PUBLISH ONLY

PUB001 EGFR TKI Erlotinib in Patients with Advanced Squamous Cell Carcinoma of the Lung: A Retrospective Analysis from India Devavrat Arya, Manish K. Singhal *Medical Oncology, Fortis International Oncology Centre, Noida, Uttar Pradesh/India*

Background: Erlotinib has proven efficacy in patients with advanced non-small cell lung cancer, especially adenocarcinoma which harbour activating EGFR mutations. In squamous cell carcinomas, it has been used in second line treatment and beyond, especially in patients with poor performance status. The aim of this study was to evaluate the efficacy of erlotinib in patients with advanced squamous cell carcinoma of lung (SCC). **Methods:** We retrospectively reviewed medical records and serial chest images of lung cancer patients with SCC histology and history of erlotinib treatment. The primary objective was to assess overall response rate (ORR) and disease control rate (DCR) and the secondary objective was to assess progression-free survival (PFS) and overall survival (OS). **Results:** A total of 20 patients were analyzed (18 men and 2 women, median age of 63 years).Seventeen patients were current or former smokers and three were non smokers. Ninety percent of patients had a poor performance status (Eastern Co-operative Oncology Group Performance Status 2 or 3). Three patients achieved partial response and 7 had stable disease. The ORR was 15 % and the DCR was 50%. The median PFS was 4.3 months (range, 1.0 – 8.0 months). Overall Survival (OS) data was not mature at the time of reporting. EGFR mutation status of three patients subjected to EGFR analysis were all negative. The PFS was longer in patients who were non smokers as compared to those who gave a history of current or former smoking (median PFS, 5.3 vs. 4.1 months). Five patients (25%) had PFS more than six months. **Conclusion:** A significant proportion of lung SCC patients derive a clinical benefit from erlotinib treatment. This needs further evaluation that includes testing for activating EGFR mutations in these patients particularly those who have longer progression free survivals.
Keywords: Erlotinib, Squamous Cell Carcinoma Lung, Disease Control Rate, Progression Free Survival

PUB002 Accidental Intrathoracic Disseminated pM1a - Distinguished Lung Cancer with Favorable Prognosis Wei Li, Wen-Zhao Zhong, Xue-Ning Yang, Ri-Qiang Liao, Qiang Nie, Song Dong, Xu-Chao Zhang, Yi-Long Wu *Guangdong Lung Cancer Institute, Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhou/China*

Background: In the 7thedition of lung cancer TNM stage, the prognosis of the pM1aⅣ is better than pⅢB. Subgroups of lung cancer patients who underwent incomplete resection (R1/R2) gain favorable prognosis. This study compares the prognosis between accidental local residue and intrathoracic disseminated pM1a after incomplete resection. **Methods:** Patient characteristics, histological and molecular profiles of lung cancer patients who receiving accidental incomplete resection were retrospectively collected. All patients were divided into local residual group and intrathoracic disseminated pM1a group. Progression-free survival (PFS) and overall survival(OS) were evaluated by Kaplan–Meier and Cox regression. **Results:** From 2008 to 2013, 1483 lung cancer patients received thoractomy in Guangdong Lung Cancer Institute. 58 patients receiving incomplete resection(R1/R2) were enrolled, including 38 patients of local residue(2.6%) and 20 patients of disseminated pM1a (1.3%). Compared to local residual group, disseminated pM1a group includes more female(P=0.002), more patients younger than 60 years old(P=0.01), more non-smokers(P=0.037), higher R2/R1 resection ratio(P=0.013), less patients with lymph nodes metastasis(P=0.013), higher stage Ⅳ/ⅢB ratio P<0.001), more adenocarcinomas(P<0.001), more adenocarcinomas with lepidic pattern(P<0.001), higher EGFR mutation rates(P<0.001), lower EGFR expression (P=0.022) . Median PFS of local residue and disseminated pM1a were 8.7 and 18.8 months(P=0.120), and median OS were 11.9 and 36.0 months(P=0.002), respectively. Cox regression analysis revealed that group (local residue vs. disseminated pM1a) was the only independent prognostic factor(P=0.005) for OS. **Conclusion:** Accidental intrathoracic disseminated pM1a is a distinguished lung cancer subtype with favorable prognosis comparing to patients of local residue. The prolong PFS and OS might contribute to the natural history of the distinguished subtype and the favorable response to EGFR-TKI.

