ONO PHARMACEUTICAL CO., LTD.

Q2 Financial Results for the Fiscal Year Ending March 2023

November 1, 2022

[Number of Speakers]	7	
	Gyo Sagara	President, Representative Director, and Chief Executive Officer
	Toshihiro Tsujinaka	Senior Executive Officer, Executive Director, Corporate Strategy and Planning, Human Resources Planning Department
	Toichi Takino	Senior Executive Officer, Executive Director of Discovery and Research
	Kiyoaki Idemitsu	Executive Officer, Executive Director of Clinical Development
	Satoshi Takahagi	Corporate Officer, Executive Director, Sales and Marketing, Primary Care Business Division
	Kazuhiro Nagahama	Director of Finance and Accounting Department
	Yukio Tani	Corporate Executive Officer, Head of Corporate Communications, Sustainability Promotion Department

Revenue

Revenue	YoY Change
¥ 216.7 billion	+ 24.5 %

Breakdown of Revenue

(Billion yen)

	FY 2021 Q2	FY 2022 Q2	YoY Change
Revenue of Goods and Products	119.2	144.9	+ 21.6 %
Royalty & other revenue	54.9	71.8	+ 30.8 %
Total	174.1	216.7	+ 24.5 %

Sagara: I will now begin my explanation of Q2 results. First, sales revenue.

Revenue was JPY216.7 billion, increased by JPY42.6 billion, or 24.5%, YoY. Revenue of goods and products increased by JPY25.7 billion to JPY144.9 billion, and royalties and other revenues increased by JPY16.9 billion to JPY71.8 billion.

The breakdown of royalties is as follows: royalties from BMS increased by JPY8.2 billion to JPY42.1 billion, and those from Merck, which are related to sales of Keytruda, increased by JPY7.2 billion to JPY21.4 billion.

The positive effect of the exchange rate lead to the increase of JPY7.5 billion for royalties from BMS, and JPY3.7 billion for royalties from Merck. We believe that this is being taken advantage of by the exchange rate.

As you know, we had set the US dollar to yen exchange rate at JPY110 at the beginning of the period, but the resulting figure for Q2 was JPY133.

Revenue

Sales of Major Products

(Billion yen)

	FY 2021 Q2	FY 2022 Q2	YoY Change
Opdivo	56.1	**69.9**	+ 24.6 %
Forxiga	15.6	**26.4**	+ 68.8 %
Orencia SC	11.2	**12.5**	+ 11.0 %
Glactiv	12.7	**11.7**	- 8.0 %
Kyprolis	4.2	**4.4**	+ 6.5 %
Parsabiv	4.5	**4.3**	- 5.3 %
Velexbru	2.9	**4.1**	+ 43.4 %
Ongentys	0.9	**2.4**	+ 156.1 %
Onoact	2.3	**2.1**	- 9.6 %
Braftovi	1.4	**1.6**	+ 21.8 %
Mektovi	1.1	**1.3**	+ 17.5 %

Regarding the sales by products, the market for Opdivo is expanding for gastric and esophageal cancer indications with sales increased by JPY13.8 billion to JPY69.9 billion.

Regarding Forxiga, in addition to steady growth in the diabetic market, the market for chronic heart failure and chronic kidney disease also contributed to the expansion of the market, resulting in an increase of JPY10.8 billion. Roughly speaking, the sales by indication is about JPY16 billion for diabetes, JPY4 billion for heart failure, and JPY6 billion for kidney disease.

The other two products that contributed to the increase in sales were Velexbru and Ongentys.

Revenue

Sales of Long-term Listed Products

(Billion yen)

	FY 2021 Q2	FY 2022 Q2	YoY Change
Opalmon	2.4	**2.3**	- 5.9 %
Onon capsule	1.8	**1.2**	- 35.3 %

Long-term listed products are as shown. Both were negative.

Operating Profit

Operating Profit	YoY Change
¥ 80.3 billion	+ 38.0 %

Costs, etc.

(Billion yen)

	FY 2022 Q2	YoY Change
・Cost of Sales	53.7	(+ 17.9%)
・R&D Expenses	39.6	(+ 21.7%) ①
・SG&A Expenses	42.9	(+ 14.0%) ②
①+② Total	82.6	(+ 17.6%)
・Other Income	0.5	(- 31.8%)
・Other Expenses	0.6	(- 24.7%)

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Operating profit increased by JPY22.1 billion to JPY80.3 billion.

Cost of sales increased by JPY8.1 billion to JPY53.7 billion due to an increase in product sales itself. The cost to sales ratio improved by 1.4 points to 24.8%.

R&D expenses are steadily expanding with clinical trials. It increased by JPY7.1 billion to JPY39.6 billion. The amount of work in the area of drug discovery in our research laboratories is also expanding rapidly.

SG&A expenses other than R&D expenses increased by JPY5.3 billion to JPY42.9 billion. It was due to increases of co-promotion fee in association with sales increase of Forxiga, as well as IT/digital-related expenses. The figure is as originally scheduled.

Profit for the Period
(Owners of the Parent Company)

Profit for the Period (Owners of the Parent Company)	YoY Change
¥ 62.3 billion	+ 34.7 %

Income tax expense

¥ 18.6 billion (YoY Change + 44.0 %)

(Major change factors)

Increase in profit before tax	¥ 21.8 billion
Increase in corporate tax	¥ 5.7 billion

Profit for the period increased by JPY16 billion to JPY62.3 billion. Both revenues and profits for the interim period were the highest ever.

Financial Forecasts for FY 2022

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

(Billion yen)

	FY 2021 (Result)	FY 2022 (Previous Forecast)	FY 2022 (Revised Forecast)
Revenue	361.4	**425.0 (+ 17.6%)**	**440.0 (+ 21.8%)**
Operating profit	103.2	**145.0 (+ 40.5%)**	**149.0 (+ 44.4%)**
Profit before tax	105.0	**146.0 (+ 39.0%)**	**150.0 (+ 42.8%)**
Profit for the year (Owners of the Parent Company)	80.5	**110.0 (+ 36.6%)**	**114.0 (+ 41.6%)**

Exchange rate
FY 2022 (Previous Forecast): 1USD = 110 yen
FY 2022 (Revised Forecast (2nd Half)): **1USD = 130 yen**

Next, I will explain our financial forecasts for the fiscal year ending March 2023.

The forecast has been revised upward. It was due to a revision of the assumed exchange rate. We set an assumed exchange rate of JPY110, and the result for H1 was JPY133. We have revised our earnings forecast upward by re-setting H2 at JPY130, the same level as H1.

Revenue (Forecasts)

Revenue	YoY Change
¥ 440.0 billion	+ 21.8 %

Breakdown of Revenue

(Billion yen)

	FY 2021 (Result)	FY 2022 (Forecast)	YoY Change
Revenue of Goods and Products	246.0	290.0	+ 17.9 %
Royalty & other revenue	115.4	150.0	+ 30.0 %
Total	361.4	440.0	+ 21.8 %

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Revenues are projected to be JPY440 billion, an increase of JPY15 billion from the initial forecast.

Due to the impact of foreign exchange rates, the royalty portion of the profits in H1 alone was up about JPY11 billion. Therefore, assuming the same process in H2, we expect an increase of about JPY11 billion in H2, which would be an increase of JPY22 billion. You might expect more increase in royalty, but one of the reasons for this is that the foundation of royalty itself is a little lower than expected. The other thing is that this is already reflected on the net, is that the weak euro has had a negative impact on royalties. So, we have taken into account various factors to increase revenues by JPY15 billion in only the royalty portion is increased. JPY290 billion in revenue of goods and products have not been touched. Those are the revisions we made.

In terms of expenses, R&D expenses increased by JPY4 billion, and other SG&A expenses increased by JPY2 billion, which are also due to the impact of foreign exchange rates. As I have mentioned, the structure is such that for every JPY1, there is a JPY1.1 billion plus and a JPY300 million negative, resulting in a net positive of about JPY800 million. Regarding R&D investment, the negative JPY300 million portion is increasing expenses.

Revenue (Forecasts)

Sales Forecasts of Major Products

(Billion yen)

	FY 2021 (Result)	FY 2022 (Forecast)	YoY Change
Opdivo	112.4	155.0	+ 37.8 %
Forxiga	36.7	47.0	+ 28.2 %
Orencia SC	22.9	23.0	+ 0.5 %
Glactiv	24.5	23.0	- 6.3 %
Kyprolis	8.4	9.0	+ 7.6 %
Parsabiv	8.9	8.0	- 9.9 %
Velexbru	6.3	7.0	+ 11.7 %
Ongentys	2.9	5.0	+ 73.6 %
Onoact	4.9	4.5	- 7.6 %
Braftovi	2.7	3.5	+ 27.4 %
Mektovi	2.2	2.5	+ 11.7 %

We have not changed our forecast by product this time because we would like to wait and see what happens, although there is a possibility of an upward or downward swing for each product.

Revenue (Forecasts)

Sales Forecasts of Long-term listed products

(Billion yen)

	FY 2021 (Result)	FY 2022 (Forecast)	YoY Change
Opalmon	4.7	**3.5**	**- 26.0 %**
Onon capsule	3.6	**2.5**	**- 29.7 %**

We have not changed our forecast by product this time because we would like to wait and see what happens, although there is a possibility of an upward or downward swing for each product.

Operating Profit (Forecasts)

Operating Profit	YoY Change
¥ 149.0 billion	+ 44.4 %

Costs, etc.

(Billion yen)

	FY 2022 (Forecast)	YoY Change	
・Cost of Sales	109.0	(+ 16.6 %)	
・R&D Expenses	91.0	(+ 19.9 %)	①
・SG&A Expenses	90.0	(+ 16.8 %)	②
①+② Total	181.0	(+ 18.4 %)	
・Other Income	0.5	(- 49.0 %)	
・Other Expenses	1.5	(- 88.2 %)	

Operating profit has been revised upward by JPY4 billion to JPY149 billion.

Cost of sales increased by JPY5 billion, R&D expenses increased by JPY4 billion, and other SG&A expenses increased by JPY2 billion, roughly.

Profit before Tax (Forecasts)

Profit before Tax	YoY Change
¥ 150.0 billion	+ 42.8 %

Net financial income, etc.

+ ¥ 1.0 billion (YoY Change - ¥ 0.8 billion)

Profit before tax is JPY150 billion.

Profit for the Period /Owners of the Parent Company (Forecasts)

Profit for the Period (Owners of the Parent Company)	YoY Change
¥ 114.0 billion	+ 41.6 %

Income tax expense

¥ 35.8 billion (YoY Change + 47.1 %)

(Major change factors)

Increase in profit before tax	¥	45.0 billion
Increase in corporate tax	¥	11.5 billion

Profit for the year is JPY114 billion. This means a JPY4 billion upward revision.

In summary, the upward revision is for a JPY15 billion increase in revenue and a JPY4 billion increase in profit.

The annual dividend is planned to be JPY66 per share as announced.

This is all about the status of the financial results.

Reduction plan of Cross-shareholdings

(published on November 1, 2021)

➢ Reduction plan

- Period: October 2021 to March 2025 (3 and a half years)
- Details of reduction plan:

30% reduction from the end of September 2021 (141.8 billion yen)

※The company plans to reduce its cross-shareholdings to less than 20% of its net assets by the end of March 2022.

	End of September 2021	Expected at the end of March 2025	Plan	
			Reduction	Reduction rate
Market price at the end of September 2021	¥ 141.8 bil	¥ 99.3 bil	¥ 42.5 bil	-30.0%

➢ Medium-to long-term plan

We aim for the ratio of strategic shareholdings to net assets (on a balance sheet basis) to be less than 10%.

I will report the status of the reduction of policy shareholdings.

As of September last year, we had JPY141.8 billion in cross-shareholdings, and have announced a plan to reduce this by 30% over the next three and a half years.

The amount of reduction is JPY42.5 billion in terms of the market value at that time.

Status of reduction of Cross-shareholdings

	End of September 2021	End of September 2022	Reduction*	Reduction rate
Market price at the end of September 2021	**¥ 141.8 bil**	**¥ 115.5 bil**	**¥ 26.3 bil**	**-18.5%**

*Contain the growth investments after October 2021

(Reference)

	End of September 2021	End of September 2022	Change	Ratio of Cross-shareholdings to net assets
Balance sheet accounting amount	**¥ 141.8 bil**	**¥ 104.8 bil**	**¥ 37.0 bil**	**14.8%**

As of one year after the announcement of the 30% reduction in three and a half years, we have already reduced the amount by 18.5%. The remainder would be 11.5% in two and a half years. We are trying to bring the ratio to net assets to below 10% as quickly as possible, and it is currently at 14.8%. We would like to move forward with this project in a solemn manner.

One more thing, I would like to report on the patent term of Forxiga. It was launched in May 2014 for the treatment of Type 2 diabetes. Its patent term was April 2025.

Later, as you know, the indications of Type 1 diabetes, chronic heart failure, and chronic kidney disease were added. Currently, the patent term for Type 1 diabetes and chronic heart failure has been extended to May 2028. As for chronic kidney disease, we are currently in negotiations and have not yet concluded, but we expect that we will probably get the same extension as for Type 1 diabetes and chronic heart failure.

