ONO PHARMACEUTICAL CO., LTD.

Q1 Financial Results Briefing for the Fiscal Year Ending March 2022

July 30, 2021

[Number of Speakers]	6	
	Toshihiro Tsujinaka	Member of the Board of Directors, Senior Executive Office, Executive Director of Corporate Strategy & Planning
	Kiyoaki Idemitsu	Member of the Board of Directors, Corporate Executive Officer, Executive Director of Clinical Development
	Hiroshi Ichikawa	Corporate Senior Executive Officer, Executive Director, Sales and Marketing
	Yukio Tani	Corporate Executive Officer, Head of Corporate Communications
	Satoshi Takahagi	Business Unit Director, Oncology Business Unit, Sales and Marketing
	Kazuhiro Nagahama	Director of Finance and Accounting Department

Revenue

Revenue	YoY Change
¥ 87.4 billion	+ 16.6 %

Breakdown of Revenue

(Billion yen)

	FY 2020 Q1	FY 2021 Q1	YoY
Revenue of Goods and Products	53.6	**60.5**	+ 13.0 %
Royalty & other revenue	21.3	**26.8**	+ 25.7 %
Total	74.9	**87.4**	+ 16.6 %

Nagahama: Revenue for the first quarter of the current fiscal year increased by JPY12.4 billion, 16.6%, compared with the same period of the previous fiscal year, to JPY87.4 billion.

As for the breakdown of revenue, product sales increased by JPY7 billion YoY, or 13%, to JPY60.5 billion. This was due to steady increase in sales of products such as Opdivo intravenous infusion, Forxiga tablets, Orencia subcutaneous injection, Parsabiv intravenous injection for dialysis, and Kyprolis for intravenous injection, while sales of long-term listed products decreased.

Royalty and other revenue increased by JPY5.5 billion YoY, or 25.7%, to JPY26.8 billion. In royalty and other revenue, royalty from Bristol Myers Squibb totaled JPY17 billion, an increase of JPY3 billion YoY. Royalty related to Keytruda from Merck was JPY6.8 billion, an increase of JPY1.1 billion YoY.

Revenue

Sales of Major Products

(Billion yen)

	FY 2020 Q1	FY 2021 Q1	YoY Change
Opdivo	24.4	**29.0**	+ 18.7 %
Forxiga	5.2	**7.5**	+ 43.3 %
Glactiv	6.5	**6.5**	- 1.1 %
Orencia SC	5.4	**5.7**	+ 4.5 %
Parsabiv	1.9	**2.2**	+ 15.3 %
Kyprolis	1.7	**2.0**	+ 18.9 %
Velexbru	0.1	**1.4**	+ 1663.5 %
Onoact	1.0	**1.2**	+ 15.3 %
Braftovi	0.2	**0.7**	+ 280.1 %
Mektovi	0.2	**0.5**	+ 236.3 %
Ongentys	–	**0.2**	–
New Products（FY2021）	–	**0.3**	–

By product, sales of Opdivo increased by JPY4.6 billion YoY, or 18.7%, to JPY29 billion. This is mainly due to its expanded use in the first-line treatment of lung cancer and second-line treatment of esophageal cancer, despite intensifying competition from competing products.

As for other major new products, sales of Forxiga, a treatment for diabetes and chronic heart failure, increased by JPY2.3 billion, or 43.3%, to JPY7.5 billion. Sales of Orencia for rheumatoid arthritis treatment increased by JPY200 million, or 4.5%, to JPY5.7 billion. Sales of Parsabiv, for secondary hyperparathyroidism under hemodialysis, increased by JPY300 million, or 15.3%, to JPY2.2 billion. Sales of Kyprolis, for multiple myeloma, grew steadily by JPY300 million, or 18.9%, to JPY2 billion.

On the other hand, sales of Glactiv, for type 2 diabetes, decreased by JPY100 million YoY, or 1.1%, to JPY6.5 billion.

Revenue

Sales of Long-term Listed Products

(Billion yen)

	FY 2020 Q1	FY 2021 Q1	YoY Change
Opalmon	1.5	**1.2**	- 17.5 %
Rivastach	2.0	**0.8**	- 60.7 %
Onon capsule	0.7	**1.1**	+ 67.6 %

Sales of long-term listed products decreased due to the impact of measures to promote the use of generics. Sales of Opalmon decreased by JPY300 million YoY, or 17.5%, to JPY1.2 billion. Sales of Rivastach decreased by JPY1.2 billion YoY, or 60.7%, to JPY800 million.

Operating Profit

Operating Profit	YoY Change
¥ 29.8 billion	+ 10.2 %

Costs, etc.

(YoY Change)

・Cost of Sales	¥ 22.8 billion	(+ 10.9%)
・R&D Expenses	¥ 15.2 billion	(+ 23.5%) ①
・SG&A Expenses	¥ 19.0 billion	(+ 33.5%) ②
①+② Total	¥ 34.2 billion	(+ 28.9%)
・Other Income	¥ 0.2 billion	(+ 106.5%)
・Other Expenses	¥ 0.8 billion	(- 11.3%)

Operating profit increased by JPY2.7 billion YoY, or 10.2%, to JPY29.8 billion. In terms of expenses, cost of sales increased by JPY2.2 billion YoY, or 10.9%, to JPY22.8 billion. This is mainly due to an increase in product sales.

R&D expenses increased by JPY2.9 billion YoY, or 23.5%, to JPY15.2 billion. This was mainly due to the gradual recovery of development activities, including the enrollment of patients, as well as an increase in expenses related to development and research.

As for selling, general and administrative (SG&A) expenses excluding R&D expenses, although there were some restrictions on activities such as coronavirus-related voluntary suspension of MR hospital visits, marketing activity expenses increased due to the aggressive implementation of web lectures. In addition, there was an increase in expenses related to the launch of new products and co-promotion fees associated with the expansion of sales of Forxiga. SG&A expenses excluding R&D expenses increased by JPY4.8 billion YoY, or 33.5%, to JPY19 billion.

Profit before Tax

Profit before Tax	YoY Change
¥ 30.8 billion	+ 8.8 %

Net financial income, etc.

+ ¥ 1.0 billion (YoY Change - ¥ 0.3 Billion)

Finance income :	**¥ 1.3 Billion**
(Dividend income received and gain on sale of investment securities, etc.)	
Finance costs :	**¥ 0.3 billion**
(Loss on valuation of investment securities and interest expense arising from lease obligations, etc.)	

Profit before tax increased by JPY2.5 billion YoY, or 8.8%, to JPY30.8 billion. This was due to financial income of JPY1.3 billion, financial expenses of JPY300 million, and a decrease in net and other financial income by JPY300 million to JPY1 billion.

Profit for the Period (Owners of the Parent Company)

Profit for the Period (Owners of the Parent Company)	YoY Change
¥ 24.1 billion	+ 12.0 %

Income tax expense

¥ 6.7 billion (YoY Change - 1.1 %)

(Major change factors)

Increase in profit before tax	¥ 2.5 billion
Decrease in corporate tax	¥ 0.1 billion

Next, quarterly profit attributable to owners of the parent.

The profit for the period attributable to owners of the parent increased by JPY2.6 billion YoY, or 12%, to JPY24.1 billion, due to an increase in profit before tax. Both revenue and profit at each level were record highs for the first quarter.

As for the full-year forecast for the fiscal year ending March 31, 2022, there is no change from the forecast announced on May 13, 2021.

We plan to pay an interim and year-end dividend of JPY28 per share, or JPY56 per share for the full year. There is no change at present. Since the previous fiscal year's annual dividend was JPY50 per share, so the dividend for the current fiscal year will increase by JPY6 per share.

Tani: I would just like to add a few words.

Although we have not revised the overall forecast, we have slightly revised the forecast for individual products.

At the time of the last revision of the business forecast on May 13, we revised the forecast for Opdivo from JPY120 billion to JPY110 billion.

We have made some corrections to a few other individual products at this time.

The initial forecast for Forxiga was JPY30 billion, but we have now revised it to JPY35 billion. In addition, the previous forecast for Velexbru was JPY3.5 billion, but we have revised it to JPY5 billion, an increase of JPY1.5 billion.

On the other hand, the sales forecast for new products launched in the current fiscal year was originally set at JPY7 billion, but we have now revised the forecast downward to JPY2.5 billion, a decrease of JPY4.5 billion.

In addition to the current steady sales progress of Forxiga, the approval timing for the indication of chronic renal failure will be earlier than expected. So, we have added JPY5 billion to the previous forecast.

In consideration of the steady progress in the first quarter, we have revised the forecast for Velexbru upword by JPY1.5 billion to JPY5 billion.

On the other hand, 2 products were launched in the current fiscal year, Adlumiz and JOYCLU. The blue letter was issued on June 1 for JOYCLU, by which we have made revisions considering significant changes in the environment.

As for the royalties from Bristol Myers Squibb and Merck, Mr. Nagahama has just provided you with the figures. We are sorry to say that we are unable to disclose the detaied figures for royalties from Roche. However, you can refer to the figures for Europe on page 12 of the financial report for information on sales revenue by region.

As for royalties from Roche, royalties on sales of Tecentriq were recorded in the third quarter last year. Therefore, there were no royalties from Roche in the first quarter, so I hope you can understand that most of the difference here is due to that.

Development pipeline

Idemitsu: As for the materials, pages 13 to 16 of the financial results show the main progress of the development products. First, we will use this financial summary to explain the parts that have been updated since the fiscal year ended March 31, 2021.

The structure of this document is as follows: first the oncology field, and then the non-oncology field. In addition, the order is as follows: approval, application, Phase III, Phase II, Phase I, and those in advanced stages of development. Let me start with the oncology field.

(4) Main Status of Development Pipelines (Oncology)

As of July 26, 2021

<**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	Malignant pleural mesothelioma *1	Injection	Japan S. Korea	In-license (Co-development with Bristol-Myers Squibb)

★: Combination with Opdivo.
Changes from the announcement of financial results for the fiscal year ended March 2021
*1: Applications were approved in Japan and South Korea for combination therapy of Opdivo and Yervoy for the treatment of unresectable advanced or recurrent malignant pleural mesothelioma.