PUB003 Prognostic Analysis of High Selected En-Bloc Resected Chest Wall Involving Non-Small Cell Lung Cancers Rui Mao, Chang Chen *Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China*

Background: Factors influencing long term survival of NSCLC invading chest wall have been under debates. Considering the advances in examinations and treatments during the past several decades, this study is an attempt to investigate the possible prognostic factors of this group of patients. **Methods:** We reviewed data of all patients with NSCLC invading chest wall, who underwent complete(R0) surgical treatment of en-bloc resection at our hospital from 1994 to 2014. Superior sulcus tumors, neoadjuvant therapy receivers and patients need vertebrectomy and reconstruction were excluded. All patients were classified according to the current TNM classification. **Results:** One hundred and four patients were included. Adjuvant therapy(chemoradiotherapy or chemotherapy) was administered according to the various advises of referring physicians, so no uniform protocol was employed. All tumors received en-bloc resection. Complete resection was achieved in all cases. There were 61 IIB tumors(T3N0) and 41 IIIA tumors (T3N1, 18 patients; T3N2, 22 patients; T4N1, 1 patients) and 2 IIIB(T4N2) tumors according to the current TNM classification. Lobectomy, bilobectomy, pneumonectomy, wedge/segmentctomy and sleeve lobectomy/plastic lobectomy were required in 80, 2, 9, 3 and 10 cases. Adjuvant therapy was administrated in 61 patients while 33 patients needn't. Depth of invasion limited to partial pleura or intercostal soft issue in 60 cases, infiltrated into rib in 44 patients. Of 66 CT available cases, tumor's location arrived at spine was found in 19 and away from in 47 cases. furthermore, distance to transverse process was more far than 5cm in 28 while closer in 19. There were 4(3.85%) perioperative mortalities caused by PE or respiratory failure. Overall 5 year survival was 41.6%. Local-regional recurrence occurred in 5 patients with 45 patients developing systemic recurrence. The adjuvant therapy (yes versus no,p=0.0005), depth of invasion(rib versus other, p<0.0001), tumor size(≤3 versus >3cm, p=0.017) and tumor's location(arrival versus away, p=0.034; near versus far, p=0.019)(fig. 1) were found as prognostic factors in univariate analysis. I have to mention that the near goup can surprisely better the suvival as opposite to what we have historically thought. Two independent factors affecting long term survival are adjuvant therapy (p=0.002) and depth of invasion(p=0.028) according to multivariate analysis.

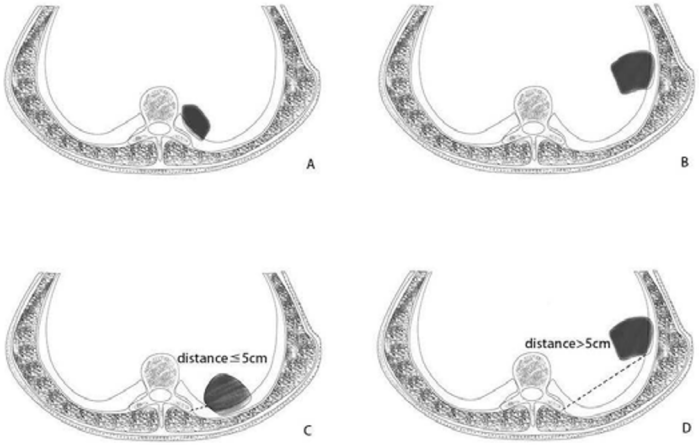
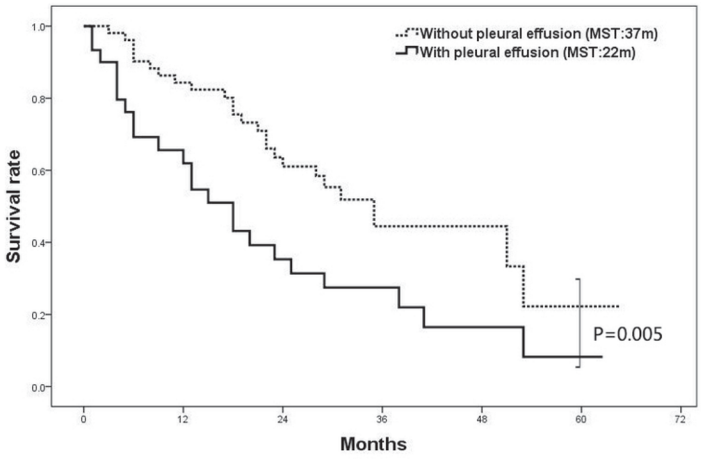
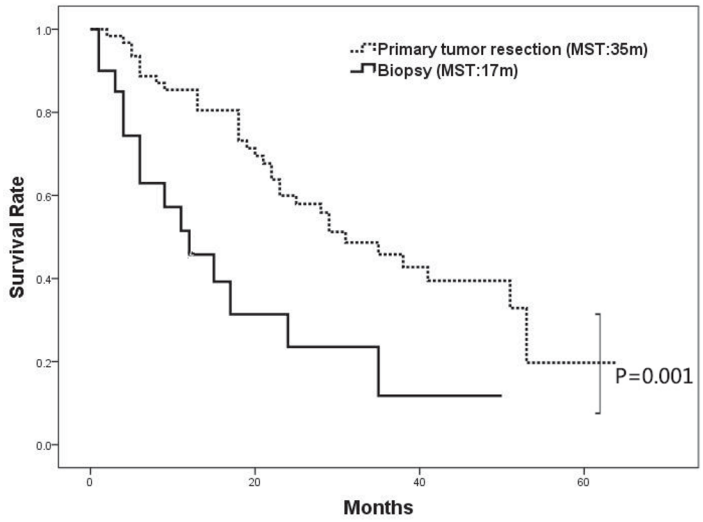