So, the patent will expire in May 2025, according to the current rules, and the generic will be launched in December, but once it is launched, it will only be available for the indication of Type 2 diabetes at that time.

That is all from me.

Development pipeline

Idemitsu: Today, I will use the supplemental material for the financial report to explain the updated development progress situation since Q1 of the fiscal year ending March 31, 2023.

I. Main Status of Development Pipelines (Oncology)

As of October 24, 2022

<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)

<Yervoy> *) : "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
Yervoy Injection ★ / Ipilimumab	Additional indication	Gastric cancer	Injection	Japan S. Korea Taiwan	III	In-license (Co-development with Bristol-Myers Squibb)
	Additional indication	Esophageal cancer	Injection	S. Korea	III	In-license (Co-development with Bristol-Myers Squibb)
	Additional indication	Urothelial carcinoma	Injection	Japan S. Korea Taiwan	III	In-license (Co-development with Bristol-Myers Squibb)
	Additional indication	Hepatocellular carcinoma	Injection	Japan S. Korea Taiwan	III	In-license (Co-development with Bristol-Myers Squibb)

No change.

<I-O Related> ***) :** "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-4686 ★ (BMS-986207)	New chemical entities	Solid tumor / Anti-TIGIT antibody	Injection	Japan	I / II	In-license (Co-development with Bristol-Myers Squibb)
ONO-4482 ★ (BMS-986016) / Relatlimab	New chemical entities	Melanoma / Anti-LAG-3 antibody	Injection	Japan	I / II	In-license (Co-development with Bristol-Myers Squibb)
ONO-7475 ★	New chemical entities	Solid tumor / Axl/Mer inhibitor	Tablet	Japan	I	In-house
ONO-4578 ★	New chemical entities	Colorectal cancer / Prostaglandin receptor (EP4) antagonist	Tablet	Japan	I	In-house
	New chemical entities	Pancreatic cancer / Prostaglandin receptor (EP4) antagonist	Tablet	Japan	I	In-house
	New chemical entities	Non-small cell lung cancer / Prostaglandin receptor (EP4) antagonist	Tablet	Japan	I	In-house
	New chemical entities	Solid tumor・Gastric cancer / Prostaglandin receptor (EP4) antagonist	Tablet	Japan	I	In-house
ONO-7913 ★ /Magrolimab	New chemical entities	Pancreatic cancer / Anti-CD47 antibody	Injection	Japan	I	In-license (Gilead Sciences, Inc.)
	New chemical entities	Colorectal cancer / Anti-CD47 antibody	Injection	Japan	I	In-license (Gilead Sciences, Inc.)
ONO-7119 ★ /Atamparib	New chemical entities	Solid tumor / PARP7 inhibitor	Tablet	Japan	I	In-license (Ribon Therapeutics, Inc.)
ONO-7122 ★	New chemical entities	Solid tumor / TGF-β inhibitor	Injection	Japan	I	In-license (Co-development with Bristol-Myers Squibb)
ONO-7914 ★	New chemical entities	Solid tumor / STING agonist	Injection	Japan	I	In-house

No change.

<Others> *) : "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-7913 / Magrolimab	New chemical entities	TP53-mutant acute myeloid leukemia / Anti-CD47 antibody	Injection	Japan	III	In-license (Gilead Sciences, Inc.)
	New chemical entities	Acute myeloid leukemia / Anti-CD47 antibody	Injection	S. Korea Taiwan	III	In-license (Gilead Sciences, Inc.)
Braftovi Capsules / Encorafenib	Additional indication	Thyroid cancer / BRAF inhibitor	Capsule	Japan	II	In-license (Pfizer Inc.)
Mektovi Tablets / Binimetinib	Additional indication	Thyroid cancer / MEK inhibitor	Tablet	Japan	II	In-license (Pfizer Inc.)
ONO-4059 /Tirabrutinib Hydrochloride	New chemical entities	Primary central nervous system lymphoma / BTK inhibitor	Tablet	USA	II	In-house
ONO-7475	New chemical entities	EGFR-mutated non-small cell lung cancer / Axl/Mer inhibitor	Tablet	Japan	I	In-house
ONO-7913 / Magrolimab	New chemical entities	Solid tumor / Anti-CD47 antibody	Injection	Japan	I	In-license (Gilead Sciences, Inc.)
	New chemical entities	Myelodysplastic syndromes (MDS) / Anti-CD47 antibody	Injection	Japan	I	In-license (Gilead Sciences, Inc.)
ONO-4578	New chemical entities	Hormone receptor-positive, HER2-negative breast cancer / Prostaglandin receptor (EP4) antagonist	Tablet	Japan	I	In-house
ONO-4685	New chemical entities	T-cell lymphoma / PD-1 x CD3 bispecific antibody	Injection	USA	I	In-house
ONO-7018 *1	New chemical entities	Non-Hodgkin lymphoma, Chronic lymphocytic leukemia / MALT1 inhibitor	Tablet	USA	I	In-license (Chordia Therapeutics Inc.)

★: Combination with Opdivo.

The changes from the announcement of financial results for the first quarter of the fiscal year ending March 2023 are as follows:

*1: Phase I of ONO-7018, MALT1 inhibitor, was initiated in the USA for the treatment of non-Hodgkin lymphoma or chronic lymphocytic leukemia.

* Phase II of Opdivo for the treatment of pancreatic cancer was conducted in Japan, but the project was discontinued.
* Phase I/II of combination therapy with Opdivo and Yervoy for the treatment of virus positive / negative solid carcinoma was conducted in Japan, South Korea and Taiwan, but the project was discontinued due to strategic reasons.
* Phase I/II of ONO-7475, Axl / Mer inhibitor, for the treatment of acute leukemia was conducted in the USA, but the project was discontinued due to strategic reasons.

In the case of clinical development of the oncology drugs in the same indication, the most advanced clinical phase is described.

At the bottom, we added ONO-7018. ONO-7018 is a MALT1 inhibitor in-licensed from Cordia. Phase I has been initiated in the US for non-Hodgkin's lymphoma and chronic lymphocytic leukemia.

The note describes projects that have been discontinued and removed from this document. First, we were conducting Phase II of Opdivo for pancreatic cancer, and then Phase II for virus-positive and -negative solid tumors, but we decided to discontinue the development of both and not to proceed to the next phase.

In addition, for ONO-7475, an Axl/Mer inhibitor, Phase I/II of this compound for acute leukemia was being conducted in the US, but development for this indication was discontinued for strategic reasons.

II. Main Status of Development Pipelines (Areas other than Oncology)

As of October 24, 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
Onoact for Intravenous Infusion / Landiolol Hydrochloride	Additional indication for pediatric use	Tachyarrhythmia in low cardiac function*2 / Short-acting selective β_1 blocker	Injection	Japan	In-house

The change from the announcement of financial results for the first quarter of the fiscal year ending March 2023 is as follows:
*2: An application of Onoact for Intravenous Infusion, short-acting selective β_1 blocker, was approved in Japan for the treatment of tachyarrhythmia (supraventricular tachycardia, atrial fibrillation and atrial flutter) in pediatric patients with low cardiac function.

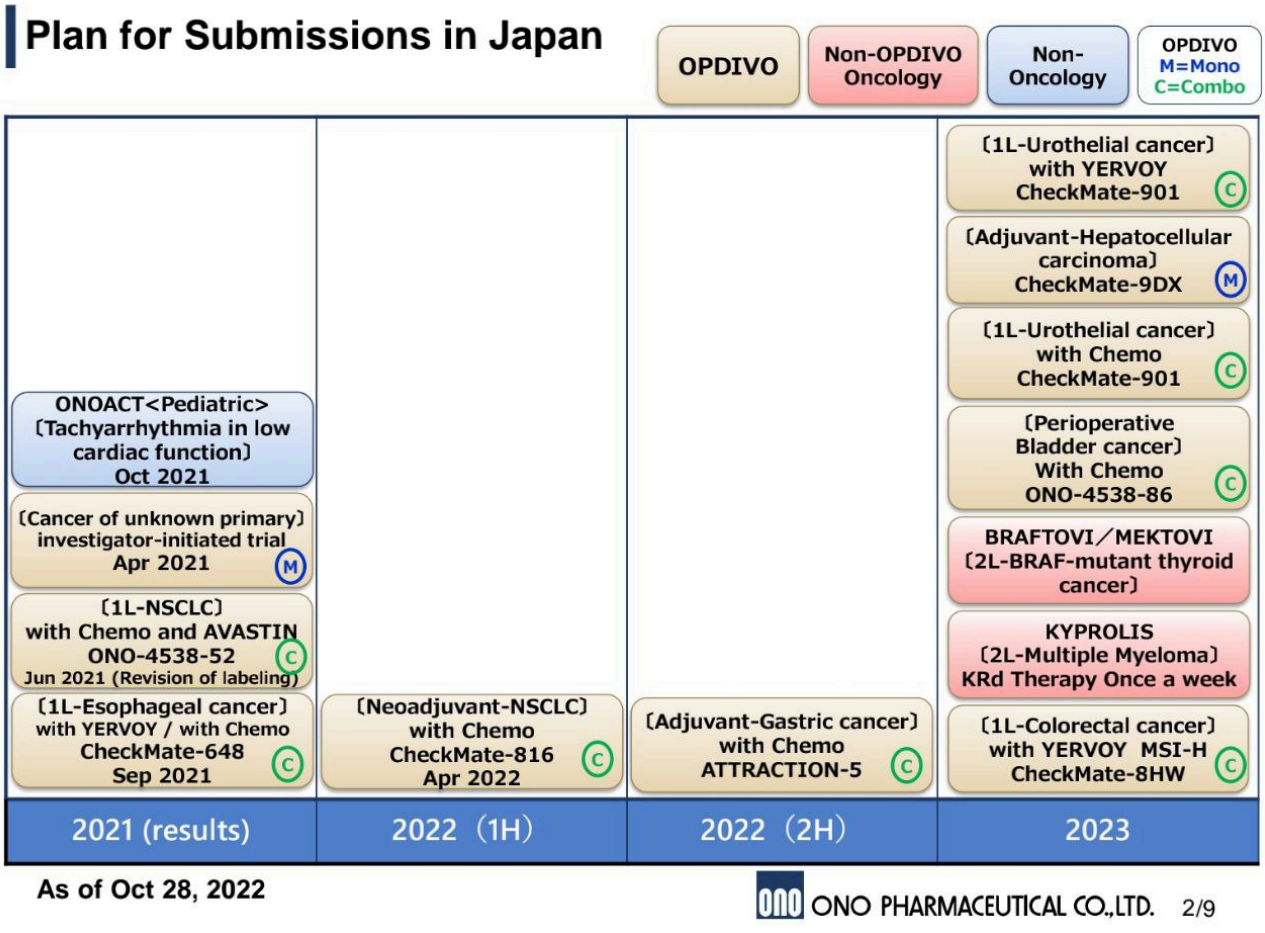
<Clinical Trial Stage> ***) :** "In-house" compounds include a compound generated from collaborative research.

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
Velexbru Tablets / Tirabrutinib Hydrochloride	Additional indication	Systemic sclerosis / BTK inhibitor	Tablet	Japan	I	In-house
ONO-2020	New chemical entities	Neurodegenerative disease / Epigenetic regulation	Tablet	USA	I	In-house

The change from the announcement of financial results for the first quarter of the fiscal year ending March 2023 is as follows:
*Phase I of ONO-2909, Prostaglandin receptor (DP1) antagonist, for the treatment of narcolepsy was conducted in Japan, but the project was discontinued due to the results not being able to confirm anticipated efficacy.

This shows the main development progress in non-oncology area. Please look at the top row of the approved development products. Onoact was approved for pediatric indication this August.

ONO-2909, an antagonist of DP1, one of the prostaglandin receptors, was being developed for narcolepsy. Efficacy confirmation in narcolepsy patients was conducted in Phase I, but the expected efficacy was not achieved, and development was discontinued.



The table shows the schedule for future domestic applications.

