

Medical Treatment Expenses for Lung Cancer in Japan

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ABSTRACT

BACKGROUND: Since 1993 lung cancer has been the leading cause of death due to cancer in Japan. In December 2015, nivolumab was approved for the treatment of lung cancer in this country and dramatic effects have been noted in many patients. However, its price is very high, which is one of the causes of rising national medical expenses.

MATERIALS: In 2009 the Ministry of Health, Labour and Welfare of the Japanese Government began to publish the data of medical treatment expenses for the main malignant neoplasms. The numbers of deaths due to malignant neoplasms, including lung cancer, and medical treatment expenses from 2009 to 2017 were obtained from the data published on the sites of the ministry.

RESULTS: From 2015 to 2016, the number of deaths from lung cancer decreased, though it increased from 2009 to 2015. The medical treatment expenses for this cancer increased from 2009 to

2015, but from 2015 to 2016 they increased largely for all age groups (45-64, 65-74 and 75+ years). The increase in the percentage of the expenses spent by the group aged 45-64 years at outpatient clinics from 2015 to 2016 was the highest (10.1 points), and was about 2 times larger than that of those aged 75 and older (4.58). The expense to decrease one death from lung cancer (about \$200,000) in the group aged 65-74 years was the smallest, being about 40% of that for the group aged 75 and older (about \$500,000). The greater part of the increase in the sale of nivolumab from 2015 to 2016 (about 80%) may be accounted for by medical treatment expenses for lung cancer. **DISCUSSION:** It is certain that the introduction of nivolumab for the treatment of lung cancer brought about the increase in the medical treatment expenses from 2015 to 2016. There is a possibility that the cost and quality of life due to treatment with this drug differ by age.

Key words: Japan; Lung cancer; Medical expense; Nivolumab

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INTRODUCTION

In Japan cancer has been the leading cause of death since 1981 and its crude mortality rate has been increasing^[1]. On the other hand, national medical expenses have also been increasing and now have become a burden on the national budget.

Since 1993 lung cancer has been the leading cause of death due to cancer. In December 2015, nivolumab, a molecular targeted drug, was introduced for the treatment of lung cancer, and dramatic effects have been noted in many patients. However, its price is very high, and is one of the causes of rising national medical expense. In this article, the recent changes in medical treatment expenses for lung cancer in Japan are reported.

MATERIALS AND METHODS

1. Medical treatment expenses

In the statistics of the Japanese Government, the total medical expenses consist of: (1) medical treatment expenses; (2) dental treatment expenses;

(3) pharmacy dispensation expenses; (4) visiting care expenses; (5) meal and living expenses during hospitalization; (6) others.

In this article, only medical treatment expenses are examined, and an arbitrary exchange rate of Yen 100 = 1\$US is used.

2. Numbers of deaths from malignant neoplasms and lung cancer

The numbers of deaths due to malignant neoplasms, including lung cancer, were obtained from the vital statistics indicated on the site of the Ministry of Health, Labour and Welfare of the Japanese Government.

https://www.e-stat.go.jp/stat-search/files?page=1&layout=datalis t&toukei=00450011&tstat=00001028897&cycle=7&year=20180 &month=0&tclass1=00001053058&tclass2=00001053061&tclass3=00001053065&result_back=1.

3. Medical treatment expenses

Medical treatment expenses for each of the main diseases have been available since 2009 on the site of the Ministry of Health, Labour and Welfare.

<https://www.mhlw.go.jp/toukei/list/37-21.html>.

Data about the medical treatment expenses for malignant neoplasms, including lung cancer, from 2009 to 2017 were obtained from this site. The data are indicated by age groups for the ages of 0-14, 14-44, 45-64, 65-69, 70-74 and 75+ years. The medical treatment expenses of the group aged 65-74 years were calculated employing these data. Since the percentages of the medical treatment expenses for the patients aged 44 years or younger were only about 2% every year, they were omitted from this article.

4. Average annual increase in the number of deaths due to lung cancer from 2009 to 2015

From 2009 to 2015, the number of deaths from lung cancer increased. The average annual increase was calculated by adding the number of deaths in 2009 to that in 2015 and dividing the result by 6. Employing this value as the “expected value” and the change from 2015 to 2016 as the “observed value”, the chi-square test was performed.

The difference between the “expected value” and the “observed value” was regarded as the “estimated decrease in the number of deaths.” This value was employed for the calculation of the expense to decrease the number of deaths by one.

