ONO PHARMACEUTICAL CO., LTD.

Q1 Financial Results for the Fiscal Year Ending March 2023

August 1, 2022

[Number of Speakers] 5

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Satoshi Takahagi	Corporate Officer, Executive Director, Sales and Marketing, Primary Care Business Division
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Revenue

Revenue	YoY Change
¥ 106.7 billion	+ 22.2 %

Breakdown of Revenue

(Billion yen)

	FY 2021 Q1	FY 2022 Q1	YoY Change
Revenue of Goods and Products	60.5	72.2	+ 19.2 %
Royalty & other revenue	26.8	34.6	+ 28.8 %
Total	87.4	106.7	+ 22.2 %

Nagahama: I will now explain our financial results for Q1 of the fiscal year ending March 2023.

Revenue for Q1 was JPY106.7 billion, increased by JPY19.4 billion, or 22.2%, compared to the same period last year.

Revenue of goods and products increased by JPY11.6 billion, or 19.2%, to JPY72.2 billion due to solid sales growth of Opdivo for intravenous infusion, Forxiga tablets, Orencia subcutaneous injection, Velexbru tablets, and Ongentys tablets, despite a decline in sales of long-term listed products.

Royalty & other revenue increased by JPY7.7 billion, or 28.8% to JPY34.6 billion compared to the same period last year. Royalty income from Bristol-Myers Squibb for Opdivo increased by JPY3.8 billion to JPY20.8 billion, and royalty income from Merck for Keytruda increased by JPY3 billion to JPY9.8 billion.

Revenue

Sales of Major Products

(Billion yen)

	FY 2021 Q1	FY 2022 Q1	YoY Change
Opdivo	29.0	**34.1**	+ 17.4 %
Forxiga	7.5	**13.1**	+ 75.3 %
Orencia SC	5.7	**6.2**	+ 9.4 %
Glactiv	6.5	**6.0**	- 6.7 %
Kyprolis	2.0	**2.2**	+ 12.6 %
Parsabiv	2.2	**2.1**	- 3.1 %
Velexbru	1.4	**2.1**	+ 45.1 %
Ongentys	0.2	**1.2**	+ 399.8 %
Onoact	1.2	**1.1**	- 8.7 %
Braftovi	0.7	**0.9**	+ 30.6 %
Mektovi	0.5	**0.7**	+ 29.5 %

By product, sales of the anti-cancer agent Opdivo for intravenous infusion increased by JPY5.1 billion, or 17.4%, to JPY34.1 billion, mainly due to expanded use for first-line treatment of gastric cancer, adjuvant treatment of esophageal cancer, and first-line treatment of non-small cell lung cancer, despite intensified competition with other products.

Among other major new products, Forxiga tablets, the treatment for diabetes, chronic heart failure, and chronic kidney disease, increased by JPY5.6 billion, or 75.3%, to JPY13.1 billion.

Sales of Orencia subcutaneous injection, for rheumatoid arthritis treatment, increased by JPY0.5 billion, or 9.4%, to JPY6.2 billion.

Kyprolis for intravenous infusion, the treatment of multiple myeloma, increased by JPY0.3 billion, or 12.6%, to JPY2.2 billion.

Sales of anti-cancer agent Velexbru tablets increased by JPY0.6 billion, or 45.1%, to JPY2.1 billion.

Sales of Ongentys tablets, for Parkinson's disease, increased steadily by JPY1 billion to JPY1.2 billion.

On the other hand, sales of Glactiv tablets, for type 2 diabetes treatment, decreased by JPY0.4 billion or -6.7% to JPY6 billion.

Sales of Parsabiv for intravenous dialysis, the treatment of secondary hyperparathyroidism on hemodialysis, decreased by JPY0.1 billion, or -3.1%, to JPY2.1 billion.

Revenue

Sales of Long-term Listed Products

(Billion yen)

	FY 2021 Q1	FY 2022 Q1	YoY Change
Opalmon	1.2	**1.1**	- 6.5 %
Onon capsule	1.1	**0.7**	- 36.3 %

Regarding the long-term listed products, due to the impact from the NHI price revision, sales of Opalmon tablets, for the improvement of peripheral circulatory disturbance, decreased by JPY0.1 billion, or -6.5%, to JPY1.1 billion, and sales of Onon capsules, for bronchial asthma and allergic rhinitis, decreased by JPY0.4 billion, or -36.3%, to JPY0.7 billion.

Operating Profit

Operating Profit	YoY Change
¥ 38.2 billion	+ 28.1 %

Costs, etc.

(Billion yen)

	FY 2022 Q1	YoY Change
・Cost of Sales	26.9	(+ 18.1%)
・R&D Expenses	19.4	(+ 27.3%) ①
・SG&A Expenses	21.7	(+ 14.6%) ②
①+② Total	41.1	(+ 20.3%)
・Other Income	0.1	(- 43.8%)
・Other Expenses	0.6	(- 22.4%)

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Next is operating profit. Operating profit increased by JPY8.4 billion, or 28.1%, to JPY38.2 billion compared to the same period last year.

In terms of expenses, cost of sales increased by JPY4.1 billion or 18.1%, YoY to JPY26.9 billion, mainly due to an increase in revenue of goods and products.

R&D expenses increased by JPY4.2 billion, or 27.3%, YoY to JPY19.4 billion, mainly due to an increase in research-related expenses and development costs related to early-stage clinical trials.

Selling, general and administrative expenses, excluding R&D expenses, increased by JPY2.8 billion, or 14.6%, YoY to JPY21.7 billion due to increased co-promotion expenses associated with the sales expansion of Forxiga tablets and expenses associated with the strengthening of IT and digital-related information infrastructure.

Profit before Tax

Profit before Tax	YoY Change
¥ 39.0 billion	+ 26.7 %

Net financial income, etc.

+ ¥ 0.9 billion (YoY Change - ¥ 0.1 billion)

Finance income : (Dividend income received, etc.)	¥ 1.2 billion
Finance costs : (Exchange losses, etc.)	¥ 0.3 billion

Next is profit before tax.

Finance income and finance costs totaled JPY1.2 billion and JPY0.3 billion, respectively, and net financial income, etc. decreased by JPY0.1 billion YoY to JPY0.9 billion. Profit before tax was JPY39 billion, increased by JPY8.2 billion, or 26.7%, from the same period last year YoY.

Profit for the Period
(Owners of the Parent Company)

Profit for the Period (Owners of the Parent Company)	YoY Change
¥ 29.5 billion	+ 22.4 %

Income tax expense

¥ 9.5 billion (YoY Change + 42.1 %)

(Major change factors)

Increase in profit before tax	¥ 8.2 billion
Increase in corporate tax	¥ 2.8 billion

Due to the increase in profit before tax, profit for the period attributable to owners of the parent company increased by JPY5.4 billion or 22.4% YoY to JPY29.5 billion. Both revenue and profit at each stage reached record highs for Q1.

Financial Forecasts for FY 2022

Financial forecasts are unchanged from those announced on May 11, 2022

(Billion yen)

	FY 2021 (Result)	FY 2022 (Forecast)	YoY Change
Revenue	361.4	**425.0**	+ 17.6 %
Operating profit	103.2	**145.0**	+ 40.5 %
Profit before tax	105.0	**146.0**	+ 39.0 %
Profit for the year (Owners of the Parent Company)	80.5	**110.0**	+ 36.6 %

Exchange rate FY 2022: 1USD = 110 yen

I would like to explain our forecast for the full year ending March 2023.

Although the current yen's exchange rate to the dollar is moving at a weaker level than the assumed rate, there is no change to the full-year earnings forecast announced on May 11, 2022.

The assumed exchange rate is JPY110 to the dollar, and a JPY1 depreciation of the yen will result in a JPY1.1 billion increase in revenue and a JPY0.8 billion increase in profit for the full year. In addition, the sales forecasts for each major product shown on page 12 of the financial results summary remain unchanged from the figures announced at the beginning of the fiscal year.

The Company plans to pay an interim and year-end dividend of JPY33 per share, or JPY66 per share for the full year, with no change in the current status. As the annual dividend for the previous fiscal year ended March 31, 2022 was JPY56 per share, this represents an increase of JPY10.

Tani: I will make a supplementary statement regarding sales of Opdivo. It was mentioned that sales increased 17.4% to JPY34.1 billion. Although the NHI price of Opdivo was revised downward in August last year, the volume-based sales increased by about 33% YoY.

Development pipeline

Idemitsu: I will give an update on the progress of main development pipelines. There are two points to be updated this time.

(4) Main Status of Development Pipelines (Oncology)

As of July 25, 2022

<Approved> *) : "In-house" compounds include a compound generated from collaborative research.

Product Name / Development Code / Generic Name	Classification	Target Indication / Pharmacological Action	Dosage Form	Area	In-house*) / In-license
Yervoy Injection ★ / Ipilimumab	Additional indication	Esophageal cancer *1	Injection	Japan Taiwan	In-license (Co-development with Bristol-Myers Squibb)

★: Combination with Opdivo

The change from the announcement of financial results for the fiscal year ended March 2022 is as follows:

*1: Applications for the combination therapy of Opdivo and Yervoy, and the combination therapy of Opdivo and chemotherapy were approved in Japan and Taiwan for the treatment of unresectable advanced or recurrent esophageal cancer.

<Clinical Trial Stage>

<Opdivo> *) : "In-house" compounds include a compound generated from collaborative research.

Product Name / Development Code / Generic Name	Classification	Target Indication / Pharmacological Action	Dosage Form	Area	Phase	In-house*) / In-license
Opdivo Intravenous Infusion / Nivolumab	Additional indication	Hepatocellular carcinoma	Injection	Japan S. Korea	III	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Ovarian cancer	Injection	Japan S. Korea Taiwan	III	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Bladder cancer	Injection	Japan S. Korea Taiwan	III	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Prostate cancer	Injection	Japan S. Korea Taiwan	III	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Pancreatic cancer	Injection	Japan S. Korea Taiwan	II	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Virus positive・negative solid carcinoma	Injection	Japan S. Korea Taiwan	I / II	In-house (Co-development with Bristol-Myers Squibb)

First is the section on approved products on page 13. Yervoy was approved for treatment of esophageal cancer in combination with Opdivo in Japan in May and Taiwan in July.

(5) Main Status of Development Pipelines (Areas other than Oncology)

As of July 25, 2022

<Filed> *) : "In-house" compounds include a compound generated from collaborative research.

Product Name / Development Code / Generic Name	Classification	Target Indication / Pharmacological Action	Dosage Form	Area	In-house*) / In-license
Onoact for Intravenous Infusion / Landiolol Hydrochloride	Additional indication for pediatric use	Tachyarrhythmia in low cardiac function / Short-acting selective β_1 blocker	Injection	Japan	In-house

<Clinical Trial Stage> *) : "In-house" compounds include a compound generated from collaborative research.

