

To estimate the **Potential Peak Sales** for pembrolizumab (Keytruda) in the indication of metastatic or locally advanced esophageal or gastroesophageal junction (GEJ) carcinoma 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 specific data on patient numbers, pricing, and market penetration may not be publicly available in real-time, I will outline the methodology and use reasonable assumptions based on available data and industry trends. If you have access to specific data (e.g., exact patient numbers or pricing), I can refine the calculations accordingly.

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

The indication is for patients with **metastatic or locally advanced esophageal or GEJ carcinoma** who are not candidates for surgical resection or definitive chemoradiation. We will estimate the number of eligible patients in each geography.

#### Incidence and Prevalence Data (Approximate):

- **Esophageal Cancer Incidence (2020, GLOBOCAN estimates):**

- US: ~18,000 new cases annually.

- EU5: ~45,000 new cases annually (combined for Germany, France, Italy, Spain, UK).

- China: ~320,000 new cases annually (highest incidence globally).

- Japan: ~25,000 new cases annually.

- **Proportion of Metastatic or Locally Advanced Cases:** Approximately 50-60% of esophageal cancer cases are diagnosed at a metastatic or locally advanced stage.

- **Proportion Not Eligible for Surgery or Chemoradiation:** Of these, ~30-40% may not be candidates for surgical resection or definitive chemoradiation due to comorbidities, tumor location, or other factors.

#### Estimated Eligible Patients (Annual New Cases):

Using the above data and assuming ~55% of cases are advanced and ~35% of those are not eligible for surgery/chemoradiation:

- US:  $18,000 * 0.55 * 0.35 = \sim 3,465$  patients.

- EU5:  $45,000 * 0.55 * 0.35 = \sim 8,663$  patients.

- China:  $320,000 * 0.55 * 0.35 = \sim 61,600$  patients.

- Japan:  $25,000 * 0.55 * 0.35 = \sim 4,813$  patients.

- **Total Eligible Patients:** ~78,541 patients annually across these geographies.

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## **Step 2: Estimate Market Penetration (20-30% Share of Treated Patients)**

Pembrolizumab is used in combination with chemotherapy, and its adoption depends on factors like reimbursement, competition (e.g., other PD-1 inhibitors like nivolumab), and clinical guidelines.

Assuming a **20-30% market share** of treated patients:

- At 20% share:  $78,541 * 0.20 = 15,708$  patients treated.
- At 30% share:  $78,541 * 0.30 = 23,562$  patients treated.

#### Breakdown by Geography (at 25% average share for simplicity in distribution):

- US:  $3,465 * 0.25 = \sim 866$  patients.
- EU5:  $8,663 * 0.25 = \sim 2,166$  patients.
- China:  $61,600 * 0.25 = \sim 15,400$  patients.
- Japan:  $4,813 * 0.25 = \sim 1,203$  patients.
- **Total Treated Patients at 25% Share:**  $\sim 19,635$  patients.

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### **Step 3: Estimate Annual Treatment Cost per Patient**

Pembrolizumab's pricing varies by region due to differences in healthcare systems, negotiations, and discounts. Approximate annual costs (based on historical data for Keytruda in oncology indications, typically dosed every 3 weeks):

- US:  $\sim \$150,000$  per patient per year (list price, before discounts).
- EU5:  $\sim \$100,000$  per patient per year (varies by country due to negotiations).
- China:  $\sim \$50,000$  per patient per year (lower due to pricing controls and local competition).
- Japan:  $\sim \$120,000$  per patient per year (similar to EU but with specific pricing agreements).

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### **Step 4: Calculate Potential Peak Sales (20-30% Share)**

Peak sales are calculated by multiplying the number of treated patients by the annual treatment cost per patient in each geography.

#### At 20% Share (15,708 patients):

- US:  $(3,465 * 0.20) * \$150,000 = 693 * \$150,000 = \$103.95$  million.
- EU5:  $(8,663 * 0.20) * \$100,000 = 1,733 * \$100,000 = \$173.3$  million.
- China:  $(61,600 * 0.20) * \$50,000 = 12,320 * \$50,000 = \$616$  million.
- Japan:  $(4,813 * 0.20) * \$120,000 = 963 * \$120,000 = \$115.56$  million.
- **Total Peak Sales at 20% Share:**  $\$103.95M + \$173.3M + \$616M + \$115.56M = \sim \$1,008.81$  million ( **$\sim \$1.01$  billion**).

#### At 30% Share (23,562 patients):

- US:  $(3,465 * 0.30) * \$150,000 = 1,040 * \$150,000 = \$156$  million.

- EU5:  $(8,663 * 0.30) * \$100,000 = 2,599 * \$100,000 = \text{\$259.9 million}$ .
- China:  $(61,600 * 0.30) * \$50,000 = 18,480 * \$50,000 = \text{\$924 million}$ .
- Japan:  $(4,813 * 0.30) * \$120,000 = 1,444 * \$120,000 = \text{\$173.28 million}$ .
- **Total Peak Sales at 30% Share:**  $\$156\text{M} + \$259.9\text{M} + \$924\text{M} + \$173.28\text{M} = \text{\$1,513.18 million}$  (**~\\$1.51 billion**).

#### Range of Potential Peak Sales:

- **\\$1.01 billion (20% share) to \\$1.51 billion (30% share)** annually for this indication across the US, EU5, China, and Japan.

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## **Step 5: Calculate \$ Value of 1% Share of Treated Patients**

A 1% share of treated patients corresponds to 1% of the total eligible patients (78,541).

- **1% of Eligible Patients:**  $78,541 * 0.01 = \sim 785$  patients.

#### Breakdown by Geography:

- US:  $3,465 * 0.01 = \sim 35$  patients.
- EU5:  $8,663 * 0.01 = \sim 87$  patients.
- China:  $61,600 * 0.01 = \sim 616$  patients.
- Japan:  $4,813 * 0.01 = \sim 48$  patients.

#### Revenue from 1% Share:

- US:  $35 * \$150,000 = \text{\$5.25 million}$ .
- EU5:  $87 * \$100,000 = \text{\$8.7 million}$ .
- China:  $616 * \$50,000 = \text{\$30.8 million}$ .
- Japan:  $48 * \$120,000 = \text{\$5.76 million}$ .
- **Total \$ Value of 1% Share:**  $\$5.25\text{M} + \$8.7\text{M} + \$30.8\text{M} + \$5.76\text{M} = \text{\$50.51 million}$ .

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## **Final Summary:**

1. **Potential Peak Sales for Pembrolizumab** in this indication (metastatic or locally advanced esophageal/GEJ carcinoma) across the US, EU5, China, and Japan:

- At 20% share: **~\\$1.01 billion annually**.
- At 30% share: **~\\$1.51 billion annually**.

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

- ~\$50.51 million annually.

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### **Caveats and Assumptions:**

- **Patient Population:** Estimates are based on GLOBOCAN data and general oncology trends for esophageal cancer. Actual eligible patient numbers may vary based on local epidemiology and diagnostic practices.

- **Pricing:** Costs are approximate and may differ due to discounts, biosimilar competition, or local pricing policies (especially in China).

- **Market Share:** The 20-30% range assumes moderate to strong adoption, but competition from other immunotherapies (e.g., nivolumab) and evolving treatment paradigms could impact this.

- **Treatment Duration:** Assumes full-year treatment; actual duration may be shorter based on progression or tolerability.

- **Geographic Variability:** Access to pembrolizumab and reimbursement policies vary widely, especially in China.

If you have access to more precise data (e.g., exact patient numbers, pricing, or market share forecasts), I can adjust the calculations accordingly. Let me know!