

# 10-022 Prospective observational cohort study of second-line chemotherapy administration after first-line platinum-based chemotherapy for patients with advanced NSCLC in Japan (SAPPHIRE study)

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## Background

Standard care of advanced NSCLC

- First-line platinum-based chemotherapy (first-line CT)
- Second-line chemotherapy (second-line CT) after the progression of the first-line CT

Maintenance therapy after the first-line CT

- Recently, maintenance therapy has been reported to be beneficial.
- Its impact on overall survival appears to be marginal or negligible, when most patients could receive timely active second-line CT after progression.

## Objective

- To investigate the proportion of patients who had progression during observation after CR/PR/SD of first-line CT actually received the second-line CT
- To elucidate factors associated with second-line CT administration in advanced NSCLC patients.

## Methods

Study design

- Cohort (prospective observational) study

Primary endpoint

- Proportion of patients who received second-line CT after first-line CT

Patient inclusion

- Patients with advanced NSCLC who received platinum-based first-line CT
- From April 2010 to September 2011, at 30 institutions in Japan

Data collection

- Baseline characteristics (age, gender, ECOG-PS, smoking status, comorbidities, body mass index, histological subtype, EGFR/ALK status, CBC/chemistry at registration)
- Regimens and responses to the first/second/third-line CT (regimen, response)
- Administration of maintenance CT
- Reason for not receiving second-line CT (if it was not administered)

• Survival

Data cutoff

- Interim report describing patients with at least 6 months of follow up at April 2012

Support

- Supported by the Public Health Research Center Foundation CSPOR

## Results

- A total of 865 eligible patients with advanced NSCLC provided patient characteristics and details of the first-line CT.
- At the time of cut off, 797 patients were assessable for response of the first-CT. A total of 572 patients had CR/PR/SD.
- Administration of the second-CT was analyzed for 506 patients who had progression after first-line CT (primary study population)
- Maintenance therapy was administered to 144 patients. Of those,
  - 7 patients did not progress.
  - of 137 patients progressed, 25 patients (17.2%) could not receive second-line CT.
- Observation with no maintenance therapy was done in 362 patients. Of those,
  - 40 patients did not progress.
  - of 322 patients progressed, 89 patients (27.6%) could not receive second-line CT.
- Decline of PS was the principal reason for not receiving second-line CT in both patients with and without maintenance CT.

Figure 1

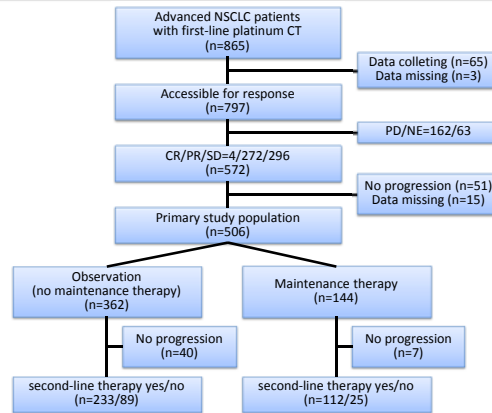


Table 1. Patient characteristics

Characteristics	No. of patients (n=865)	%
Sex male/female	628/237	73/24
Age median (range) 70 or more	65 (24-86) 250	29
Histology Adeno Squamous NSCLC (NOS) Others	602 174 73 16	70 20 8 2
PS 0/1/2/3-4/unknown	343/449/65/7/1	40/52/7/1/0
Smoking never/ever/unknown	173/687/5	20/79/1
Comorbidities none/any	654/211	76/24
EGFR status mutant/wild/unknown	87/515/263	10/60/30
ALK-EML translocation positive/negative/unknown	11/42/812	1.3/4.9/93.9

Table 2. Summary of first-line CT

	No. of patients	%
First-line platinum CT	865	
Cisplatin	331	38.3
Carboplatin	501	57.9
Nedaplatin	33	3.8
Accessible for response	797	
CR	4	0.5
PR	272	34.1
SD	296	37.1
PD	162	20.3
NE	63	7.9
Maintenance therapy	144	18.1

Table 3. Summary of Maintenance CT

	No. of patients (n=144)	%
Bevacizumab	54	38.0
Pemetrexed	51	35.9
TS-1	13	9.2
Pemetrexed+Bevacizumab	9	6.3
TS-1+Bevacizumab	7	4.9
Docetaxel	4	2.8
Gemcitabine	2	1.4
Erlotinib	1	0.7
Pemetrexed+Gefitinib	1	0.7
Other	2	1.4

