中文題目：持續使用 Bevacizumab 合併多線化學治療在肺腺癌的病人－一份個案報告

英文題目：Continuous Bevacizumab with multiple line chemotherapy after failure of induction therapy in patient with advanced Adenocarcinoma : a case report

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Introduction

Non-small-cell lung cancer (NSCLC) is one of the most common carcinomas in the world, and adenocarcinoma is the most common type of it. Patients with advanced NSCLC have 4–6 months median progression-free survival (PFS) and 8–10 months median overall survival (OS). Chemotherapy is the preferred option for advanced lung adenocarcinoma without epidermal growth factor receptor (EGFR) mutation and Anaplastic lymphoma kinase (ALK) rearrangement. Platinum-based doublet chemotherapy is the traditionally standard treatment. However, the efficacy of traditional chemotherapy already reached a plateau. Bevacizumab (BEV) has been the first-line therapy in combination with chemotherapy for advanced nonsquamous NSCLC patients for over 10 years. In this case report, we report a lung cancer patient who presented with no EGFR mutations or ALK rearrangements, and were treated with BEV with multiple lines of chemotherapy.

Case presentation

A 67-year-old male visited Kaohsiung Medical University Hospital with initial presentation of dry cough and wheez for one month. The left upper lobe mass with infiltration was found in chest X-ray (CXR). Chest computed tomography (CT) revealed tumor growth at left upper lobe with bilateral pulmonary fine nodules and left pleural effusion, and CT-guided percutaneous needle biopsy proved adenocarcinoma, with wild-type EGFR and negative EML4/ALK rearrangement. The patient received induction chemotherapy with BEV, carboplatin, and pemetrexed administered every 3 weeks. After 6 cycles of induction therapy and 16 months of maintenance chemotherapy with Premetrexed and BEV, CXR revealed RUL nodular lesion increased, disease progression (PD) was impressed. The patient received subsequent chemotherapy with docetaxel and BEV every 3 weeks. However, whole body skin rash with chills was noted after docetaxel uses for 2 cycles, and chemotherapy was shifted to gemcitabine with BEV. After 4 cycles chemotherapy of BEV and gemcitabine, the CXR remained stable disease (figure 6). Gemcitabine with BEV (7.5 mg/kg) was used for totally 7 cycles. After PD, navelbine with BEV was used for 4 cycles. This patient received BEV with chemotherapy for totally 35 cycles.

Discussion

BEV, a recombinant humanized IgG1 monoclonal antibody, can block tumor angiogenesis and suppress tumor growth by inhibiting vascular endothelial growth factor A, thereby blocking the biological effects of vascular endothelial growth factor. The role of BEV after PD is still unclear in the multiline treatment strategy of advanced NSCLC. AvaALL, a multinational, open-label, randomized phase III trial, assessed continuous BEV and standard chemotherapy beyond first PD

(PD1) in patients with NSCLC following first-line treatment with platinum-based chemotherapy plus BEV. After second PD (PD2) and third PD (PD3), patients received third-line or fourth-line standard of chemotherapy ± Bev treatment, respectively. Primary endpoint was overall survival (OS). The result of this trial showed that BEV plus chemotherpay resulted in benefit in median OS compared to chemotherapy alone (11.9 months versus 10.2 months), however, the primary endpoint was not met (416 OS events were required, at 10% two-sided significance level). Besides, the OS rates were 10% higher in the bevocizumab group than chemotherapy alone at 6-, 12- and 18-months. Median PFS, even in second (PFS2) or third (PFS3), was also improved significantly in BEV group (PFS2: 4.9 momths with BEV vs 3.8 momths with chemotherapy, PFS3: 3.5 momths for BEV vs 2.4 months for chemotherapy). Although the primary endpoint was not met, efficacy data suggest a positive trend for continued BEV plus chemotherapy after PD1 compared with chemotherapy alone. Our case, patient with adenocarcinoma without driver mutation, continued bevocizumab plus chemotherapy even after PD1, PD2 and PD3. The PFS1 was about 20 months, and the PFS2 was about 7 months. The PFS3 was about 5 months. The overall survival was 37 months. Based on the results from clinical trials and our experience, continuous BEV with other chemotherapeutic agents after failure of induction chemotherapy improves PFS, and maybe OS, of lung cancer patients compared to those patients without continuous BEV use.