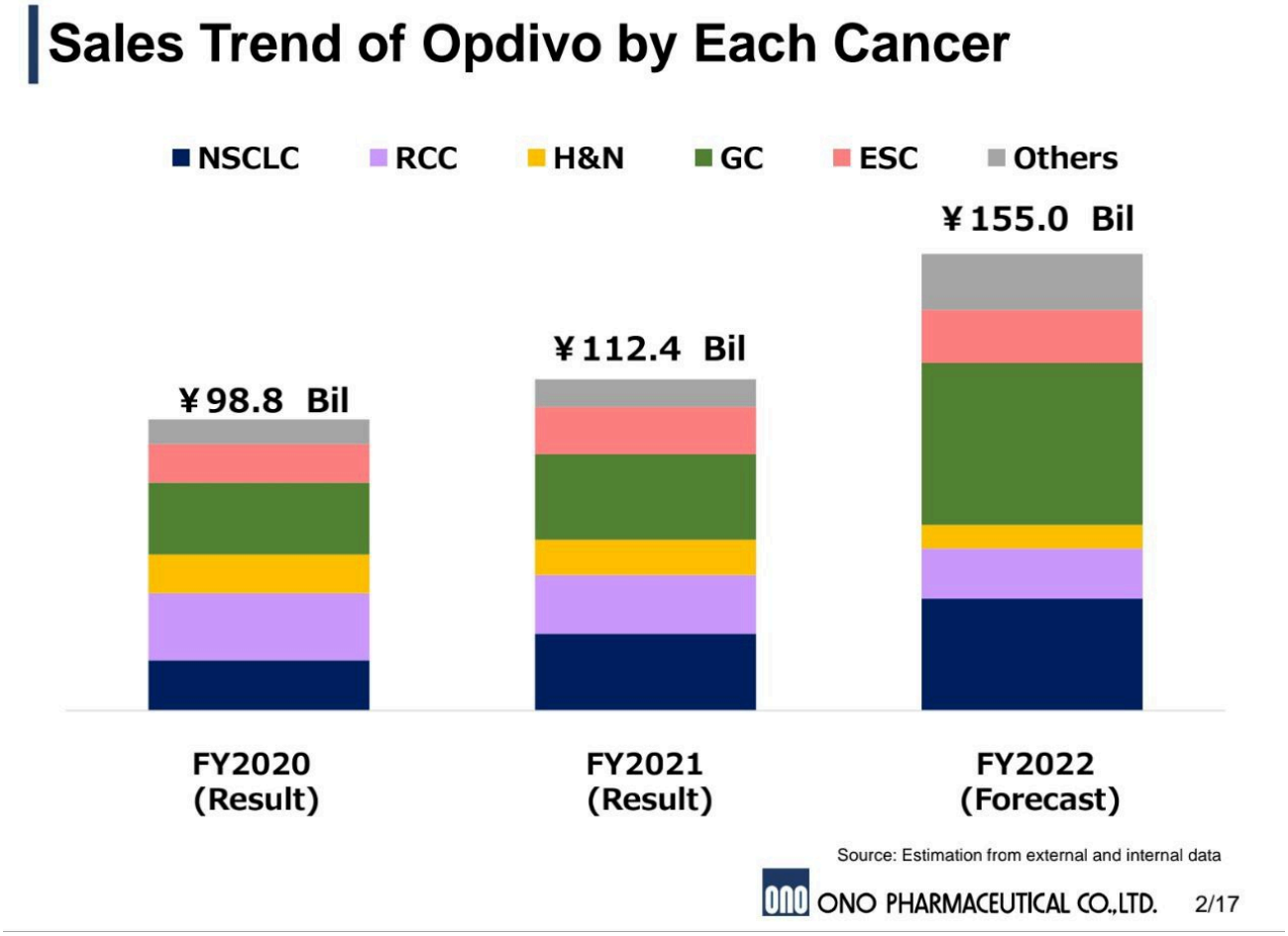
On the far left, the results for FY2021, as I mentioned earlier, we obtained the pediatric indication for Onoact this August.

Next, on the far right, in FY2023, is the combination of Opdivo and Yervoy for first- line treatment of urothelial carcinoma on the top row, and the postoperative adjuvant treatment of hepatocellular carcinoma, both of which were placed in H2 of FY2022 in the previous document, but the timing of obtaining the results was expected to be later than originally planned. Therefore, we have changed the timing of the application to FY2023.

That's all for the update on the domestic application schedule.

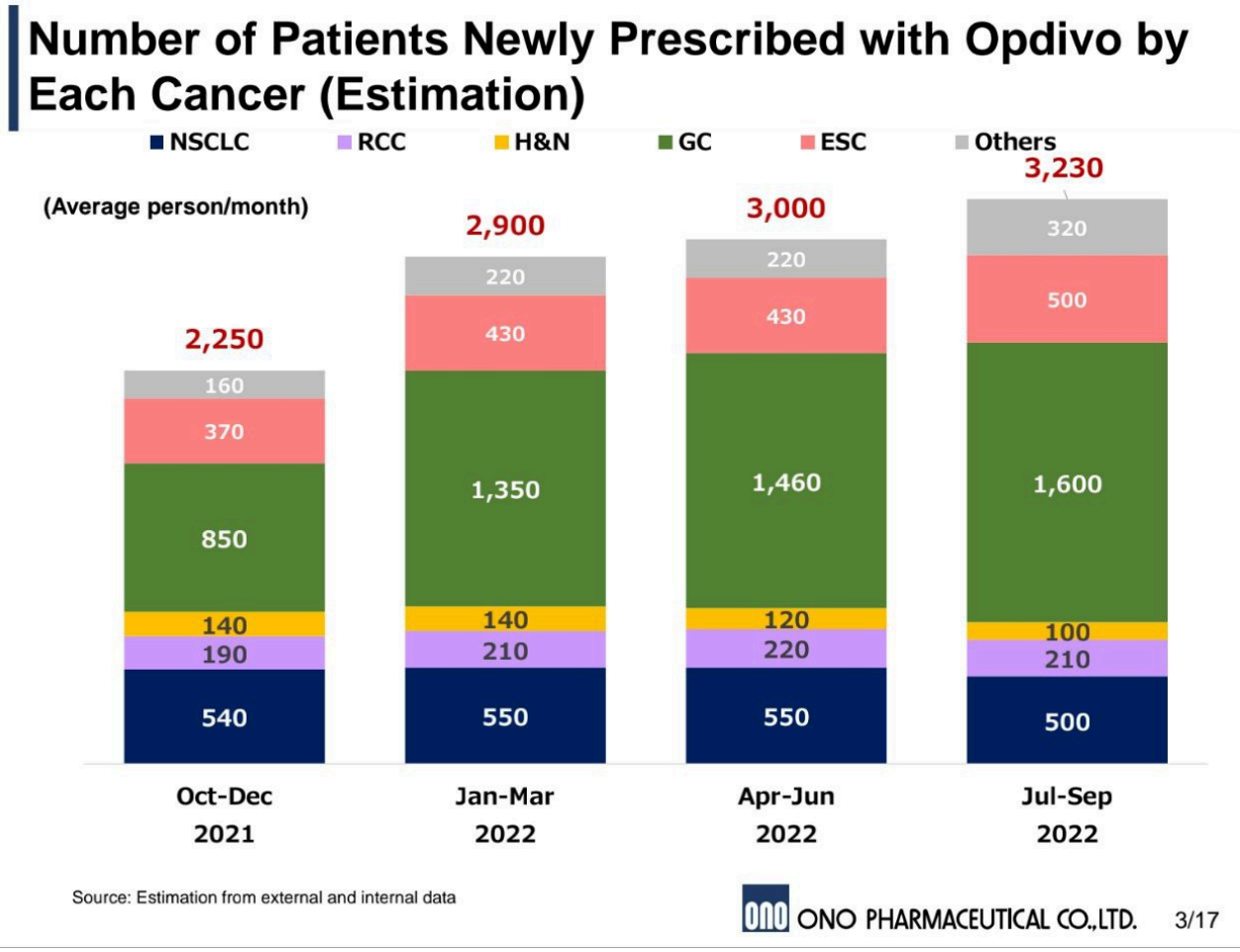
Trend of Opdivo

Takahagi: I will explain the Opdivo trend. Today, I would like to explain sales, the number of new prescriptions, and the status in each cancer type: lung cancer, gastric cancer, esophageal cancer, renal cell carcinoma, and urothelial carcinoma.



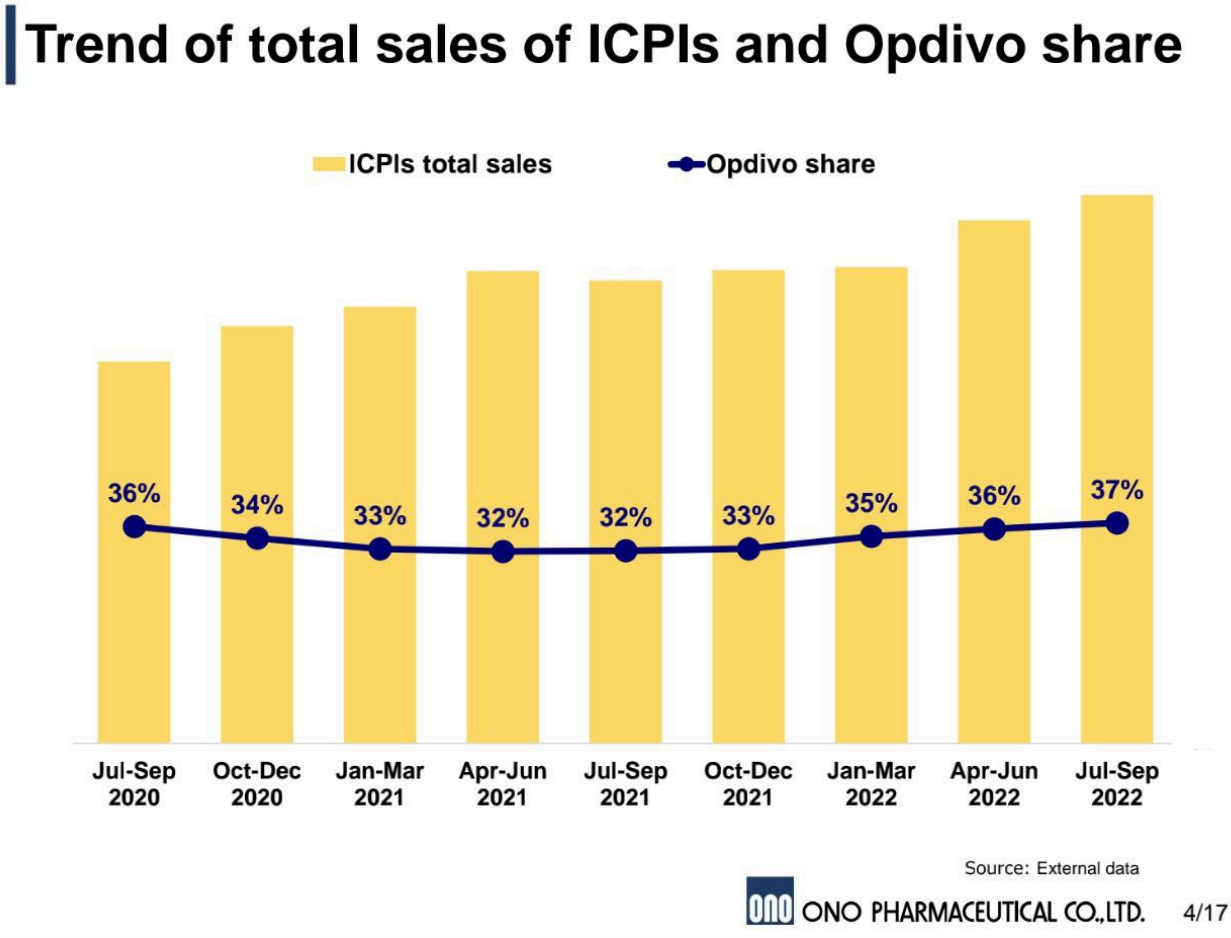
Here is an overview of Opdivo sales.

In FY2021, sales was JPY112.4 billion, and in the current fiscal year, sales is expected to be JPY155 billion. There is no change here.



This shows number of patients newly prescribed with Opdivo by cancer type which represents an average person per month quarterly.