fig.1: A: arrival; B: away; C: near; D: far. **Conclusion:** Adjuvant therapy and depth of invasion are independent factors influencing prognosis of en-bloc resected chest wall involving non-small cell lung cancers, the role of tumor's location needs more investigations.
Keywords: complete resection, non-small cell lung cancer, en-bloc, prognostic factor

PUB004 Primary Tumor Resection Showed Survival Benefits for Non-Small-Cell Lung Cancers with Unexpected Malignant Pleural Dissemination Yijiu Ren, Yunlang She, Chenyang Dai, Gening Jiang, Ke Fei, Pengqing Ying, Chang Chen *Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China*

Background: Although non-small-cell lung cancer (NSCLC) with malignant pleural nodules is generally contraindicated for surgery, there is no consensus concerning on-site operative decisions for unexpectedly intra-operatively encountered malignant pleural disseminations. The rationale underlying the primary tumor removal and other aggressive interventions remains controversial. **Methods:** All surgical NSCLC cases of Shanghai Pulmonary Hospital between January 2005 and December 2013 were reviewed. Among them, 83 cases met the definition of "unexpected" malignant pleural nodules, despite routine preoperative evaluations for tumor metastasis. No pleural effusion was visualized in 52 cases during operations, and 31 had pleural effusion in minimal volume. Survivals were calculated with Kaplan–Meier method and risk factors were evaluated by the log-rank test. **Results:** The overall 3- and 5-year survival rates were 36.1% and 16.8%, respectively. The median survival time (MST) after surgery was significantly longer in the group without pleural effusion (37 months) compared to group with pleural effusion (22 months, p=0.005) (Fig 1). Patients with primary tumor resection had significantly better outcome compared to biopsy (MST: respectively, 35 vs. 17 months, 3-year survival 45.8% vs. 11.8%, p=0.001) (Fig 2). No baseline differences emerged in characteristics between biopsy (n=21) and primary tumor resection (n=62) groups including targeted therapy. Multivariate analysis showed that primary tumor resection (HR: 3.678, p=0.014), no pleural effusion (HR: 3.409, p=0.001), N0/1 status (HR: 5.937, p=0.002), and adenocarcinoma (HR: 5.481, p=0.002) were favorable prognostic factors in patients with malignant pleural nodules.





