

Table 1. Characteristics of Three Patients with APL during Treatment with Gefitinib for Recurrence of Non–Small-Cell Lung Cancer.*

Patient	Pathological Type of NSCLC	Initial Clinical Stage	Primary Chemotherapy	Surgery	Primary Radiotherapy	Postoperative Chemotherapy	Interval from Initial Treatment until Gefitinib Treatment, mo	Response to Gefitinib†	Duration of Gefitinib Treatment, mo	Interval from Gefitinib Treatment until APL, mo	Characteristics of APL	Treatment for APL
1	Adenocarcinoma	IV (T1N0M1)	Cisplatin (60 mg/m ²) on day 1, docetaxel (60 mg/m ²) on day 1, and irinotecan (50 mg/m ²) on day 2 for two cycles	No	Cyberknife for brain metastasis (22.993 Gy)	None	21	Partial response	15	15	Normal karyotype, PML-RAR α positive	Response to all-trans-retinoic acid (ATRA) followed by cytarabine + mitoxantrone consolidation
2	Squamous-cell carcinoma	IIIB (T4N3M0)	Cisplatin (80 mg/m ²) on day 1, mitomycin (8 mg/m ²) on day 1, and vinorelbine (20 mg/m ²) on days 1 and 8 for two cycles in neoadjuvant setting	Yes	Fractionated radiotherapy (2 Gy \times 25)	Uracil-tegafur (300 mg/m ² /day) for 2 mo in adjuvant setting	23	Partial response	25	25	Normal karyotype, PML-RAR α positive	Response to ATRA followed by cytarabine + mitoxantrone, cytarabine + daunorubicin, and cytarabine + idarubicin consolidation
3	Adenocarcinoma	IA (T1N0M)	Carboplatin and paclitaxel for one cycle (doses unknown)	Yes	None	Total doses: cisplatin, 71 mg/m ² ; carboplatin, 371 mg/m ² ; irinotecan, 1168 mg/m ² ; docetaxel, 71 mg/m ² ; gemcitabine, 6857 mg/m ² ; vinorelbine, 129 mg/m ² ; paclitaxel, 150 mg/m ² ; and amrubicin, 320 mg/m ²	43	Progressive Disease	5 + 4‡	26	Normal karyotype, PML-RAR α positive	Response to ATRA

* All three patients were men. Patient 1 was 49 years of age, Patient 2 was 65 years of age, and Patient 3 was 72 years of age. APL denotes acute promyelocytic leukemia, NSCLC non–small-cell lung cancer, and PML-RAR α promyelocytic leukemia retinoic acid receptor α .

† The response to gefitinib was defined by World Health Organization criteria.

‡ Patient 3 discontinued and then restarted gefitinib treatment.

ters for Disease Control and Prevention, is less than or equal to 10 µg per deciliter but may soon be lowered to 5 µg per deciliter.²

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APL during Gefitinib Treatment for Non–Small-Cell Lung Cancer

TO THE EDITOR: Gefitinib is an orally active inhibitor of tyrosine kinase epidermal growth factor,¹ with clinical effectiveness in the control of non–small-cell lung cancer. We describe 3 patients with possible treatment-related acute promyelocytic leukemia (APL) among 108 consecutive patients with advanced, recurrent non–small-cell lung cancer who were treated with gefitinib between November 2001 and December 2004 at our institution (Table 1, facing page). Other than these three patients, no patients with other cancers have been identified in this cohort.

Chemotherapy, including the use of topoisomerase II inhibitors (e.g., anthracyclines), and radiotherapy are known as predisposing factors for treatment-related APL,² and all our patients had been exposed to cytotoxic agents as well as radiation before the initiation of gefitinib therapy. Therefore, it is difficult to identify gefitinib as the sole cause of the treatment-related APL. However, the incidence of this complication in our gefitinib-treated cohort is far beyond that expected on the basis of our clinical experience of treatment for non–small-cell lung cancer before gefitinib was commercially available. Considering that 3 percent of treatment-related acute myeloid leukemias are

APL,³ the cluster of treatment-related APL in our cohort suggests that gefitinib, alone or in combination with other environmental factors, such as cytotoxic drugs or radiotherapy, is a risk factor for APL. We believe that further evaluation in a large-scale epidemiologic study is required to elucidate the association between gefitinib and treatment-related APL.

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