

## Trend of Opdivo

### **1. Status of estimated new prescriptions (April 2017 – March 2018)**

- Opdivo was used in about 17,000 patients per year during April 2017 – March 2018.
- Estimated number of new patients by each cancer is about 7,300 patients with non-small cell cancer (NSCLC), which is more than 40% of whole patients, about 4,200 with gastric cancer, about 2,400 with head and neck cancer (HNC), about 2,200 with renal cell carcinoma (RCC), etc.

### **2. Sales forecast by each cancer**

- Of the total sales of Opdivo of ¥90.1 billion in FY 2017, ¥50.4 billion is estimated to account for NSCLC.
- While the sales will be affected by drug price revision in FY 2018, the sales is estimated to remain unchanged with ¥90.0 billion (Calculating by the former drug price, it will increase by about 30% to ¥118.3 billion.). Although there will be some minus impact in sales for NSCLC, it is estimated to be covered in sales of RCC, HNC and gastric cancer.

### **3. Estimated average treatment period by each cancer**

- There is no significant change in the period from the previous result (half-year ago).

### **4. Status of NSCLC (Squamous and non-squamous types)**

- Regarding a prescription trend of the 2<sup>nd</sup> line non-squamous NSCLC, while the prescription of pembrolizumab remarkably increased in March 2018, the prescription rate of Opdivo did not decrease and the one of docetaxel decreased.
- The company thinks that the share of Immuno-Oncology (I-O) medicines, pembrolizumab in addition to Opdivo has been increasing. The company needs to continuously follow-up this trend.
- In the 2<sup>nd</sup> line squamous NSCLC, Opdivo continuously was chosen.

### **5. Squamous/Non-squamous NSCLC – Integrated analysis**

- In the results of integrated analysis of the CM-017 study in patients with squamous NSCLC and the CM-057 study in patients with non-squamous NSCLC, the hazard ratio was 0.70.

### **6. Estimated patients by each treatment line in advanced or recurrent gastric cancer (Internal survey)**

- The estimated number of patients by each treatment line in advanced or recurrent gastric cancer is about 26,000 patients for 1<sup>st</sup> line, about 19,000 for 2<sup>nd</sup> line and about 10,000 for 3<sup>rd</sup> line.
- The median overall survival in whole treatment period of 1<sup>st</sup> line to 4<sup>th</sup> line is about 14 months.

**7. Number of patients newly treated with Opdivo in advanced or recurrent gastric cancer (Result from MR reports in FY 2017)**

- The number of patients newly treated patients who could be followed by MRs of both Ono and Bristol-Myers Squibb was about 3,600 patients.
- Opdivo was more frequently used for the 4<sup>th</sup> line or later at the beginning when the indication of gastric cancer was supplementally approved, but is recently used in about 70% of patients in the 3<sup>rd</sup> line, who have been followed-up.

**8. Continuous treatment rate of Opdivo in advanced or recurrent gastric cancer**

- In the results of clinical studies, we initially anticipated that less than 20% of patients would continue to treat with Opdivo for 6 months, but actually about 30% of patients have been continuously treated.

**9. Treatment rate of Opdivo in 3<sup>rd</sup> line patients (Assuming 100% in 2<sup>nd</sup> line patients)**

- Assuming that 100% of patients is treated in the 2<sup>nd</sup> line patients as of August 2017, prior to approval, about 50% of patients were treated in 3<sup>rd</sup> line, but currently increased to 55% due to approval of Opdivo.
- On the other hand, about 30% of patients has moved to the best supportive care (BSC) after the 2<sup>nd</sup> line treatment. In the future, the company will provide the information relating to this stage.

**10. Number of patients treated with drugs for advanced or metastatic RCC in Japan (Estimation by internal survey)**

- The number of patients with RCC is about 5,400 patients for 1<sup>st</sup> line, about 3,600 for 2<sup>nd</sup> line and about 1,700 for 3<sup>rd</sup> line.

**11. Change in patients newly treated with Opdivo (share) in the 2<sup>nd</sup> line advanced or metastatic RCC**

- Axitinib, a Tyrosine Kinase Inhibitor (TKI), has been used so far as a standard of treatment and was used about 70% of patients in the 2<sup>nd</sup> line RCC.
- The share of axitinib and Opdivo was almost same in November 2017, and then Opdivo has been used more frequently than the standard therapy drug with the current share of 47%.

**12. Number of patients treated with drugs in advanced or metastatic RCC in Japan**

- About 80% of approximately 5,400 1<sup>st</sup> line patients account for the intermediate or poor risk patients. The therapy of Opdivo in combination with ipilimumab which is now under filing is a regimen showing an efficacy in this field where existing treatment drugs are not so effective, and high unmet medical need still remains.

### **13. IMDC risk classification (Risk classification used for molecular targeted drugs)**

- Among 6 risk factors, the ratio of classification is 23% of whole patients meeting “no factor”, 51% meeting “1 or 2 factors (intermediate risk)” and 26% meeting “3 or more factors (poor risk)”.
- It is mentioned that the existing TRIs show a good result in patients with favorable risk, but the efficacy cannot be expected in intermediate or poor risk patients, along an increase in risk factors.
- The clinical study with the combination therapy of Opdivo and ipilimumab mainly in intermediate and poor risk patients was stopped early with efficacy and the combination therapy is expected especially in intermediate and poor-risk patients.

### **14. Opportunity for Opdivo after supplemental approval for 1<sup>st</sup> line RCC**

- The therapy of Opdivo in combination with ipilimumab is aimed as standard therapy drugs in the area of intermediate or poor-risk RCC.
- When TKIs are first used in favorable risk patients, or even when TRIs are used in the 1<sup>st</sup> line intermediate or poor-risk patients, the company thinks that Opdivo mono-therapy is one of treatment options as a standard treatment drug in the 2<sup>nd</sup> line.