5. Average annual increase in the medical treatment expenses for lung cancer from 2009 to 2015

From 2009 to 2015, the medical treatment expenses for lung cancer increased. The average annual increase was calculated by adding the medical treatment expenses in 2009 to those in 2015 and dividing the result by 6.

Employing this value as the “expected value” and the change from 2015 to 2016 as the “observed value”, the chi-square test was performed.

The difference between the “expected value” and the “observed value” was regarded as the “estimated increase in the expenses.” Through dividing the “estimated increase in the expenses” by the “estimated decrease in the number of deaths”, the expense to reduce the number of deaths by one was calculated.

6. Prices and net sales of nivolumab

Prices and net sales of nivolumab were obtained from the data on the site “Answers News”, which is an information site on medical drugs in Japan.

<https://answers.ten-navi.com/pharmanews/14616/>

RESULTS

1. Numbers of deaths from malignant neoplasms and lung cancer

Table 1 shows the numbers of deaths due to malignant neoplasms, including lung cancer. The numbers of deaths from malignant neoplasms increased from 2009 through 2017, and those due to lung cancer from 2009 to 2015. However, the total number of deaths from lung cancer decreased significantly from 2015 to 2016.

2. Medical treatment expenses for lung cancer

Table 2 shows the changes in the medical treatment expenses for malignant neoplasms and lung cancer. The increase from 2015 to 2016 of those for malignant neoplasms was not significant, but that for lung cancer was significantly high.

In all the age groups the increases from 2015 to 2016 were significant and the largest among the changes between each of the years from 2009 to 2017 (Table 3).

3. Percentages of medical treatment expenses for lung cancer at outpatient clinics

The changes in the percentages of medical treatment expenses for lung cancer at outpatient clinics within the total expenses spent by each of the age groups are shown in Table 4. In each of the age groups, the increase from 2015 to 2016 was the largest among the changes between each of the years from 2009 to 2017. The increase in the percentage of the expenses for the group aged 45-64 years at outpatient clinics from 2015 to 2016 was the highest (10.1 points) among the 3 age groups, and was about 2 times larger than that of the group aged 75 years and older (4.58).

4. Medical treatment expenses to decrease the number of deaths from lung cancer by one

Table 5 shows the medical treatment expenses to decrease the number of deaths from lung cancer by one.

The calculation of the “Total” expenses was as follows: (1) The “expected value” of the number of deaths was 1132.50, and the “observed value” was -540.0 (Table 1). Therefore, the estimated decrease in the number of deaths was 1672.5 (1132.5+540). (2) The “expected value” of the medical treatment expenses for lung cancer was \$174 million, and the “observed value” was \$658 million (Table 3). Therefore, the estimated increase in the expenses was \$484 million (658-174). (3) The medical treatment expense to decrease the number of deaths due to lung cancer by one was \$484million/1672.5, which comes to \$289,387.1.

The expense for the group aged 65-74 years (about \$200,000) was the smallest among the 3 age groups, being about 40% of that of the group aged 75 and older (about \$500,000).

5. Prices and net sales of nivolumab

Table 6 shows the prices and net sales of nivolumab. In September 2014, nivolumab became available, and its price was \$7,298.5 per 100mg. In December 2015, the Japanese Government approved it for the treatment of non-small cell lung cancers. This may be one of the main causes of the increase in medical treatment expenses after 2015. The increase in the net sales from 2015 to 2016 was about \$817 million (1039 - 212), and the increase in the medical treatment expenses for lung cancer from 2015 to 2016 was \$658 million (Table 2). Thus, the greater part of the increase in the sale of nivolumab from 2015 to 2016 (about 80%) may be accounted for by medical treatment expenses for lung cancer.

Table 1 Numbers of deaths due to malignant neoplasms and lung cancer.

Year	Malignant neoplasms	Lung cancer Age (years)			
		45-64	65-74	75+	Total
2009	344105	10630	17641	38751	67583
2010	353499	10714	18241	40364	69813
2011	357305	10778	18149	40857	70293
2012	360963	10443	18681	41899	71518
2013	364872	10039	19315	42894	72734
2014	368106	9259	20475	43214	73396
2015	370362	8512	21243	44174	74378
2016	373088	7763	20859	44794	73838
2017	373365	6999	20480	46285	74120
Change					
2009-2015#	4376.17	-353.00	600.33	903.83	1132.50
2015-2016	2726.00	-749.00	-384.00	620.00	-540.00
	**	**	**	**	**

#annual average, **p < 0.001.

Table 3 Medical treatment expenses for lung cancer by age group (million \$).

