

498P Case series of small cell lung cancer transformation post tyrosine kinase inhibitor failure

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Background: Patients with epidermal growth factor receptor (EGFR) mutant advanced non-small cell lung cancer (NSCLC) developed resistance to first- or second-generation EGFR-tyrosine kinase inhibitor (TKI) after 9-13 months and third-generation EGFR-TKI after 10 months, respectively. Small cell lung cancer (SCLC) transformation is a rare resistance mechanism in these patients.

Methods: Tissue re-biopsy in 35 patients with EGFR mutant advanced NSCLC who failed first-line EGFR-TKI; and 4 patients with acquired T790M mutant advanced NSCLC who failed third-generation EGFR-TKI, to look for SCLC transformation.

Results: SCLC transformation was identified in 2 out of 35 (5.7%) patients who failed first-line EGFR-TKI and 1 out of 4 (25.0%) patients who failed third-generation EGFR-TKI. All 3 patients were never smoker. The first patient was a 70-year-old male with exon 19 deletion stage IV lung adenocarcinoma. He had partial response (PR) to gefitinib 250 mg daily but developed symptomatic progressive disease (PD) after 26 months. Re-biopsy of his enlarging primary lung lesion showed SCLC transformation. The second patient was a 43-year-old male with exon 19 deletion stage IV lung adenocarcinoma. He had PR to gefitinib 250 mg daily but developed symptomatic PD after 15 months. Re-biopsy of his enlarging primary lung lesion showed SCLC transformation and plasma was positive for T790M mutation. The third patient was a 62-year-old female with exon 21 L858R stage IV lung adenocarcinoma. She had PR to gefitinib 250 mg daily but experienced symptomatic PD after 8 months' of gefitinib therapy. Re-

biopsy of her primary lung tumor revealed T790M mutation and treatment was switched to osimertinib 80 mg daily. After an initial PR, she developed PR in the 12th month. Biopsy from metastatic inguinal lymph node showed SCLC. The first and second patients were given standard chemotherapy but did not respond. The third patient sought treatment in another hospital.

Conclusions: Re-biopsy is recommended in patients with symptomatic PD while on EGFR-TKI treatment. SCLC transformation is an emerging challenge to the management of advanced NSCLC. New treatment strategies should be explored to improve outcome of patients who develop SCLC transformation.

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