<**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
Opdivo Intravenous Infusion / Nivolumab	Additional indication	Urothelial cancer	Injection	Japan	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Esophageal cancer	Injection	Japan	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Cancer of unknown primary *2	Injection	Japan	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication for pediatric use	Hodgkin lymphoma *3	Injection	Japan	In-house (Co-development with Bristol-Myers Squibb)

Changes from the announcement of financial results for the fiscal year ended March 2021
*2: An approval application for Opdivo was filed in Japan for the treatment of cancer of unknown primary.
*3: An approval application for Opdivo was filed in Japan for the treatment of pediatric patients with hodgkin lymphoma.

<**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	Esophageal cancer	Injection	S. Korea Taiwan	III	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Hepatocellular carcinoma	Injection	Japan S. Korea	III	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Ovarian cancer	Injection	Japan	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	Biliary tract 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)

As for Yervoy, which is listed on page 13, it was approved in Japan in May and in South Korea in June for use in combination with Opdivo for malignant pleural mesothelioma.

Next, in the application of Development Pipeline section, the third line of the table, we filed an application for approval of Opdivo for the treatment of unknown primary cancer in April and for pediatric use for Hodgkin's lymphoma in January.

<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	Japan S. Korea Taiwan	III	In-license (Co-development with Bristol-Myers Squibb)
	Additional indication	Urothelial cancer	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)
	Additional indication	Virus positive / negative solid carcinoma	Injection	Japan S. Korea Taiwan	I / II	In-license (Co-development with Bristol-Myers Squibb)

<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-7701 ★ (BMS-986205) / Linrodostat	New chemical entities	Bladder cancer / IDO1 inhibitor	Tablet	Japan S. Korea Taiwan	III	In-license (Co-development with Bristol-Myers Squibb)
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-7807 ★ (BMS-986258)	New chemical entities	Solid tumor / Anti-TIM-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-7911 ★ (BMS-986321) / Bempegaldesleukin	New chemical entities	Solid tumor / PEGylated IL-2	Injection	Japan	I	In-license (Co-development with Bristol-Myers Squibb)
ONO-4578 ★	New chemical entities	Colorectal cancer / PG receptor (EP4) antagonist	Tablet	Japan	I	In-house
	New chemical entities	Pancreatic cancer / PG receptor (EP4) antagonist	Tablet	Japan	I	In-house
	New chemical entities	Non-small cell lung cancer / PG receptor (EP4) antagonist	Tablet	Japan	I	In-house
	New chemical entities	Solid tumor・Gastric cancer / PG receptor (EP4) antagonist	Tablet	Japan	I	In-house
ONO-7913 ★ /Magrolimab	New chemical entities	Pancreatic cancer*4 / Anti-CD47 antibody	Injection	Japan	I	In-license (Gilead Sciences, Inc.)
	New chemical entities	Colorectal cancer*4 / Anti-CD47 antibody	Injection	Japan	I	In-license (Gilead Sciences, Inc.)

Next, in the section on products under development in clinical trials, ONO-7913, an anti-CD47 antibody, has started Phase I trials in combination with Opdivo for pancreatic cancer and colorectal cancer, at the bottom of the I-O-related table on page 14.

<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
Braftovi Capsules / Encorafenib	New chemical entities	Colorectal cancer / BRAF inhibitor	Capsule	S. Korea	III	In-license (Pfizer Inc.)
	New chemical entities	Melanoma / BRAF inhibitor	Capsule	S. Korea	III	In-license (Pfizer Inc.)
Mektovi Tablets / Binimetinib	New chemical entities	Colorectal cancer / MEK inhibitor	Tablet	S. Korea	III	In-license (Pfizer Inc.)
	New chemical entities	Melanoma / MEK inhibitor	Tablet	S. Korea	III	In-license (Pfizer Inc.)
ONO-7912 (CPI-613) / Devimistat	New chemical entities	Pancreatic cancer / Cancer metabolism inhibitor	Injection	S. Korea	III	In-license (Rafael Pharmaceuticals, Inc.)
	New chemical entities	Acute myeloid leukemia / Cancer metabolism inhibitor	Injection	S. Korea	III	In-license (Rafael Pharmaceuticals, 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 *5 / BTK inhibitor	Tablet	USA	II	In-house
ONO-7475	New chemical entities	Acute leukemia / Axl/Mer inhibitor	Tablet	USA	I / II	In-house
	New chemical entities	Non-small cell lung cancer*6 / Axl/Mer inhibitor	Tablet	Japan	I	In-house
ONO-7912 (CPI-613) / Devimistat	New chemical entities	Pancreatic cancer / Cancer metabolism inhibitor	Injection	Japan	I	In-license (Rafael Pharmaceuticals, Inc.)
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)*7 / Anti-CD47 antibody	Injection	Japan	I	In-license (Gilead Sciences, Inc.)

★: Combination with Opdivo.
Changes from the announcement of financial results for the fiscal year ended March 2021
*4: Phase I of combination therapy of Opdivo and ONO-7913 was initiated in Japan for the treatment of pancreatic cancer and colorectal cancer.
*5: Phase II of ONO-4059 was initiated in the USA for the treatment of primary central nervous system lymphoma.
*6: Phase I of ONO-7475 was initiated in Japan for the treatment of non-small cell lung cancer.
*7: Phase I of ONO-7913 was initiated in Japan for the treatment of myelodysplastic syndromes (MDS).
* Development of ONO-4483 for the treatment of solid tumor was discontinued in Japan due to strategic reasons.
* Development involving combination therapy of Opdivo and Yervoy for the treatment of head and neck cancer was discontinued because it did not meet primary endpoints.

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

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ONO-4059, a BTK inhibitor, has started Phase II in the US for primary central nervous system lymphoma.

And below that, ONO-7475, an inhibitor of Axl/Mer, has started Phase I in Japan for non-small cell lung cancer.

At the bottom, ONO-7913, the anti-CD47 antibody that I mentioned earlier that we started a new study in combination with Opdivo, has started Phase I for myelodysplastic syndromes, commonly known as MDS.

Also, please see the note regarding cancelled projects. ONO-4483, an anti-KIR antibody, had been in Phase I for solid tumors, but was discontinued for strategic reasons. In addition, a Phase III study in combination Opdivo and Yervoy for head and neck cancer was being conducted, but the development was discontinued due to failure to meet the primary endpoint.

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

As of July 26, 2021

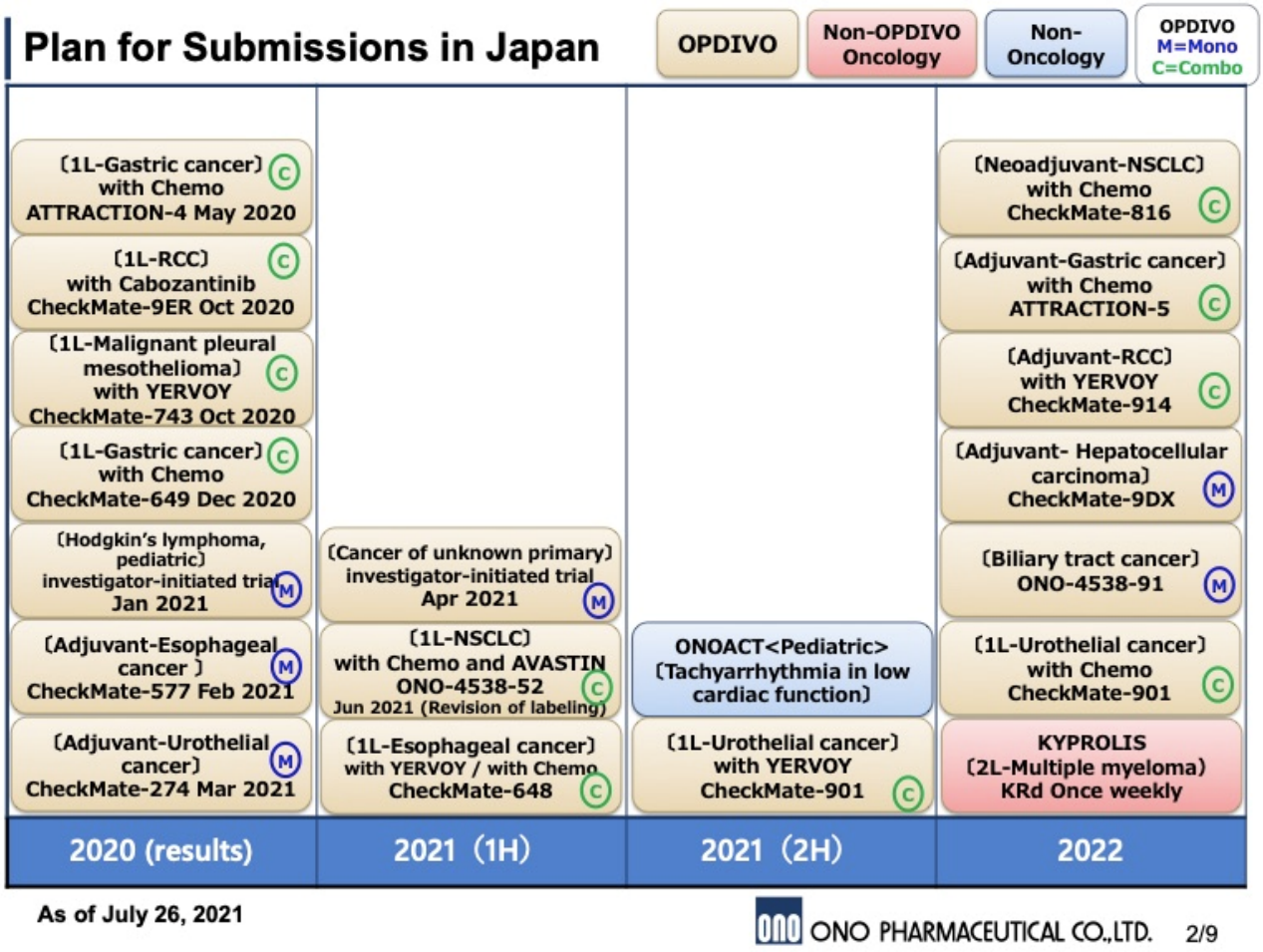
<**Clinical Trial Stage**> *) : "In-house" compounds include a compound generated from collaborative research.

