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Initial report of cohort study in patients with non-small-cell lung cancer (NSCLC) who were treated with 1st-line platinum-based chemotherapy (SAPPHIRE study)

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Comprehensive Support Project

【Abstract】

Background
Although 2nd-line chemotherapy comprises the standard of care for NSCLC, not every patient could receive one. How many and why did they miss the opportunity are not fully investigated.

Methods
We prospectively registered consecutive patients with NSCLC treated with platinum-based 1st-line therapy from April 2010 to September 2011 from 30 institutions in Japan. Baseline characteristics, regimens and responses for the 1st-line therapy, whether the patients received 2nd-line chemotherapy or not, and if not treated, the reason was recorded. This study was supported by the Public Health Research Center Foundation CSPOR.

Results
A total of 866 patients were registered. Patient characteristics were: median age, 65 (24 - 80); female patients, 27.5%; ECOG PS 0 or 1, 91.6%; adenocarcinoma, 69.6%; squamous cell carcinoma, 20.1%; never smoker, 20.1%; EGFR activating mutation positive, 10.2%. Maintenance chemotherapy was administered to 28.9% (131 / 454) of patients whose disease did not progress during the course of 1st-line chemotherapy. Among 592 patients with at least 6 months of follow-up, 193 were excluded (129 PD during the course of 1st-line chemotherapy, 20 ongoing 1st-line chemotherapy, and 44 others). The remaining 399 patients were analyzed with regard to administration of 2nd-line chemotherapy. A total of 135 patients (33.8%) did not receive 2nd-line chemotherapy, and the reasons were: without disease progression, 42 (31.1%); declined PS, 55 (40.7%); patient refusal, 20 (14.8%); death of any cause, 5 (3.7%). Therefore, approximately 20% of patients missed their opportunity to receive appropriate 2nd-line chemotherapy during follow-up period after completion of effective 1st-line therapy.

Conclusions
This is the largest prospective observational study exploring the proportion and the reasons for NSCLC patients not receiving 2nd-line chemotherapies. Further investigations to identify predictive factors for 'missing the opportunity for 2nd-line chemotherapy' are underway.

【Background】

- Second-line chemotherapy comprises the standard of care for non-small-cell lung cancer (NSCLC)[1-3].
- However, not all patients could receive appropriate 2nd-line chemotherapy.
- Recent studies demonstrated that maintenance chemotherapy prolongs survival in patients with NSCLC[4-7].
- Subgroup of patients who are benefited by maintenance chemotherapy is still to be determined.
- The proportion of patients who could not receive 2nd-line chemotherapy and the reason for undertreatment is not fully investigated.

【Objectives】

- To investigate the proportion of patients with NSCLC who received 2nd-line chemotherapy after platinum-based 1st-line chemotherapy.
- To elucidate the reasons and factors which hinder patients from receiving 2nd-line chemotherapy.

【Methods】

Study Design
- Cohort study

Primary Endpoint
- Proportion of patients who received 2nd-line chemotherapy after platinum-based 1st-line chemotherapy

Patient Inclusion
- Patients with advanced or recurrent NSCLC
- Platinum-based 1st-line chemotherapy between April 2010 and September 2011 from 30 institutions in Japan
- Platinum-naïve
- Without history of other malignancy

Data Collection
- Patient characteristics including age, gender, performance status (ECOG), smoking status, comorbidities (diabetes mellitus, cardiac disease, interstitial lung disease), body mass index, histological subtype, EGFR mutation, ALK translocation, CBC/chemistry at registration
- Details of 1st-, 2nd-, 3rd-line, and maintenance chemotherapy; including regimen, response
- Reason for administration or omitting 2nd-line chemotherapy
- Survival

【Result】

- Data cutoff at April 2012; updated from abstract submission
- Data of 866 patients were assessable for patient characteristics and details of 1st line treatment; 788 for response; 620 for maintenance chemotherapy; 547 for 2nd line chemotherapy; 479 for analysis of factors which hinders patients from receiving 2nd-line chemotherapy

