Appendix file 1: Cases of patients 1,2

Patient 1:
We report the case of a 59 year-old Caucasian female who presented generalized seizure revealing multiple cerebral metastases and a right superior lobar lesion of a lung adenocarcinoma (CK20-,CK7+,RE-,-RP-,TTF1+) (cT1N0M1) in September 2006. This patient was a former smoker (20 packs year) and had a history of breast cancer, treated in February 2002 by surgery and radiotherapy (pT1N0M0, grade 2, RH+). Up to now, she remains free from breast cancer. She was first delivered in toto cerebral radiotherapy (30Gy) and was then prescribed conventional chemotherapy. After 6 cycles of Cisplatin-Gemcitabine (April 2007), CT scan evaluation revealed stable disease (both cerebral and thoracic sites). Three months later, progressive disease was demonstrated with the increase of the right superior lobar lesion and the occurrence of controlateral mediastinal lymph node (cT1N3M1) (Figure 1). She was then prescribed Erlotinib (150 mg/d per os) as 2nd line therapy from July 2007. During the following 27 months-treatment, all the consecutive CT scans progressively demonstrated the complete regression of the left anterior mediastinal lymph node and the partial regression of the right superior lobar lesion while brain metastases were stable (Figure 1). Up to now, this patient is still under treatment with Erlotinib. Tolerance is excellent since she only presented transient skin rash grade 2 (from month 1 to month 3). She does not take any concomitant drug. In September 2007, mutation assays (direct sequencing and pyrosequencing methods) performed on paraffin-embedded tumor blocks (right superior lobar lesion at diagnosis) revealed mutant KRAS gene (exon 2, G12C) and wild type EGFR gene (screened exons: 18-21). Another assay performed in an independent laboratory confirmed the KRAS mutation and the EGFR wild type status.
Patient 2:
We report the case of a 51 year-old Caucasian female who was diagnosed with advanced lung adenocarcinoma in January 2006. Initial work-up (cerebral and thoraco-abdominal CT-Scan) revealed left lobar superior lesion and mediastinal lymph nodes (cT2N2M0). This patient was a former smoker (20 packs year). She had a history of venous thromboembolic event (treated by tinzaparin, stopped in December 2006) and of mental depression (treated by paroxetine). She underwent left superior lobectomy with mediastinal lymphadenectomy (pT2aN2M0) in January, 2006. She was then delivered cisplatin-based adjuvant chemotherapy (gemcitabine was switched for docetaxel after the first cycle due to hypersensitivity reaction). Unfortunately, she presented bone and liver metastases after the third cycle of this adjuvant line. Evaluation performed after six cycles of this regimen (July 2006) concluded to stable disease (both bone and liver sites). She was then prescribed Erlotinib from August 2006. All the consecutive evaluations (CT scan and bone scan) progressively demonstrated partial response (both bone and liver mets). Up to now, the patient is still considered in partial response after 37 months under Erlotinib. Mutation assays (direct sequencing method) were performed in April 2009 on paraffin-embedded tumor blocks (left lobar superior lesion, surgical piece). Mutant KRAS gene (exon 2, G12C) and wild type EGFR gene (screened exons: 18-21) were demonstrated. This regimen is well tolerated since only grade 1 toxicities were noted: intermittent diarrhea (from month 6 until now), skin xerosis (from the beginning of treatment) and folliculitis (from the beginning of treatment). Concomitant drugs are: paroxetine, bromazepam, and loperamide.