Product Name / Development Code / Generic Name	Classification	Target Indication / Pharmacological Action	Dosage Form	Area	Phase	In-house*) / In-license
Orencia SC / Abatacept	Additional indication	Polymyositis・Dermatomyositis / T-cell activation inhibitor	Injection	Japan	III	In-license (Co-development with Bristol-Myers Squibb)
Onoact for Intravenous Infusion / Landiolol Hydrochloride	Additional indication for pediatric use	Tachyarrhythmia in low cardiac function / Short-acting selective β_1 blocker	Injection	Japan	II / III	In-house
Joyclu Intra-articular Injection / ONO-5704 / SI-613	Additional indication	Enthesopathy / Hyaluronic acid-NSAID	Injection	Japan	II	In-license (Seikagaku Corporation)
Velexbru Tablets / Tirabrutinib Hydrochloride	Additional indication	Pemphigus / BTK inhibitor	Tablet	Japan	II	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	I	In-house
ONO-7684	New chemical entities	Thrombosis / FXIa inhibitor	Tablet	Europe	I	In-house
ONO-2808	New chemical entities	Neurodegenerative diseases / 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

Changes from the announcement of financial results for the fiscal year ended March 2021

* Phase III of protease enzyme inhibitor Foipan Tablets for the treatment of COVID-19 in Japan was discontinued because the clinical trial did not demonstrate efficacy.

We were conducting Phase III of Foipan for COVID-19, but efficacy was not observed and development was discontinued. That's it for the financial summary.



Next, I will focus on the areas that are being updated using the documents on the progress of the development pipeline that are posted on the website.

Please refer to page 2 for the schedule of future applications in Japan.

As you can see in the table, beige columns indicate Opdivo, red indicates non-Opdivo cancer areas, and blue indicates non-cancer areas. For Opdivo, the bottom right corner of the column says M for single agent and C for combination.

As for the timing of the application, please note that this is the fastest schedule if the project proceeds as planned, and the situation may change.

From left to right are the results for FY2020, followed by the schedule for the first half of FY2021, then the second half, and finally the schedule for FY2022 on the far right.

I will now focus on the changes from the previous earnings announcement in May.

First of all, the second section from the left, the first half of FY2021, the application for Opdivo in the top row for cancer of unknown primary was submitted in April. This is as explained in the financial statement.

In June, the package insert of Opdivo was revised for combination treatment with chemotherapy and Avastin for first-line non-small cell lung cancer.

In the previous document, the timing of the application for COVID-19 for Foipan was included in the first half of FY2021, but it was removed due to lack of efficacy.

Next, we will skip 1 step and go to FY2022. The top line, regarding the combination of Opdivo with chemotherapy as preoperative adjuvant for non-small cell lung cancer, the previous data indicated that the application would be submitted in the second half of FY2021, but the timing of the application has been changed to FY2022 due to a delay in the occurrence of events for EFS, one of the primary endpoints. The application period has been changed to FY2022.

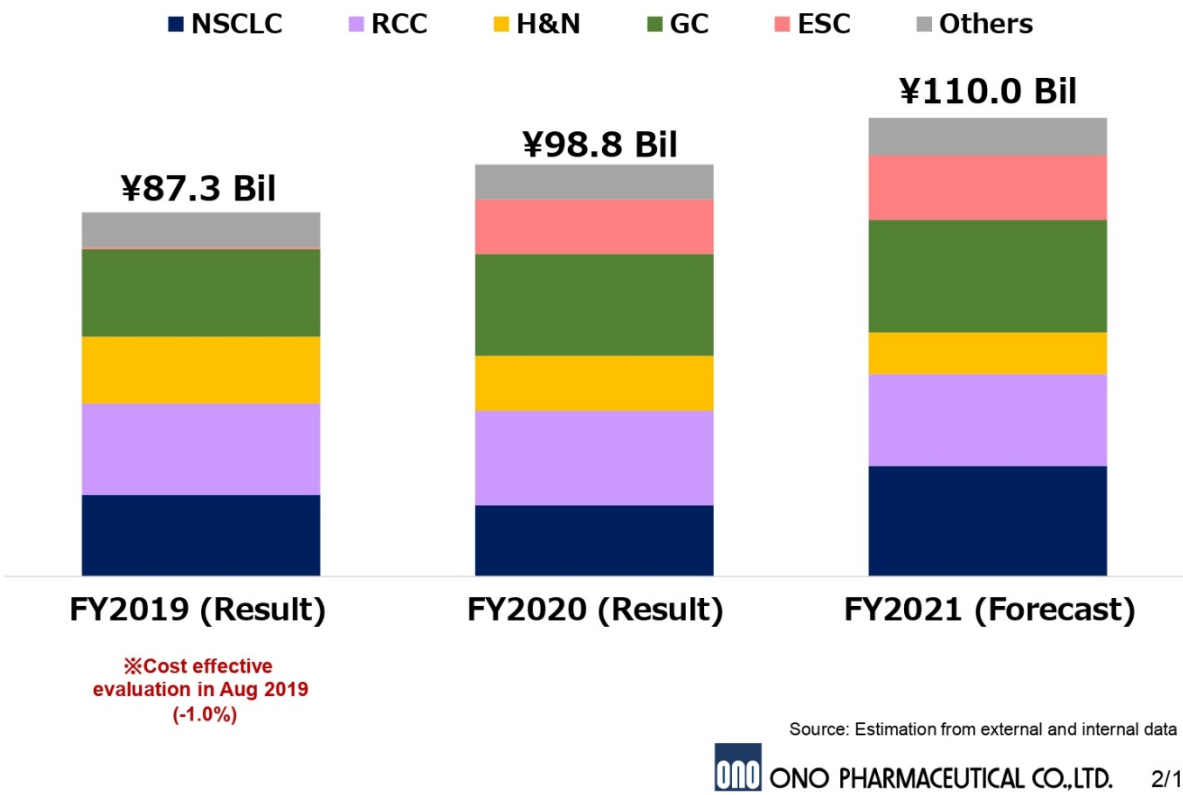
We have changed the timing of the application of Opdivo in the combination with chemotherapy for postoperative adjuvant gastric cancer from the second half of FY2021 to FY2022. This is based on the results of the interim analysis conducted recently where the Independent Data Monitoring Committee deemed that the study continue.

In addition, in the previous document, there was a plan to file an application for combination Opdivo and Yervoy for the first-line treatment of head and neck cancer in the second half of FY2021. As I mentioned in the financial summary, we were unable to achieve the primary endpoint, so it has been removed from the document.

That concludes the section on domestic applications.

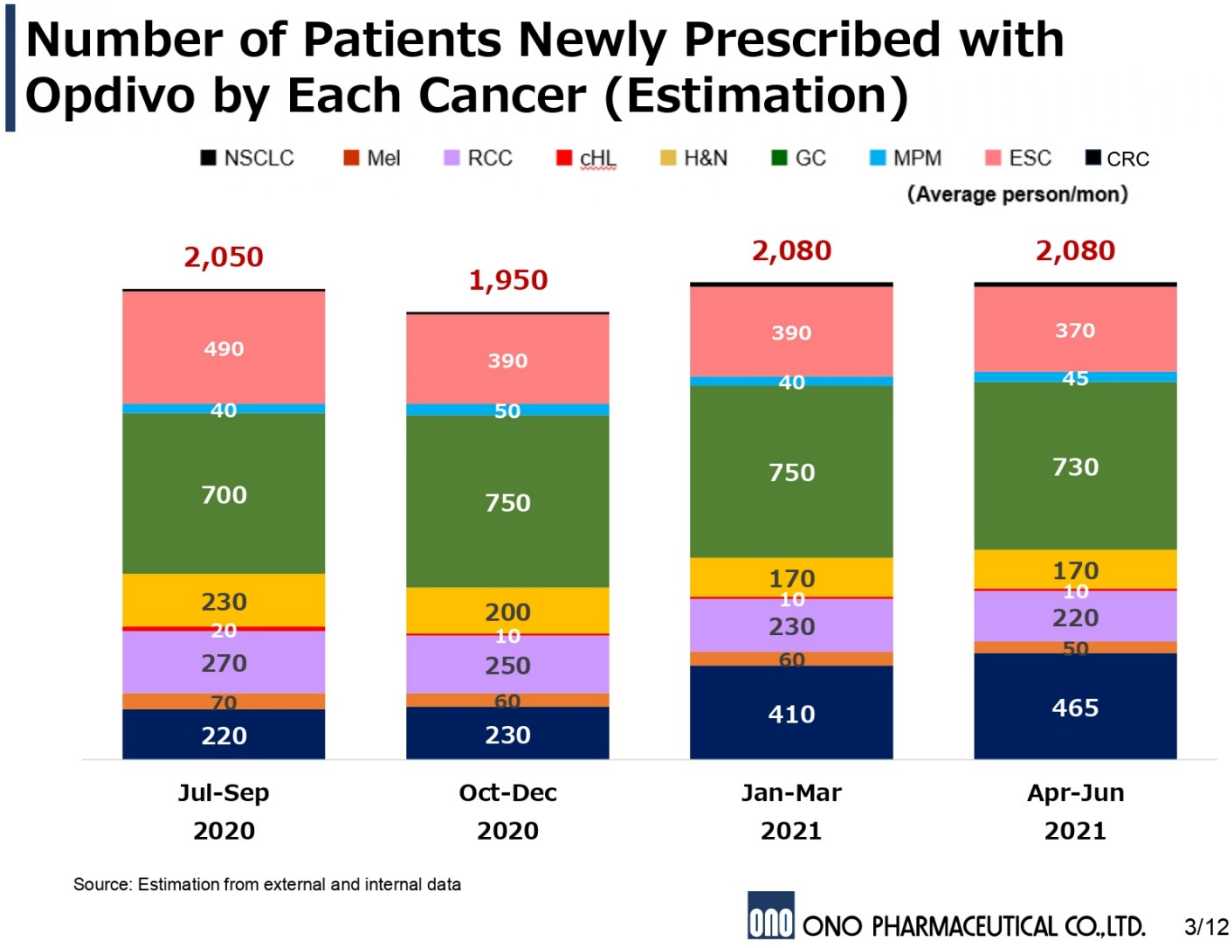
The following pages show the status of the development project, which we hope you will find useful.

