LBA48_PR - CTONG 1103: Erlotinib versus Gemcitabine plus Cisplatin as Neo-adjuvant Treatment for Stage IIIA –N2 EGFR-mutation Non-small-cell lung cancer (EMERGING): a Randomised Study

Presentation Number: LBA48_PR
Lecture Time: 09:15 - 09:30
Speakers: Wen-Zhao Zhong (Guangzhou, CN)

Abstract

Background

Cisplatin-based doublet chemotherapy as neoadjuvant treatment for IIIA-N2 non-small cell lung cancer (NSCLC) give patients 5% survival benefit. EGFR-TKIs have been proved to prolong PFS of advanced EGFR-mutant NSCLC. CTONG1104 trial shown adjuvant gefitinib could improve 10 months (disease free survival) DFS than chemotherapy in N1/N2 resected NSCLC. It raises the possibility that EGFR-TKIs may play a beneficial role in the neoadjuvant setting. We conducted this randomized trial to compare the efficacy of erlotinib (E) and gemcitabine plus cisplatin (GC) as neoadjuvant/adjuvant treatment.

Methods

Eligible patients with N2 disease were randomly assigned in 1:1 ratio to E group for 42 days as neoadjuvant therapy and then for 12 months after surgery or GC group for 2 cycles neoadjuvant chemotherapy and 2 cycles after complete resection. The primary endpoint is objective response rate (ORR). secondary endpoints included downstaging rates of pathological lymph nodes, pathological complete response (pCR), progression-free survival (PFS), overall survival (OS), safety, and tolerability.

Results

A total of 386 patients from 17 centers were screened, 72 were randomized and included in the intention-to-treat population. The ORR for neoadjuvant E versus GC was 54.1% (95% CI, 37.2% to 70.9%) vs 34.3% (95% CI, 17.7% to 50.8%) (OR 2.26; 95% CI, 0·87–5.84; p=0·092). After neoadjuvant therapy, 31 patients (83·8%) in the E group and 24 (68·6%) in the GC group underwent surgery. Overall, lymph node downstaging occurred in 13% in the E and 4·2% in the GC group. The major pathological response (MPR) occurred in 3 of 28 patients (10.7%) in the E group and 24 (68·6%) in the GC group underwent surgery. Median PFS was significantly longer with E (21·5 months; 95% CI, 19·3–23·6) versus GC (11·9 months; 95% CI, 9·1–14·7; HR 0·42; 95% CI, 0·23–0·76; p=0·003), whereas OS data was immature. The incidence of grade 3/4 toxicities was lower in the E group (0%) than that in the GC group (29·4%). No unexpected AEs were found.

Conclusions

Neoadjuvant/adjuvant erlotinib improved ORR, and significantly prolonged PFS compared with GC chemotherapy in patients with stage IIIA-N2 EGFR mutation NSCLC.

Clinical trial identification: NCT01407822

Editorial Acknowledgement: No
**1370P - The results of treatment of non-small cell lung cancer stage III with a preoperative vinorelbine/carboplatin and personalized adjuvant chemotherapy**

Presentation Number: 1370P  
Lecture Time: 12:50 - 12:50  
Speakers: Evgeny O. Rodionov (Tomsk, RU)

**Abstract**

**Background**

Individual chemotherapy based on the determination of molecular biomarkers of chemosensitivity is a new way to treat patients with NSCLC. Promising markers for chemosensitivity are monoresistance genes such as BRCA1, RRM1, ERCC1, TOP1, TOP2α, TUBB3, TYMS, and ABCC5.

**Methods**

We enrolled and analyzed 62 patients with stage III NSCLC. All the patients have received 2 courses of neoadjuvant chemotherapy vinorelbine/carboplatin and surgery. Then patients were randomly assigned (1:1 ratio) to either the personalized adjuvant chemotherapy arm (main group) or the adjuvant chemotherapy vinorelbine/carboplatin arm (control group). In the main group, carboplatin-containing doublets were assigned based on monoresistance gene expression levels ABCC5, RRM1, ERCC1, BRCA1, TOP1, TOP2α, TUBB3 and TYMS. RNA was extracted from tumor after neoadjuvant chemotherapy using “RNeasy Plus Mini Kit” (QIAGEN, Germany). The analysis of monoresistance genes expression was done by qRT-PCR method. A χ² test was used to analyze gene expression in relation to clinicopathological parameters. The survival rates were calculated by the Kaplan-Meier method.

**Results**

The follow-up period was 4 - 76 months. In the main group, the disease progression was observed in 6 patients (19.4%), in the control group - 15 patients (48.4%). Three-year disease-free survival in the main group was 80.7% (median DFS not achieved), in the control group - 51.6%, median DFS - 34 months (HR: 2.56, 95% CI: 1.09 - 6.03); differences are statistically significant: Log-Rank test χ²=4.196, p = 0.041. There was no difference in three-year overall survival (main group: 87.1%, control group: 67.7%, HR: 2.27, 95% CI: 0.79 - 6.47).

**Conclusions**

Personalized postoperative chemotherapy based on the determination of monoresistance gene expression after neoadjuvant chemotherapy allows significant increase of patients 3-year disease-free survival by 29.1%.

**Legal entity responsible for the study**

Cancer Research Institute, Tomsk National Research Medical Center, Russian Academy of Sciences, Tomsk, Russia.

