated patients (aged older than 18 years) with inoperable locally advanced non-small-cell lung cancer suitable for chemoradiotherapy and an Eastern Cooperative Oncology Group performance status of less than 3 were included. Undergoing 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET) and computed tomography (CT) for treatment planning, patients were randomly assigned (1:1) using a random number generator and block sizes between four and six to target volume delineation informed by 18F-FDG PET and CT plus elective nodal irradiation (conventional target group) or target volumes informed by PET alone (18F-FDG PET-based target group). Randomisation was stratified by centre and Union for International Cancer Control stage. In both groups, dose-escalated radiotherapy (60-74 Gy, 2 Gy per fraction) was planned to the respective target volumes and applied with concurrent platinum-based chemotherapy. The primary endpoint was time to locoregional progression from randomisation with the objective to test non-inferiority of 18F-FDG PET-based planning with a prespecified hazard ratio (HR) margin of 1:25. The per-protocol set was included in the primary analysis. The safety set included all patients receiving any study-specific treatment. Patients and study staff were not masked to treatment assignment. This study is registered with ClinicalTrials.gov, NCT00697333.

FINDINGS:

From 13 May 2009 to 5 December 2016, 205 of 311 recruited patients were randomly assigned to the conventional target group (n=99) or the 18F-FDG PET-based target group (n=106; the intention-to-treat set), and 172 patients were treated per protocol (84 patients in the conventional target group and 88 in the 18F-FDG PET-based target group). At a median follow-up of 29 months (interquartile range (IQR) 9-54), the risk of locoregional progression in the 18F-FDG PET-based target group was non-inferior to, and in fact lower than, that in the conventional target group in the per-protocol set (14% [95% Confidence Interval (CI) 5-21] vs. 29% [17-38] at one year; HR 0.57 [95% CI 0.30-1.06]). The risk of locoregional progression in the 18F-FDG PET-based target group was also non-inferior to that in the conventional target group in the intention-to-treat set (17% [95% CI 9-24] vs. 30% [20-39] at one year; HR 0.64 [95% CI 0.37-1.10]). The most common acute grade 3 or worse toxicity was oesophagitis or dysphagia (16 [16%] of 99 patients in the conventional target group vs. 17 [16%] of 105 patients in the 18F-FDG PET-based target group); the most common late toxicities were lung-related (12 [12%] vs. 11 [10%]). A total of 20 deaths potentially related to study treatment were reported (seven vs. 13).

INTERPRETATION:

18F-FDG PET-based planning could potentially improve local control and does not seem to increase toxicity in patients with chemoradiotherapy-treated locally advanced non-small-cell lung cancer. Imaging-based target volume reduction in this setting is, therefore, feasible, and could potentially be considered standard of care. The procedures established might also support imaging-based target volume reduction concepts for other tumours.