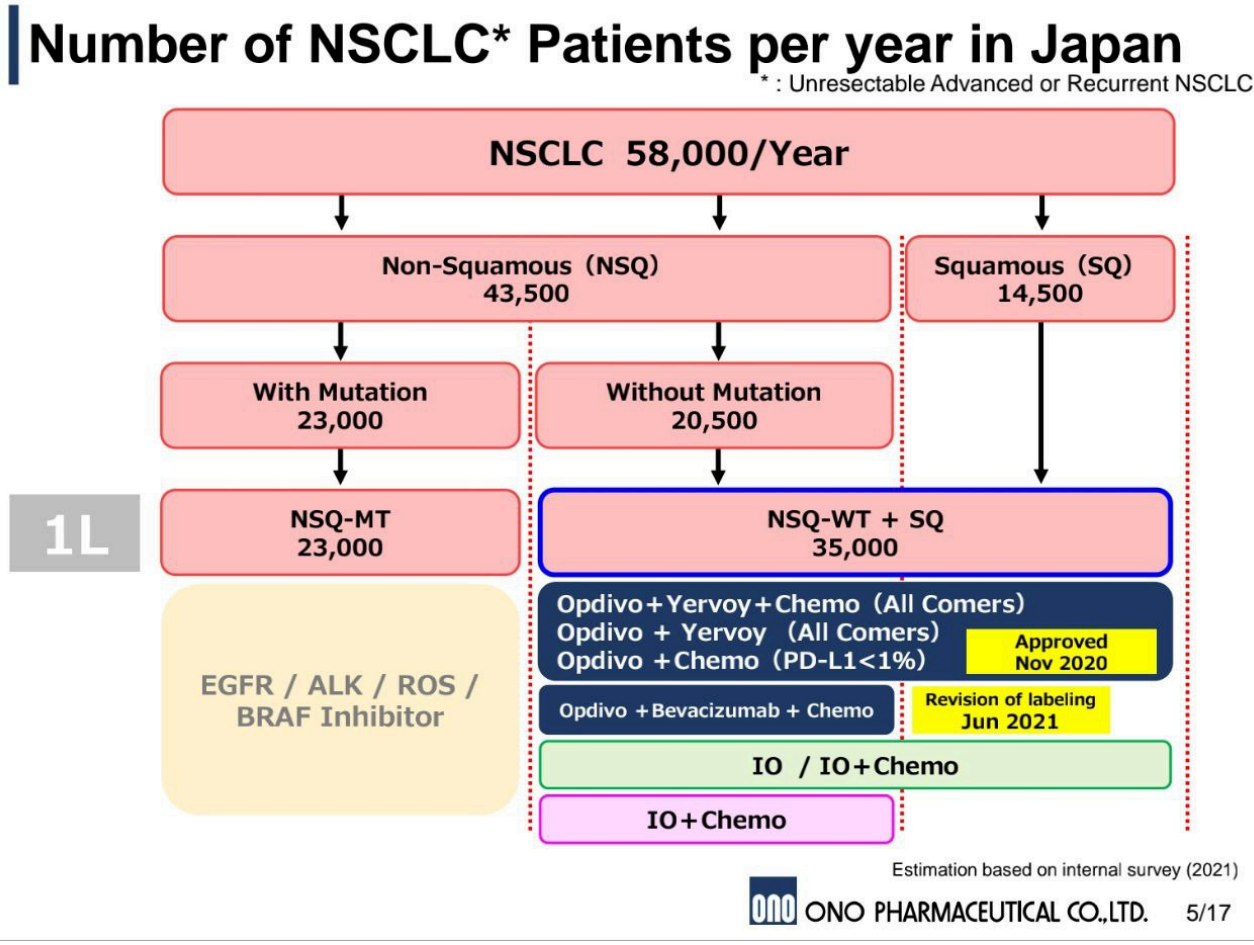
Although this is only an estimate, 1,600 cases of gastric cancer, 500 cases of esophageal cancer, and 500 cases of lung cancer initiated the prescription in July to September 2022. The monthly average is 3,230 cases.



This shows trends of total sales of immune checkpoint inhibitors launched in Japan and Opdivo's market share.

The yellow bar graph shows the total sales of immune checkpoints inhibitors, and the dark blue line graph shows the market share of Opdivo.

Sales of immune checkpoint inhibitors have been increasing steadily, and despite the NHI price revision in FY2022, total sales have grown with respect to all products. In this context, Opdivo has a 37% market share and is performing well.

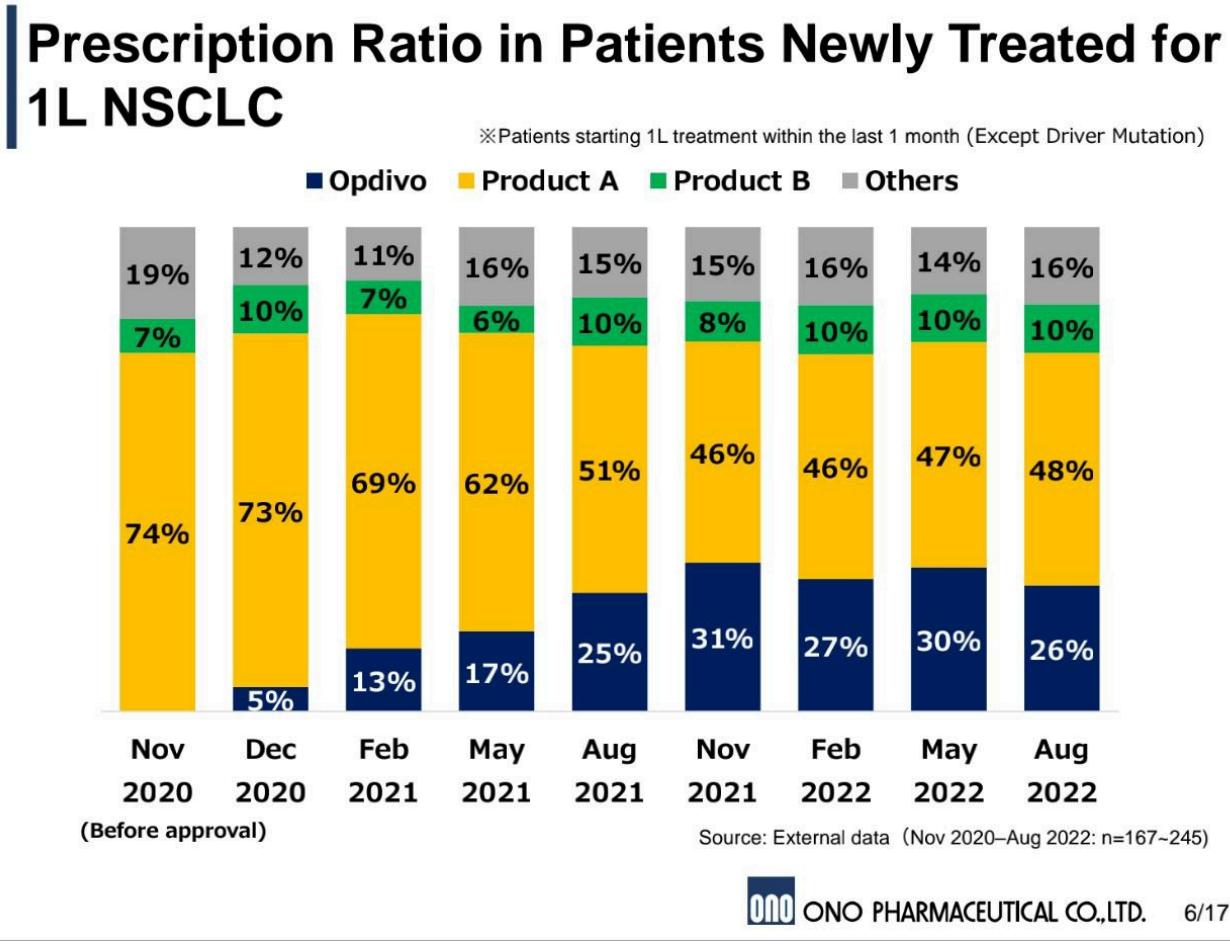


From here, I would like to explain by type of cancer.

First, non-small cell lung cancer.

The annual number of patients with unresectable advanced recurrent non-small cell lung cancer is 58,000, according to our own estimate. Among them, non-small cell lung cancer is divided into non-squamous and squamous cell types by histologic type. Further, non-squamous cell type is divided into those with and without genetic mutations.

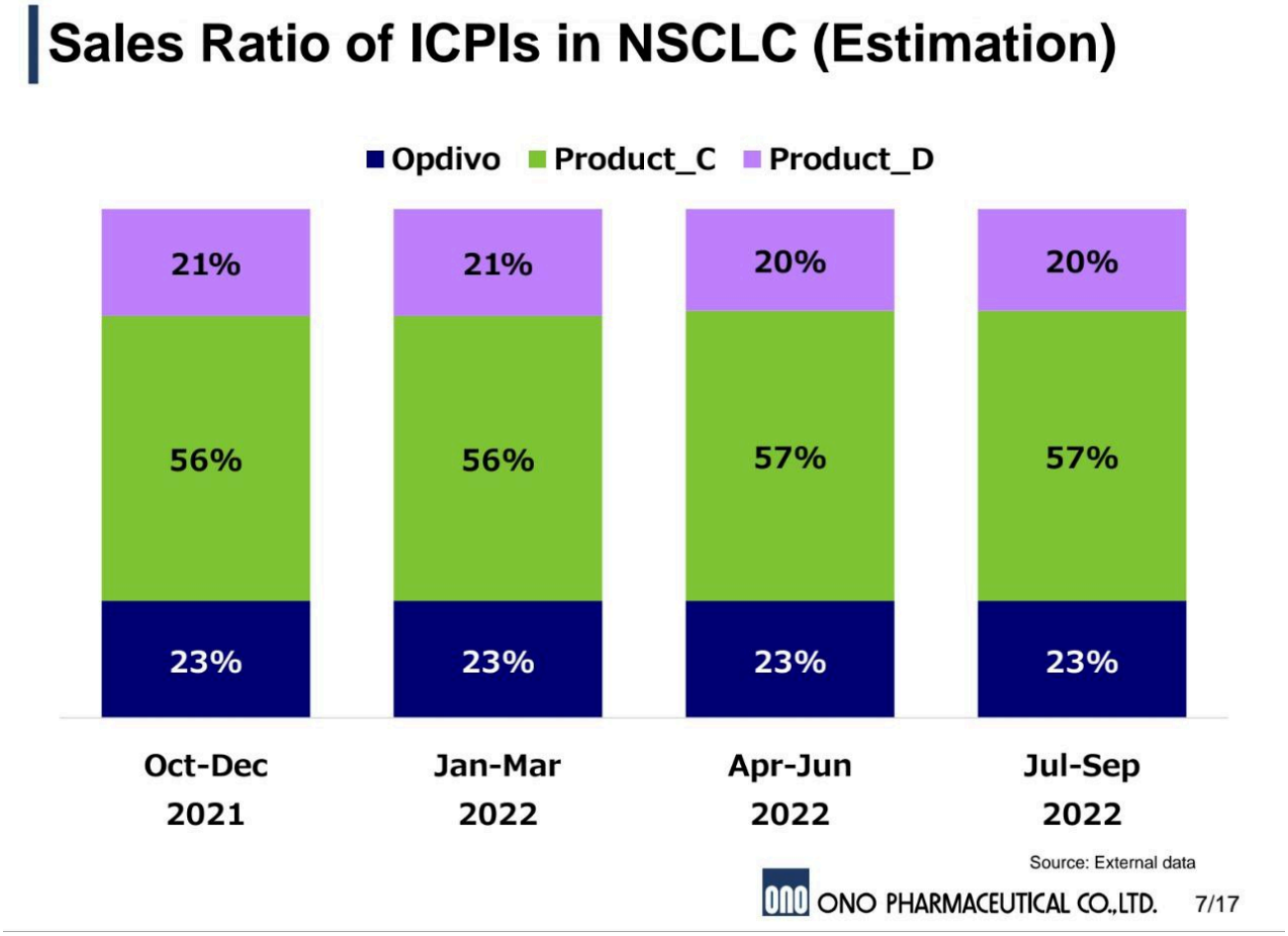
The market for immune checkpoint inhibitors such as Opdivo in the first-line treatment of lung cancer is very large, estimated at 35,000 patients per year, for squamous cell carcinoma, and non-squamous cell carcinoma without genetic mutations. We are currently developing our Opdivo regimen activities in a very competitive environment.



This shows the share of new patients in first-line treatment of lung cancer.

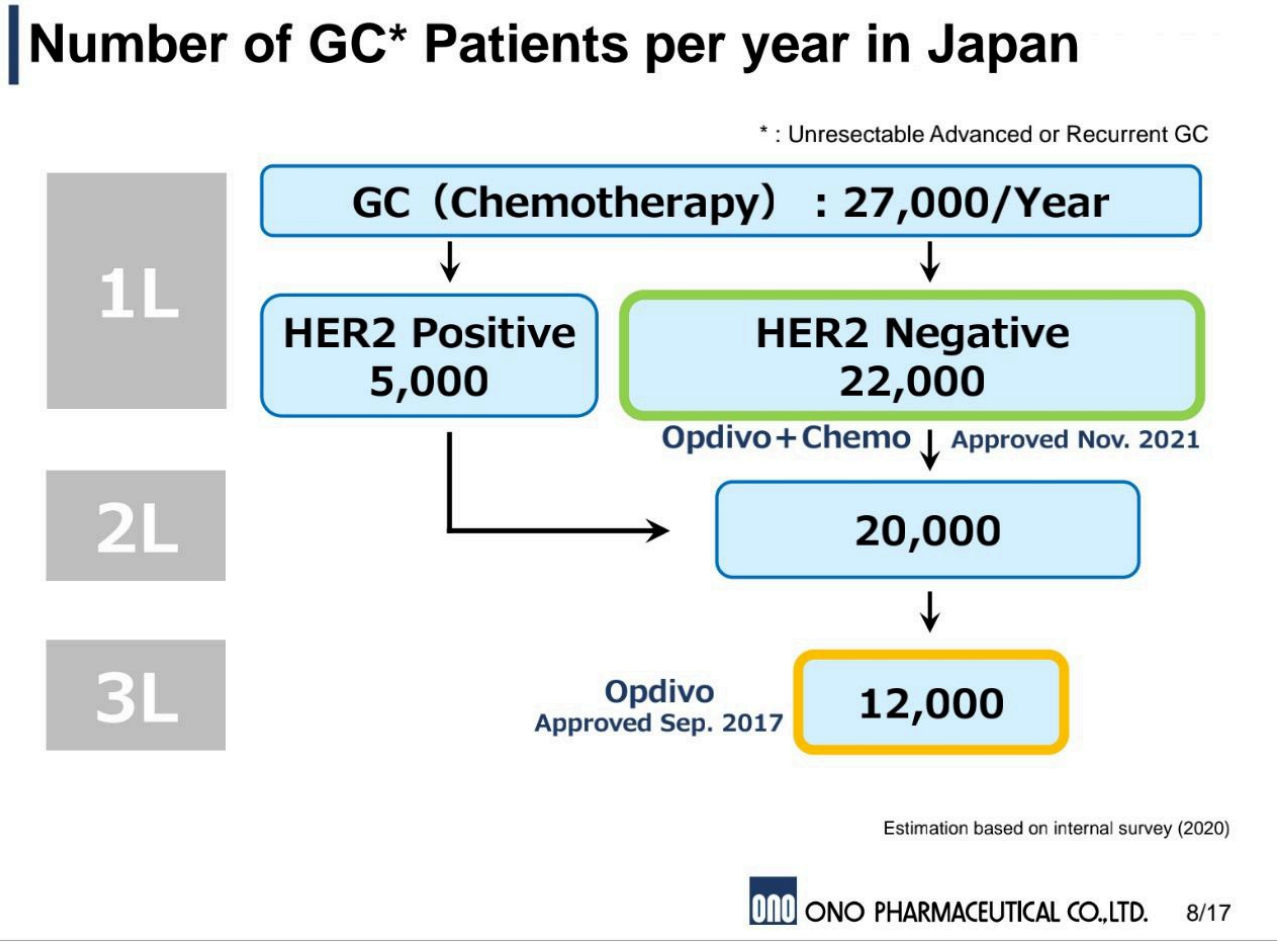
Opdivo's share of new patient prescriptions was 26% as of August and is currently in a bit of a stagnant trend.