Year	Age (years)			Total
	45-64	65-74	75+	
2009	975	1195	1212	3459
2010	1125	1309	1290	3811
2011	1201	1450	1329	4070
2012	1205	1552	1383	4236
2013	1128	1645	1391	4255
2014	1057	1747	1421	4315
2015	1061	1869	1476	4503
2016	1214	2179	1661	5161
2017	1178	2164	1801	5249
Change				
2009-2015#	14.33	112.33	44.00	174.00
2015-2016	153.00	310.00	185.00	658.00
	**	**	**	**

#annual average; **p < 0.001.

Table 5 Estimated change in the number of deaths, medical treatment expenses and expenses to decrease deaths due to lung cancer from 2015 to 2016 by one.

	Age (years)			Total
	45-64	65-74	75+	
Estimated decrease in the number of deaths	396.0	984.3	283.8	1672.5
Estimated increase in the expenses (million \$)	138.7	197.7	141.0	484.0
Expense to decrease deaths by one (\$)	350168.4	200812.7	496770.4	289387.1

DISCUSSION

Nivolumab has the benefits of prolonging overall survival and disease-free survival^[2,3]. From the viewpoint of cost, however, there is room for argument.

Many cost-effectiveness analyses of nivolumab were reported, but there is little evidence showing that its cost effectiveness is excellent. According to a report by Goeree et al^[4], nivolumab was found to have the highest expected per-patient cost, but also improved per-patient life years and QALYs. Nivolumab cost an additional \$151,560 per QALY gained compared to docetaxel. Matter-Walstra et al^[5] reported that compared with docetaxel, nivolumab was not cost effective for

Table 2 Medical treatment expenses for malignant neoplasms and lung cancer (million \$).

Year	Malignant neoplasms	Lung cancer
2009	29159	3459
2010	30312	3811
2011	31831	4070
2012	33267	4236
2013	33792	4255
2014	34488	4315
2015	35889	4503
2016	37067	5161
2017	38192	5249
Change		
2009-2015#	1121.67	174.00
2015-2016	1178.00	658.00
		**

#annual average; **p < 0.001.

Table 4 Percentages of the total medical treatment expenses for lung cancer spent at outpatient clinics(%).

Year	Age (years)			Total
	45-64	65-74	75+	
2009	27.2	25.1	25.1	26.0
2010	27.2	25.4	22.5	25.2
2011	28.1	25.2	22.9	25.6
2012	28.6	25.3	23.4	25.9
2013	30.2	26.6	24.3	27.1
2014	31.2	27.4	24.9	27.9
2015	33.6	29.2	25.9	29.5
2016	43.7	37.1	30.5	36.9
2017	45.1	38.2	32.5	38.1
Change				
2009-2015#	1.06	0.68	0.13	0.58
2015-2016	10.10	7.92	4.58	7.34

#annual average.

Table 6 Prices and net sales of nivolumab.

Year	Month		Price/100mg (\$)	Net sales (million \$)
2014	September	Came to market	7298.49	25
2015	December	Approval of insurance coverage for non-small cell cancer		212
2016				1039
2017	February		3649.25	901
2018	April		2780.29	
2018	November		1737.68	

the treatment of nonsquamous non-small cell lung cancer. Li et al^[6] reviewed many reports and concluded that nivolumab was not cost effective as a first-line treatment.

In Japan, in 2018, the price was reduced to \$1,737.7 per 100mg. This might contribute to a decrease in the medical treatment expenses. However, the reduction in price might lead to the easy use of this medicine and, as a result, it is possible that the total medical treatment expenses could increase. If a patient dies, there are no more treatment expenses. However, if the overall survival rate is improved, the number of patients who continue treatment increases and, consequently, this leads to an increase in expenses.

When the survival rate is improved, many patients receive their

treatment at outpatient clinics after remission induction therapy is completed. The increase in the percentages of medical treatment expenses at outpatient clinics may be accounted for by the improvement in the survival rate. In the present study, the increase in the percentage of the expenses at outpatient clinics for the group aged 45-64 years was the largest. If the treatment is done at outpatient clinics, the quality of life of the patient is much improved.

The costs to reduce cancer deaths by one were different by age, as well. Thus, there is a possibility that the cost or quality of life with regard to treatment with nivolumab differs by age. Therefore, the age factor should not be ignored in analyses about cost and quality of life when this drug is employed.

In Japan, the smoking rates were the highest in 1966 (about 80% for males and about 16% for females)^[1]. Since that year, the smoking rate has been decreasing and, therefore, it is expected that the incidence rate of lung cancer will decrease in the future. However, if expensive drugs are used for many of the patients, medical treatment expenses will remain high.

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