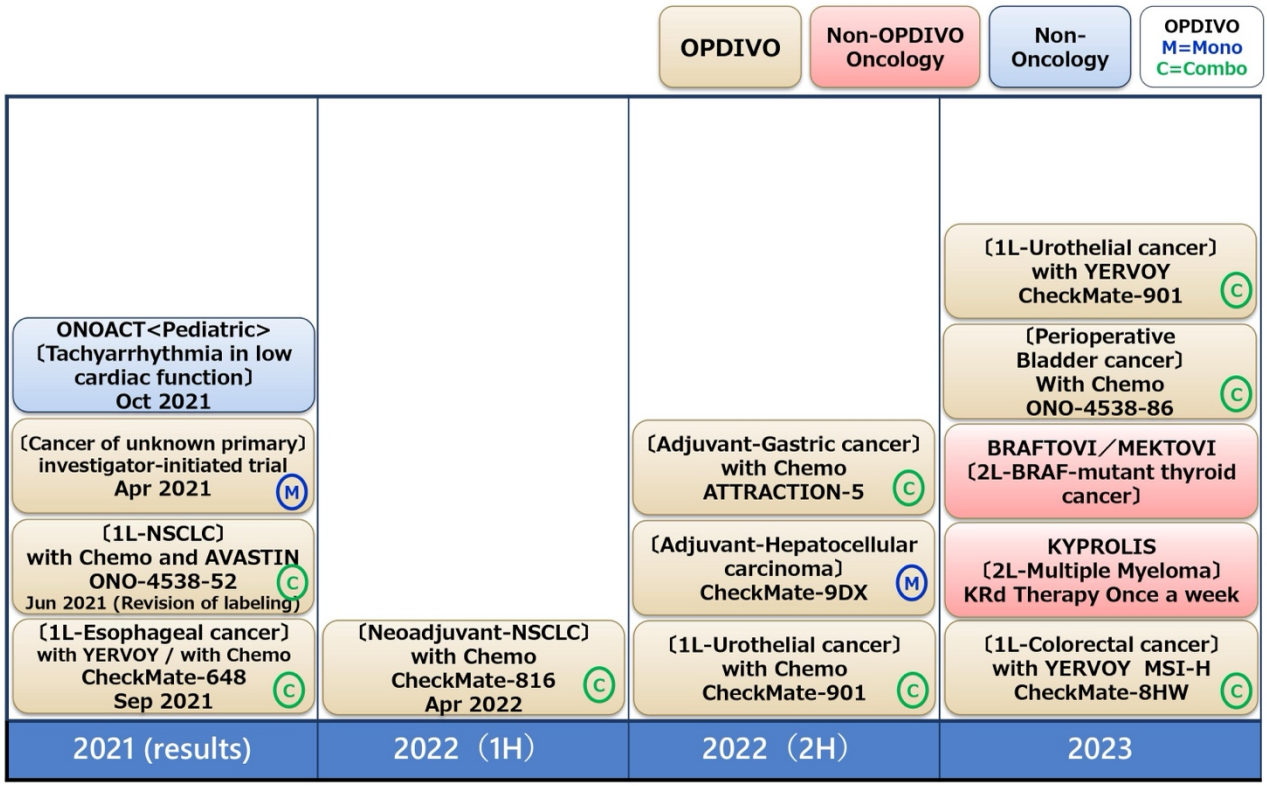
Product Name / Development Code / Generic Name	Classification	Target Indication / Pharmacological Action	Dosage Form	Area	Phase	In-house*) / In-license
ONO-2017 / Cenobamate	New chemical entities	Primary generalized tonic-clonic seizures / Inhibition of voltage-gated sodium currents/positive allosteric modulator of $GABA_A$ ion channel	Tablet	Japan	III	In-license (SK Biopharmaceuticals)
	New chemical entities	Partial-onset seizures / Inhibition of voltage-gated sodium currents/positive allosteric modulator of $GABA_A$ ion channel	Tablet	Japan	III	In-license (SK Biopharmaceuticals)
Velexbru Tablets / Tirabrutinib Hydrochloride	Additional indication	Pemphigus / BTK inhibitor	Tablet	Japan	III	In-house
ONO-2910	New chemical entities	Diabetic polyneuropathy / Schwann cell differentiation promoter	Tablet	Japan	II	In-house
ONO-4685	New chemical entities	Autoimmune disease / PD-1 x CD3 bispecific antibody	Injection	Japan Europe	I	In-house
ONO-7684	New chemical entities	Thrombosis / FXIa inhibitor	Tablet	Europe	I	In-house
ONO-2808	New chemical entities	Neurodegenerative disease / S1P5 receptor agonist	Tablet	Japan Europe	I	In-house
ONO-2909	New chemical entities	Narcolepsy / Prostaglandin receptor (DP1) antagonist	Tablet	Japan	I	In-house
Velexbru Tablets / Tirabrutinib Hydrochloride	Additional indication	Systemic sclerosis / BTK inhibitor	Tablet	Japan	I	In-house
ONO-2020 *2	New chemical entities	Neurodegenerative disease / Epigenetic Regulation	Tablet	USA	I	In-house

The change from the announcement of financial results for the fiscal year ended March 2022 is as follows:
*2: Phase I of ONO-2020 (Epigenetic Regulation) was initiated in the U.S. for the treatment of neurodegenerative disease.

ONO-2020 has been newly added this time. Phase I in the US will begin. ONO-2020 is a compound that acts on epigenetics and targets neurodegenerative diseases.

Epigenetics is a mechanism by which cells regulate gene function without changing the DNA base sequence itself. It is reported that epigenetic abnormalities are observed in neurons and surrounding cells in neurodegenerative disease. ONO-2020 is expected to restore nerve function by normalizing epigenetic modification status in the brain, thereby improving various symptoms of neurodegenerative diseases.

Plan for Submissions in Japan



As of July 29, 2022

Next is the plan for submissions in Japan. As for the timing of the submission, this is the fastest possible schedule if everything goes according to plan, and the situation may change.

For the second column from the right, the submission of postoperative adjuvant for renal cell carcinoma in combination with Opdivo and Yervoy using CheckMate-914, which was planned for 1H of FY2022, was removed late last week, as the expected results were unfortunately not obtained.

The second is the submission for Opdivo for the first-line treatment of urothelial carcinoma in CheckMate-901, which is listed at the bottom of 2H of FY2022. In addition to the chemotherapy combination treatment as shown in this document, the combination with Yervoy was also listed in the previous document. The submission for the combination with Yervoy, which was planned for 2H of FY2022, was related to a PD-L1-positive cohort. Unfortunately, we could not obtain the expected results. Therefore, we will not be able to file an application at this timing.

On the other hand, with regard to the combination with Yervoy, there is another cohort for cisplatin nonadherence, the results will be available after 2023. Therefore, we have now added the submission for Opdivo for the first-line treatment of urothelial carcinoma in combination with Yervoy to the top row of the right-sided column for FY2023.

Development status of OPDIVO (1)

As of July 29, 2022

Target disease	Line of Therapy	Treatment	Phase				
			Japan	Korea	Taiwan	US	EU
Melanoma	Adjuvant・1st・2nd	Monotherapy, with Ipi (1st line only)	Approved	Approved	Approved	Approved	Approved
Non-small cell lung cancer	Neo-adjuvant	with Chemo	Filed	III	III	Approved	Filed
	1st	with Ipi	Approved	Approved	Approved	Approved	–
		with Ipi + Chemo	Approved	Approved	Approved	Approved	Approved
		with Chemo	Approved	–	–	–	–
		with Chemo (NSQ)	Revision of labeling	Approved	Approved	–	–
	2nd	Monotherapy	Approved	Approved	Approved	Approved	Approved
Renal cell carcinoma	1st	with Ipi	Approved	Approved	Approved	Approved	Approved
		with TKI	Approved	Approved	Approved	Approved	Approved
		with Ipi + TKI	–	III	III	III	III
	2nd	Monotherapy	Approved	Approved	Approved	Approved	Approved
Hodgkin's lymphoma	Relapsed /Refractory	with Brentuximab	III	–	–	III	–
		Monotherapy	Approved	Approved	Approved	Approved	Approved
Head and neck cancer	2nd	Monotherapy	Approved	Approved	Approved	Approved	Approved
Malignant pleural mesothelioma	1st	with Ipi	Approved	Approved	Approved	Approved	Approved
	SOC refractory	Monotherapy	Approved	–	–	–	–

Red: Update after May 2022

The development status of Opdivo is updated on this page and next page.

Development status of OPDIVO (2)

As of July 29, 2022

Target disease	Line of Therapy	Treatment	Phase				
			Japan	Korea	Taiwan	US	EU
Gastric cancer	Adjuvant	with Chemo	III	III	III	–	–
	1st	with Chemo	Approved	Approved	Approved	Approved	Approved
		with Ipi + Chemo	III	III	III	–	–
	3rd	Monotherapy	Approved	Approved	Approved	–	–
Esophageal cancer	Adjuvant	Monotherapy	Approved	Approved	Approved	Approved	Approved
	1st	with Ipi, with Chemo	Approved	III	Approved	Approved	Approved
	2nd	Monotherapy	Approved	Approved	Approved	Approved	Approved
Colorectal cancer	1st	with Chemo	II / III	–	–	II / III	II / III
	MSI-H／dMMR (1st)	with Ipi	III	–	–	III	III
	MSI-H／dMMR (3rd)	Monotherapy	Approved	–	Approved	Approved	-
		with Ipi	Approved	Approved	Approved	Approved	Approved*
Hepatocellular carcinoma	Adjuvant	Monotherapy	III	III	III	III	III
	1st	with Ipi	III	III	III	III	III
	2nd	Monotherapy, with Ipi	II	II	Approved**	Approved**	II

* 2nd line
* * With Ipi (US),Monotherapy only (Taiwan)

Red: Update after May 2022

The Opdivo development status is summarized on pages 3 and 4. The changes are shown in red, including the approval in Japan and Taiwan for the first-line treatment of esophageal cancer, which I explained earlier using the financial summary.

Global devlopment projects (Other than OPDIVO)

As of July 29, 2022

Product name/ Development code (Generic name)	Target indication	Pharmacological action	Area
【Phase Ⅲ】			
ONO-7913 (Magrolimab)	Acute myeloid leukemia	Anti-CD47 antibody	KR・TW
【Phase Ⅱ】			
ONO-4059 (Tirabrutinib)	Primary central nervous system lymphoma	BTK inhibitor	US
【Phase Ⅰ/Ⅱ】			
ONO-7475	Acute leukemia	Axl / Mer inhibitor	US
【Phase Ⅰ】			
ONO-7684	Thrombosis	FXIa inhibitor	EU
ONO-2808	Neurodegenerative disease	S1P5 receptor agonist	EU
ONO-4685	T-cell lymphoma	PD-1 x CD3 bispecific antibody	US
	Autoimmune disease		EU
ONO-2020	Neurodegenerative disease	Epigenetic Regulation	US

Red: Update after May 2022

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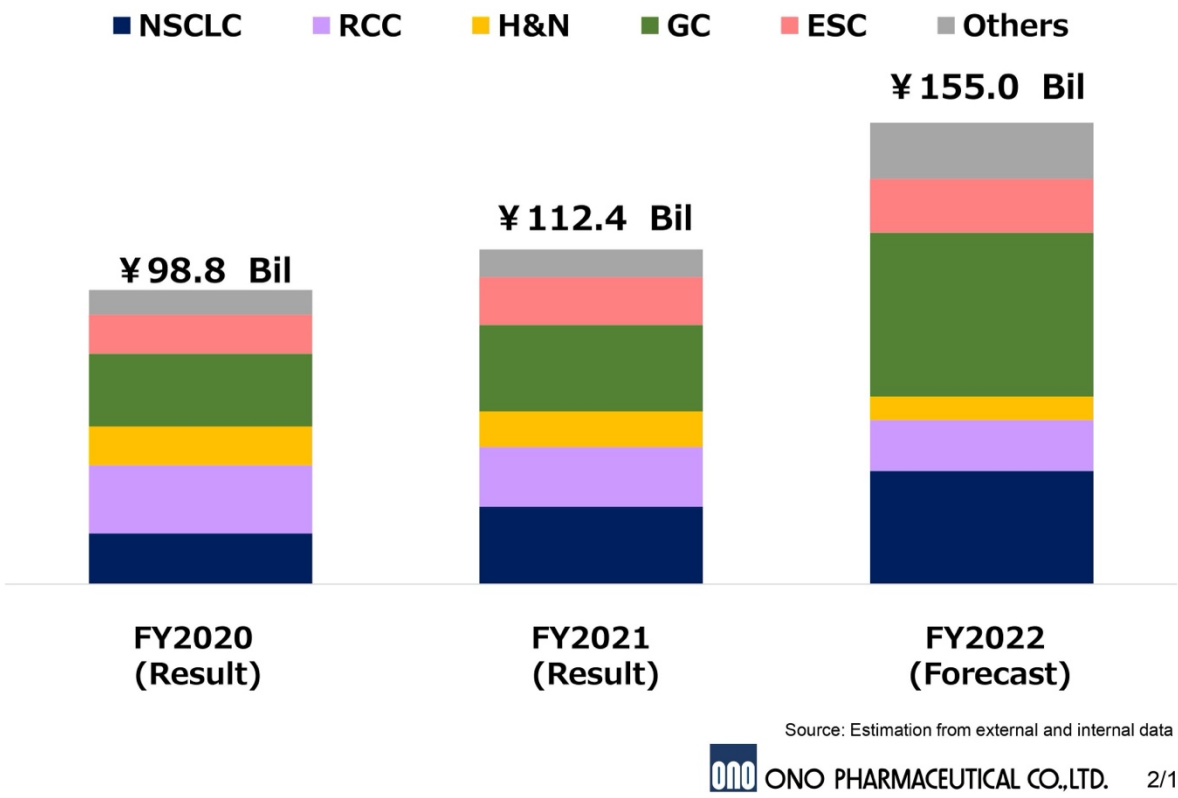
On page 9, you find the description of ONO-2020 that I mentioned earlier. That's all for the progress of developed products.

