for the management of subsolid pulmonary nodules detected by computed tomography state that FDG-PET is of limited value, potentially misleading, and therefore not recommended for solitary pure ground-glass nodules >5 mm and pure ground-glass nodules >5 mm without a dominant lesion [Naidich DP et al. *Radiology*. 2013].

In conclusion, Prof Sculier stated that evidence suggests that PET is not a good imaging modality in the diagnosis of lung cancer. He suggested that the study authors consider repeating their assessment by DWI and FDG-PET after reclassifying the study specimens according to their radiologic presentation.

ESTERN: Neoadjuvant Erlotinib Showed Promise in NSCLC Patients With *EGFR* Mutations

Written by Francesca Coltrera

Neoadjuvant erlotinib treatment showed promise in a phase 2 trial of patients with advanced-stage non–small cell lung cancer (NSCLC) with *EGFR* mutations. A poster [Han B et al. *Ann Oncol*. 2015] was presented on behalf of Baohui Han, MD, PhD, Shanghai Chest Hospital, Shanghai, China, that detailed findings from the single-arm ESTERN study [NCT01217619].

Out of 155 patients with previously untreated NSCLC screened at the hospital between October 2010 and June 2014, 44 had stage IIIA-N2 tumors confirmed by endobronchial ultrasound. Twenty-five of these patients with exon 19 or 21 *EGFR* mutations ultimately enrolled in the study.

All participants had adenocarcinoma and an ECOG performance status of 1. Overall median age was 59 years. Of 25 participants, 13 were men and 12 were current or former smokers. Sixteen (64%) had an exon 19 deletion, and 10 (40%) had an exon 21 *L858R* mutation (1 patient had both).

The primary end point was radical resection rate. Secondary end points were pathologic complete response rate, objective response rate, disease-free survival (DFS), overall survival (OS), quality of life, safety profile, and exploratory biomarkers.

On days 1-28, patients received 150 mg/d of erlotinib, a tyrosine kinase inhibitor effective in first-line therapy for advanced NSCLC patients with EGFR mutations. After evaluation for disease progression, participants received the same dose regimen on days 29-56.

Nine patients did not proceed to radical resection surgery because of disease progression (n=5), severe adverse events (SAE; n=2), or unsuitability for surgery (n=2, surgery not feasible due to either tumor shrinkage or surgery history in other lung). Sixteen reaped sufficient benefit from erlotinib to have the surgery. Most were women (n=10) and never-smokers (n=11).

The primary end point of radical resection rate was reached in 15 patients (60%) in the intention-to-treat (ITT) analysis and in 15 of 16 (93.8%) patients in the surgery group. One patient in the ITT group (4.0%) and 1 patient in the surgery group (6.3%) had a pathologic complete response. An objective response rate was seen in 8 patients (32.0%) and 7 patients (43.8%) in the ITT and surgery groups, respectively, and progressive disease was seen in 6 patients (24.0%) and 1 (6.3%) patient, respectively.

Data for OS were not yet available. Median progression free survival in all patients was 7.9 months (95% CI, 5.6 to 10.2 months). From the start of study treatment, median DFS was 12.2 months (95% CI, 7.3 to 17.1 months). Median DFS after surgery was 10.4 months (95% CI, 5.4 to 15.4 months).

Most patients received adjuvant therapy after surgery. Median time from surgery to discharge was 8 days. Rash occurred in 28% of patients; 4% experienced diarrhea. Three patients had grade 3/4 AEs (4% leukocytopenia; 4% abnormal liver function; 4% cerebral infarction, considered unrelated to treatment). The investigators concluded toxicity was well tolerated.

In 3 patients with EGFR mutations detected in preoperative biopsies, surgical samples were subsequently tested and found to be EGFR wild-type. Tumor marker carcinoembryonic antigen, which helps track several cancers, was considerably lower following neoadjuvant erlotinib therapy in patients who went on to surgery (n=16) compared with those who did not (n=9). The baseline levels of 54.2 and 120.8 µg/L were reduced to 10.6 and 106.8 µg/L, respectively, at 7 weeks. In the ITT group (n=25), the carcinoembryonic antigen level was 33.2 µg/L at 7 weeks, reduced from 78.2 µg/L at baseline.

Limitations were the small sample size, single-arm design, and lack of OS data. Although findings must be confirmed in randomized studies, treatment toxicity was largely well tolerated and neoadjuvant erlotinib followed by radical resection appeared promising for some advanced-stage NSCLC patients with specific *EGFR* mutations.