Conclusion: Patients with malignant pleural nodules but without pleural effusion had better survival compared to those with effusions. Primary tumor resection had survival benefits for patients with unexpected intra-operatively proven malignant pleural nodules.
Keywords: lung cancer, Surgery, Malignant pleural dissemination, Prognosis

PUB005 Therapeutical Effect of Intrapleural Circular Hyperthermic Perfusion Chemotherapy on Malignant Pleural Effusion under VATS Feng Xing[1], Hong Jiang[1], Shenglin Ma[2] [1]*Department of Thoracic Surgery, Hangzhou First People'S Hospital, Hangzhou, P. R. China, Hangzhou/China,* [2]*Department of Radiation Oncology, The First People' S Hospital of Hangzhou Medical Group, Hangzhou/China*

Background: Malignant pleural effusion (MPE) is defined as the identification of malignant cells in plural fluid or on pleural biopsy, which is often caused by primary pleural malignancy and tumors with pleural extension. It is a common complication of advanced malignant disease. According to the recently UICC revised staging system, the presence of MPE was upstaged from T4 to M1a with poor prognosis. The 30-day mortality is 29 to 50% and the median survival is 3 to 12 months. Given these considerations, the management of MPE is usually palliative, with promptly relieving of symptoms, reducing discomfort, and raising the patient's quality life. There is no standard treatment for patients with these malignancies. And the therapeutic outcomes remain to be unsatisfactory. Recent reports have demonstrated the effectiveness of hyperthermic pleural perfusion with cisplatin. But only few MPE patients had adopted the therapy in several institutions reports. The true long-time therapeutic effect, toxic side reactions, and the patient's remaining days were still to be greatly expected. The purpose of this study is to assess the feasibility, toxicity, and final results of intrapleural circular hyperthermic perfusion chemotherapy on MPE under VATS **Methods:** Between February 1999 and March 2012, eighty patients with symptomatic MPEs were performed on ICHPC under video-assisted thoracoscopic surgery (VATS). All had been proved to be as pleural spreads with malignant effusion due to primary or pleural malignancy. After breaking up the pleural adhensions under VATS, the 43℃ distilled water 3000ml containing cisplatin (200 mg/m^2) was circularly perfused into the pleural cavity for one hour through extracorporeal circulation unit. The improvement on patient's symptoms - the change for Karnofsky score(KPS)、the effect on MPEs, and the adverse reaction were observed after the treatment. The concentration change of carcino-embryonic antigen (CEA), cytokeratin-19 fragments(CYFRA21-1), neuron-specific enolase(NSE) were compared before and after the treatment. Meanwhile, the pathological and electron microscopic morphological change with pleural carcinomatoid tissue, as well as paraneoplastic normal tissue were observed after ICHPC. **Results:** The symptoms such as dyspnoea, shortness of breath disappeared. And MPEs were effectively controlled with total response rate of 100%. All patients KPS exceeded seventy. Moreover, the concentration of CEA CYFRA21-1 NSE dramatically descended with tolerably adverse effects. Mass necroses with pleural carcinomatoid were observed in post-treatment microscope. And chromatin condensation、apoptotic body occurrence and nuclear fragmentation in tumor cells were also found in post-treatment electron microscope. **Conclusion:** ICHPC has the evident therapeutical effect on MPE with less adverse reactions and invasiveness. And it is also suitable for the old and rigid patients with MPEs. We think it would be highly valued in controlling the MPEs
Keywords: Video-assisted thoracic surgery, intrapleural perfusion hyperthermic chemotherapy, lung cancer, malignant pleural effusion

PUB006 The Efficacy and Safety of Higher-Dose Icotinib in Non-Small Cell Lung Cancer Patients after Progression with Normal Dose Xiaoqing Liu[1], Weixia Wang[1], Chuanhao Tang[1], Xiaoyan Li[1], Jianjie Li[1], Wanfeng Guo[1], Haifeng Qin[1], Lili Qu[1], Hongjun Gao[1], Fenlai Tan[2], Lieming Ding[2] [1]*Department of Pulmonary Oncology, 307 Hospital of the Academy of Military Medical Sciences, Cancer Center, Beijing/China,* [2]*Betta Pharmaceuticals Co.Ltd., Hangzhou/China*