Trend of Opdivo

Takahagi: I will provide information on general status, sales, number of newly prescribed patients, composition of IO inhibitors, status by cancer type, such as lung cancer, gastric cancer, esophageal cancer, and urologic cancer.

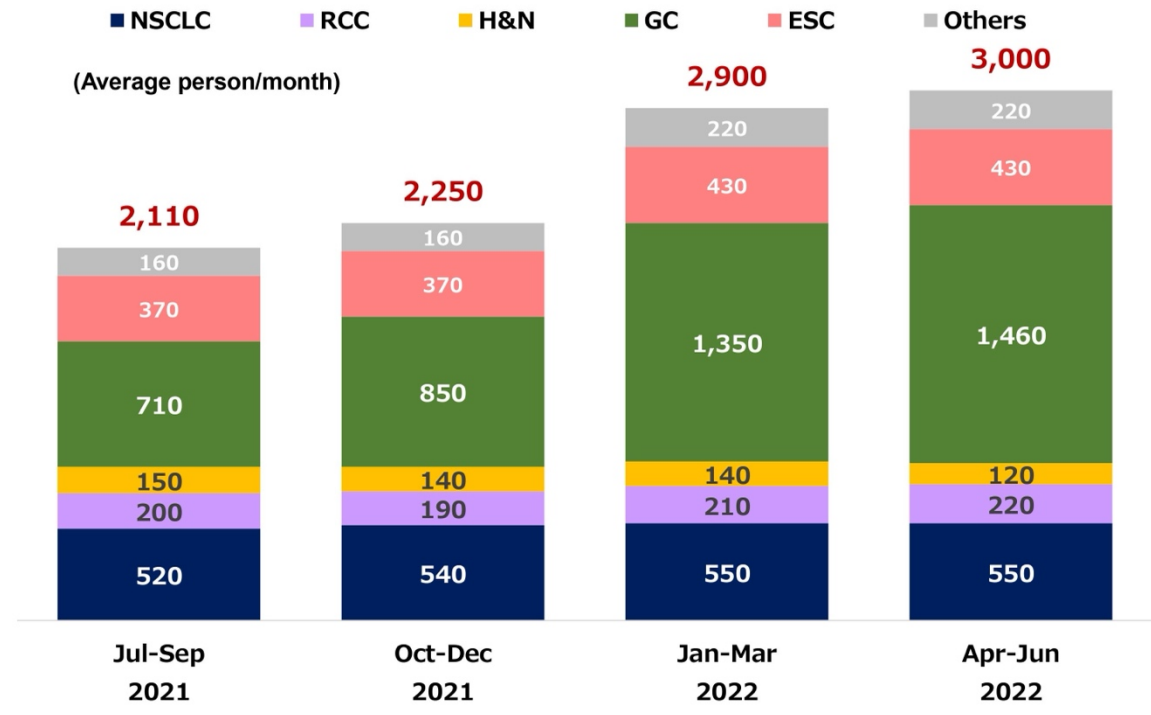
Sales Trend of Opdivo by Each Cancer



Source: Estimation from external and internal data

Sales for Opdivo in FY2021 were JPY112.4 billion. We expect sales of JPY155 billion in this FY .

Number of Patients Newly Prescribed with Opdivo by Each Cancer (Estimation)



Source: Estimation from external and internal data

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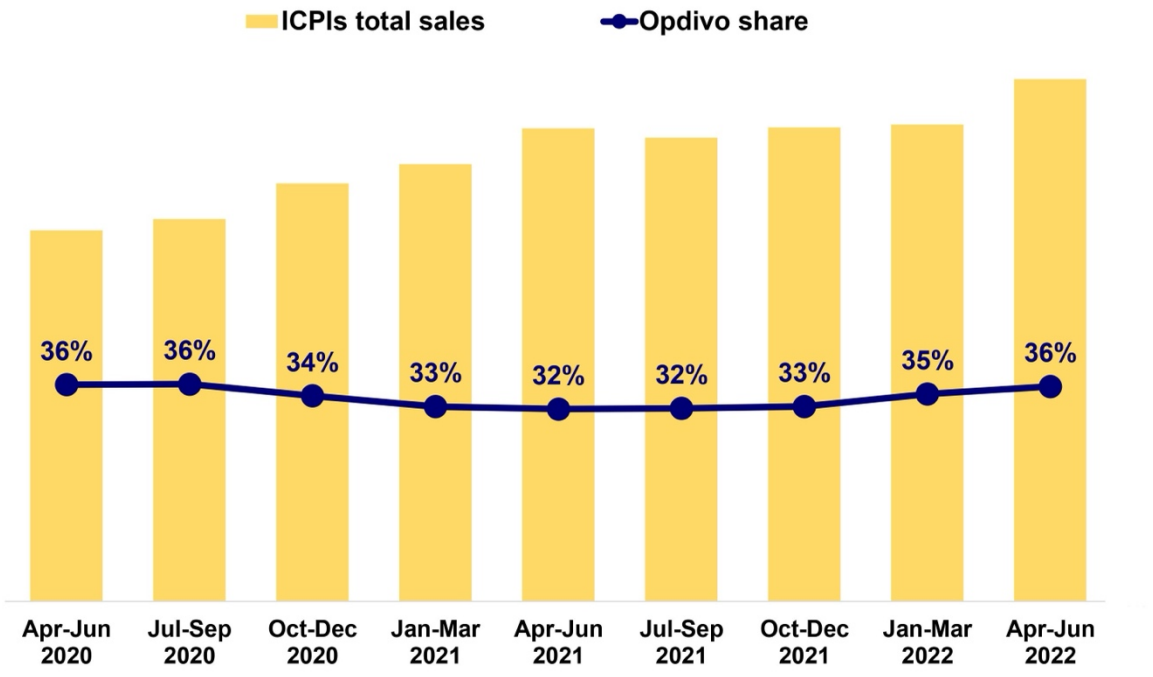
You see the estimated number of patients newly prescribed with Opdivo by cancer type broken down by quarter, from July to September 2021 to April to June 2022, with the average number of patients per month.

As an estimate, in April to June 2022, there were 1,460 cases of gastric cancer, of which nearly 800 were the first-line treatment. In esophageal cancer, there were 430 cases, of which about 100 were the adjuvant therapy. In lung cancer, there were 550 cases, including 420 for the first-line treatment. On average, there were 3,000 cases for new prescriptions per month.

Trend of total sales of ICPIs and Opdivo share

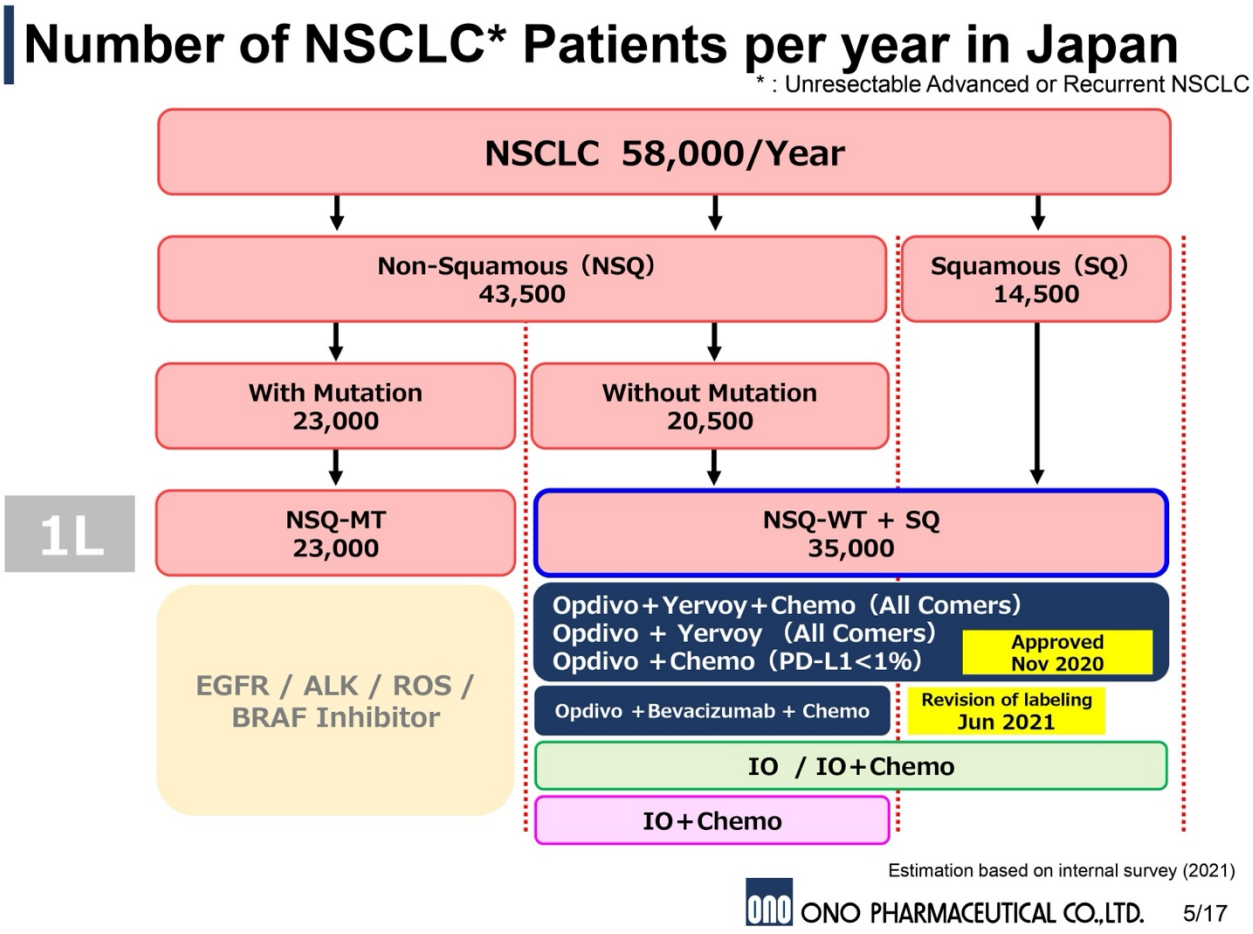


Source: External data

This slide shows trend of total sales of immune checkpoint inhibitors marketed in Japan and Opdivo's market share.

The yellow bar graph shows the total sales of immune checkpoint inhibitors, and the dark blue line graph shows the change in Opdivo's market share.