We believe that further promotion for the efficacy and safety of the combination therapy of Opdivo with Yervoy (IO/IO), which is currently not available for the competitive drugs, is necessary. We are continuing to work on this promotion.



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

Opdivo accounted for 23%, and we believe that further growth is needed in the area of first-line lung cancer treatment.

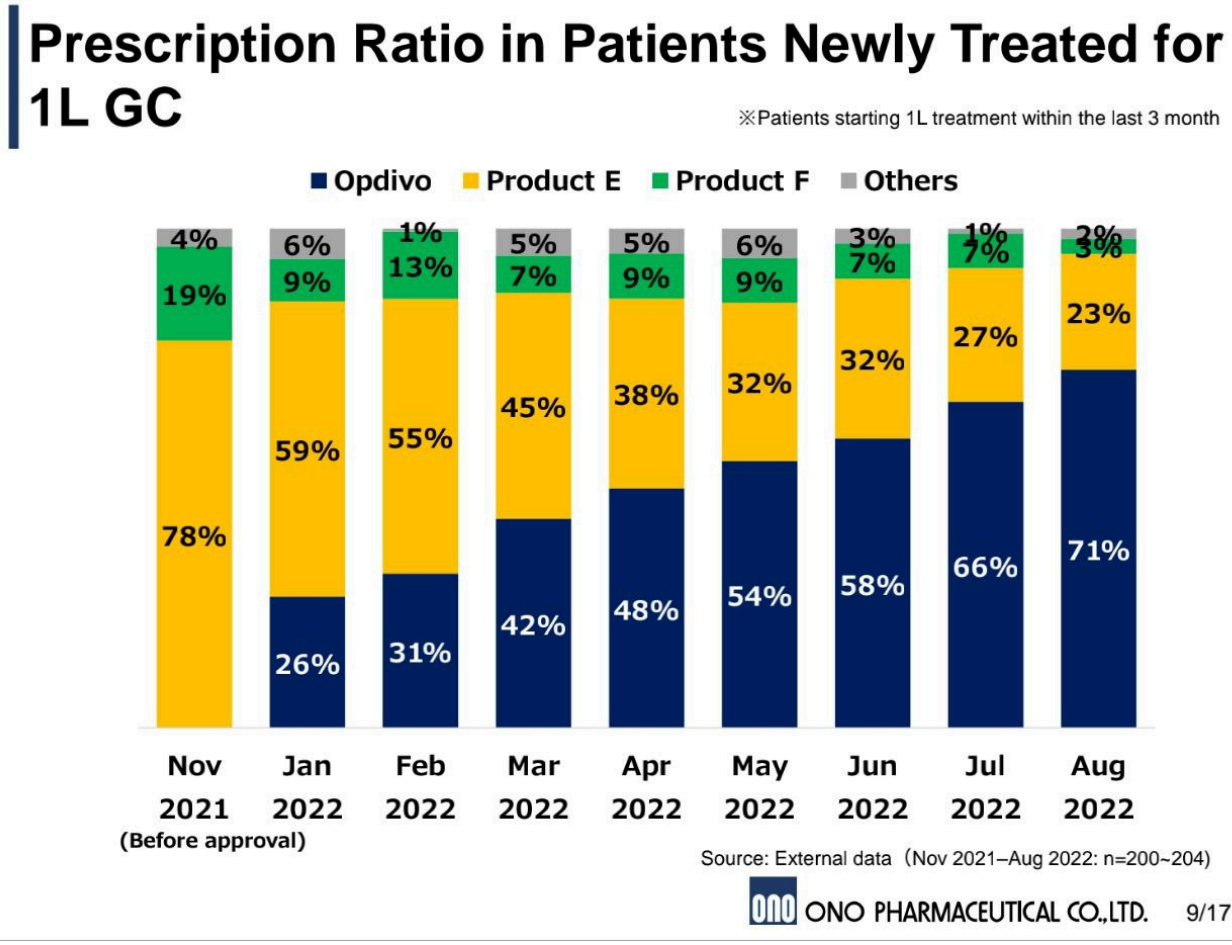


Next, I would like to explain the gastrointestinal field.

First is gastric cancer.

The annual number of patients with unresectable advanced recurrent gastric cancer is estimated at 27,000, according to our own estimate.

In November 2021, Opdivo was approved in combination with chemotherapy for first-line HER2-negative treatment. The number of patients is 22,000, and promotions are currently underway to address this number.



This table shows the prescription share in new patients for the first-line treatment of gastric cancer.

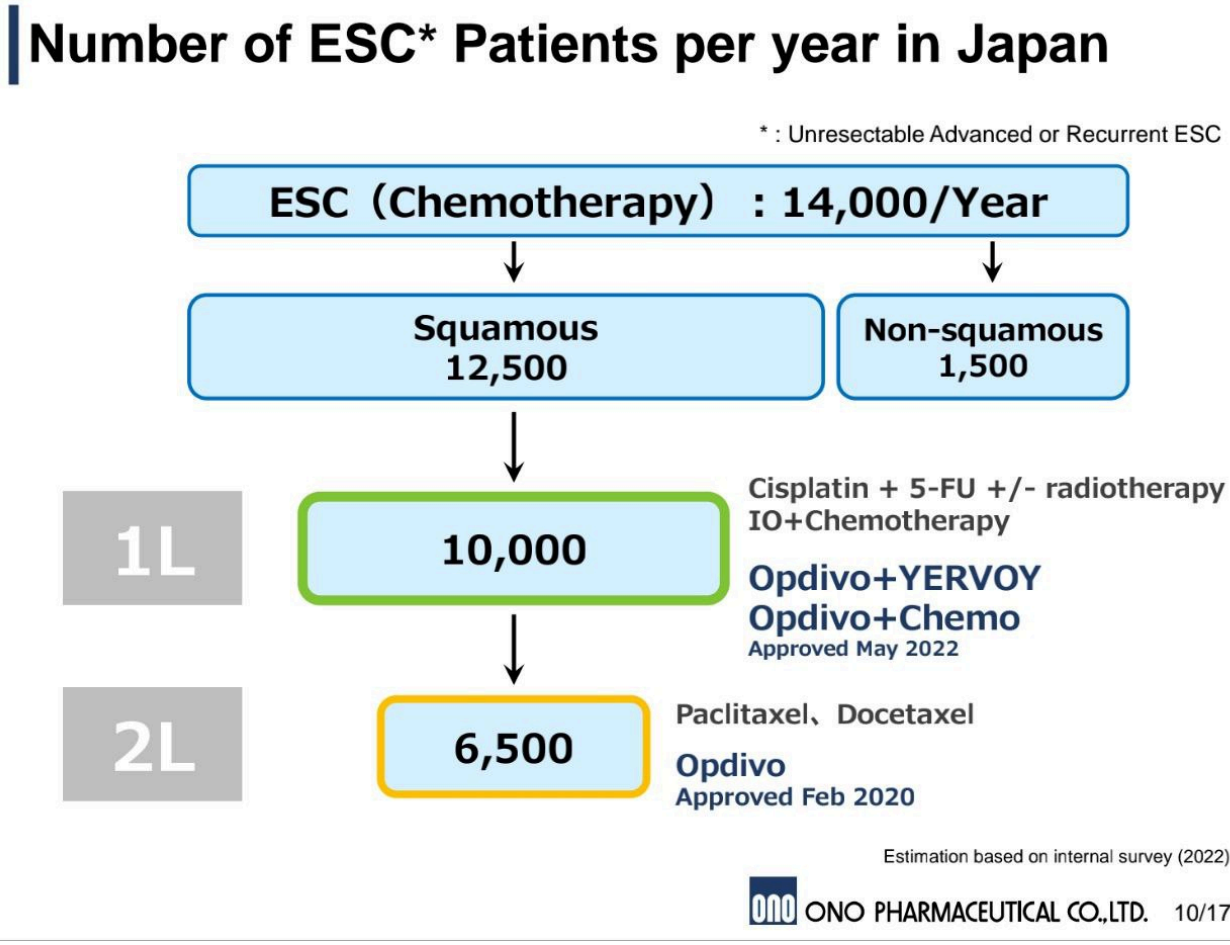
Prescriptions for Opdivo are steadily increasing with a 71% share of new patients for first-line treatment.

As I indicated earlier for lung cancer, it is slightly stagnant. The average duration of administration for first-line treatment of lung cancer is 5.7 months, and for this first-line treatment of gastric cancer, it is 8.5 months. We believe that the number of patients receiving and using the drug will continue to accumulate over the next few years. We expect significant peak sales in this gastric cancer area in the future and hope to manage to cover the stagnant lung cancer area.

This is not in the document but is for reference only. This slide shows the share of new patients in the third line treatment of Opdivo for gastric cancer and the second line treatment of Opdivo for esophageal cancer up to 18 months from the time of approval.

It is said that the peak time for the share of new patients in general regimens is about two years, but Opdivo's third line for gastric cancer and second line for esophageal cancer have shown a rapid increase in the share of new prescriptions, reaching 70% of the target in 18 months.

If we overlay the results of the first-line treatment for gastric cancer on this graph, we have reached 71% as of this nine-month period. It shows a rapid uptake, and we are firmly committed to bringing this Opdivo regimen to patients in the first-line treatment of gastric cancer.

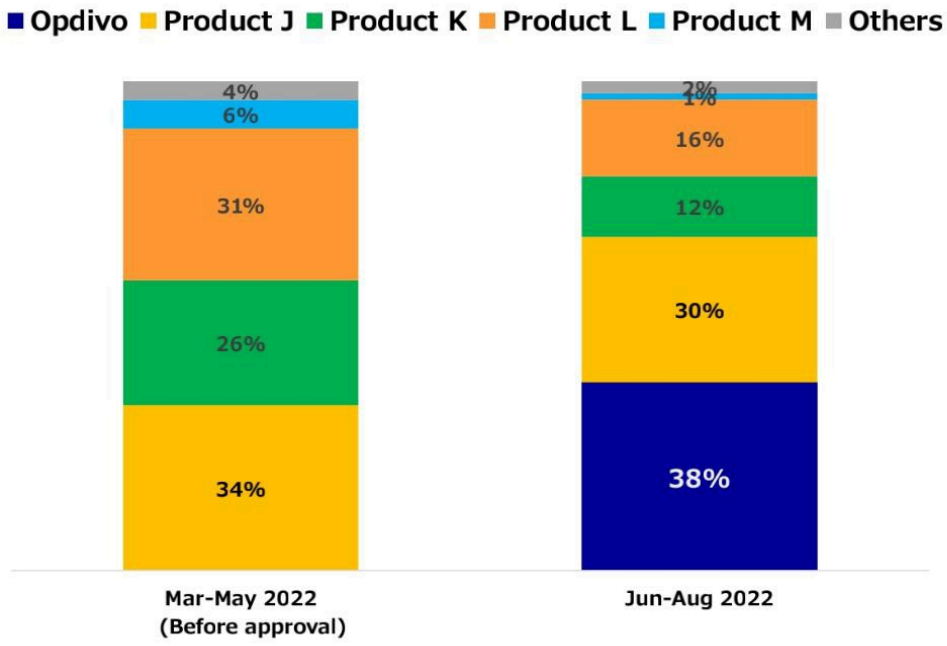


Next is esophageal cancer.