Background: Icotinib, an oral EGFR tyrosine kinase inhibitor, had shown antitumor activity and favourable toxicity in clinical trials. A phase III clinical study revealed icotinib was non-inferior to gefitinib in efficacy with favorable safety. Phase I trials established that icotinib anti-tumor efficacy increases with dose escalation. The objective of this study is to investigate the efficacy and safety of higher-dose icotinib in non-small cell lung cancer (NSCLC) patients after disease progression with normal-dose icotinib. **Methods:** Patients with NSCLC would be administered with higher-dose icotinib (250 mg three times per day) after disease progression with 125-mg icotinib, until second progression or intolerable toxicity. The primary endpoint was progression-free survival (PFS1) following progression at standard dose of icotinib (125 mg), secondary endpoints included objective response rate (ORR), disease control rate (DCR) and safety. The safety and efficacy of 375-mg icotinib will also be explored in those patients experiencing a second progression. This study is registered at ClinicalTrial.gov as NCT01465243. **Results:** A total of 32 NSCLC patients were enrolled, mostly stage IV (29/32), ECOG score 0-1 (32/32), adenocarcinoma (29/32) and non-smokers (21/32). The median PFS of 125-mg icotinib (PFS0) was 150.0 days (95% CI 111.0 - 267.0 days). All 32 patients experienced disease progression and thereafter were given 250-mg icotinib three times daily. All patients had progressed disease and were evaluable for efficacy. Median PFS in icotinib 250 mg tid extension period (PFS1) was 64.0 days (95% CI 50.0-103.0 days). Six patients were further given 375-mg icotinib after disease progression with 250-mg icotinib with a median PFS2 (PFS in 375-mg extension period) of 68.5 days (95% CI 30.0 ~ 117.0 days). In the extension period of 250mg and 375mg, the ORR was 15.6% (5/32) and 0% (0/0), DCR was 62.5% (20/32) and 66.7%(4/6), respectively. The PFS1 was significantly longer in patients with PFS0 > 3 months, compared to patients with PFS0 < 3 months (91.0 vs. 43.0 days, long-rank p = 0.0046). Thirty-two patients were included in safety analysis, the incidence of overall adverse reactions (ADR) was 56.3% (18/32). The most common ADRs were rash (34.4%), diarrhea (9.4%), and transaminase elevation (18.8%). Only one serious adverse event (SAE) was reported (grades 3 urine leukocytosis), which was unrelated to drug by investigator evaluation. No interstitial lung disease (ILD) or treatment-related deaths were reported. **Conclusion:** Higher-dose icotinib continuation was well tolerated with favorable efficacy in NSCLC patients after disease progression with normal dose, especially for patients with a median PFS more than 3 months in 125-mg period.
Keywords: higher dose, icotinib, non-small cell lung cancer, progression

PUB007 TTF-1 Expression Is Significantly Associated with Mutations in Exon 21 of the EGFR Gene in Chinese Patients with Lung Adenocarcinoma Ying Li, Hongyu Liu, Qingchun Zhao, Yongwen Li, Jun Chen *Tianjin Medical University General Hospital, Tianjin/China*

Background: Non-small cell lung cancers (NSCLCs) make up 85% of lung cancers, with a 5-year survival rate of only 15%–17%. Adenocarcinoma of the lung is one of the main subtypes of NSCLC. With the identification of epidermal growth factor receptor (EGFR) gene mutations in NSCLCs and the development of the EGFR tyrosine kinase inhibitors (TKIs), such as gefitinib and erlotinib, the survival and quality of life of adenocarcinoma patients have improved greatly. Along with EGFR mutations, thyroid transcription factor-1 (TTF-1), a biomarker for lung adenocarcinoma, was reported to have a much higher rate of expression in the lung adenocarcinoma specimens of Asian, female, and nonsmoking lung cancer patients. The NEJ 002 clinical trial also found that the rate of EGFR mutations was significantly higher in lung adenocarcinoma specimens that were positive for TTF-1 expression than in specimens that were TTF-1 negative. Therefore, clarifying whether there is a relationship between EGFR mutations and TTF-1 positivity in lung adenocarcinomas and whether TTF-1 can be a biomarker of EGFR mutation status is essential, especially for some patients with advanced lung cancer with inadequate specimens for evaluating EGFR status. **Methods:** There were 200 lung adenocarcinoma patients who were enrolled in this study. Tumor specimens of these patients were investigated for TTF-1 expression using immunohistochemistry and mutations in *EGFR* were determined by a liquidchip platform for DNA analysis of slides with sections of formalin-fixed, paraffin-embedded specimens. **Results:** The rates of TTF-1 expression and *EGFR* mutations were 81.5% and 45.5%, respectively, in the lung adenocarcinoma specimens of recruited patients. Among female nonsmokers (n = 72), 93.1% of specimens were positive for TTF-1 expression, and 63.9% had *EGFR* mutations. Of 89 patients with *EGFR* mutations, 83 (50.9%) specimens were simultaneously positive for TTF-1 expression. Kaplan-Meier analysis of all patient specimens found that postoperative survival time was not significantly associated with