Total sales of immune checkpoint inhibitors have been increasing steadily, and despite the impact of the NHI price revision in FY2021, sales of all five products have been growing, with Opdivo share at 36%, remaining strong.



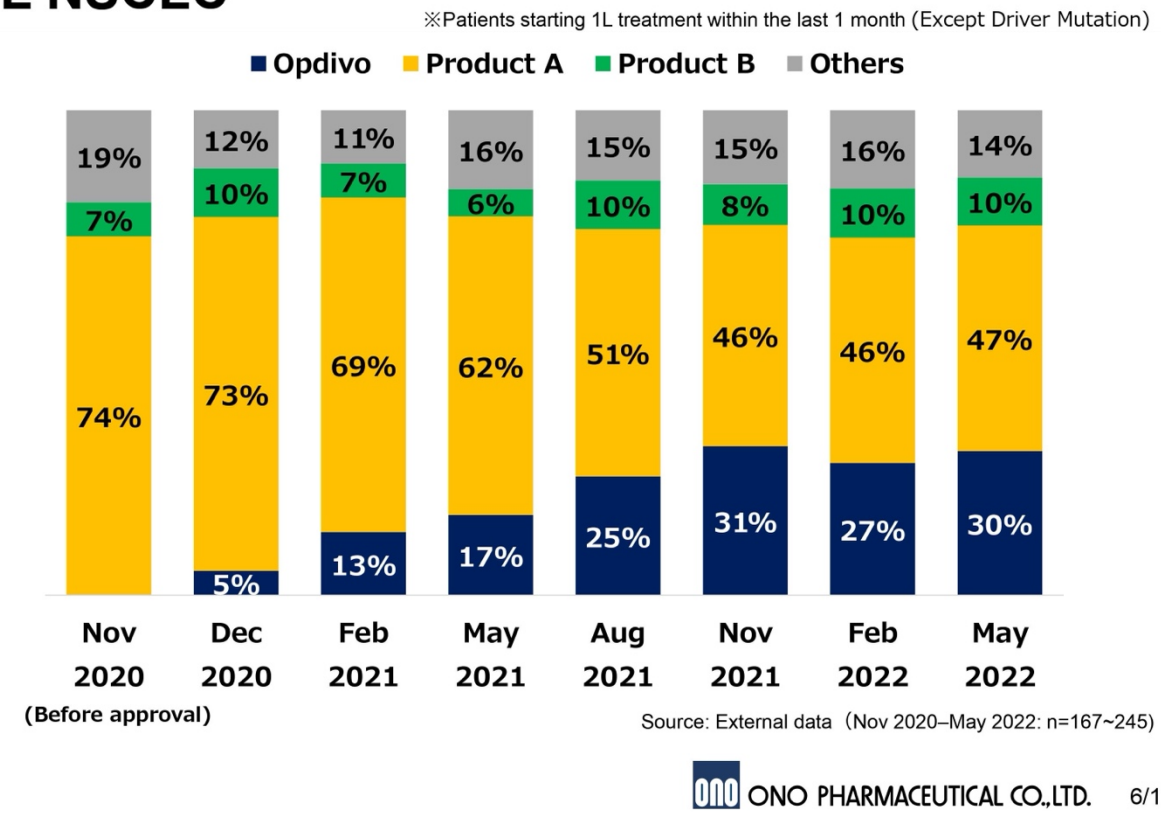
I will explain the annual patient number for non-small cell lung cancer in lung cancer area.

The annual number of patients with unresectable advanced or recurrent non-small cell lung cancer is estimated at 58,000 per year, although this is only our own estimate.

Non-small cell lung cancer is divided into non-squamous and squamous cell carcinoma by histologic type, and non-squamous carcinoma is further divided by the diagnosis with or without genetic mutation. The target indications for immune checkpoint inhibitors such as Opdivo in the first-line treatment of lung cancer are squamous cell carcinoma and non-squamous cell carcinoma without genetic mutations, where an estimated number of patients are 35,000 patients per year.

Although the competitive environment is currently severe, the two Opdivo combination regimens have been approved and available on the market in November 2020 and June 2021, respectively.

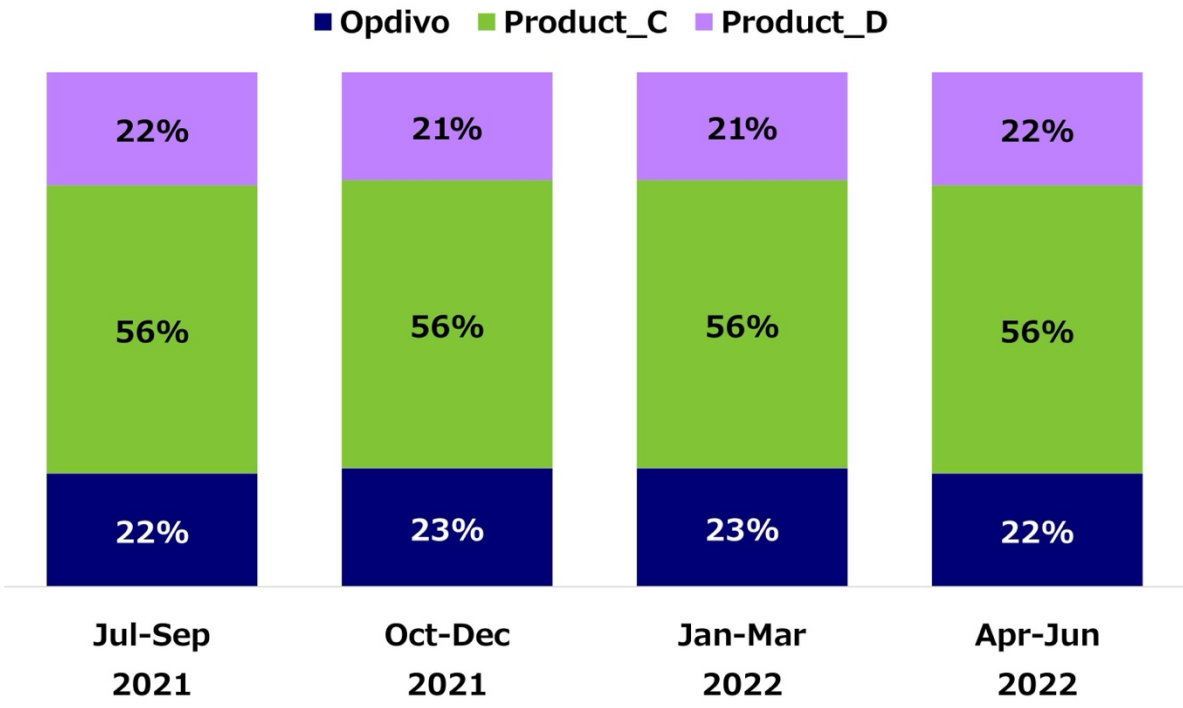
Prescription Ratio in Patients Newly Treated for 1L NSCLC



This slide shows the prescription ratio in patients for the first-line treatment of lung cancer.

Opdivo's share of new prescriptions was 30% as of May. Since the trend has been stagnant recently, we will further promote the usefulness of the IO/IO combination therapy of Opdivo and Yervoy, which is not available in competing products.

Sales Ratio of ICPIs in NSCLC (Estimation)

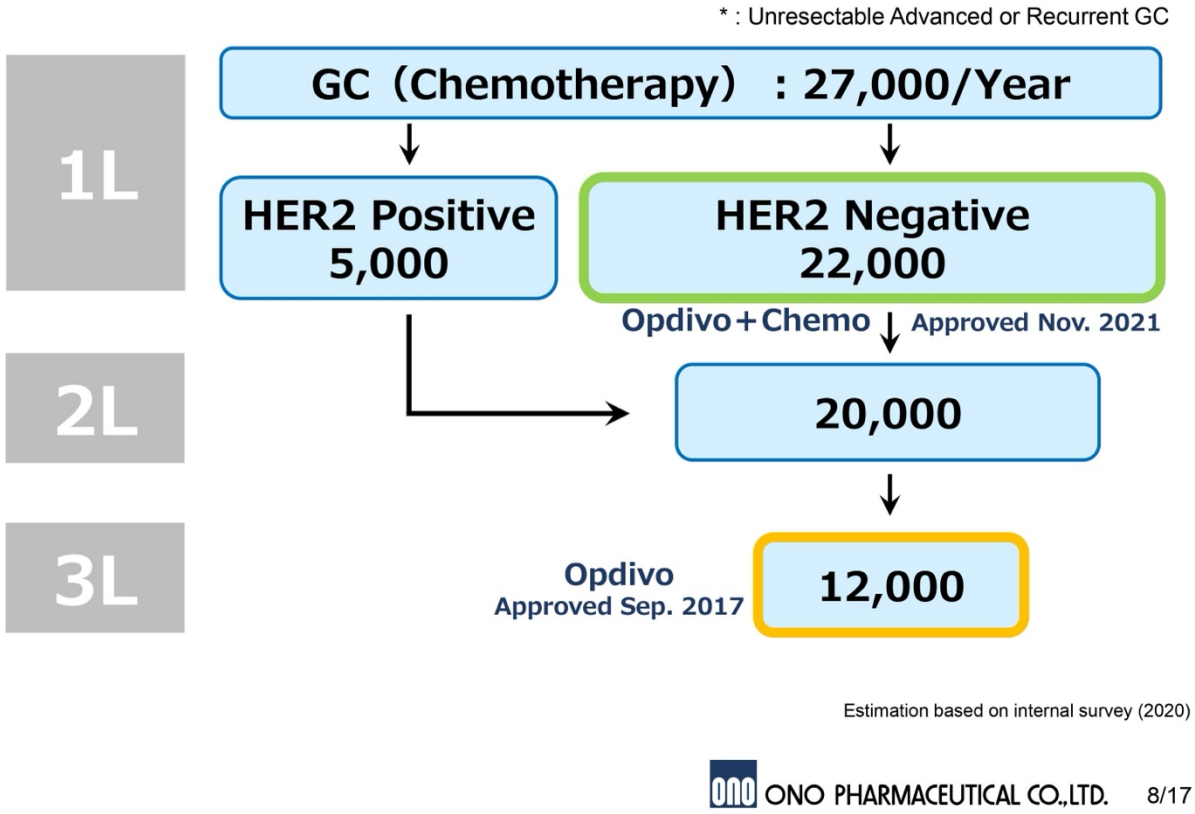


Source: External data

This slide shows the sales composition of immune checkpoint inhibitors in all non-small cell lung cancer lines, including first-line treatment and second-line treatment and beyond.

From the left, we show results for July to September 2021 through April to June 2022, broken down by quarter. In the April to June period, Opdivo accounted for 22% of the market, and we will strive for further growth in the first-line treatment of lung cancer.

