

To estimate the **Potential Peak Sales** for pembrolizumab (Keytruda) in the indication of first-line treatment of locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma with PD-L1 expression (CPS  $\geq 1$ ) in the US, EU5 (Germany, France, Italy, Spain, UK), China, and Japan, as well as the **\$ value of a 1% share of treated patients** in these geographies, we need to follow a structured approach. Since exact data on patient populations, pricing, and market dynamics may not be fully available, I will make reasonable assumptions based on publicly available information, epidemiology data, and market trends for oncology drugs. The analysis will be broken into steps.

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## **Step 1: Define the Target Patient Population**

The indication is for first-line treatment of HER2-positive gastric or GEJ adenocarcinoma with PD-L1 expression (CPS  $\geq 1$ ). We need to estimate the number of eligible patients in each geography.

#### Epidemiology of Gastric and GEJ Cancer:

- **Incidence of gastric cancer** (including GEJ) varies by region:
- **US**: ~27,000 new cases annually (SEER data).
- **EU5**: ~60,000 new cases annually (combined estimate based on GLOBOCAN).
- **China**: ~400,000 new cases annually (highest incidence globally, GLOBOCAN).
- **Japan**: ~130,000 new cases annually (GLOBOCAN).
- **HER2-positive subset**: Approximately 15-20% of gastric/GEJ cancers are HER2-positive.
- **PD-L1 expression (CPS  $\geq 1$ )**: Around 40-60% of gastric/GEJ cancers express PD-L1 at CPS  $\geq 1$  (based on clinical trial data for pembrolizumab).
- **Locally advanced unresectable or metastatic**: About 50-60% of gastric/GEJ cancer patients present with advanced or metastatic disease at diagnosis.

#### Eligible Patient Population (First-Line Treatment):

Assuming:

- 17.5% of cases are HER2-positive (midpoint of 15-20%).
- 50% of cases have PD-L1 CPS  $\geq 1$  (midpoint of 40-60%).
- 55% of cases are advanced/metastatic (midpoint of 50-60%).

We calculate the eligible population as a percentage of total incidence:

- Eligible % = 17.5% (HER2+)  $\times$  50% (PD-L1+)  $\times$  55% (advanced/metastatic) = ~4.8% of total gastric/GEJ cancer incidence.

Now, estimate the number of eligible patients:

- **US**: 27,000  $\times$  4.8% = ~1,300 patients.
- **EU5**: 60,000  $\times$  4.8% = ~2,900 patients.

- **China:**  $400,000 \times 4.8\% = \sim 19,200$  patients.
- **Japan:**  $130,000 \times 4.8\% = \sim 6,200$  patients.
- **Total:**  $\sim 29,600$  patients across these geographies.

#### Share of Treated Patients (20-30%):

Assuming pembrolizumab captures 20-30% of the eligible treated population:

- **Midpoint (25%) treated patients:**

- US:  $1,300 \times 25\% = 325$  patients.
- EU5:  $2,900 \times 25\% = 725$  patients.
- China:  $19,200 \times 25\% = 4,800$  patients.
- Japan:  $6,200 \times 25\% = 1,550$  patients.
- Total:  $\sim 7,400$  patients.

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## **Step 2: Estimate Annual Cost of Treatment per Patient**

Pembrolizumab pricing varies by region due to differences in healthcare systems, negotiations, and discounts. The drug is typically administered every 3 weeks at a dose of 200 mg (flat dose). Annual cost estimates are based on reported figures and market insights:

- **US:**  $\sim \$150,000$  per patient per year (based on list price; actual net price may be lower due to rebates).
- **EU5:**  $\sim \$80,000$ - $\$100,000$  per patient per year (varies by country; using  $\$90,000$  as average).
- **Japan:**  $\sim \$80,000$  per patient per year (similar to EU pricing after adjustments).
- **China:**  $\sim \$40,000$  per patient per year (lower due to price negotiations and inclusion in National Reimbursement Drug List with significant discounts).

#### Duration of Treatment:

In first-line gastric/GEJ cancer, median progression-free survival (PFS) with pembrolizumab + chemo is around 6-9 months (based on KEYNOTE-590 and KEYNOTE-811 trial data). However, some patients may continue treatment for 1-2 years if they respond well. We assume an **average treatment duration of 1 year** for simplicity.

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## **Step 3: Calculate Potential Peak Sales**

Peak sales are calculated as:

**Peak Sales = Number of Treated Patients  $\times$  Annual Cost per Patient**

Using the 25% midpoint share of treated patients:

- **US:**  $325 \text{ patients} \times \$150,000 = \text{\$48.8 million}.$

- **EU5:** 725 patients × \$90,000 = **\$65.3 million**.
- **China:** 4,800 patients × \$40,000 = **\$192.0 million**.
- **Japan:** 1,550 patients × \$80,000 = **\$124.0 million**.
- **Total Peak Sales:** \$48.8M + \$65.3M + \$192.0M + \$124.0M = **\$430.1 million annually**.

#### Range of Peak Sales (20-30% Share):

- At 20% share: Total treated patients = ~5,920 → Peak Sales = **~\$344 million**.
- At 30% share: Total treated patients = ~8,880 → Peak Sales = **~\$516 million**.

Thus, **Potential Peak Sales** range from **\$344 million to \$516 million annually**, with a midpoint of **\$430 million**.

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## **Step 4: Calculate \$ Value of 1% Share of Treated Patients**

A 1% share of treated patients corresponds to 1% of the eligible population being treated with pembrolizumab.

Eligible population = ~29,600 patients → 1% = ~296 patients.

Now, calculate revenue for 296 patients using the regional pricing:

- **US:** (1,300 × 1%) = 13 patients × \$150,000 = **\$1.95 million**.
- **EU5:** (2,900 × 1%) = 29 patients × \$90,000 = **\$2.61 million**.
- **China:** (19,200 × 1%) = 192 patients × \$40,000 = **\$7.68 million**.
- **Japan:** (6,200 × 1%) = 62 patients × \$80,000 = **\$4.96 million**.
- **Total Value of 1% Share:** \$1.95M + \$2.61M + \$7.68M + \$4.96M = **\$17.2 million**.

Thus, the **\$ value of a 1% share of treated patients** across these geographies is approximately **\$17.2 million annually**.

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## **Final Answer:**

1. **Potential Peak Sales for Pembrolizumab** in this indication (first-line HER2-positive gastric/GEJ adenocarcinoma with PD-L1 CPS ≥1) across the US, EU5, China, and Japan, assuming a 20-30% share of treated patients:

- Range: **\$344 million to \$516 million annually**.
- Midpoint (25% share): **\$430 million annually**.

2. **\$ Value of 1% Share of Treated Patients** across these geographies:

- Approximately **\$17.2 million annually**.

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### **Caveats and Assumptions:**

- Patient population estimates are based on approximate epidemiology data and may vary with more precise local data.
- Pricing is assumed based on public information and may differ due to discounts, reimbursement policies, or biosimilar competition.
- Market share assumptions (20-30%) account for competition from other therapies (e.g., trastuzumab, other IO agents) and potential label expansions or restrictions.
- Treatment duration is approximated as 1 year; actual duration may vary based on real-world outcomes.
- Peak sales assume steady-state market penetration, which may take a few years post-launch to achieve.

If you have access to more specific data (e.g., exact patient numbers, pricing, or trial outcomes), I can refine the calculations further.