Sales Trend of Opdivo by Each Cancer



Source: Estimation from external and internal data

Takahagi: Starting from the bar graph on the left, we have the results for FY2019, FY2020, and the forecast for FY2021. Sales was JPY98.8 billion in FY2020, and we forecast sales of JPY110 billion in the current fiscal year.

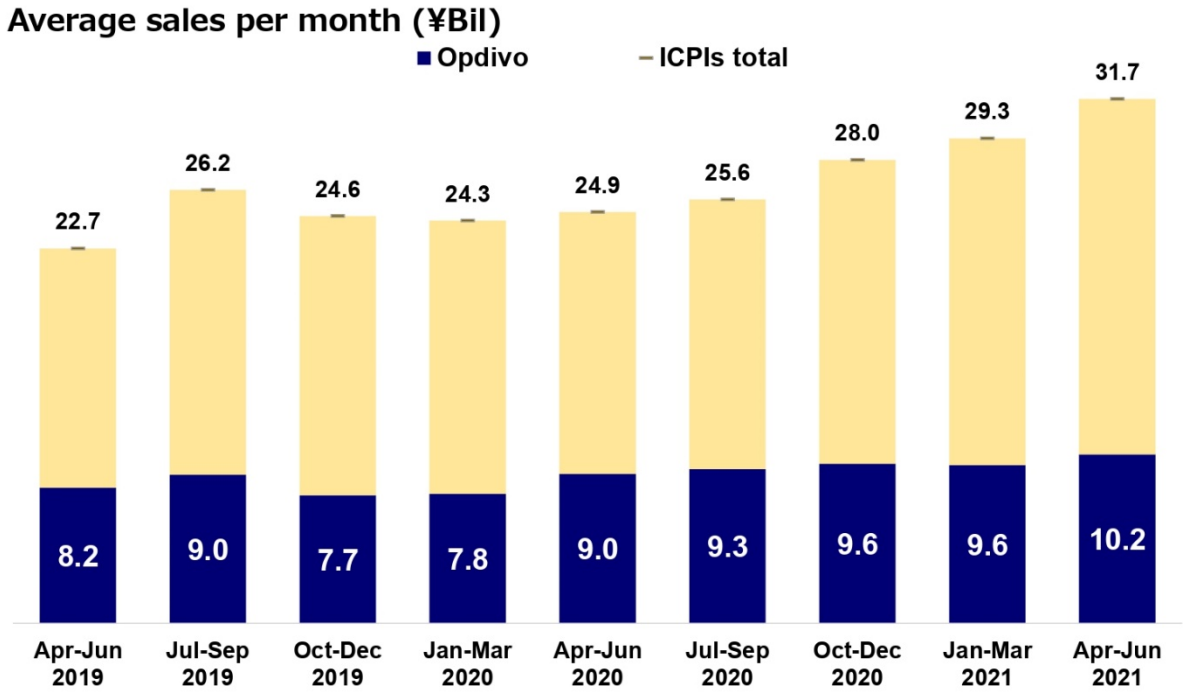


The bar graph on the left shows the quarterly number of new prescriptions for Opdivo by cancer type and the estimated number of new prescriptions from July-September of FY2020 to April-June of FY2021, and also shows the average number of patients per month.

In April-June 2021, the drug was used in an estimated 730 cases for gastric cancer and 370 for esophageal cancer. In lung cancer, it was used in an estimated 465 cases per month on average, including both first- and second-line use. On average, we received 2,080 new prescriptions per month.

The number of newly prescribed patients for the first-line treatment of lung cancer, for which approval was obtained in November last year, was approximately 1,600 from December last year to June this year, with more than 300 new prescriptions obtained in June alone.

Sales Trend of ICPIs (NHI price basis)



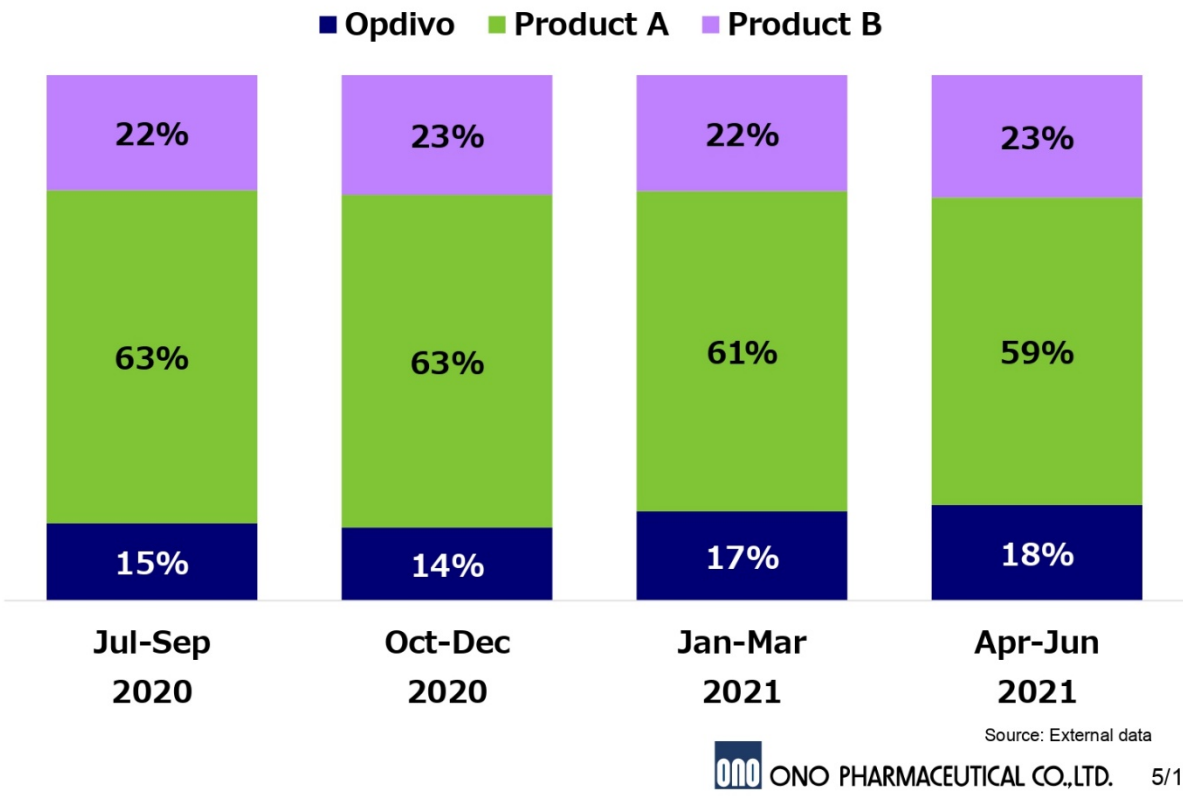
Source: External data

The table shows the monthly average sales of all immune checkpoint inhibitors launched in Japan, on a NHI price basis, from April to June of FY2019 to April to June of FY2021, broken down by quarter.

The numbers on the bar graph represent the sales of all immune checkpoint inhibitors, and the dark blue color shows the sales trend of Opdivo. Sales of immune checkpoint inhibitors have been increasing steadily, and the total sales of all 5 products exceeded JPY300 billion in the market in FY2020.

In this context, sales of Opdivo are increasing with the currently approved 9 types of cancer.

Sales Ratio of ICPIs in NSCLC (Estimation)