Number of GC* Patients per year in Japan



Estimation based on internal survey (2020)

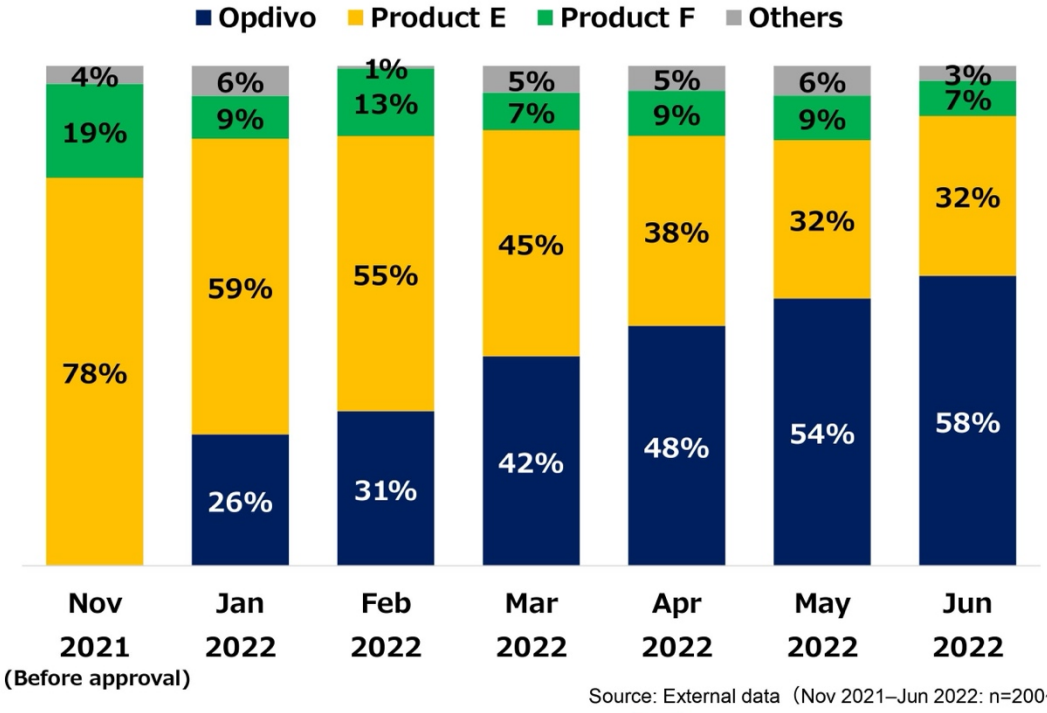
This slide shows the annual number of patients with gastric cancer.

The annual number of patients with unresectable advanced or recurrent gastric cancer is estimated at 27,000, although this is only an in-house estimate.

In November 2021, Opdivo was approved in combination with chemotherapy in first-line HER2 negative patients. Therefore, we estimate that the number of patients who are eligible for Opdivo is 22,000 per year.

Prescription Ratio in Patients Newly Treated for 1L GC

※Patients starting 1L treatment within the last 3 month



Source: External data（Nov 2021–Jun 2022: n=200~204）

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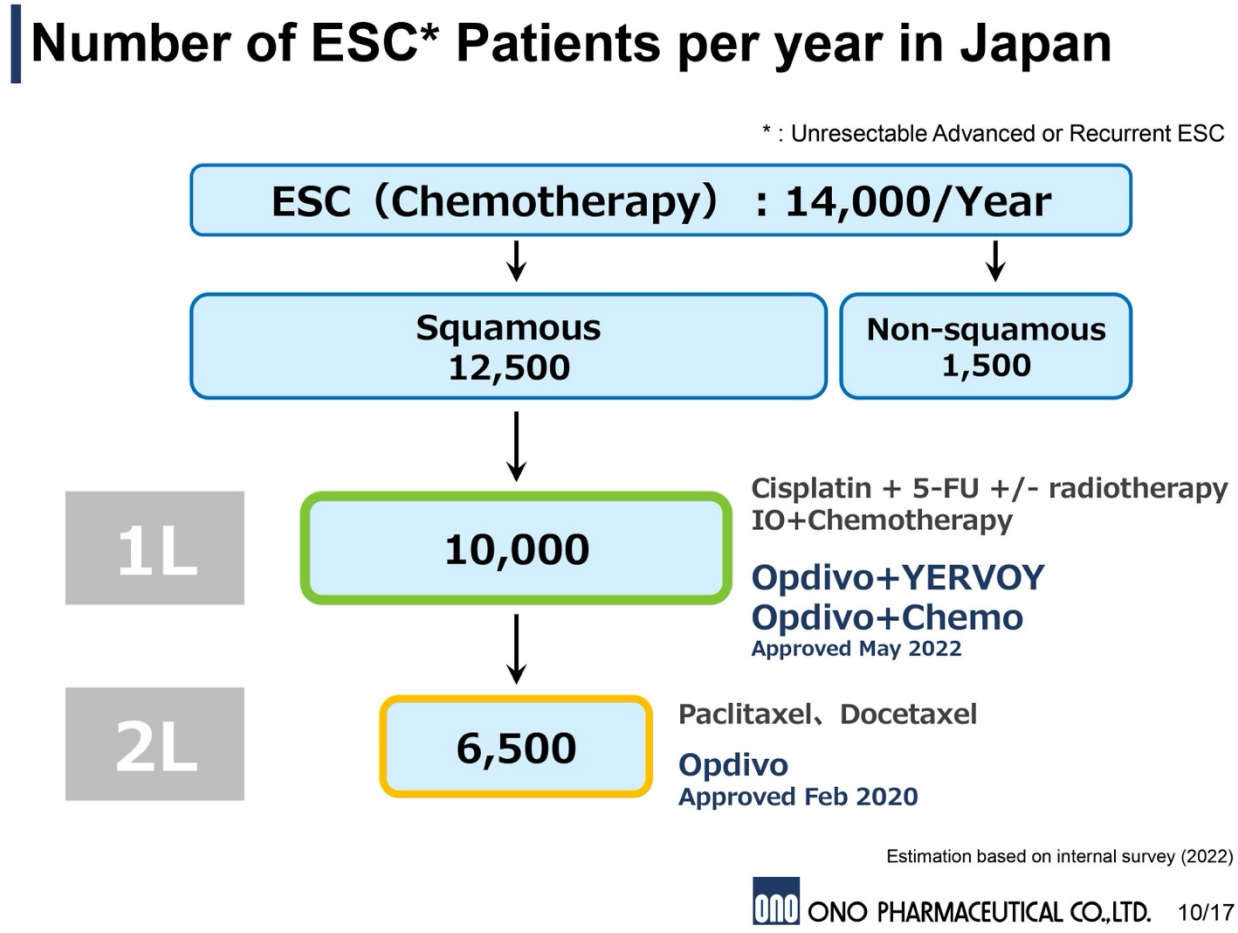
The slide shows the share of new prescriptions in the first-line treatment of gastric cancer.

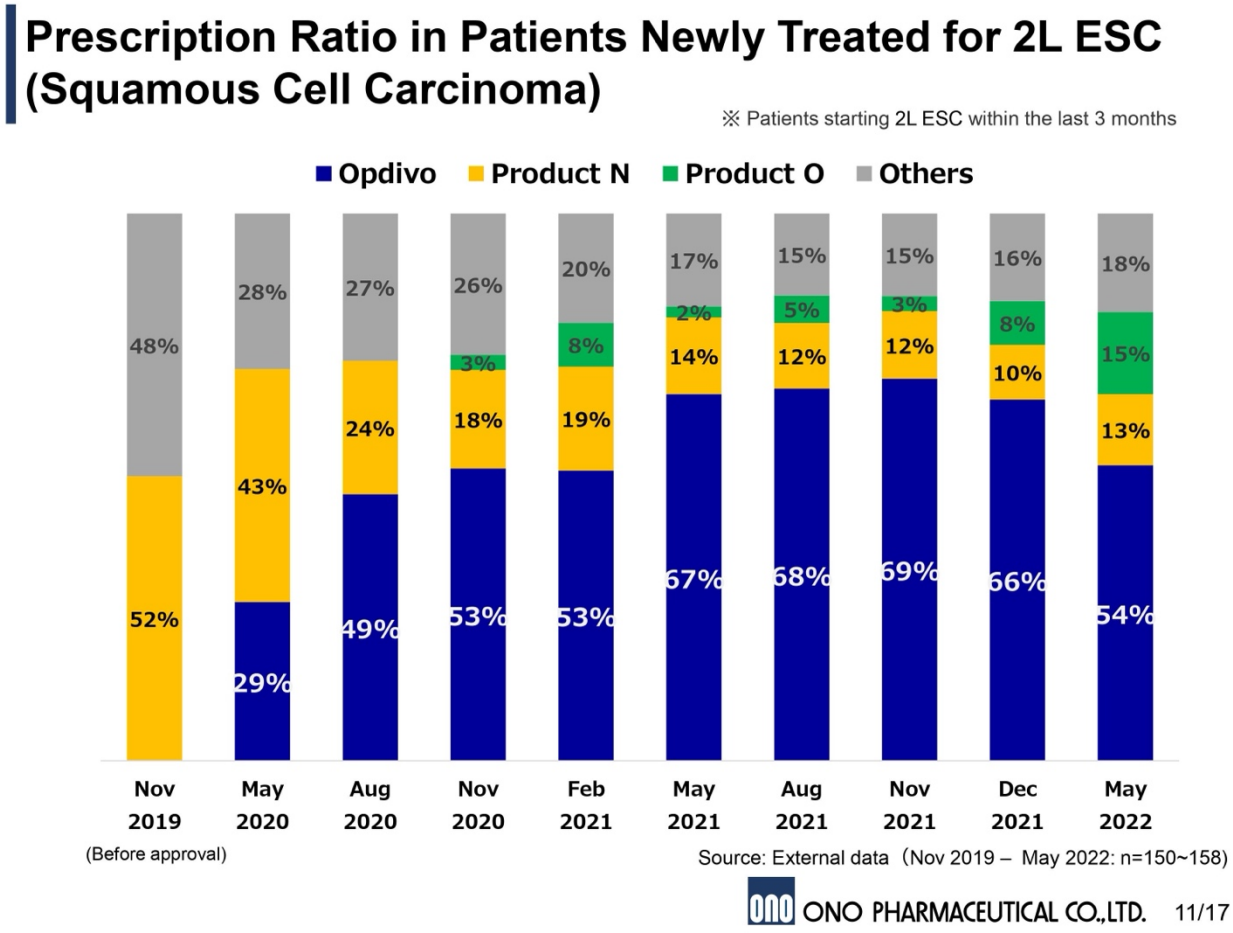
As of June, Opdivo's share of new prescriptions for first-line therapy was 58%.

Prescriptions are steadily increasing, and we expect to reach our target peak market share of 65% within 18 months of approval, with significant peak sales expected over the next several years as the number of patients newly treated builds up.



Next is the area of esophageal cancer.

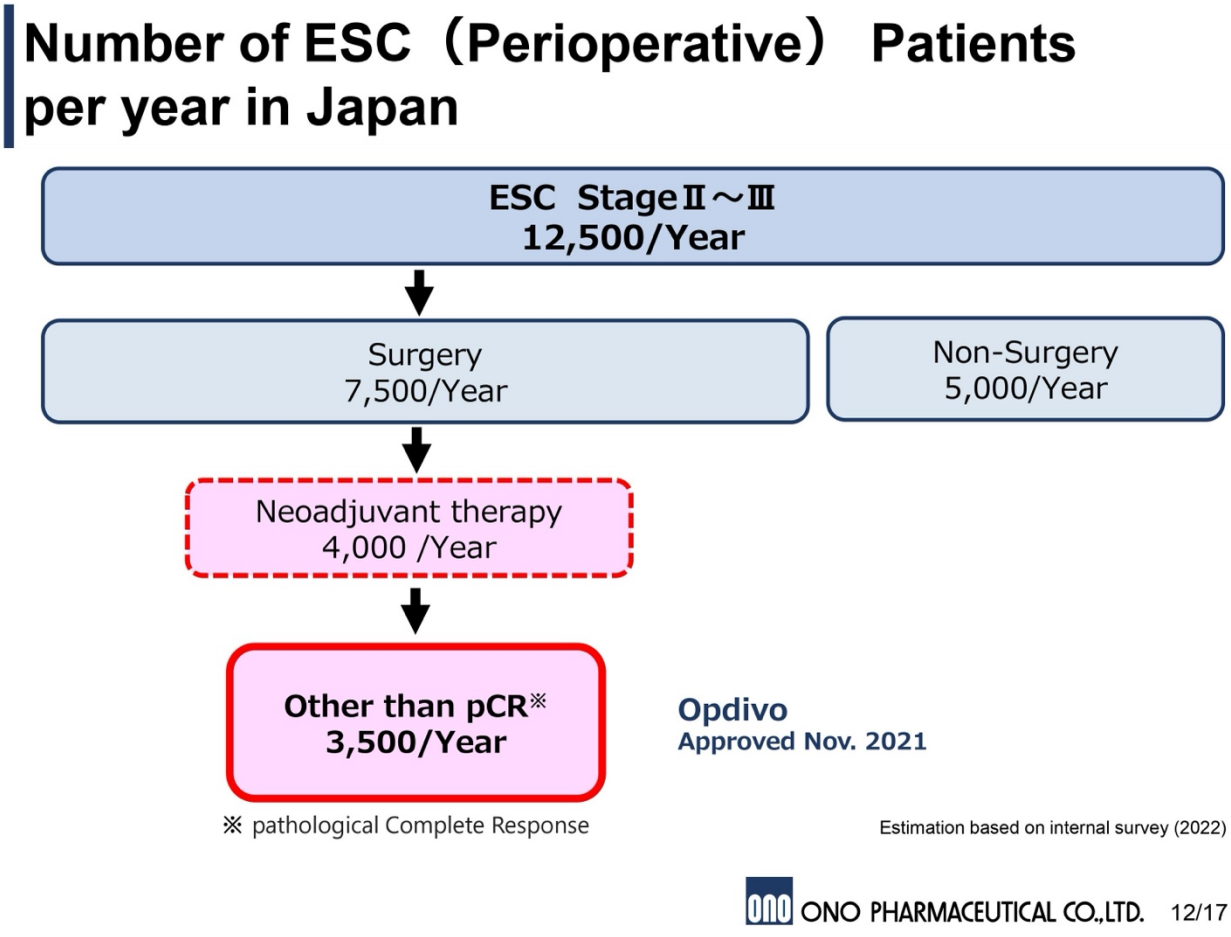
In May 2022, we received approval for the combination of Opdivo and Yervoy, as well as Opdivo and chemotherapy regimen, for the first-line treatment of unresectable advanced or recurrent esophageal cancer. The first-line treatment target is squamous cell carcinoma, and the number of eligible patients is considered to be 10,000.