Patient characteristics	Number of patients (N=866)	%
Age (median, years) (range)	65 (24 – 86)	
Gender male/female	628/238	72.5/27.5
PS (ECOG) 0/1/2/3-4	343/450/65/7	39.6/52.0/7.5/0.8
Comorbidities none/any	654/212	75.5/24.5
Histology		
adenocarcinoma	603	69.6
squamous cell carcinoma	174	20.1
large cell carcinoma	9	1.0
other	80	9.2
EGFR mutation (+)	88	10.2
exon21 L858R/exon19 del	42/36	4.8/4.2
EGFR mutation (−)	514	59.4
ALK translocation (+)/(−)/unknown	11/42/813	1.3/4.8/93.9
Smoking history		
never/experienced/current	174/435/252	20.1/50.2/29.1
Body mass index (median) (range)	22.1 (13-39.6)	

1st line Treatment delivery	Number of patients (N=866)	%
CDDP-based	332	38.3
CDDP+PEM/CDDP+PEM+BV	152/10	17.6/1.2
CDDP+GEM	51	5.9
CDDP+VNR	21	2.4
CDDP+DOC/CDDP+DOC+BV	47/20	5.4/2.3
CDDP+S-1	5	0.6
CBDCA-based	501	57.9
CBDCA+PEM/CBDCA+PEM+BV	125/28	14.4/3.2
CBDCA+GEM	30	3.5
CBDCA+PTX/CBDCA+PTX+BV	173/89	20.0/10.3
CBDCA+S-1	34	3.9
BV containing regimen	168	19.4

	Number of patients	%
Response to 1st line chemotherapy	788	100
CR/PR/SD/PD/NE	4/266/295/161/62	0.5/33.8/37.4/20.4/7.9
Maintenance therapy	620	100
none	429	69.2
PEM/PEM+BV	62/21	10.0/3.4
BV	67	10.8
Erlotinib	3	0.5
S-1/S-1+BV	13/11	2.1/1.8
Other	12	1.9
2nd-line chemotherapy	547	100
none	179	32.7
DOC	149	27.2
PEM	69	12.6
Erlotinib/Gefitinib	27/16	4.9/2.9
S-1	18	3.3
other	89	16.3

【Result (cont.)】

- 179 patients did not receive 2nd-line chemotherapy at the time of data cutoff; the reasons were as follows: without disease progression, 50 (27.9%); declined PS, 75 (41.9%); patient refusal, 28 (15.6%); death of any cause, 6 (3.4%).

Factor		2nd line therapy (N=479) Number of patients (%)		Univariate P value*
		No (n=125)	Yes (n=354)	
male		98 (78.4)	254 (71.8)	p = 0.1587
female		27 (21.6)	100 (28.2)	
age	<65	43 (34.4)	168 (47.5)	**0.0120**
	≧65	82 (65.6)	186 (52.5)	
PS	0	31 (24.8)	170 (48.0)	**<0.0001**
	1-4	94 (75.2)	184 (52.0)	
Smoking	never	15 (12.0)	76 (21.5)	**0.0237**
	exp/current	110 (88.0)	278 (78.5)	
Comorbidity※	none	84 (67.2)	271 (76.6)	**0.0440**
	any	41 (32.8)	83 (23.4)	
BMI	<20	46 (36.8)	87 (24.6)	**0.0106**
	≧20	79 (63.2)	267 (75.4)	
EGFR	mutation (+)	5 (3.9)	30 (8.2)	0.2598
	mutation (−)	79 (61.2)	219 (59.5)	

*Fisher's test, ※DM, cardiac disease, ILD

Factor	Odds ratio	95% CI	Multivariate P value**
Age (≧65 vs <65)	0.648	0.416 – 1.011	0.0558
PS (1-4 vs 0)	0.395	0.247 – 0.631	**0.0001**
Smoking (ex/current vs never)	0.500	0.270 – 0.923	**0.0268**
Comorbidities (any vs no)	0.649	0.405 – 1.040	0.0722
BMI (≧20 vs <20)	1.565	0.989 – 2.477	0.0558

**Logistic regression model

【Summary and Conclusion】

- This is the largest cohort study exploring the proportion of patients with NSCLC and reasons for omitting 2nd-line chemotherapies.
- Maintenance therapy (either switch or continuation) was administered in approximately 30% of patients.
- Although data were immature, approximately 30% of patients did not receive appropriate 2nd-line chemotherapy.
- Declined PS was the most common reason for hindering 2nd-line chemotherapy.
- Advanced age, declined PS, smoking history, comorbidity, low BMI were correlated with hindrance to 2nd-line therapy in univariate analysis; however EGFR mutation was not significantly correlated.
- In multivariate analysis, declined PS and smoking history were associated with hindrance to 2nd-line chemotherapy.
- Further investigation to establish predictive model is currently underway.

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【Any question?】

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