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Case Report

Response to Afatinib, an Irreversible EGFR-TKI in a Patient with Advanced Squamous Carcinoma of lung

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Introduction

Advanced squamous cell carcinoma of the lung, accounts for 20-30% of cases of non-small-cell lung cancer [1]. After the failure of first-line platinum-based doublet chemotherapy, there are very few treatment options available to patients suffering from advanced squamous cell carcinoma of the lung [2]. There is a dearth of approved drugs targeting driver mutations which are responsible for carcinogenesis in squamous carcinoma of lung, despite specific molecular targets being identified (e.g., FGFR1 amplification, PIK3K3 abnormalities, DDR2 mutations) [3]. On the other hand, many targeted therapies have been approved for the treatment of adenocarcinoma of the lung. Erlotinib (an EGFR tyrosine kinase inhibitor) and Docetaxel are already approved in second-line treatments for squamous cell carcinoma [2]. Molecular data suggest a role for over expression or gene amplification of EGFR in the pathobiology of squamous cell carcinoma. Several studies [4,5] suggest that EGFR over expression is more common in squamous tumors (up to 82% of cases) than in adenocarcinoma. The rationale for targeting EGFR in patients with squamous cell carcinoma of the lung is supported by trials [6,7] showing an improvement in overall survival when the anti-EGFR monoclonal antibodies Cetuximab or Necitumumab were added to first-line platinum doublet chemotherapy compared with doublet chemotherapy only. In addition to EGFR, other members of the ErbB family, including HER2 [8–10] HER3 [11] and HER4 [11] as well as their cognate ligand NRG1 [12] have been implicated in the pathogenesis of squamous cell carcinoma. Hence it was hypothesized that Afatinib, an irreversible ErbB-family inhibitor which selectively blocks signalling from all homodimers and heterodimers formed by EGFR, HER2, HER3 and HER4 will act against squamous carcinoma of lung [13].

Case description: A 61 year male, a known smoker, had presented with fever and cough, and was diagnosed as a case of Carcinoma Right Lung. CT scan Whole Thorax done on 21/05/2013 showed heterogeneous mass lesion in the right upper lobe with mitotic changes and moderate emphysematous changes in lungs bilaterally. Bronchoscopic biopsy done on 23/05/2013 reported squamous cell carcinoma. Video bronchoscopy done on 23/05/2013 reported infiltrating growth seen at carina and right upper lobe bronchus, completely occluded with soft tissue lesion, lesion was visualised under narrow band showed abnormal tortuous vascularity and rest of the visualized trachea and bronchial tree was normal. CT scan Chest done on 22/06/2013 reported central speculated lobulated heterogeneous mass in right lung mainly involving apical and posterior segment of upper lobe and part of apical segment of lower lobe encasing right main stem bronchus and truncus anterior artery causing narrowing of stem bronchus and cutting off right upper lobe bronchus with adjacent interlobular septal thickening, fibrosis and nodularity and centri-lobular and para-septal emphysematous changes in rest of the bilateral lung fields. The 99 m Tc-MDP bone Scan done on 22/06/2013 reported no abnormal area of increased osteoblastic uptake was noted to suggest skeletal metastases. He was diagnosed with squamous cell carcinoma Right Lung T3 N2 M0. His EGFR mutation status was unknown. He was treated with External Beam Radiotherapy using Image guided radiotherapy technique with weekly Cisplatin (50 mg) based concurrent chemotherapy from 25/06/2013 till 08/08/2013.

He was started on Tab. Gefitinib 250 mg. OD from 27/08/2013, lesion size decreased as per CT Scan Thorax of 05/10/2013 but a PET CT scan done on 17/02/2014 showed residual disease. So he was put on Gemcitabine + Cisplatin based palliative chemotherapy for 6 cycles from 05/03/2014 to 28/07/2014. But once again, the PET CT scan of 11/08/2014 shows residual disease.

He had residual disease even after 2nd line of palliative chemotherapy. He was advised Afatinib 30 mg, orally daily from 15 December 2014. As there were limited therapeutic options available, this therapy was likely to benefit the patient. The PET CT scan of 20/02/2015 showed stable disease. The patient's ECOG performance status improved from 4 to 2. The patient was free of progression for more than 6 months even after receiving Afatinib in fourth line. Patient did not suffer from any side effects like diarrhoea or skin rashes.

The PET CT of 26/06/2015 however, showed peripherally thick enhancing lesion in left frontal lesion involving cortical and subcortical areas. Patient was administered WBRT 30 Gray/10 fractions following which Afatinib was continued for another 5 months, till 27th November 2015. Patient developed septicaemia and was admitted on 19/12/2015. Investigation showed that the patient

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had urinary tract infection with E. Coli. Patient also had creatinine and urea abnormalities along with decreased renal clearance. However, the patient had Stable disease in lung and brain. Patient succumbed to his illness on 30/01/2016, due to renal failure.

Discussion

Lung cancer is the leading cause of cancer-related death worldwide, with NSCLC accounting for 85 % of all lung cancers [1]. Lung squamous carcinoma forms 20 – 30 % of NSCLC; however, the incidence is higher in India. The strongest risk factors for lung cancer are tobacco use and age. Passive smoking, asbestos exposure and air pollution are also known to cause lung cancer [14,15].

The incidence of adenocarcinoma of lung is higher in western population. Probably, this is the reason why disproportionately higher amount of research is concentrated on targeted treatments directed towards driver mutations of adenocarcinoma. Hence, even today the treatment options available in squamous cell carcinoma of lung are limited.

Many molecular targets are similar in both adeno and squamous carcinomas of lung. Therefore, it makes logical sense to try targeted therapies which have shown overall survival benefits in adenocarcinoma of lung, especially after all the established treatment modalities are exhausted.

Here, the patient received first line single agent chemotherapy with Cisplatin along with EBRT for one and a half month. After progression with this therapy, he received Gefitinib for almost 6 months. He received doublet chemotherapy with Gemcitabine + Cisplatin based palliative chemotherapy for 6 cycles from 05/03/2014 to 28/07/2014 following progression with Gefitinib. Finally, the patient received Afatinib following tumour progression while on treatment with Gemcitabine + Cisplatin.

The patient continued receiving Afatinib for almost an entire year. His ECOG performance status also improved. He had progression free survival of more than 6 months with Afatinib in fourth line in squamous cell carcinoma of lung which is more than the progression free survival seen in LUX-Lung 8 trial, where patients received Afatinib in second line [16]. Hence, this is a unique case to show that Afatinib benefits patients with squamous cell carcinoma of lung.

Conclusion

Afatinib can be considered as a good treatment option in squamous cell carcinoma of lung when first line chemotherapy fails.

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