Since the first-line treatment of esophageal cancer is just approved, today I will introduce the new prescription ratio for the second-line treatment.

Since an IO competing product was approved for first-line treatment last year and its use has been expanding, the number of IO-naive patients in second-line treatment has decreased, and the prescription rate of Opdivo for second-line treatment is 54% now. But, if we focus on IO-naive patients, Opdivo is used in nearly 70% of them.

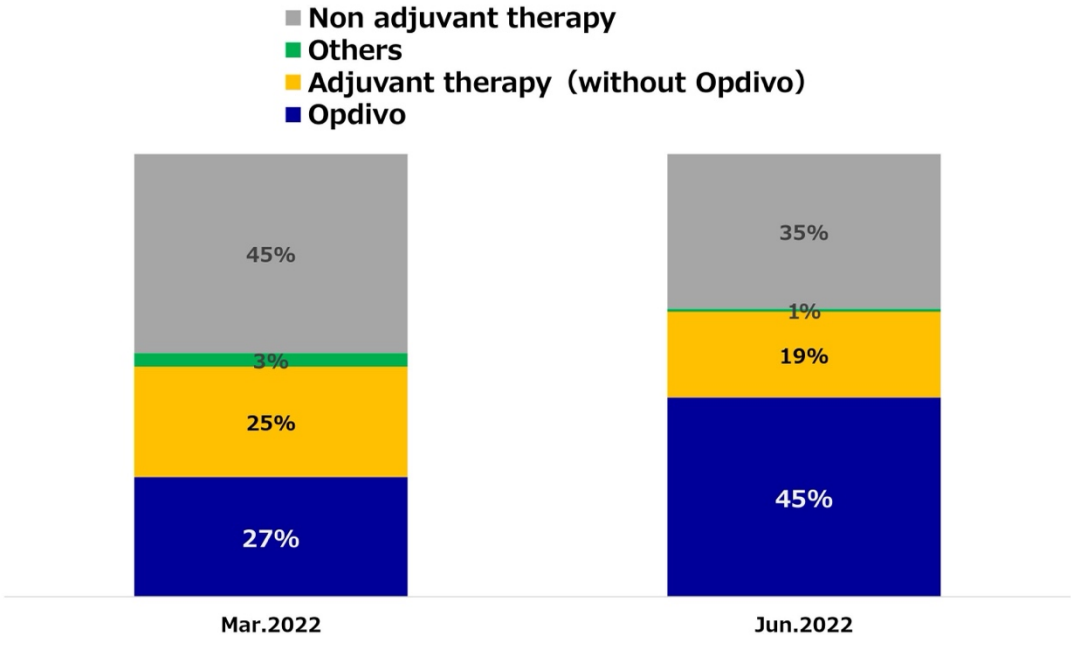
The Opdivo regimen was approved for first-line treatment in May 2022. As for the results of the number of prescriptions for the single month of June, we have confirmed more than 100 new prescriptions based on MR reports. We will continue to aim to further expand prescriptions in the first-line treatment area.



Then, I will explain the number of patients with perioperative esophageal cancer, which we received approval for November 2021.

The number of patients with stage II to III esophageal cancer is estimated to be 12,500 per year, of which 7,500 are eligible for surgery. Of those patients, we estimate that 4,000 will receive neoadjuvant therapy and 3,500 will be eligible for Opdivo adjuvant therapy with non-pathologic complete response.

Prescription Ratio in Patients Newly Treated for ESC (adjuvant therapy)



Source: External data (Mar 2022 – Jun 2022: n=150)

※Patients starting treatment within the last 3 month

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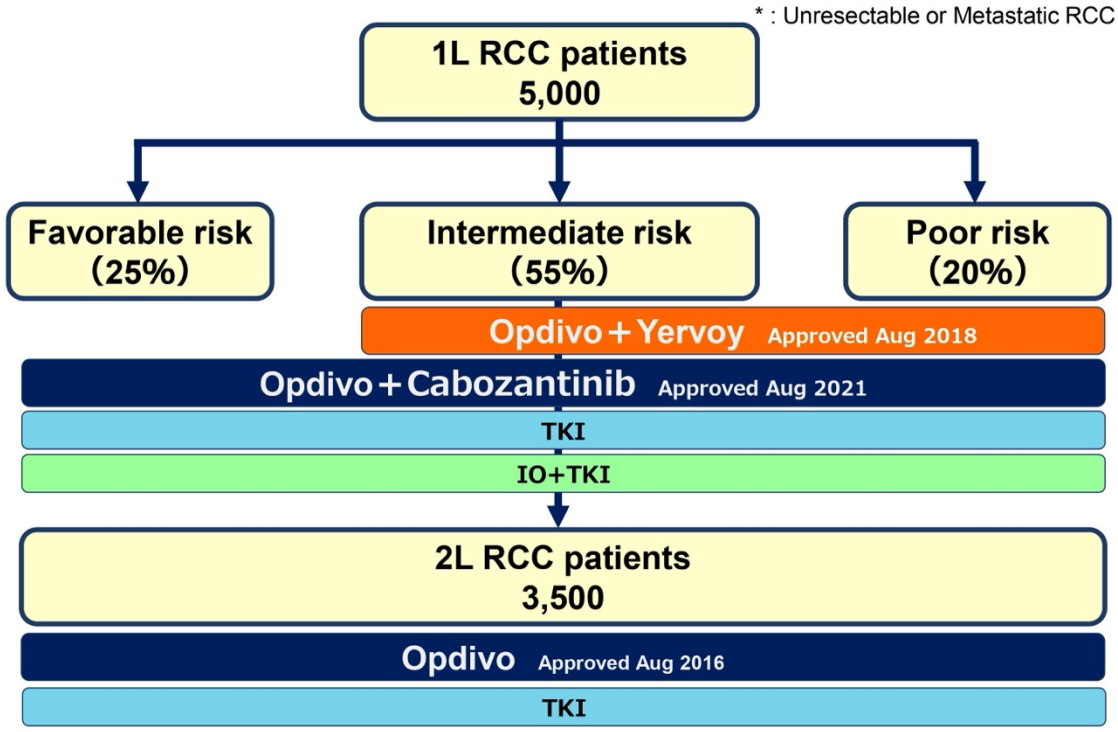
The Opdivo share in the area of ESC adjuvant therapy, which we received an approval in November 2021, was 45% as of June. It has been evaluated by KOL as a useful treatment option for patients who did not receive CRT before surgery or did not achieve pathologic complete response after surgery, without safety concerns, and is being considered for introduction, taking into account the risks and benefits.

However, there remain many patients who have not yet received postoperative adjuvant chemotherapy, and we will continue to raise awareness about the benefits of Opdivo.

Number of RCC* Patients per year in Japan

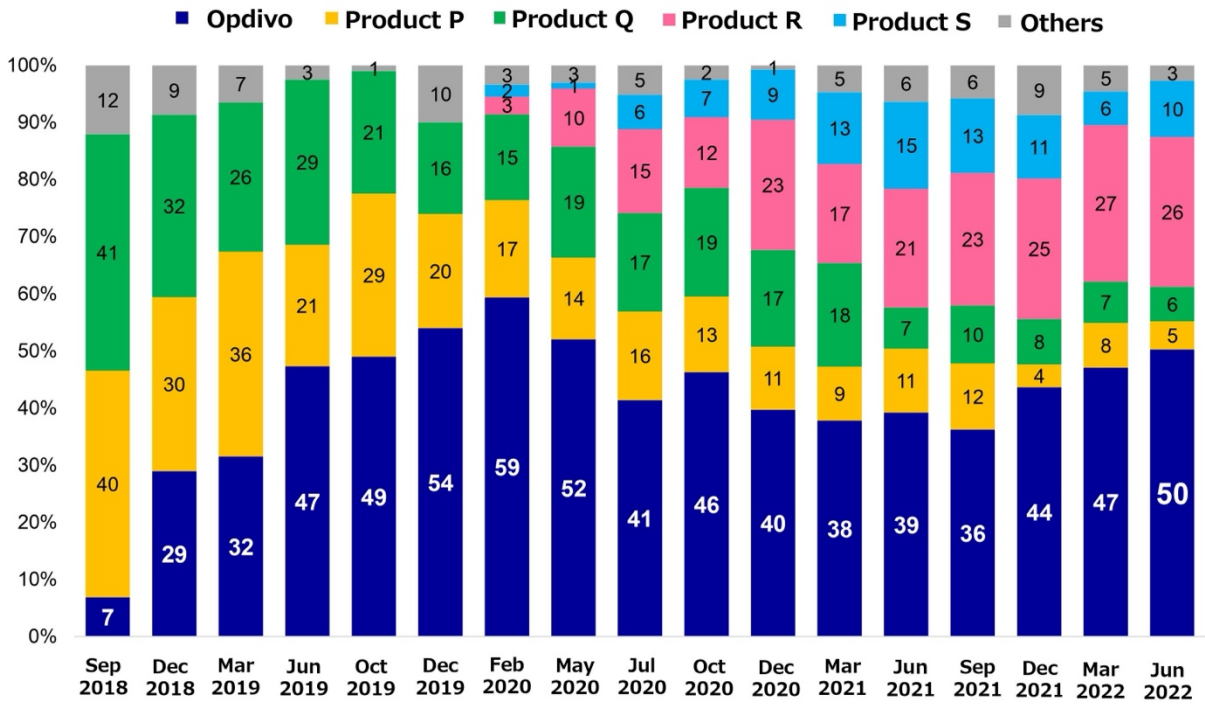


Estimation based on internal survey (2022)

Next is renal cell carcinoma.

Opdivo has all the evidence for first-line and second-line treatment and beyond, and we are working to bring Opdivo to all renal cell carcinoma patients.