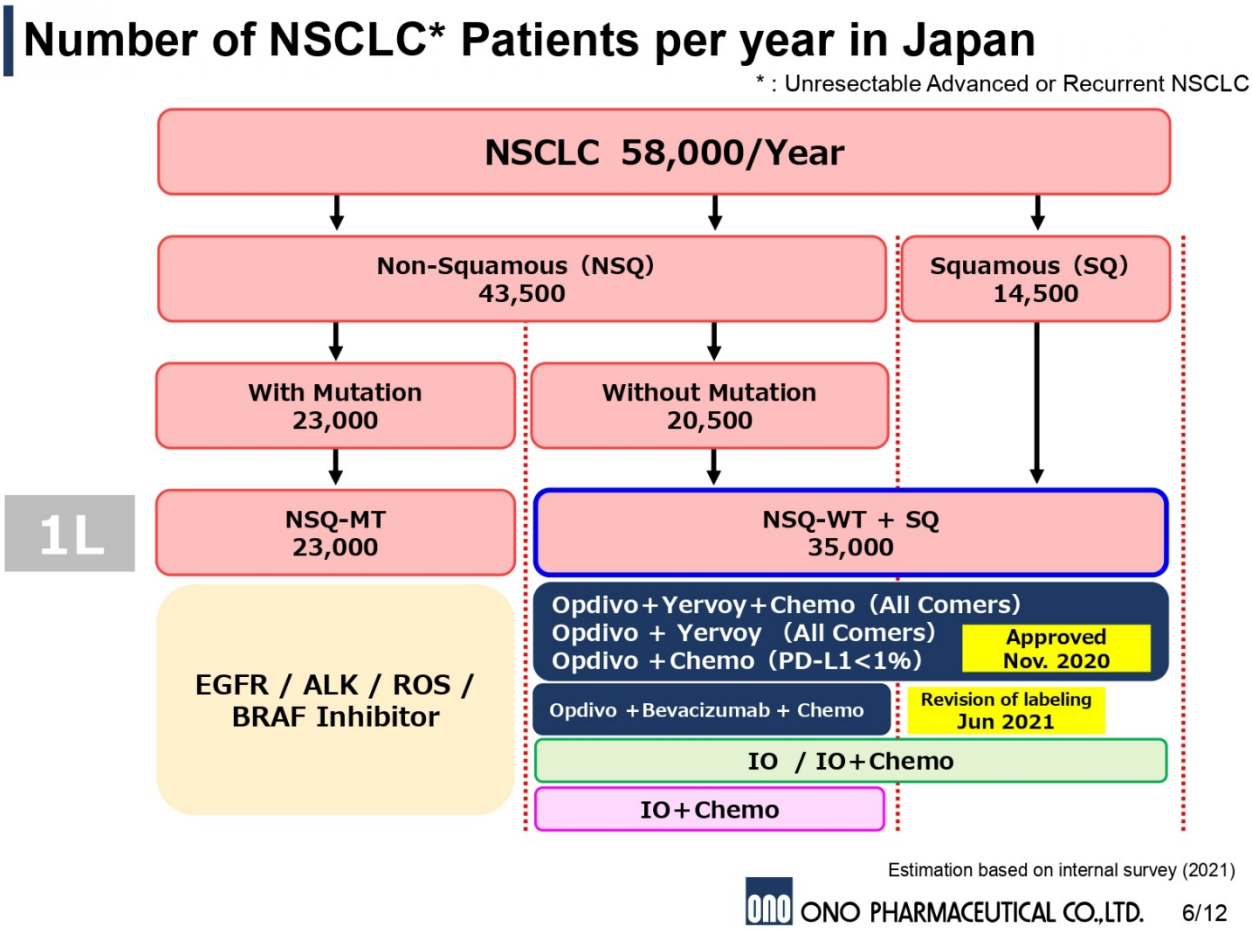


Source: External data

I will introduce the sales by cancer type, starting from the lung cancer field.

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

From the bar graph on the left, we show the period from July to September in FY2020 to April to June in FY2021, by quarter. In the April-June period of 2021, Opdivo accounted for 18% of the market, and we will work to gain further ground in the first-line lung cancer treatment area.



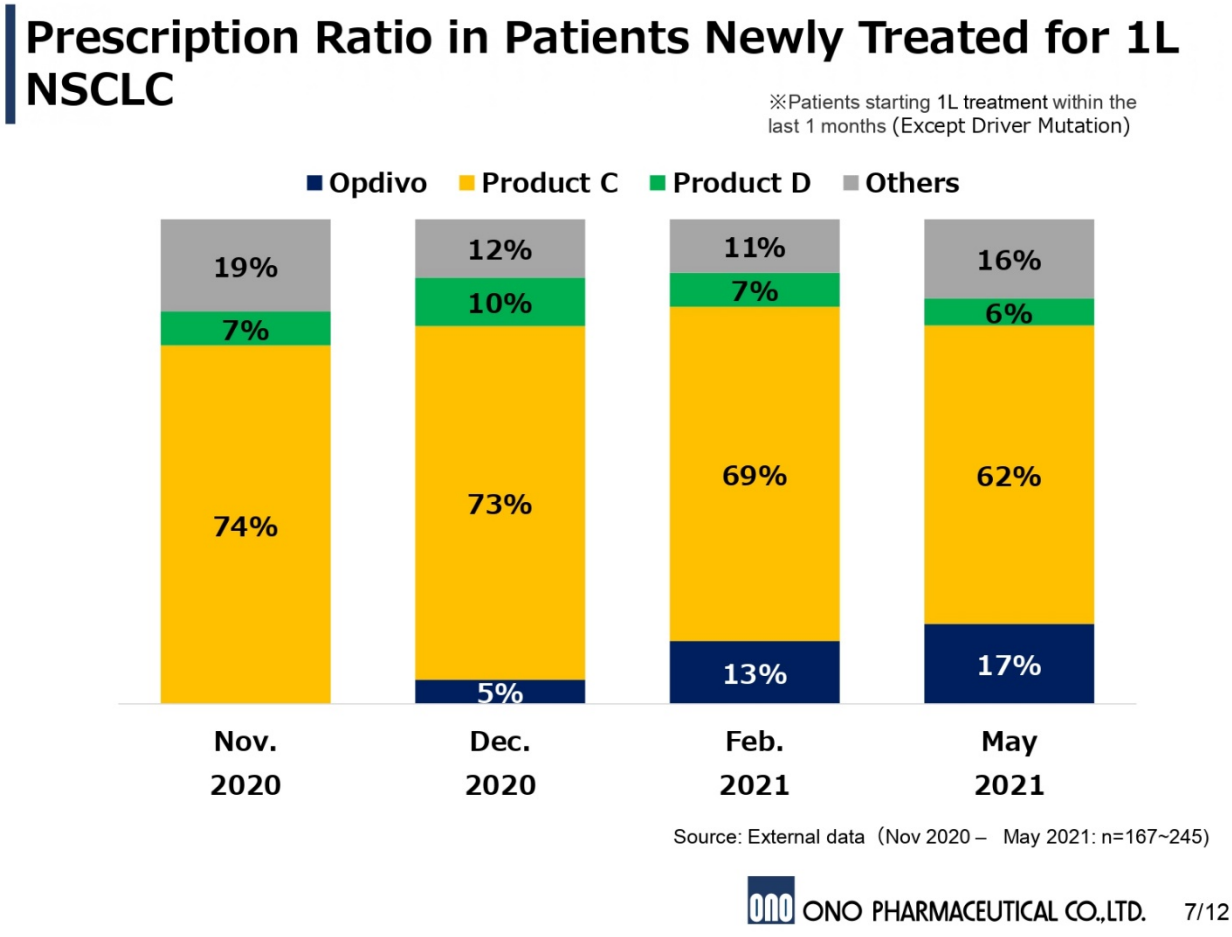
The annual number of patients with non-small cell lung cancer is shown.

The annual number of patients with unresectable advanced or recurrent non-small cell lung cancer is estimated to be 58,000, although this is only an in-house estimate.

Non-small cell lung cancer is divided into non-squamous cell carcinoma and squamous cell carcinoma by histological type, and non-squamous cell carcinoma is further divided by diagnosis with or without genetic mutation.

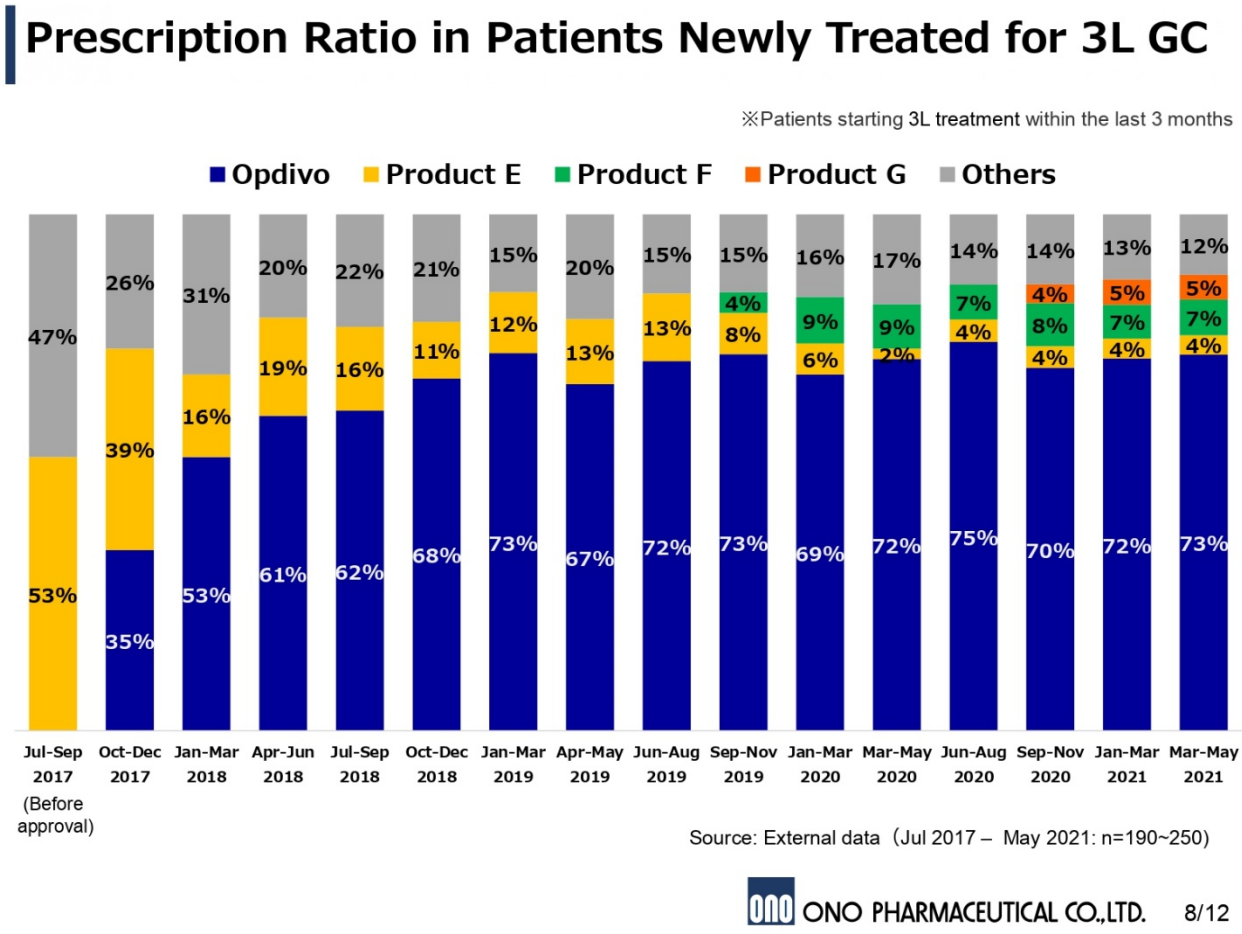
Immune checkpoint inhibitors such as Opdivo in the first-line treatment of lung cancer target squamous cell carcinoma and non-squamous cell carcinoma without genetic mutation, and the market is very large, estimated at 35,000 patients per year.

