Letter to the Editor

Good response to erlotinib in a patient after progression on osimertinib: A rare case of spatiotemporal T790M heterogeneity in a patient with epidermal growth factor receptor-mutant nonsmall cell lung cancer

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Dear Editor,

We report a rare case of spatiotemporal heterogeneity T790M mutation with repeated response and clinical benefit to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) in a 51-year-old woman with nonsmall cell lung cancer. The patient presented was evaluated for shortness of breath elsewhere found to have mass lesion in the left upper lobe with massive pleural effusion and referred to our center. She was evaluated further and found to have multiple pleural deposits, bilateral pulmonary nodules, and lymph nodal involvements. Pleural effusion was positive for malignant cells, and cell block was suggestive of adenocarcinoma. Computed tomography-guided biopsy from the left lung lesion was thyroid transcription factor-1 positive and was suggestive of adenocarcinoma lung. Molecular studies of EGFR mutational analysis by amplified refractory mutation system-polymerase chain reaction was positive for in-frame

DELETION (746–750) in exon 19, and anaplastic lymphoma kinase fusion studies were negative by immunohistochemistry. ROS and MET gene rearrangements were negative by FISH. PDL-1 testing done by Ventana SP263 was negative. After therapeutic drainage of pleural fluid, pleurodesis was done by Talc and she was started on gefitinib 250 mg once daily. She tolerated the TKI well and she had progression of disease after 8 months with a new left perihilar lesion in the lung. In view of progression, bronchoscopic guided rebiopsy from new lesion was done and a blood sample for cell-free DNA analysis for EGFR mutational analysis by Droplet Digital PCR (ddPCR) was sent. Rebiopsied formalin-fixed block showed the expression of Deletion 19 mutation along with T790M mutation in exon 20. Digital Droplet PCR also picked up T790M mutation. The patient has chosen the option of chemotherapy for TKI. She was started on pemetrexed-based chemotherapy. After three cycles, she had a good response, and after 6 cycles, she had disease progression. She was counselled again and was started on osimertinib 80 mg/day. She responded for 4½ months and had disease progression. She was given six cycles of gemcitabine-based chemotherapy again had disease progression with appearance of new lymph nodes in mediastinum. Rebiopsy was done from the newer lymph node which was suggestive of adenocarcinoma and had revealed the presence of EGFR DEL 19 mutation without T790M mutation which was present in earlier biopsy. In view of possibility of tumor heterogeneity, ddPCR was done in both blood and urine samples which also revealed EGFR del 19 mutation but the absence of T790M mutation. She was started on erlotinib 150 mg/day. She has a good clinical response and she progressed after 6 months of TKI therapy. As she was not willing for further biopsies, she was started on nivolumab-based immunotherapy at present after progression on erlotinib.

T790M heterogeneity was reported in some studies where this mutant clone can disappear after TKI-free interval with reappearance following retreatment with TKI.[1-3] This is interesting case report in which the patient had responded to first-generation TKI following treatment with third-generation TKI revealing spatiotemporal heterogeneity of this mutation.

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Conflicts of interest

There are no conflicts of interest.

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