Prescription Ratio in Patients Newly Treated for 1L RCC

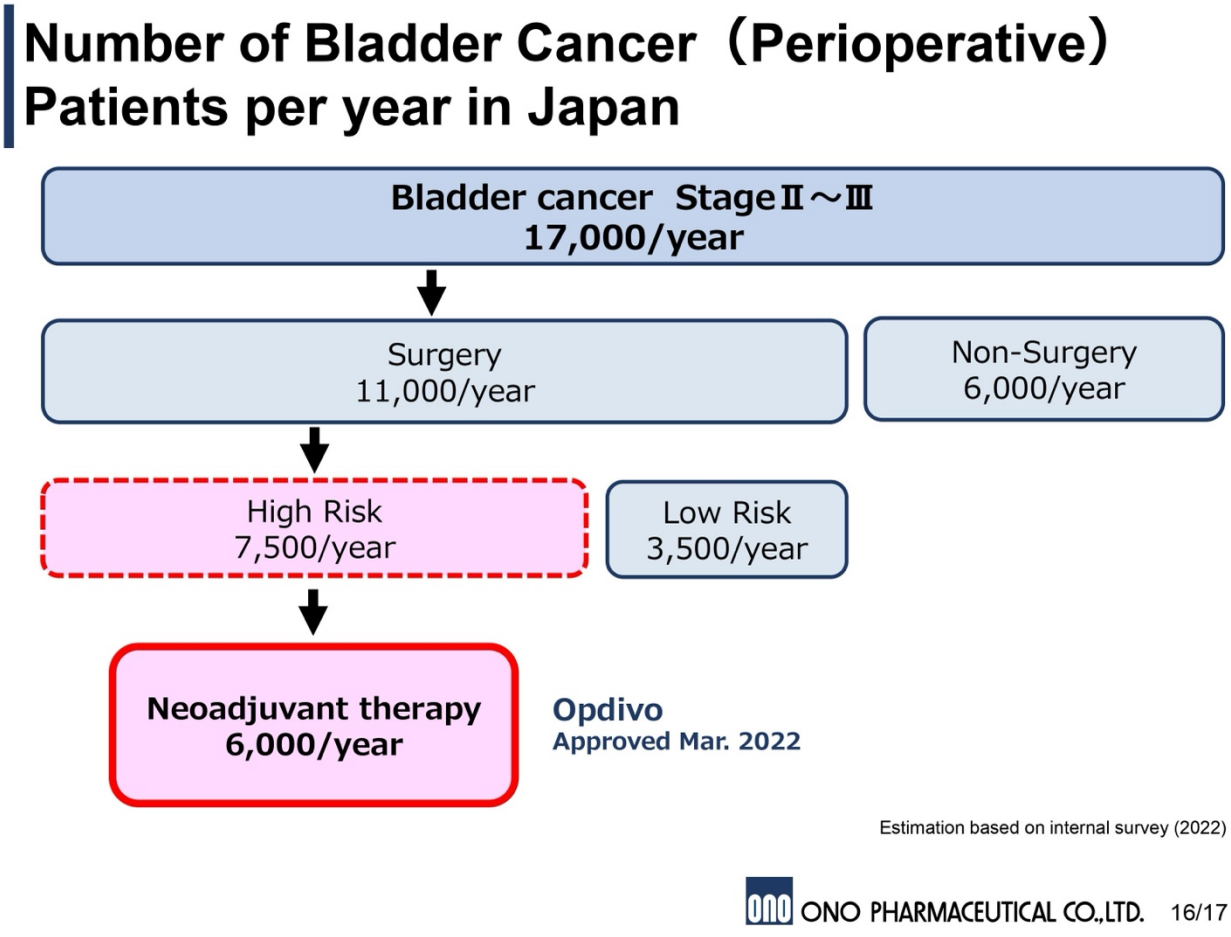


Source: External data（Sep 2018–Jun 2022: n= 46~110)

This slide shows the prescription ratio in patients newly treated for first-line renal cell carcinoma.

In first-line treatment, prescriptions for IO combination therapy have been expanding, with nearly 90% of cases being recently treated with IO combination therapy.

The prescription ratio in patients newly treated for Opdivo/Yervoy and Opdivo/TKI combination therapy is 50%, with new acquisition share of 15% for low risk, 50% for intermediate risk, and 75% for high risk.

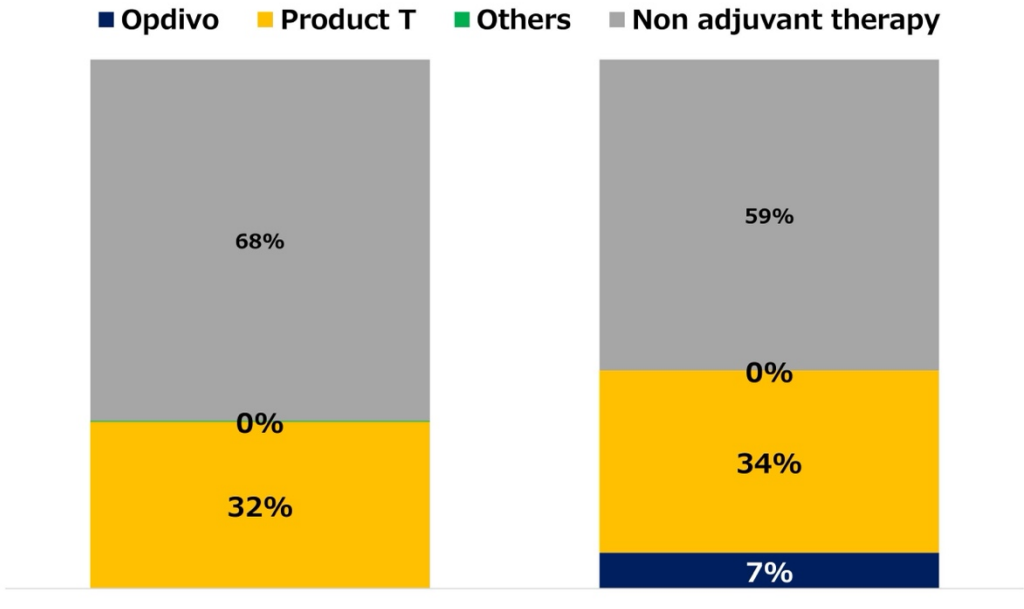


Finally, urothelial carcinoma.

Urothelial carcinoma is a cancer that develops in the inner urothelial mucosa of the renal pelvis, ureter, bladder, and urethra. In Japan, bladder cancer accounts for 80% of all urothelial carcinoma. Today, I will introduce the number of patients with adjuvant treatment of bladder cancer.

The number of patients with stage II to III bladder cancer is estimated to be 17,000 per year, of which 11,000 are eligible for surgery. Among these patients, we believe that the number of high-risk patients with a high recurrence rate is 7,500, and the number of patients who are eligible for postoperative adjuvant therapy with Opdivo and who will receive preoperative adjuvant therapy is estimated to be 6,000.

Prescription Ratio in Patients Newly Treated for Bladder Cancer（adjuvant therapy）



※Patients starting treatment within the last 3 month

Source: External data（Jan 2022–Jun 2022: n=200）

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As of June, Opdivo had a 7% share of new prescriptions for adjuvant treatment of urothelial cancer, for which we received an approval in March of this year. Opdivo has not yet penetrated the market.

The KOL says that post-resection recurrent patients with muscle layer invasive urothelial carcinoma have a poor prognosis and no treatment options, and therefore, it is important to prevent recurrence. It has also suggested that Opdivo postoperative adjuvant therapy holds great promise as a promising option to improve DFS and prevent recurrence.

Since 60% of patients do not receive postoperative adjuvant therapy, we will continue to raise awareness of the usefulness of the Opdivo regimen so that it can be evaluated as a necessary treatment option.

I introduced the general situation of Opdivo, in areas of lung cancer, gastric cancer, esophageal cancer, and urologic cancer. We will continue to strive to meet the unmet needs of cancer patients.

Question & Answer

Questioner 1: Please advise me of the actual royalty for the period, for example, the impact of the exchange rate on royalty income, average exchange rate for the period?

Nagahama: The assumed exchange rate was JPY110. During Q1, the average exchange rate was in a range of around JPY128 and JPY129.

Questioner 1: Is it right to think that there is a possibility of a review of the exchange rate including Q2?

Nagahama: We will continue to consider the necessity to revise the assumed exchange rate, but would appreciate it if you could consider that it is necessary to assess the exchange rate at this point.

Questioner 1: Regarding ONO-2020, epigenetics, I think that it has been leading the way in some areas of anticancer drugs. I would appreciate it if you could briefly introduce your company's approach to epigenetics and your expectations for ONO-2020 in the future.

Idemitsu: As for ONO-2020, it came from research on epigenetics for neurodegenerative diseases. Please understand that it does not come from the research on epigenetics regardless of therapeutic areas, but from the project of epigenetics targeting at neurodegenerative diseases. It is still in early clinical development stage. As we have high expectations, we hope you could wait and see a little more.

Questioner 1: Although you commented on the target indication still in a broad sense, is it possible to narrow it down?

Idemitsu: I hope you will wait a little longer.

Questioner 1: Lastly, about Opdivo, the new prescription ratio for adjuvant therapy for esophageal cancer is expanding to 45%, while it is decreasing to 35% from 45% in non-adjuvant therapy. Can I understand the share change?

Takahagi: There was originally no standard adjuvant therapy for esophageal cancer. Therefore, most of patients have not received adjuvant therapy for esophageal cancer. Since Opdivo has entered the market, the awareness of adjuvant therapy for postoperative esophageal cancer has been gradually expanding. However, only about 60% of patients are still receiving adjuvant therapy, including Opdivo and other drugs, so the remaining nearly 40% of patients are still untreated. We will strive to acquire this remaining 40% mainly for Opdivo regimen.

Questioner 1: On page 12, you said that the target patients would be around 3,500. May I understand that you have reached the point where you can acquire about half of them.

Takahagi: Yes. You are right.

Questioner 2: I think you are steadily expanding your market share of Opdivo first-line treatment for gastric cancer. In the past six months, has there been any anything of concern in terms of actual results, such as duration of administration, or discontinuation rate?

Takahagi: Overall, we consider the situation to be solid. However, as an issue, there is strong evidence that Opdivo has been favorable for CPS 5 and above. On the other hand, I heard that there are many cases in which doctors are not sure whether to use Opdivo regimen for patients with CPS less than 5 or negative CPS, or

patients whose CPS has not been measured. For this reason, it is also true that the intention to prescribe remains at about 40% in patients whose CPS is less than 5 or whose CPS is not measured. Therefore, we would like to further raise awareness of its usefulness in such patient population, in order to further expand this segment. However, we have just started it, and my impression is that there are not so many concerns in the administration period and other factors.

Questioner 2: Thank you very much. I think you are almost at the point of achieving 65% or 70% penetration by the end of this fiscal year. I think that after the 70% penetration by the end of the fiscal year, there will be an increase in sales due to the increase in the number of patients for a little less than a year. Is it correct to assume that the growth of the first line for gastric cancer will stop in the same way as for lung cancer?

Takahagi: As for the new prescription ratio in patients, we expect to bring it to a peak around this fiscal year. As for the sales that will come out of this, especially this fiscal year and next fiscal year, I think it will probably take about 1.5 to two years after peak share is reached for peak sales to be reached. Therefore, we have the image that sales from Opdivo for the first-line treatment of gastric cancer will gradually grow still in FY2024.

Questioner 2: Lastly, I looked at Bristol's financial results. Please tell us briefly about the domestic schedule of Opdualag, the combination with anti-LAG-3- antibody.

Idemitsu: Opdualag, a combination drug with anti-LAG-3-antibody, is currently in Phase I and II in Japan. We are currently discussing with BMS future application policy, and we will decide the specific schedule and other details in the future.

Questioner 2: I guess, we shouldn't have expectations too much in Japan, as this is for melanoma, right?