Although the competitive environment is currently severe, we entered the market in November last year with combination Opdivo and Yervoy, and in June this year, the combination therapy with bevacizumab was added.

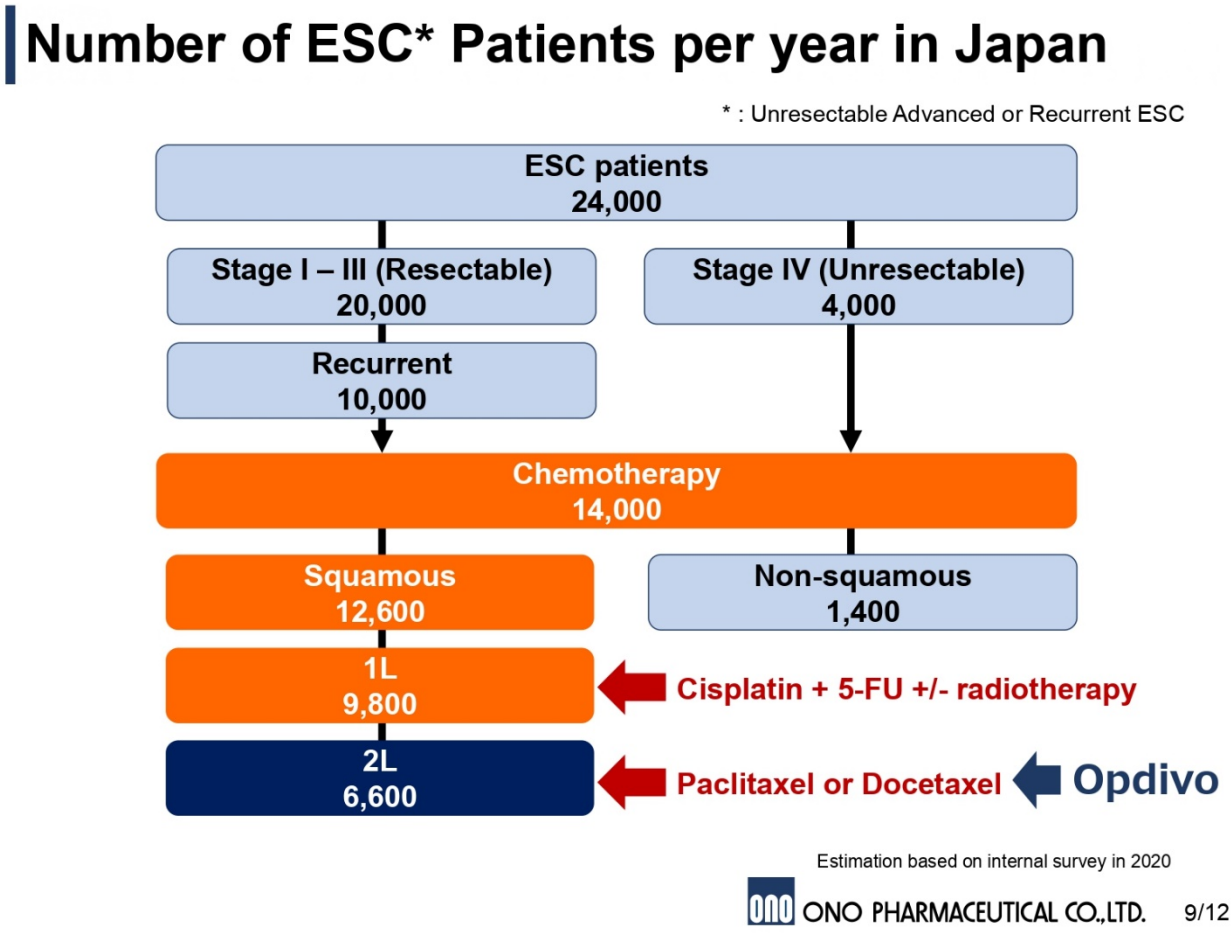


The table shows the changes in the share of new patients in the first-line treatment of lung cancer.

As of May, Opdivo's share of new patient prescriptions was 17%, and we are working to achieve a 30% share this fiscal year.



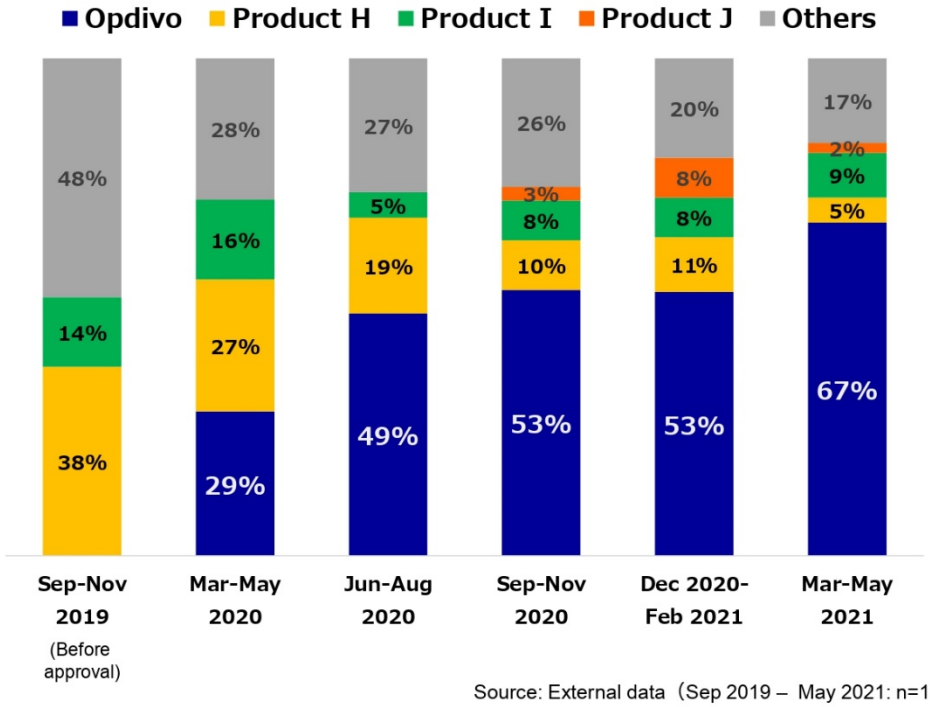
This is the trend of the share of new patients in the third-line treatment of gastric cancer. Opdivo's share of new patient prescriptions for third-line treatment is still above the target of 70%, despite the entry of competing products.



Following gastric cancer, I would like to introduce the second-line treatment of esophageal cancer. Its use in the second-line treatment of unresectable advanced or recurrent esophageal cancer has been steadily expanding since its approval in February last year.

Prescription Ratio in Patients Newly Treated for 2L ESC (Squamous Cell Carcinoma)

※ Patients starting 2L ESC within the last 3 months



Source: External data（Sep 2019 – May 2021: n=150~158）

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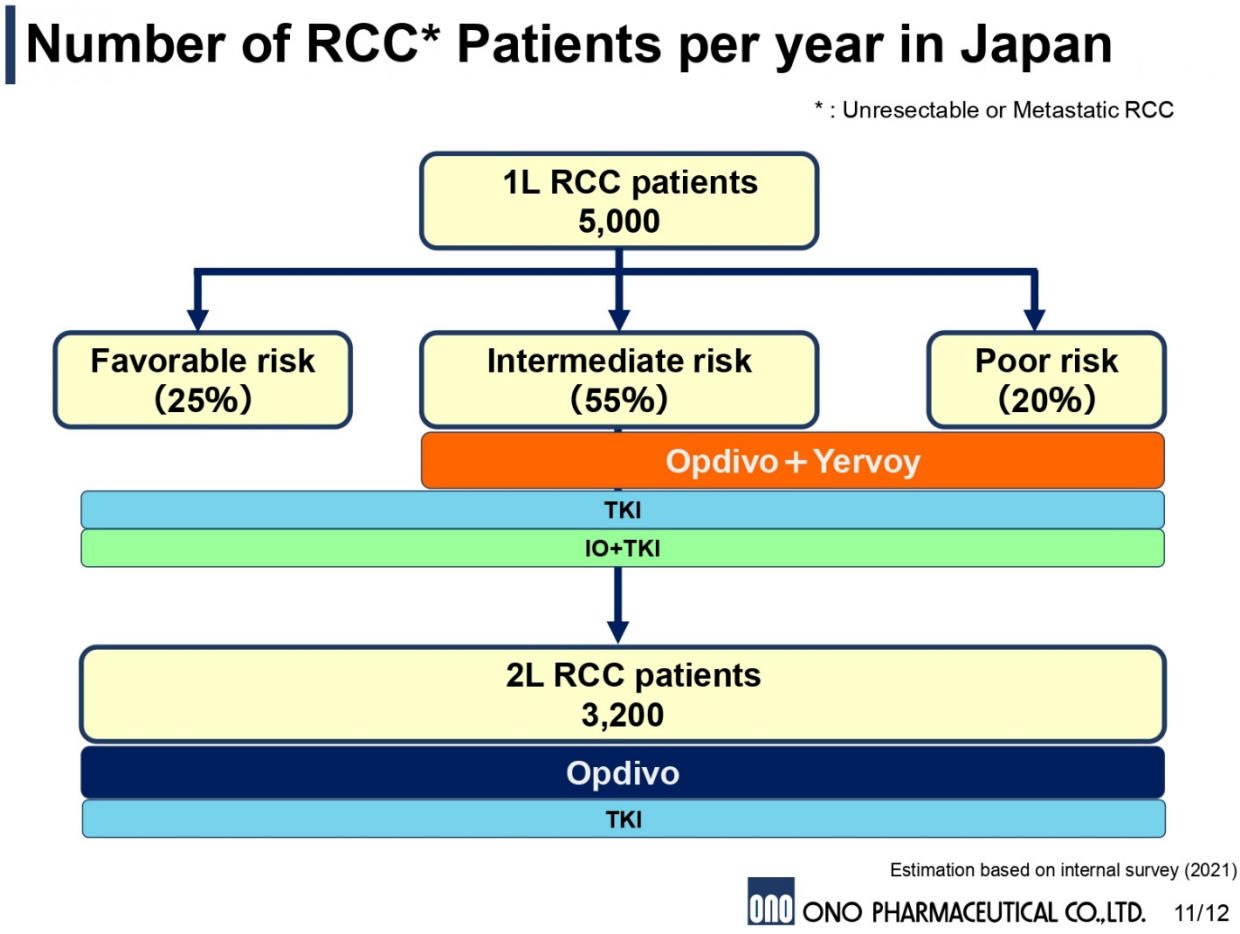
While competing products are entering the market, Opdivo's share of new patient prescriptions for second-line treatment has risen to 67%, and we will aim for our target of 70%, which is already in sight. We will continue to raise awareness of the benefits of Opdivo in the gastrointestinal field.