In the first-line treatment of unresectable advanced recurrent esophageal cancer, the combination regimens both of Opdivo and Yervoy, and Opdivo and chemotherapy were approved in May this year, and we started promotions.

The first-line treatment target is squamous cell carcinoma, and we believe that the number of patients eligible for this treatment is 10,000.

Prescription Ratio in Patients Newly Treated for 1L ESC (Squamous Cell Carcinoma)



※Patients starting treatment within the last 3 month

Source: External data (May 2022–Aug 2022: n=150~155)

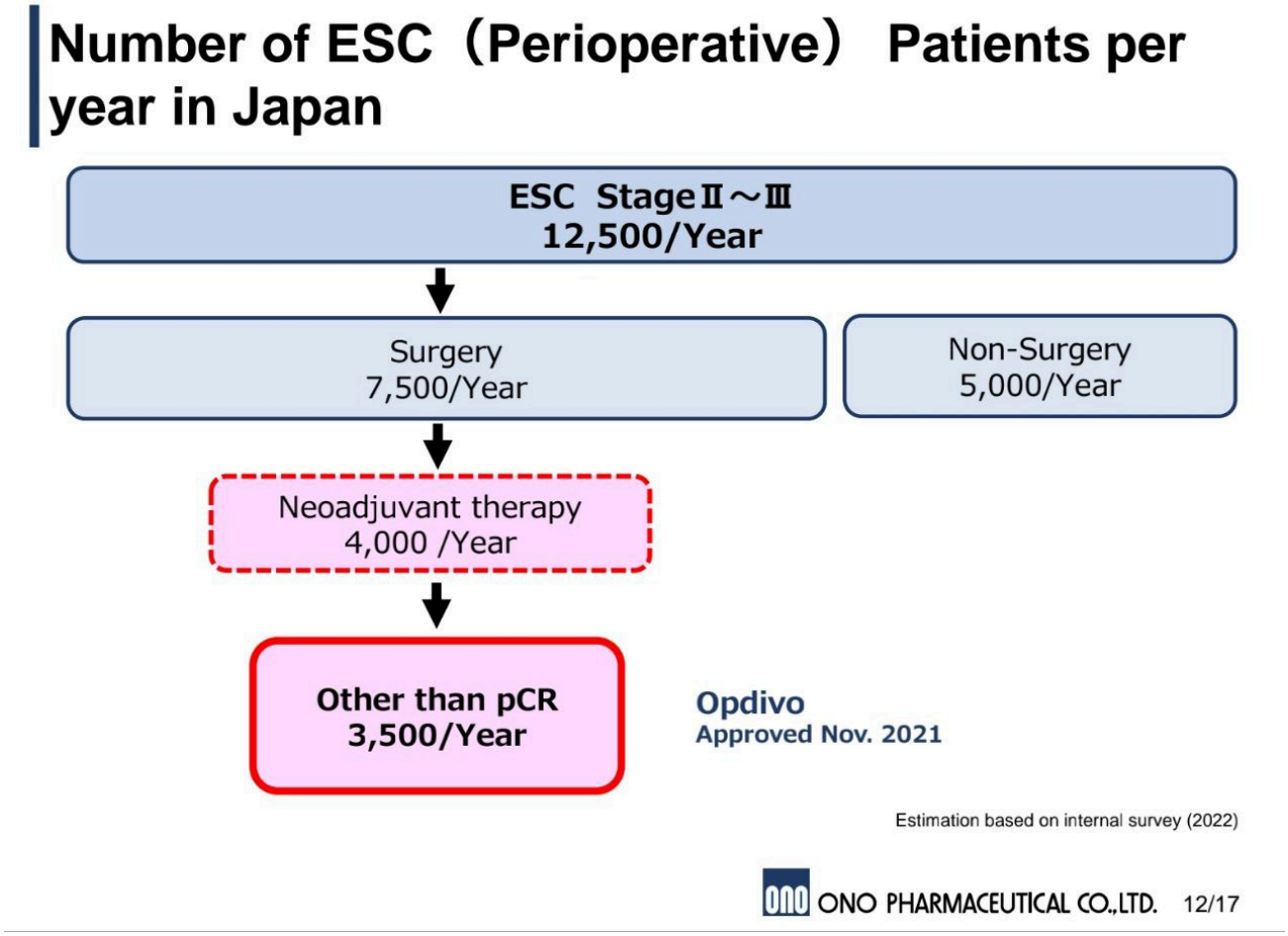
ONO PHARMACEUTICAL CO.,LTD. 11/17

This table shows the prescription share in new patients for the first-line treatment of esophageal cancer.

As you are all aware, a combination of the competitive product of IO and chemotherapy regimen entered the market in November last year, and as of this May when we entered the market, about 30% of new patients were prescribed with the competitive IO product.

With the entry of the Opdivo regimen into first-line treatment in May this year, IO's total market share has grown from roughly 50% to 60%. Among these, the Opdivo regimen has a 38% share of new patients, higher than the competitive drugs, and prescriptions are steadily expanding.

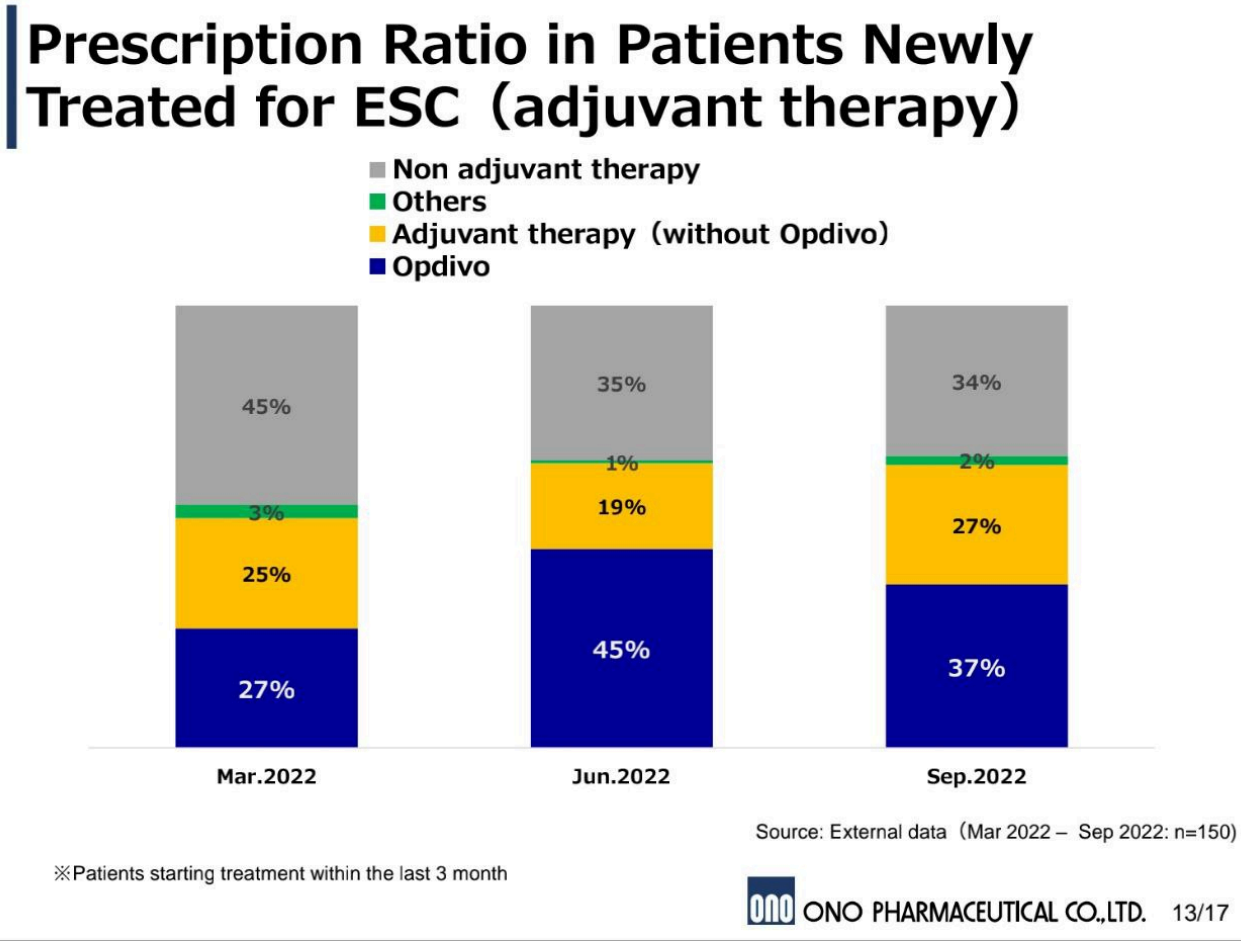
As I mentioned earlier for gastric cancer, we believe that the number of prescriptions for esophageal cancer will similarly increase in the future, leading to significant sales.



In esophageal cancer, additional indications have been approved for postoperative adjuvant therapy in the perioperative period.

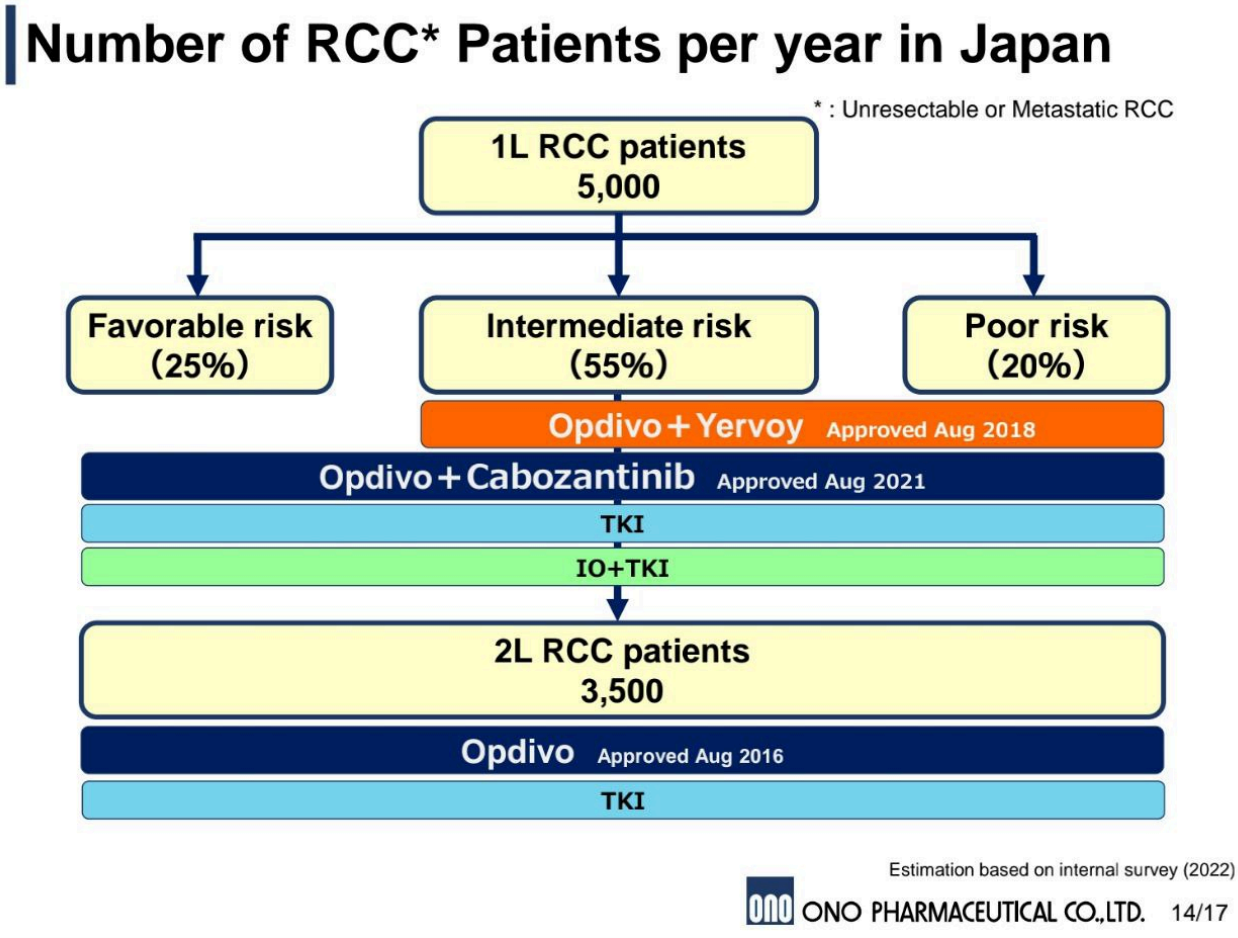
As for the number of patients undergoing surgery for esophageal cancer, of which indication was approved in November last year, the number of patients with stage II - III esophageal cancer is 12,500 per year, of which 7,500 are said to be eligible for surgery.