Idemitsu: Regarding expectations, do you mean sales?

Questioner 2: Yes.

Idemitsu: With regard to the sales for melanoma, we need to examine in the future.

Tsujinaka: I would like to add some additional explanation on the impact of the exchange rate on the royalty income. If we look only at BMS and Merck, total royalty income from BMS was JPY3.8 billion, local sales were JPY0.6 billion, and the impact of foreign exchange was JPY3.2 billion. Total royalty income from Merck was JPY3 billion, local sales were JPY1.6 billion, and a positive currency impact was about JPY1.5 billion.

Questioner 3: In the presentation on Opdivo, you explained neoadjuvant for esophageal cancer and bladder cancer. How much is the neoadjuvant therapy contributing to sales? In addition, you expect that the submission for the expansion of the neoadjuvant application for non-small cell lung cancer will be approved in H1 of this year. I would like to know how much this will be used. Though I think there is a lot of variability in the timing, would you please advise me of your expectation?

Takahagi: Just to confirm, first of all, you are asking about postoperative adjuvant for urothelial carcinoma, right?

Questioner 3: Yes.

Takahagi: As I reported, the postoperative adjuvant for urothelial carcinoma is still difficult. The reason for this is because no standard therapy has not been established for postoperative adjuvant therapy for urothelial carcinoma. Therefore, Opdivo has opened the door to this standard of postoperative adjuvant therapy. For this reason, we do not anticipate any major sales for the current fiscal year.

However, we believe that this field will grow in the future, and we would like to bring our total sales up to the level of the sales in the field of renal cell carcinoma, where we have been working in the field of urology. We would like to proceed with the activities to ensure the efficacy and safety of the product. That is the situation about urothelial carcinoma.

Questioner 3: For urothelial carcinoma, you have already received an approval for neoadjuvant therapy, right?

Takahagi: No, we have received the approval for postoperative adjuvant therapy.

Questioner 3: Not yet received for preoperative period?

Takahagi: No, not yet.

Questioner 3: Could you tell us about non-small cell lung cancer, esophageal cancer, and bladder cancer?

Takahagi: First of all, the submission for the neoadjuvant therapy of non-small cell lung cancer is currently under review. As for neoadjuvant therapy, Opdivo should be administered up to three times at a dose of 360 mg each. Also, in terms of preoperative adjuvant therapy, as no standard treatment has not been available, we estimate that the number of patients who will be treated with Opdivo is about 5,500. In this context, we would like to deliver the product to about 50% of patients with neoadjuvant therapy for non-small cell lung cancer.

Questioner 3: Is the situation the same for esophageal cancer and bladder cancer?

Takahagi: Do you ask about postoperative adjuvant treatment for esophageal cancer? The postoperative treatment duration for esophageal cancer is within one year.

Questioner 3: Within a year. We have already discussed all cancer types for the adjuvant treatment, haven't we?

Takahagi: We are now looking at postoperative adjuvant treatment for esophageal cancer and urothelial cancer. Also, the approval of neoadjuvant treatment for non-small cell lung cancer is now underway.

Questioner 3: And just one more thing, now that you mentioned royalties, can you update us on how the lawsuit with AstraZeneca regarding Imfinzi is going right now?

Tsujinaka: The case is still pending and has not yet been settled. We would appreciate it if you could give us a little more time.

Questioner 3: Do you say that the lawsuit with Dana-Farber in the US is ongoing as well?

Nagahama: Yes, it is ongoing.

Questioner 4: I have two questions. First, I would like to know the impact of the exchange rate in Q1 period. At the beginning of the period, I think you mentioned that JPY1 depreciation would increase operating profit by JPY0.8 billion. Looking at the full-year period, can we expect that this remain the same? Would you please let us know whether the Q1 period results were positive or negative when the impact of the exchange rate is excluded in Q1 period?

Nagahama: In Q1 period of the current fiscal year, as for the foreign exchange sensitivity, we expect that JPY1 will increase operating profit by about JPY0.8 billion, as we assumed at the beginning of the fiscal year. The current revenue is just about 25% of the planned annual revenue.

We expected that revenue will gradually increase on a monthly basis toward H2 of the year. In Q1 of the current fiscal year, however, revenue has reached to approximately 25% of the annual revenue, which we did not expect, due to the so-called revenue increase effect from the exchange rate.

Questioner 4: The R&D expenses seem a bit large. Can I understand that this is due to the foreign exchange impact? Can I understand that you are progressing as planned?

Nagahama: There is a little bit exchange rate impact on the R&D expenses, but there is no big change in our current estimation of the impact on the annual R&D expenses.

Questioner 4: Secondly, regarding Opdivo adjuvant treatment, you explained adjuvant treatment for esophageal cancer and urothelial cancer. My impression is that if there is already a standard therapy for postoperative adjuvant, it would be relatively fast. I also have the impression that it will be difficult to exploit the remaining share of prescription in patients in this area where no standard therapies have established.

There is chemotherapy as a standard therapy for gastric cancer adjuvant in terms of marketing. Based on the response you are getting now, can you give an outlook, if any, on the adjuvant for gastric cancer, for which you will be getting the results of the trial in the future?

Takahagi: The market for adjuvant therapy for gastric cancer, is very large. As you say, there is a firm standard of care. In this sense, it is slightly different from what we have been experiencing now. At present, of course, we need to wait and see what kind of data will emerge in the end, but we would like to proceed with our strategy and policy in our efforts based on the data.

However, in the field of esophageal and gastric cancer, we were the first manufacturer to enter the market with Opdivo and IO. We have accumulated a great deal of experience in the area of esophageal and gastric cancers. We would like to promote the efficacy and safety of the drug to doctors once the indication is added.

We would like to continue our activities so that we can maintain our position as a top runner in the field of digestive organs.

Questioner 4: So, as there is a solid standard therapy for gastric cancer, you need to wait for the data being available.

Takahagi: You are right. We believe that it will be fully penetrated.

Nagahama: I would like to add one point regarding your earlier question on foreign exchange. As you know, the yen has been steadily weakening since the beginning of the fiscal year, but we have not changed our outlook for the dollar/yen exchange rate sensitivity of JPY0.8 billion on operating profit.

However, I would like to explain one point that the euro is now weaker against the dollar. In the European region, we will convert local Opdivo sales in Euros into US dollars, which will then be used to generate royalty income for our company, while multiplied by a certain rate. In this period, the euro has been weakening against the US dollar. Taking into consideration exchange rate sensitivity including these factors, we are investigating the impact of exchange rate on the full-year forecast results.

Questioner 5: I have two points. The first is the predictability of the Opdivo trial. I am honestly a bit shocked by the results from CheckMate-914 trial. The KEYNOTE-564 trial showed that Keytruda alone reduced the risk of death by 32% versus placebo in renal cell carcinoma, right? As Opdivo and Yervoy were co-administered in CheckMate-914 trial, I thought it had a higher chance of success.

I was wondering why this is failing. I think that adjuvant is usually successful if the first line is successful. Surgery is an act of antigen dissemination, which probably makes PD-1 more effective. I thought it was a pretty

neat story, adding CTLA-4 to it. But in fact, if we see carefully, this is your second case of adjuvant failure in combination with Yervoy, isn't it?

Considering that even the CheckMate-915 trial for melanoma adjuvant treatment failed to make a difference, I am also thinking about its effect on CheckMate-9DX for hepatocellular carcinoma. Why didn't it work with the adjuvant treatment with Opdivo and Yervoy? Can you please suggest something?

Idemitsu: We have the same idea that if Opdivo alone therapy is effective in a certain type of cancer, the effectiveness will increase when Yervoy is combined with Opdivo. Based on such an idea, we have tried the combination therapy of Opdivo and Yervoy. We need to scrutinize the data to clarify why we are not able to show the effectiveness in the combination therapy. At this point, we are not able to clearly reply to your question.

Questioner 5: Secondly, as I have just heard at financial results briefings in Europe and the United States, the focus of attention of American analysts is now on Factor XIa inhibitors. I think that J&J's AXIOMATIC-SSP trial may achieve its primary endpoint of stroke prevention and will proceed to Phase III trials. In addition, I think the competitor Bayer's asundexian also had good results. How is your ONO-7684 progressing now?

The data of PK in the Phase I study is disclosed, but even with the maximum repeated dosage of 250 mg, only about 80% to 90% of activity of the factor XIa was inhibited. When we look at asundexian, it was inhibited nearly 100%. Milvexian also inhibited considerably. I think they are doing this in the first place, because Factor XI deficiency patients are at less risk for bleeding. I think that European competitors are trying a higher dose now in the Phase I trial.

For abelacimab, the Phase III trials have been ongoing ahead in direct comparison with Eliquis in 1,655 patients. I think that the number of patients is relatively small. I wonder if they can make a difference in bleeding risk with such a small number of patients.

Idemitsu: For ONO-7684, an inhibitor of Factor XIa, it is currently in Phase I. We have been selecting the promising indication, while preparing for the next trial. For strategic reasons, we are not going to give details at this time.

Questioner 5: To make a difference in bleeding risk in comparison with the current NOAC, is it correct to understand that you don’t need many patients? I thought that you will be able to conduct Phase III by yourself.

Idemitsu: To make a difference in bleeding risk and prognosis, we need a certain number of cases.

Questioner 5: I thought that you probably need about a few thousand cases.

Idemitsu: I'm sorry, this is a strategic matter, so I'm not going to answer any further.

Questioner 6: Regarding the exchange rate for Q1, I understand that the average rate was JPY128 compared to the JPY110 assumption. Due to the weak euro, it seems that the income was affected, while I thought it was a little bigger. In addition to this, you have inventory of JPY42.6 billion, which is about 40% of revenue for Q1. I thought that this was considerably compressed due to the rapid depreciation of the yen at the end of the period, and the impact of the so-called elimination of unrealized, but isn’t this correct?

Nagahama: What did you just say about the inventory?

Questioner 6: Your company has JPY42.6 billion in inventory at the end of Q1.

Nagahama: That is product inventory.

Questioner 6: Yes, that's right. Due to the sharp depreciation of the yen at the end of the period against the foreign exchange, so naturally, you are eliminating that portion of the profit once. The so-called elimination of unrealized income in accounting. Partly due to this, I thought there was more benefit from the exchange rate in Q1, but surprisingly there wasn't.

Nagahama: As for the unrealized profit, profits from internal transactions are offset. It was not a large figure for Q1, so, there was nothing to be noted.

Questioner 6: As the operating profit of JPY145 billion is based on the assumption of JPY110, if we simply multiply by JPY135, it would be about JPY20 billion higher. Can I understand that this simply multiplied figure is not so misleading?

Nagahama: As I mentioned earlier, we need to consider the impact on the weak euro and other factors in Europe. Since the rate of return on royalties is higher in regions outside of North America, we expect that there will be a certain degree of impact. While the impact of the dollar/yen is significant, we assume that there will be some impact from Europe.

Questioner 6: So, we don't have to think so much about factors of cost increase.

Nagahama: There are also factors that can inflate costs. I would like to give you a little information on royalties. I mentioned an increase of JPY0.8 billion in profit. Although this is an internal assumption, we expect an increase of JPY1.1 billion in revenue and an increase of JPY0.3 billion in expenses for a JPY1 depreciation. We are in the process of internally estimating the impact of these factors on our year-end performance, while keeping a close eye on the situation.

Tsujinaka: Finally, we would like to reiterate the explanation about the impact of the exchange rate on royalties from Bristol and Merck. Regarding royalties from BMS, there has been an increase of about JPY3.8 billion from the previous year. Income was JPY20.8 billion. The JPY3.8 billion increase includes JPY0.6 billion from increased local sales and JPY3.2 billion from foreign exchange effects. Royalties from Merck have increased by about JPY3 billion compared to the previous year, JPY1.5 billion from local sales and JPY1.5 billion from foreign exchange.