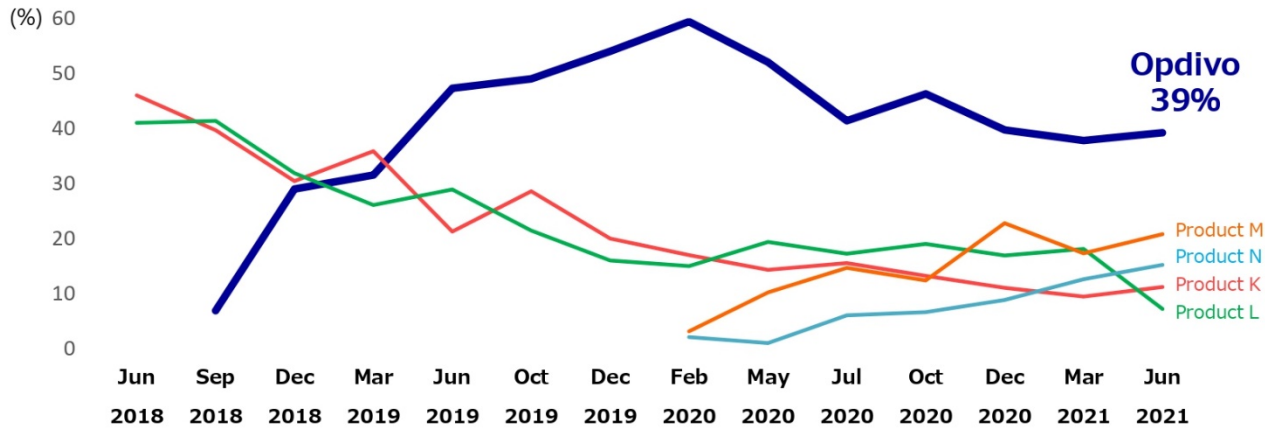


This is an introduction to the field of renal cell carcinoma.

We have evidence for Opdivo for all first-line and second-line therapies and beyond, and are working to bring Opdivo to all patients with renal cell carcinoma.

Prescription Ratio in Patients Newly Treated for 1L RCC

	2018		2019					2020			2021				
	Jun	Sep	Dec	Mar	Jun	Oct	Dec	Feb	May	Jul	Oct	Dec	Mar	Jun	
Opdivo	**-**	**7**	**29**	**32**	**47**	**49**	**54**	**59**	**52**	**41**	**46**	**40**	**38**	**39**	(%)
Product K	46	40	30	36	21	29	20	17	14	16	13	11	9	11	(%)
Product L	41	41	32	26	29	21	16	15	19	17	19	17	18	7	(%)
Product M								3	10	15	12	23	17	21	(%)
Product N								2	1	6	7	9	13	15	(%)



Source: External data（Jun 2018 – Jun 2021: n=39~100)

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This shows the changes in the share of new patients acquired in the first-line treatment of renal cell carcinoma.

In first-line treatment, IO/TKI therapy has entered the market and prescriptions are gradually expanding, and immune checkpoint inhibitors are now used in more than 70% of first-line treatment cases.

Among them, the share of new patient prescriptions for combination Opdivo and Yervoy is 39%, and if we narrow down our focus to intermediate and poor risk patients who are to be treated with Opdivo and Yervoy, the share of new patient acquisition is more than 50%.

We are expecting the approval of the combination therapy of TKI Cabometyx and Opdivo in the near future, and we would like to expand our activities to the low-risk market where we have not been able to do so far, in order to further expand the use of Opdivo regimen.

The above information is also available by cancer type.

In the current fiscal year, we will push forward and gain ground with activities for the first-line treatment of lung cancer, for which we obtained approval in the last fiscal year.

The cancer types for which we are seeking approval include gastric cancer as a first-line treatment, esophageal cancer as a postoperative adjuvant, urothelial cancer as a postoperative adjuvant, cancer of unknown primary, and pediatric Hodgkin’s lymphoma.

In particular, for the first-line treatment of HER2-negative gastric cancer, we will make use of our past experience and continue to make efforts to provide information after the approval.

In addition, cancer of unknown primary and pediatric Hodgkin's lymphoma are rare types of cancer. As there is a high unmet need in these diseases, we will strive to provide information, including disease awareness.

We will continue to deliver the benefits of single-agent Opdivo and combination therapy with Yervoy and other drugs to cancer patients.

Question & Answer

Q: I would like to confirm one more time the comment on ATTRACTION-05 that the interim analysis has already been done externally.

The previous assumption was that the description of schedule had been made based on the interim analysis results in the shortest possible time. As the trial is decided to continue this time based on the result from interim analysis, I assume that the top line result will be released in the next fiscal year and that the application will be submitted in the next fiscal year. Is that right?

Idemitsu: Yes. Your assumption is correct. As you mentioned, We had described our plan for the earliest application based on the result of the interim analysis, but the trial will be continued and the final analysis will be done in the next fiscal year.

Q: What is the timing for the next fiscal year, first or half?

Idemitsu: I'm sorry, but I will refrain from answering at this time.

Q: Thank you very much. Also, I heard that a blue letter about JOYCLU was released in June. In the prescription of the product, if anaphylaxis occurs, it seems to be difficult to deal with. This time, your company reduced the sales estimate for JOYCLU.

Should we be cautious about how we view the marketing of JOYCLU in the future? By which I mean, should we look at it as a slight change in outlook not only for the current fiscal year but also for the medium term? Or should we take a wait-and-see approach for now? What do you think about this?

Ichikawa: As you said, we are discussing carefully with Seikagaku Corporation, the manufacturer and distributors of the product.

Anaphylactic shock was reported in 10 patients. In order to ensure the proper and careful use of the product in the patient's treatment, we are currently taking measures such as allowing the patient to remain under the care of a doctor for 30 minutes, and to make phone calls, faxes, and e-mails to ensure sufficient response in case of emergency after the administration of the product. However, there is a limit to what we can do.

We are not certain this moment whether it may be 6 months or a year to find the cause of this anaphylactic shock. While we expected to provide information to medical professionals as soon as we determine the cause, we are afraid that we will need some more time to find the cause.

Q: Thank you very much. Lastly, I would like to talk about the market share of Opdivo for lung cancer treatment, and I think you mentioned that there were 300 patients in June. I think the figure is currently about 4,000 people, but I wonder if this is higher or lower than expected.

Takahagi: At present, we believe that the situation is as planned within our expectation.

Q: I was wondering if you could tell us how you are looking at the Phase III trial data of other companies' immune checkpoint inhibitors for adjuvant treatments that were presented at ASCO.

Looking at the adjuvant study of Tecentriq in non-small cell lung cancer, the adjuvant data of Keytruda in renal cell carcinoma, etc., how do you think the sales of Opdivo in non-small cell lung cancer and renal cell carcinoma will be affected in the near future?

Takahagi: I would like to answer, particularly with respect to the area of renal cell carcinoma. I think you were probably referring to the results of the KETNOTE-564 trial of adjuvant therapy with Keytruda, is that correct?

First of all, I heard that the trial of Keytruda is intended for patients with renal cell carcinoma at intermediate to poor risk of recurrence after surgery to remove the kidney. Looking at the Japanese market, 60% of the patients at the Stage IV (unresectable and metastatic) renal cell carcinoma are newly diagnosed, and 40% recur after surgery. In particular, we consider that half of the 40% of postoperative recurrences, about 20%, are in the intermediate to poor risk of recurrence.

However, in Japan, the standard treatment for postoperative adjuvant renal cell carcinoma is conservative, and it is said that the time until recurrence is very long. I don't know when Keytruda was filed or approved, so I can't say.

Since the number of eligible patients is very limited and the period of time until recurrence is long, I think that the impact on prescription of the combination of Opdivo and Yervoy for Stage IV IO patients with renal cell carcinoma is very small at present.

Q: Thank you. Can you make any comment on the impact of the IMpower010 study in any way?

Takahagi: With regard to the impact of IMpower, we will be entering the period of using it in the preoperative and postoperative periods, so I think we need to consider how it will be used in these areas in the future.

It is true that there are a certain number of patients who have recurrences after surgery. So, some of the patients at the Stage IV may indeed be affected by the progress of IO. However, as in the case of renal cell carcinoma, there are issues such as the timing of recurrence and the extent to which the disease will be treated. Depending on the results of IMpower, it may or may not become the standard of care. My impression is that it is still too early to say how much of an impact it will have.

Q: First, for adjuvant lung cancer, which has been delayed a bit in the filing timing this time, what is the impression regarding this delay?

Is it positive, negative, or neither? Can you tell me a little bit about how you see this? That's the first question.

Idemitsu: There is a delay in the event occurrence. We can consider that it is effective, or it may not be. I'm not certain.