We believe that 4,000 of these patients will receive preoperative adjuvant therapy; and 3,500 will have a pathologic non-complete response and be eligible for postoperative adjuvant therapy with Opdivo.



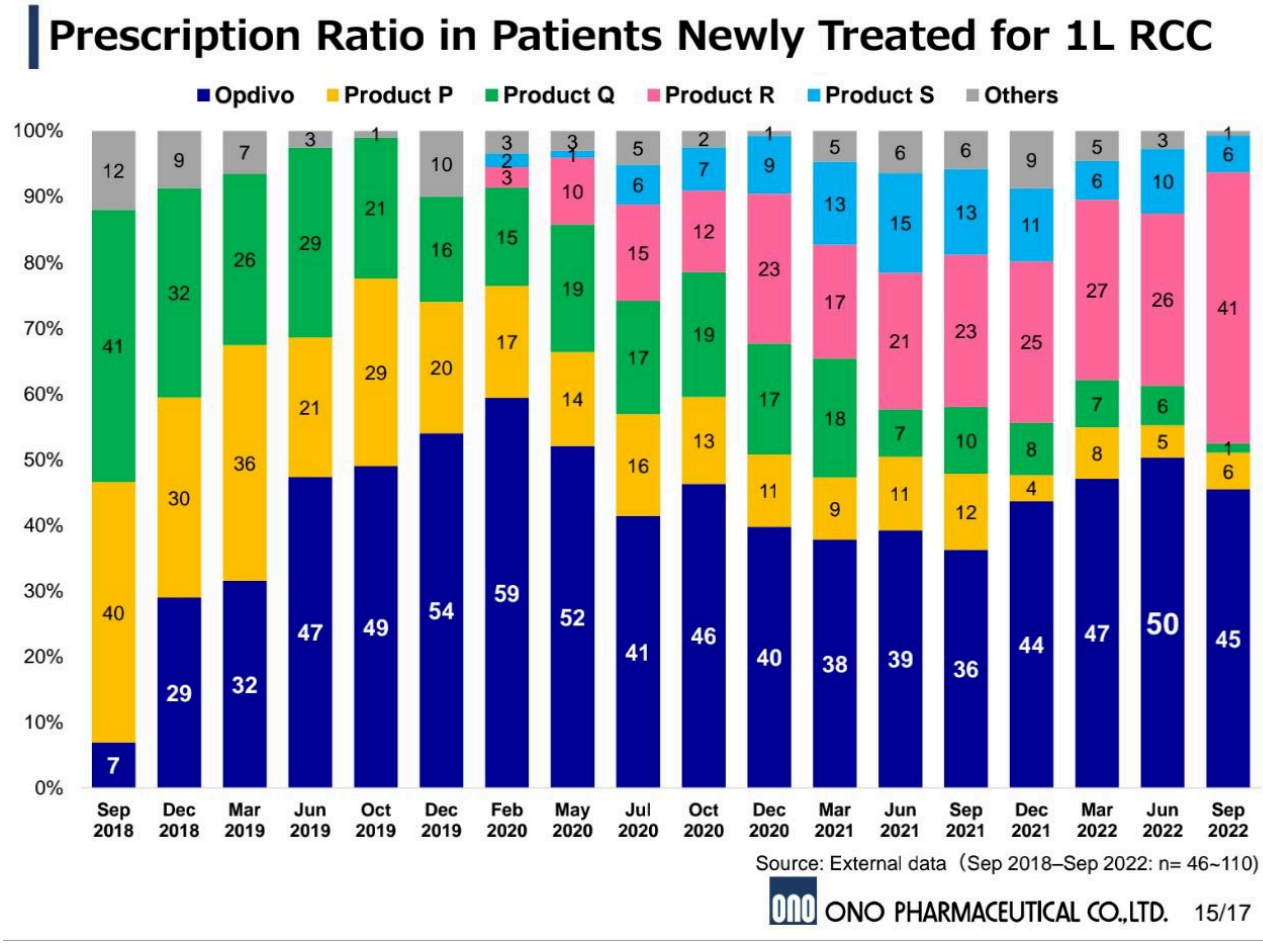
The share of new patients in postoperative adjuvant therapy for esophageal cancer was 37% as of September and has risen to nearly 40%.

The doctors who use the product have no problem with its safety, and it is highly regarded as a new treatment option. We are asking them to consider the introduction of the product after carefully reviewing the risks and benefits of the product after the surgery. We would like to increase the presence of Opdivo in the gastrointestinal field as well.



Finally, this is urology field.

We have evidence of Opdivo for first-line and second-line treatment and beyond, and are currently working to bring Opdivo to all renal cell carcinoma patients. In particular, the number of patients in this first-line treatment of renal cell carcinoma is 5,000 per year.



This chart shows the market share trend of new prescriptions in the first-line treatment of renal cell carcinoma.

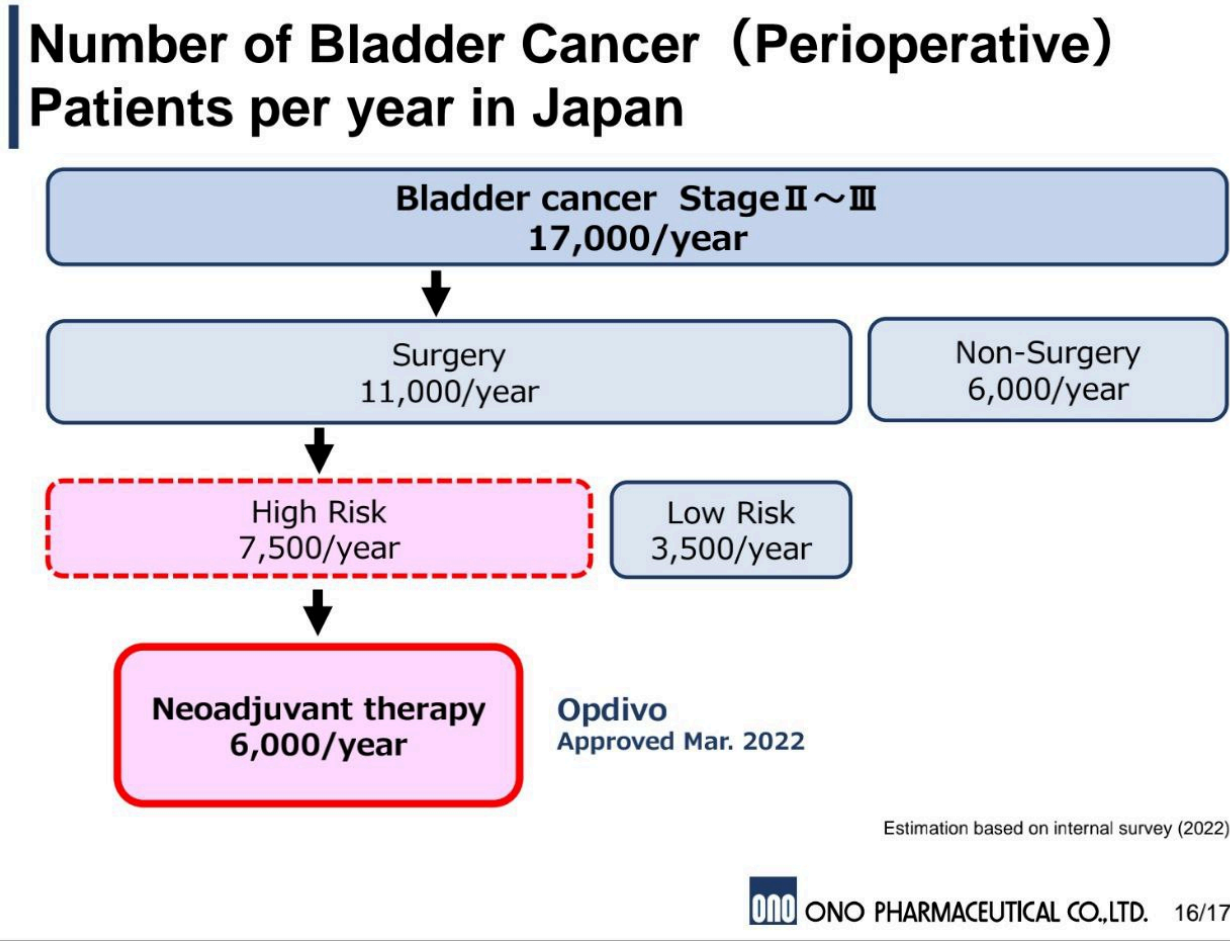
In first-line treatment, the prescription of IO combination therapy is widely used, recently with 90% of patients receiving IO combination therapy.

The share of new patient prescriptions for Opdivo, Yervoy, and the combination of Opdivo and TKI is 45%. The prescription share is 14% for faborable risk, 72% for intermediate risk, and 50% for poor risk.

We will continue to maintain the number one position in first-line treatment with the Opdivo regimen.

Finally, I would like to explain urothelial carcinoma.

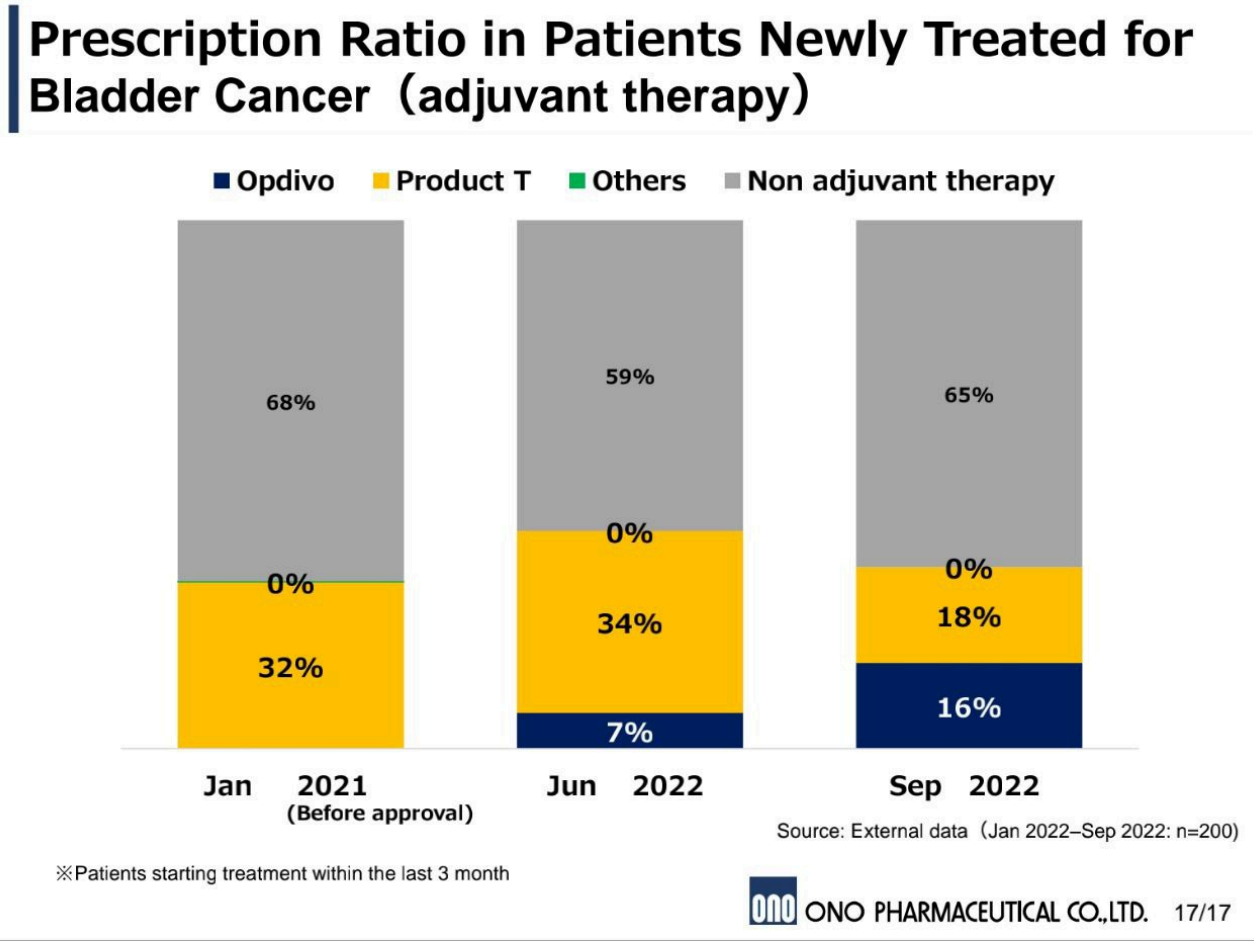
As you know, urothelial carcinoma is a cancer that develops on the urothelium or mucosa of the renal pelvis, ureter, bladder, and urethra. Bladder cancer accounts for 80% of all urothelial cancers in Japan.



For this reason, we show the number of patients in the operative stage of bladder cancer on page 16 of your handout.

The number of patients with stage II – III bladder cancer is 17,000 per year. Of these, 11,000 are said to be eligible for surgery.

