Article published online: 2022-03-28

Letter to the Editor

Objective Response with Geftinib in Non small cell Lung Cancer

Sir,

Prognosis of patient with advance non-small cell lung cancer (NSCLC) is poor). Chemotherapy is invariably used; paclitaxel, gemcitabine, cisplatin/carboplatin, vinorelbine and doxetaxel are active chemotherapeutic agents. Recently a novel drug IRESSA– Epidermal growth factor receptor tyrosine kinase inhibitor (EGFR) has been added in the list of effective agents against NSCLC. We here describe our experience of using IRESSA in two such patients.

Case 1 : Mrs. J.M., a 46 years old lady was diagnosed to have metastatic bone disease in September 2002. Bone biopsy revealed poorly differentiated adenocarcinoma. Chest x-ray revealed right parahilar opacity. CT scan of chest revealed right anterior upper lobe soft tissue nodular lesion with sub-centimeter, mediastinal lymph-adenopathy. Serum CEA –40.5 ng/ml; serum CA-125 and serum CA-19.9 were within limits. With diagnosis of primary NSCLC with bony metastasis, she received chemotherapy with gemcitabine and cis-platin. She also received inj zoledronic acid 4 mg every month. Post 3 cycles there was no relief in backache. Serum CEA was 67.9 ng/ml. In view of this , her chemotherapy was changed to docetaxel and carboplatinum. At the end of 3 cycles, she had no backache and serum CEA was 5.3 ng/ml. She received 2 more cycles of above chemotherapy and was subsequently kept on observation. In january, 2004 though asymptomatic, serum CEA was 28.5 ng/ml. She was put on oral Geftinib (IRESSA) 250 mg daily. Four months later, serum CEA was normal, chest x-ray revealed complete regression of right parahilar mass. CT scan chest also revealed significant regression of right upper lobe mass. Presently she continues to be asymptomatic and is on oral Geftinib 250mg daily.

Case 2 : Miss. L.S., a 37 years old lady presented with history of dry cough. Initially, she was treated outside with antitubercular treatment with no response. Further investigations revealed diagnosis of adenocarcinoma of lung in March 2002. She underwent surgery and right upper and middle lobectomy was done. Histology revealed moderately differentiated adenocarcinoma of lung. Postoperatively, she received adjuvant chemotherapy with gemcitabine and carboplatinum, 3 cycles till June 2002 followed by radiotherapy to right upper lobe in the dose of 5400 cGY in 30 fractions over 46 days. Subsequently, she was advised followed up. Six months later in march 2003, patient complaint of dry cough. Chest x-ray and CT scan of chest revealed multiple lung nodules in both lungs. She received 3 cycles of chemotherapy using docetaxel and cis-platinum and had stable disease. However, six months later chest x-ray and PET scan revealed evidence of progressive disease in lung and bones. She was started on oral Geftinib 250mg daily in February 2004, 12 days later, patient developed severe acneform rashes over face and upper arms. Therefore, Gefitinib was withheld for 1 month and restarted in March 2004. Presently, she is asymptomatic with complete resolution of lung nodules on chest x-ray.

Comments : Geftinib, is orally active epidermal growth factor receptor tyrosine kinase inhibitor. It blocks the signal transduction pathways implicated in the proliferation and survival of cancer cells. This drug was approved for clinical use in May 2003 as a 3rd line therapy for patients with NSCLC. Two large phase II Geftinib monotherapy studies (IRESSA dose evaluation in

advance lung cancer (IDEAL 1 and 2) in patients with pretreated advanced NSCLC further confirmed that this drug was generally well tolerated and produced durable, clinically significant antitumour activity (response rates for Geftinib 250mg/day were 18.4% and 11.8% for IDEAL 1 and 2 study, respectively). Another 30% or more of patients had stable disease. Approximately 40% of patients had improvement in disease related symptoms. These benefits were observed within 3 weeks in 75% of patients. The overall survival at 1 year was 25%. The most frequent drug-related adverse events observed in these two trials were skin rash and diarrhoea, which were generally mild (grade I-II). Retrospective analyses of large phase 2 studies of Geftinib showed that responses were frequent among patients who had never smoked, women and patients with broncho-alveolar carcinoma or adenocarcinoma with broncho-alveolar features.[2-3]

Haringhuizen et al have described their 16 months single institution experience with Geftinib in 92 pretreated non-small cell lung cancer (NSCLC) patients. Geftinib was given at a dose of 250mg day until disease progression or death. They achieved a disease control rate of 46% (objective response rate 8.7%) and 1-year survival of 29%. Multi-variate analyses revealed a significant impact of performance status on survival. The duration of response was 1.2 – 15.8 + months, 37% patients had a stable disease. The main side effects of Geftinib encountered were - grade I-II diarrhoea and skin-rash.

Incidentally both our patients are females, who had progressive disease on cytotoxic chemotherapy. Both showed objective response radiologically to oral Geftinib which was not seen previously to aggressive chemotherapy. Both the patients histologically had adenocarcinoma and had never smoked. Our observations are similar to those reported in above studies and suggest that option of treatment with Geftinib must be considered in NSCLC patients especially for those who have failed first or second line chemotherapy.

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