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**Disclosure:** All authors have declared no conflicts of interest.
1431P - TP53 mutations impair overall survival of TKI-treated patients with oncogene-driven NSCLC

Presentation Number: 1431P
Lecture Time: 12:50 - 12:50
Speakers: Petros Christopoulos (Heidelberg, DE)

Abstract

Background

Tyrosine kinase inhibitors (TKI) have considerably improved survival of patients with oncogene-driven non-small cell lung cancer (NSCLC). However, prognosis varies widely, and identification of molecular factors with a critical role for adverse outcome could facilitate further advances in management.

Methods

We retrospectively studied the clinical course of patients with metastatic epidermal growth factor receptor (EGFR)- or anaplastic lymphoma kinase (ALK)-driven NSCLC and known baseline TP53 status that received TKI at our institutions. Overall survival (OS) from the start of treatment for metastatic disease was analyzed according to Kaplan-Meier or by Cox regression.

Results

A total of n = 149 EGFR+ and n = 76 ALK+ patients were included with a median age of 62 years (interquartile range [IQR] 19), a median ECOG performance status of 0.5 (IQR 1) and a predominance of female (136/225=60%) never-/light-smokers (median number of pack-years 9, IQR 16). Median OS was 36 months for EGFR+ and 44 months for ALK+ NSCLC patients. TP53 mutations were present at diagnosis in 34% (51/149) of EGFR+ and 19% (15/76) of ALK+ patients, and they were associated with inferior OS in both EGFR+ (24 vs. 40 months in median, p = 0.027) and ALK+ NSCLC (24 vs. 53 months, p = 0.001). Their adverse effect was comparable to that of a worse initial clinical condition as reflected by an ECOG performance status of 1 compared to 0 (HR = 1.8 for ECOG vs. 1.8 for TP53 mutations in EGFR+ patients, and HR = 4.1 for ECOG vs. 3.7 for TP53 mutations in ALK+ patients, all p < 0.05 in bivariable analyses), and it was independent from that of the oncogene variant in both patient groups (HR = 1.9 for other EGFR alterations vs. exon 19 indels, and HR = 1.8 for TP53 mutations vs. wild-type in EGFR+ patients; HR = 2.3 for EML4-ALK V3 vs. V1/V2, and HR = 4.7 for TP53 mutations vs. wild-type in ALK+ patients, all p < 0.05 in bivariable analyses).

Conclusions

TP53 mutations impair overall survival of TKI-treated patients with EGFR- and ALK-driven NSCLC independent of baseline clinical status and oncogene variant. Their detection could assist selection of cases for more aggressive management. Preclinical exploration of their role in acquired TKI resistance could guide novel therapeutic strategies.

Legal entity responsible for the study

Department of Thoracic Oncology, Thoraxklinik at Heidelberg University Hospital, and Institute of Pathology, Heidelberg University Hospital, Heidelberg, Germany.

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Abstract

Background

Recently FLAURA study demonstrated significant PFS and numeric OS benefit for Osimertinib 1st line vs. 1st gen. TKI’s Erlotinib/Gefitinib. The number of pts switching from 1st gen. to 3rd gen. TKI (30%) appeared to be low and it is questionable whether these data represent real world sequencing treatment patterns. Therefore, we investigated the sequence pattern, i.e. the percentage of 2nd line therapy in EGFR mt+ pts in 3 certified lung cancer centers in Germany.

Methods

Data of 912 of 1477 pts tested for EGFR mutations were analyzed between 2009-2017. 140/144 pts with an activating EGFR mt + (16%) and treated with systemic therapy (4 pts received no therapy) were identified and their treatments were captured as well as their outcome. 36 pts were treated before accessibility to 3rd generation TKI and 104 pts after accessibility to 3rd generation TKI.

Results

130/140 pts were treated with 1st line TKI and 10 received 1st line chemotherapy. 17 pts are still on 1st line TKI, 8 pts were lost to follow-up, 3 pts died while on 1st line TKI. 112 pts were candidates for 2nd line therapy. 34/112 (30%) of these pts did not receive 2nd line therapy. Causes for not receiving 2nd line therapy were pts refusal (n = 2), bad PS (n = 26) frequently due to CNS metastases, fast progression and death (n = 6). After accessibility of 3rd gen. TKI, 20 of 66 (30%) pts did not receive 2nd line therapy. Median OS of the overall cohort was 27 months (n = 140), median OS of pts receiving 2nd line (n = 78) vs. no 2nd line (n = 62) was 36 vs. 14 months (p < 0.0001). After accessibility of 3rd gen. TKI 30/104 pts (29%) receive a 3rd gen. TKI after 1st line or 2nd line therapy. Median OS of pts receiving (n = 30) and not receiving 3rd gen. TKI (n = 110) was 55 months vs. 22 months (p < 0.0001).

Conclusions

In real world, a significant number of pts treated with 1st or 2nd gen. TKI do not reach 2nd line therapy even when 3rd gen. TKI were accessible. Reasons for not receiving 2nd line therapy are in most cases deterioration of PS and lack of possibility to test for T790M in the minority of cases (n = 28/66, 42% were not tested). These data, although favorable for the small and very selected cohort of pts treated with Osimertinib, might argue for the most effective therapy in 1st line for pts with EGFR mt+ tumors.

Legal entity responsible for the study

Carl von Ossietzky University Oldenburg Department of Internal Medicine-Oncology.

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Disclosure

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