Q: Thank you very much. Second, I would like to talk about the approval timing of first-line treatment of gastric cancer. Of course, this is a discussion with the regulatory authorities, so you may not be able to disclose it, but for example, is there an expectation that the product will be approved in the middle of this year, or will we have to wait for the launch until next year? Please let us know if there is any update on the prospects for the approval of this first-line treatment for gastric cancer.

Idemitsu: I can't give you a definite answer because it depends on the review by the authorities, but our expectation is that it will be approved by the end of this year.

Q: Will it be launched this year?

Idemitsu: It's an additional indication approval, so it will be made available as soon as we receive approval.

Q: I have 2 questions. One is that, although it has nothing to do with the financial result, the trial involving Mie University has been settled, or rather, a guilty verdict has been rendered against current employees of your Company. I read an article in a professional journal that President Sagara apologized to stakeholders at

the shareholders' meeting. I think that he once said that he would explain the review of the company's internal system and consultation by internal lawyers and others, once the judgment was issued.

The situation has changed a bit with the guilty verdict. Considering that it is an era when governance and compliance are strict, I think that it may be rather difficult to invest your company in reality. Could you tell us about the current status of this?

Tsujinaka: We are taking this point very seriously. Originally, I had hoped to report the results of the internal investigation committee as early as next week. We are a little behind on that, but we hope to open our investigation report in the not too distant future.

Based on the recommendations from the Investigation Committee, we would like to explain the future internal compliance system, the handling of various donations such as scholarship donations, and the future system of the company.

We would like to ask for your patience and understanding.

Q: Just one more question. Opdivo is doing well in gastric cancer (GI tract) and lung cancer (respiratory system), as you mentioned. Among the cancer types, hepatocellular carcinoma is one that I am wondering about. What I noticed in your table is that in the development of Opdivo on page 2, the adjuvant is scheduled to be filed in 2022, I think. I believe you are also working on the first- and second-line treatment, so I was wondering what the order will be. Is it correct to say that adjuvant treatment will appear first?

Idemitsu: Yes. The adjuvant will come out first. Phase III study with Opdivo mono-therapy was being conducted in the first-line treatment, but it did not meet the primary endpoint

Q: Is the second-line treatment still ongoing? Is the first-line treatment discontinued? Is the adjuvant treatment in Phase III?

Idemitsu: Regarding the second-line treatment for hepatocellular carcinoma, it had been granted under the accelerated approval in the US based on the result from Phase 2 study, but it was withdrawn the other day.

In Japan, we have no plan to file an application for the second-line treatment.

Q: Then this table on page 4, is that correct? There are the adjuvant, first- and second-line treatments for hepatocellular carcinoma.

Idemitsu: Phase 3 is ongoing for the first-line treatment in combination with ipilimumab. The application for the adjuvant will come first. As for the second-line treatment, the accelerated approval was granted for Opdivo mono-therapy and Opdivo + ipilimumab combination therapy in the US based on the result from Phase 2 study, but the approval for Opdivo mono-therapy was withdrawn the other day.

Q: So, is it correct to understand that there is no second-line treatment for Opdivo mono-therapy in Japan.

Idemitsu: Yes.

Q: First, I understand that the market share of Opdivo for lung cancer has been steadily increasing. Which regimens are gaining market share, and in what regiments and patient populations, and how is it being evaluated?

I understand that market share is growing, but I am not quite sure why this market share has been achieved.

Takahagi: First of all, regarding patient populations in whom prescription was made, there is no significant difference between squamous and non-squamous lung cancer. However, if you look at the ratio of regimens, 60% are the 9LA regimen, where the combination of Opdivo, Yervoy and chemotherapy was given, and 40% are the 227 regimen, where the combination regimen of Opdivo and Yervoy was given.

Currently, in the lung cancer field, treatment drugs are selected based on the expression of PD-L1. In terms of the expression of PD-L1, we are getting the highest share in PD-L1 negative patients, which accounts for about 30% of the market. We are gaining a very high share.

On the other hand, there are still many issues regarding PD-L1 expression of 1-49%. As for PD-L1 expression of 50% or higher, other regimens such as monotherapy or combination therapy with chemotherapy are mainly used.

However, our strategy for the regimen of Opdivo and Yervoy is to get the share for PD-L1 expression of 1-49% negative cases. I believe that we are progressing almost exactly according to the strategy we have set.

Q: The second question is about the development pipeline progress. On the second page of the progress of the development pipeline, regarding the timing of the interim analysis, ATTRACTION-05 will be continued based on the results of the interim analysis. In this regard, can you tell us if there are any indications that you are planning to submit based on the results of the interim analysis among the pipelines?

Idemitsu: Basically, we prepare this document based on the fastest scenario. When we do an interim analysis, the schedule for application is listed taking into account the results of interim analysis.

Q: Would you please advise in which studies the interim analysis will be conducted?

Idemitsu: I don't know in which study an interim analysis will be made, because I don't have the data at hand.

Q: I'd like to confirm a few things about the financial results. In the first quarter of this fiscal year, I understand that SG&A expenses other than R&D will account for about 26% of the plan.

Right now, your Company is making good progress on profits. Is there any possibility that your Company will invest a little more if the progress continues at this pace?

Nagahama: As for the progress of expenses, the current situation is still within the expectation of the annual forecast. We have no plans at present to change our current plan of JPY74 billion in SG&A expenses. We are looking at the current situation.

Q: Regarding royalties results, I think it's going pretty well right now, and sales of Opdivo by Bristol was good, so I think there has been a possibility that it could go up a little bit, but is it safe to say that it's getting stronger?

Tsujinaka: In terms of royalties, the situation is as you pointed out. However, royalty depends on the impact of foreign exchange rates. We initially estimated that the rate is set at JPY106 to 1 dollar. Therefore, excluding the effect of this exchange rate (the effect of the exchange rate is about 3.5%), the volume basis is about 1% higher than the initial plan, which is almost as planned.

While continuing to take foreign exchange factors and overseas market trends into consideration, we would like to announce any revision, if we see a tendency, as you pointed out. As of now, we remain it unchanged.

Q: Lastly, regarding lung cancer, I understand that you were talking earlier about 9LA and 227, with the market share being 6 : 4, but if we include the combination with Avastin which was made available in June, how will the earlier 6 : 4 ratio change? I wonder if I can expect the same level of effect in combination with Avastin.

Takahagi: First of all, regarding your question about the combination regimen of Opdivo, Avastin and chemotherapy, as you know, Tecentriq is already being approved and promoted with a similar regimen.

Based on the responses from doctors, many of them are of the opinion that the regimen including Avastin has great potential for patients with brain tumors and pleural effusions. Considering these factors, our strategy is to use 9LA and 227, and especially in combination with Yervoy, which is a different regimen from other immune checkpoint inhibitors.

In addition, I would like to promote and propose to the doctors this feature of the Avastin Combination regimen for patients with pleural effusion or brain metastasis, although the number of cases may be a little limited.

Q: On the third page of the document, royalties have increased by 26%, and both those from Bristol and Merck have seen significant growth. Are these within your expectations? When those from Bristol and Merck are excluded, the remainder is JPY3 billion, which is 80% growth. May I understand that this is mainly from the royatlty on Tecentriq?

Tani: Talking specifically about Tecentriq, as I explained earlier, the royalty on Tecentriq was zero in the previous term, but it is included in this term.

Tsujinaka: I would like to explain further. BMS had a sales plan to expand its global sales by about 25% in this fiscal year. The majority of these are in the United States, where the market is more promising. BMS expected an increase of 7% in Europe and other regions. I think the view is that a large increase in the US market is expected, and there is a conservative view about the rest.

As you know, royalty rate from BMS is 4% in the US, and 15% in other countries. I expect that the estimated royalty amount shown to Ono by BMS, is relatively certain figure.

Currently, the sales situation of BMS is slightly lower than planned in the United States. On the other hand, it has grown by more than 10% in Europe and other regions. As a result, overall loyalty to us has grown positively in the mid-1% range on a volume basis and the impact of foreign exchange has added to this, resulting in the current situation that it is about 5% higher than originally planned.

As mentioned earlier in the development section, Opdivo was tentatively approved in the US for the second-line treatment of hepatocellular carcinoma, but thereafter BMS failed in the Opdivo study while Merck succeeded in the Keytruda study. Therefore, there is a possibility that Opdivo will lose the market share for this second-line treatment of hepatocellular carcinoma in the US probably in the final quarter (January-March 2022). In other words, regarding loyalty from BMS, we have no plan to revise our expectations, taking into account the following factors: Positive factors for additional approvals for lung cancer, gastric cancer, and renal cell carcinoma and negative factors for hepatocellular carcinoma in the US may be reflected in the figures from the January-March next year and thereafter.

Q: The royalty alone increased JPY5.5 billion, but the total increase in operating profit was about JPY2.7 billion, which means that the gross profit also increased by JPY10 billion. However, The reason why the overall profit increased by only JPY2.7 billion is that the research expenses and SG & A expenses increased considerably due to various corona circumstances, so it cost money and the growth is just 10%. Is it correct?

Nagahama: I think you're almost right. The increase in royalties was better than expected. Therefore, gross profit is indeed in excess of JPY10 billion. However, the progress in SG&A expenses has been a little fast, and I think that you are aware of this on an operating profit basis.

Q: The last question from me is that the total operating profit and the forecast for this term are up 5%. Actually, the expense growth was very high in 1Q, and the progress of profit was also high. Is the progress rate of operating profit 28.9%? That being said, is it better to think that it is within the expectation?

Tsujinaka: Yes, it is as expected. The reason for the extremely high growth in expenses in the first quarter was due to the fact that we could not consume the expenses in the 1Q last year under the coronavirus circumstances. This was a time when our research laboratories were temporarily shut down due to the coronavirus pandemic, and research and development expenses as well as operating expenses were considerably reduced.

If we make a simple comparison of each individual, it seems that the expenses have increased considerably, but if we look at the change in the actual expenses in the latter half of last year, you can see that they are being used almost as planned.