Table 4. Characteristics of patients with or without maintenance therapy

Characteristics	No maintenance therapy (n=362)		Maintenance therapy (n=144)	
	No. of patients	%	No. of patients	%
Sex male/female	277/85	76.5/23.5	93/51	64.6/35.4
Age median (range) 70 or more	67 (24-86) 127	35.1	63 (34-78) 26	18.1
Histology Adeno Squamous NSCLC (NOS) Others	216 104 34 8	59.7 28.7 9.4 2.3	126 7 1 0	87.5 4.9 7.6 0
PS 0/1/2/3-4	152/185/22/3	42.0/51.1/6.1/0.9	75/62/6/1	52.1/43.1/4.2/0.7
Smoking never/ever/unknown	63/296/3	17.4/81.8/0.8	34/110/0	23.6/76.4/0
EGFR status mutant/wild/unknown	23/140/199	6.4/55.0/38.7	17/100/25	11.8/69.4/18.8

## Conclusions

- Preliminary results of this large observational study in Japan suggested that
  - Among the patients who did not receive maintenance therapy, 27.6% missed an opportunity to receive appropriate second-line CT.
  - We could not find associated factors for not receiving second-line CT.
  - As for the patients who received maintenance therapy, 17.2% did not receive second-line CT.
  - Administration of maintenance therapy did not appear to compromise the chance to receive second-line CT.
- Further investigation is needed to identify the patients who would be less likely to receive the second-CT after disease progression, and thus would be more likely to receive benefit from maintenance therapy strategy.

Table 5. Summary of second-line CT patients with confirmed progression after CR/PR/SD in first-line CT

	No maintenance therapy (n=322)		Maintenance therapy (n=137)	
	No. of patients	%	No. of patients	%
None	89	27.6	25	18.2
2nd-line CT	233	72.4	112	81.8
Docetaxel	101	31.3	42	30.7
Pemetrexed	39	12.1	23	16.8
Erlotinib	15	4.7	12	8.8
TS-1	12	3.7	3	2.2
Gemcitabine	6	1.9	8	5.8
Other	60	18.6	24	17.5

Table 6. Reasons for not receiving second-line CT after progression

Reasons	No maintenance therapy (n=89)		Maintenance therapy (n=25)	
	No. of patients	%	No. of patients	%
Declined PS	49	55.1	15	60.0
Patient refusal	14	15.7	9	36.0
Death of any cause	6	6.7	1	4.0
Loss of follow-up and others	20	2.2	0	0

Table 7. Association between baseline characteristics and administration of second-line CT yes/no (univariate analysis)

Characteristics	No maintenance therapy (n=233/129*)			Maintenance therapy (n=112/32*)		
	No. of patients	%	P OR (95% CI)	No. of patients	%	P OR (95% CI)
Sex male female	180/97 53/32	65.0/35.0 62.4/37.6	0.213 1.12(0.679-1.849)	70/23 42/9	75.7/24.4 82.4/17.6	0.404 0.652(0.281-1.521)
Age ≥70 <70	78/49 155/80	61.4/38.6 66.0/34.0	0.422 0.822(0.526-1.284)	17/9 95/23	61.4/38.6 66.0/34.0	0.118 0.457(0.184-1.134)
PS 0 1-4	102/50 131/79	67.1/32.9 62.4/37.6	0.375 1.230(0.794-1.905)	64/11 48/21	85.3/14.7 69.6/30.4	0.028 2.545(1.134-5.704)
Smoking never ever	40/23 193/106	63.4/36.6 64.5/35.5	0.886 0.955(0.545-1.673)	32/2 80/30	94.1/5.9 72.7/27.3	0.009 6.000(1.492-23.84)
Comorbidities none yes	173/93 60/36	65.0/35.0 62.5/37.5	0.710 1.116(0.689-1.807)	90/24 22/8	72.6/28.4 73.3/26.7	0.622 1.364(0.552-3.388)
Platinum regimen CDDP other	92/41 141/88	69.1/30.9 61.6/38.4	0.172 1.400(0.890-2.202)	42/8 70/24	84.0/16.0 74.5/25.5	1.800 0.753-4.283

\*Patients without progression of first-line CT are included\*

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