Among these patients, we believe that the number of patients at high risk of recurrence is about 7,500, and we estimate that the number of patients who will receive preoperative adjuvant therapy with Opdivo is 6,000 per year.



The share of new patients for postoperative adjuvant therapy for urothelial carcinoma, which was approved in March of this year, was 16% as of September, and it is just beginning to grow.

From KOL, the evaluation from the doctors who use our products is gradually expanding, and we would like to do a good job regarding this area.

This is the last slide from me, which is also a reference material.

I explained the trends of Opdivo, the general situation, and then by cancer types. Currently, Opdivo has expanded to 23 regimens for 11 cancer types and we are developing our activities by targeting at this very large market. We anticipate the approval of preoperative adjuvant therapy for non-small cell lung cancer in the future and will continue to work hard to meet the unmet needs of cancer patients.

Question & Answer

Questioner 1: I just want to confirm one thing on the current material. It's on page 16 about bladder cancer. Is this preoperative or postoperative?

Takahagi: Postoperative.

Questioner 1: After the surgery, right? This is a typo, right?

Takahagi: We use the term "preoperative" because patients who received chemotherapy before surgery are eligible for this product.

Questioner 1: So, the notation is correct?

Takahagi: Yes.

Questioner 1: My first question is about the exchange rate. As the President explained at the beginning of the presentation, the revenue should be profit as it is, but I feel that the profit was lost in the process. Is it as you expected? I just expected that the impact of the exchange rate would be a bit more.

Sagara: What do you mean by “as we expected”?

Questioner 1: I think you were talking about adding JPY16 billion on the top line because you had previously mentioned JPY800 million per JPY1 depreciation. I thought it was strange how it went in and out, because it got on the top line but didn't quite drop down, so could you explain that?

Sagara: As for JPY800 million net with JPY1.1 billion plus and JPY300 million minus, this is based on operating profit. Looking at revenue alone, we see JPY1.1 billion plus per JPY1. We expected that the rate would be JPY110 in H1. When we closed it in H1, it was JPY133. Therefore, multiplying JPY23 by JPY1.1 billion is resulting in an increase in revenue of around JPY12 billion.

However, the unexpected part was that the depreciation of the euro, without which the revenue would have been higher. Also, the expected royalties, which we have not disclosed, were a little short.

Questioner 1:I think that the yen will be depreciating by another about JPY10 depending on the situation, but it is unlikely that JPY1 depreciation will result in operating income of JPY800million. Should we assume that it will be pretty much disappeared along the way, as it did this time?

Sagara: The risk of somewhat lowering that JPY800 million could come up in relation to the euro.

Questioner 1: My second question is about Opdivo. As for the results up to the interim period compared to the full-year forecast, I heard that sales on lung cancer were a little low, but sales on gastric cancer were a little strong. You said that the sales are always skewed in the back, or the sales are still growing, even though the sales are a little less than 50%.

Can you please explain us if there are any indications that stand out to go up or down in terms of whether you can achieve the full year figures?

Sagara: Do you mean that you think it's a bit tough from the progress? Although there is a certain tendency to think that way, Opdivo is expected to grow significantly in H2, especially for gastric cancer and esophageal cancer as well.

The prescription rate itself is approaching 70% for gastric cancer, but the average duration of administration is currently eight and a half months. This may be extended, so the figures are likely to grow in H2.

What we are concerned about is that lung cancer is not doing well. This is a bit lower than planned. The point is whether we can recover from this and whether we can go above our plan in gastric and esophageal cancer. As for what will happen in this area, we are currently keeping the original figures, including the forecast, unchanged. That's how we came up with JPY155 billion.

Questioner 1: As far as the outcome is concerned, lung cancer is a little low, but gastric cancer covers it, is that right? You expect that would work.

Sagara: Yes, that's right.

Questioner 1: Lastly, you mentioned that the overseas development of ONO-7475 was discontinued for strategic reasons. Does this mean that you will no longer develop overseas, or will it be developed overseas for other indications? I mention about an Axl/Mer inhibitor. Can you comment on this?

Idemitsu: We conducted clinical study of ONO-7475 for acute leukemia in the US this time. We have discontinued development for that indication, but we are still developing for other indications, for example, lung cancer. Depending on the clinical result, we consider global development. Therefore, we did not discontinue this compound itself.

Questioner 1: So, you mean that you discontinued the development for acute leukemia in the US?

Idemitsu: We have discontinued the development for this indication regardless of any regions.

Questioner 1: Do you not have enough confidence for acute leukemia in its product profile?

Idemitsu: We thought that the possibility of fulfilling the unmet needs was not very high.

Questioner 2: I have some questions on Opdivo trends. The graph you have shown us today indicates that the situation in lung cancer seems to be declining a bit, instead of "not growing." Can you tell us if there is no risk of further decline?

I would also like you to comment on how the approval of Tecentriq for adjuvant treatment in May will affect advanced cancer.

Takahagi: First of all, we believe that the effect of adjuvant treatment is almost minimal. Since Opdivo was originally indicated for stage IV and many of those patients in that stage are not eligible for surgery, we do not expect much impact.

One more point, regarding the number of new Opdivo prescriptions in the future, as you mentioned, the situation is a bit flat right now. However, we have a five-year follow-up data for the 227 regimen and will have a long-term follow-up data for the 9LA regimen in the future and will continue to promote these data firmly as these regimens are expected to achieve a tail plateau or long-term survival.

One point of concern is that some doctors still have some doubts about the safety of the product, so we will continue to promote the usefulness of the product as well as safety measures.

Questioner 2: In the area of advanced cancer of the upper gastrointestinal tract, you mentioned that peak sales achieved the target earlier than usual. Given the current momentum, do you think there is a possibility to increase your market share even if you revise your target higher? Or are you in the situation where you

have already reached a good point quite quickly? Although you have good number already, is it difficult to increase the number of new patients any further?

Takahagi: We explained earlier that the market share for the first-line treatment of gastric cancer is 70%. In this area, the number of doctors who measure PD-L1 then use the product has been increasing significantly. They divide patients with PD-L1 CPS5 or higher, or less than CPS5. Based on Opdivo data, the share for CPS5 or higher currently accounts for up to 90% of prescriptions for new patients.

On the other hand, the segment of less than CPS5 accounts for 60%, and we believe that there is still room for growth in this segment. We would like to grow this segment further.

Questioner 2: My final question is about the adjuvant treatment for esophageal cancer. The graph shows that your market share seems to have fallen after rising once. The guidelines of the Esophagus Society of Japan were released around summer, and it is described that they could not make a decision on its recommendation.

As this information has become more widespread, I wonder if doctors who were aggressively using immediately after the approval have become a bit more cautious, as shown in these figures, and if there is a possibility of a slight decline in this trend.

Takahagi: This data is from an online survey to doctors. Since the number of doctors who took the survey was limited, we consider this to be within the margin of error.

As for the recommendation from the esophageal association, we are providing accurate information to them. However, when we ask the clinical doctors, they tell us that Opdivo came to a place where there had been no standard therapy for adjuvant treatment. We believe that doctors have fairly high expectations for this area.

As I indicated, there are still some doctors who are not giving adjuvant therapy or are using only chemotherapy. If we can emphasize the efficacy of Opdivo and the postoperative safety of Opdivo, we believe the market will grow further.

Questioner 3: I will ask you two simple questions. I think Mr. President mentioned that the royalty base of Opdivo is decreasing. What does this mean? Is it about Bristol sales or has there been some change in the royalties you are receiving from outside Bristol? I know that the royalty rate will not change until 2024, but could you please make it clear a little more?

Sagara: Bristol sales in the US is not going as planned and is a little short of the expectation.

Questioner 3: What is the reason there?

Tsujinaka: In the US, where BMS understands the situation, they set targets that are about twice as high as those outside the US, in terms of growth rate. They set relatively solid goals in other terms. In fact, in past years, they have exceeded their initial target in terms of volume.

As you know, more than 70% of our royalties come from outside the US. When they set aggressive targets in the US and even if they do not meet the targets in the US, we received royalties from outside the US where solid sales are achieved. Therefore, the total royalties received have never been less than the projected royalties.

This time, the volume-based figures outside of the US have not changed at all and are on target, but the unexpected depreciation of the euro against the US dollar has caused a sudden drop in those areas. As a result, we are in the situation where we are not able to cover the shortfall in the US based on the same target as made last year.

Therefore, although the movement is on a volume basis similar to that of previous years, the base appears to be a little worse externally due to the exchange rate.

Questioner 3: Do you think that it will have a chronic effect in the future?

Tsujinaka: No. The usage itself is generally hovering just a bit below their target in the US. This has been the trend in the past year. Outside of the US, the numbers are slightly above target, and this trend is exactly the same this year as well.

The exchange rate outside of the US, the depreciation of the euro was more pronounced than expected, so royalty income did not reach the level we had expected. The movement on a volume basis is similar to past years.

Questioner 3: Also, I would like to get an update on the Velexbru. I would like to know the domestic sales situation and the fact that you are planning to file an application for Phase II in the US. Have there been any changes in the outlook and prospects for this area? Can you please clear this up as to how this works in terms of timing?

Sagara: We would like to apply with the results of P2. We have not disclosed the timing, but since we are going with the results of P2 without P3, you can roughly imagine what we are talking about. We would like to make this public when the time is right to do so.

Questioner 3: What is the domestic sales situation, and also, this is already approved in South Korea, isn't it?

Takahagi: In South Korea, it was approved in November 2021. In Japan, we have received approvals for two indications of PCNSL and WM/LPL, and both sales are progressing very well.

The reason for the great progress is that both diseases are rare diseases, and until now, inpatient treatment has been the main regimen. There have been issues such that some patients prefer outpatient treatment, and that some elderly patients have difficulties for the currently available treatment methods.

We had a hard time finding target facilities or doctors as these are rare diseases, but the penetration of Velexbru has been very fast with the information dissemination through various digital media and websites. This, combined with the growing needs of patients, has led to a steady increase in sales for Velexbru.

Although this indication is for a rare disease, we believe that the number of patients will increase, and expect to be able to expand sales a little more.

Questioner 4: I have two questions. I have another question on Opdivo. I am looking at pages two and three, and since you explained it in detail, I understood it well. However, by simply looking at these pages, non-small cell lung cancer is a bit of a struggle.

Conversely, esophageal cancer and other cancers were better than expected, and it shows 16% increase in the number of patients, even though these are simply the number of patients and sales and I understand that they do not move in parallel. Can I understand that the 45% increase in others can be explained by bladder cancer?

Takahagi: For this, cancers of unknown primary source and bladder cancer were also included in others.

Questioner 4: This is a 16% increase in esophageal cancer simply by looking at the number of patients, but is this more than expected? Lung cancer is slightly lower than expected, right?

Takahagi: That's right. The number of prescriptions for lung cancer is slightly lower than expected, while the number of prescriptions for esophageal cancer is higher than expected, as you mentioned.

Questioner 4: And you expected that it would grow in Q3 and Q4, and that hasn't changed.

Takahagi: No.

Questioner 4: I also would like to ask about the exchange rate. As the President mentioned earlier, JPY1.1 billion minus JPY300 million is JPY800 million plus, and if we simply think about it, you have revised the exchange rate by JPY20, so it results in JPY16 billion with eight times two.

The increase was JPY4 billion, but you mentioned there was R&D expenses. The minus is JPY300 million, so three times two is JPY6 billion. I know I am a little persistent, but I am wondering if there will be a little more. Was this absorbed in the middle, or should we assume that you are being somewhat conservative and have revised the amount of such an increase?

Sagara: I think the costs have been properly included and we are being conservative.

Questioner 4: Is it safe to assume that there is a slight upward swing, or buffer, through Q3 and Q4?

Sagara: I can only comment here that it is a revised announcement. However, the cost will increase by about JPY6 billion if the minus 3 is totaled. I am not sure if we are adding more considering the costs, but that is the general idea, and we have revised it based on the concept of adding the cost firmly.

Questioner 4: My last question is about royalties. In terms of Bristol and Merck, looking at Q2 alone, Bristol royalty is JPY21.3 billion and Merck royalty is JPY11.6 billion. Of course, Merck royalty will decrease first. What is your overall vision for the future? Is it safe to assume that the slight decrease in Merck royalty will be able to be absorbed by Bristol royalty?

Sagara: We hope that it would be absorbed, but as you say, the Merck royalty is going down. As for Bristol royalty, it will last until 2031. This is a strict fact. There will be additional indications, combination therapies, and many other developments leading to an increase in Bristol's royalties. I expect that it will up.

Questioner 5: I have two brief questions. One is about ONO-2909. The development for narcolepsy has been discontinued, but are there any plans to develop the drug for other sleep disorders or other indications? This is my first question.

Idemitsu: Based on the results of Phase I in narcolepsy patients, we decided to discontinue the development because we consider that the likelihood of other sleep disorders is low.

Questioner 5: On a completely different note, please let me know if there has been any progress in the lawsuit with AstraZeneca regarding Imfinzi.

Sagara: The trial has made no progress so far. It continues. We will make further announcements as progress is made.