

To estimate the **Potential Peak Sales** for nivolumab (Opdivo) in the indication of unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy in the US, EU5 (France, Germany, 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 (e.g., exact patient numbers, pricing, or market penetration) is not provided, I will outline the methodology and use reasonable assumptions based on publicly available data, epidemiology, and market trends for oncology drugs. The final numbers are illustrative and should be validated with real-world data.

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

We need to estimate the number of eligible patients for nivolumab in this second-line treatment setting for ESCC in the specified geographies. ESCC is a subset of esophageal cancer, and the indication is for patients who have progressed after first-line chemotherapy.

### **- Epidemiology of Esophageal Cancer:**

- Esophageal cancer incidence varies by region, with higher rates in East Asia (e.g., China and Japan) compared to the US and Europe.
- ESCC accounts for approximately 70-90% of esophageal cancer cases globally, with higher prevalence in Asia.
- Of these, a subset will progress to advanced, recurrent, or metastatic stages and fail first-line therapy (fluoropyrimidine- and platinum-based chemotherapy), making them eligible for second-line treatment with nivolumab.

### **- Estimated Incidence and Eligible Population (rough estimates based on literature):**

- **US:** ~18,000 new esophageal cancer cases/year (2023 estimate, American Cancer Society). ~80% ESCC = 14,400. ~50% advanced/metastatic at diagnosis, and ~30-40% progress after first-line = ~2,000-3,000 eligible patients.
- **EU5:** ~45,000 new cases/year (combined). ~80% ESCC = 36,000. ~50% advanced, ~30-40% progress = ~5,000-7,000 eligible patients.
- **China:** ~300,000 new cases/year (highest incidence globally). ~90% ESCC = 270,000. ~50% advanced, ~30-40% progress = ~40,000-50,000 eligible patients.
- **Japan:** ~20,000 new cases/year. ~90% ESCC = 18,000. ~50% advanced, ~30-40% progress = ~2,500-3,500 eligible patients.
- **Total Eligible Patients:** ~50,000-65,000 across these geographies.

These numbers are approximate and conservative, focusing on second-line patients. Real numbers may vary based on exact progression rates and treatment patterns.

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

The problem assumes a 20%-30% share of treated patients for nivolumab. This accounts for competition from other therapies (e.g., other checkpoint inhibitors like pembrolizumab, or chemotherapy regimens) and access barriers (e.g., cost, reimbursement).

- **Total Treated Patients with Nivolumab** (at 20%-30% penetration):
- **US:** 2,000-3,000 eligible \* 20%-30% = 400-900 patients.
- **EU5:** 5,000-7,000 \* 20%-30% = 1,000-2,100 patients.
- **China:** 40,000-50,000 \* 20%-30% = 8,000-15,000 patients.
- **Japan:** 2,500-3,500 \* 20%-30% = 500-1,050 patients.
- **Total:** ~9,900-19,050 patients treated with nivolumab at peak penetration.

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### **Step 3: Pricing of Nivolumab**

Nivolumab is a high-cost immunotherapy. Pricing varies by region due to healthcare systems, negotiations, and purchasing power.

- **Estimated Annual Cost per Patient** (based on typical PD-1 inhibitor pricing):
- **US:** ~\$150,000-\$180,000 per year (list price before discounts).
- **EU5:** ~\$80,000-\$120,000 per year (varies by country, after discounts/rebates).
- **China:** ~\$30,000-\$50,000 per year (lower due to government negotiations and local pricing policies; e.g., inclusion in NRDL with significant discounts).
- **Japan:** ~\$100,000-\$130,000 per year (similar to EU, adjusted for local pricing).

These are rough estimates based on typical oncology drug pricing for PD-1 inhibitors. Actual costs may differ based on dosing (e.g., 240 mg every 2 weeks or 480 mg every 4 weeks), treatment duration, and negotiated discounts.

- **Average Treatment Duration:** For second-line ESCC, median progression-free survival (PFS) with nivolumab is ~1.5-3 months (based on clinical trials like ATTRACTION-3), but some patients (responders) may stay on treatment for 6-12 months or longer. We assume an average of **6-9 months of treatment** per patient, so annual cost may be adjusted to ~75% of full-year cost.

- **Adjusted Annual Cost per Patient** (assuming 75% of full-year cost for 6-9 months):
- **US:** ~\$112,500-\$135,000.
- **EU5:** ~\$60,000-\$90,000.
- **China:** ~\$22,500-\$37,500.
- **Japan:** ~\$75,000-\$97,500.

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## **Step 4: Calculate Potential Peak Sales**

Peak sales are calculated as: **Number of Treated Patients \* Annual Cost per Patient.**

- **Peak Sales at 20%-30% Penetration** (rounded for simplicity):
- **US:** 400-900 patients \* \$112,500-\$135,000 = **\$45M-\$121.5M.**
- **EU5:** 1,000-2,100 patients \* \$60,000-\$90,000 = **\$60M-\$189M.**
- **China:** 8,000-15,000 patients \* \$22,500-\$37,500 = **\$180M-\$562.5M.**
- **Japan:** 500-1,050 patients \* \$75,000-\$97,500 = **\$37.5M-\$102.4M.**
- **Total Peak Sales:** **\$322.5M-\$975.4M** across all geographies.

These figures represent potential peak sales for nivolumab in this specific indication (second-line ESCC) at 20%-30% market share. China contributes the largest share due to its high patient population, despite lower pricing.

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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 eligible patient population being treated with nivolumab.

- **Number of Patients for 1% Share** (based on total eligible patients):
- **US:** 2,000-3,000 \* 1% = 20-30 patients.
- **EU5:** 5,000-7,000 \* 1% = 50-70 patients.
- **China:** 40,000-50,000 \* 1% = 400-500 patients.
- **Japan:** 2,500-3,500 \* 1% = 25-35 patients.
- **\$ Value of 1% Share** (Number of Patients \* Annual Cost per Patient):
- **US:** 20-30 \* \$112,500-\$135,000 = **\$2.25M-\$4.05M.**
- **EU5:** 50-70 \* \$60,000-\$90,000 = **\$3M-\$6.3M.**
- **China:** 400-500 \* \$22,500-\$37,500 = **\$9M-\$18.75M.**
- **Japan:** 25-35 \* \$75,000-\$97,500 = **\$1.875M-\$3.4125M.**
- **Total \$ Value of 1% Share:** **\$16.125M-\$32.5125M.**

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## **Final Answer**

**1. Potential Peak Sales for Nivolumab in Second-Line ESCC (20%-30% Share of Treated Patients):**

- **US:** \$45M-\$121.5M
- **EU5:** \$60M-\$189M
- **China:** \$180M-\$562.5M
- **Japan:** \$37.5M-\$102.4M
- **Total:** **\$322.5M-\$975.4M**

## 2. \$ Value of 1% Share of Treated Patients:

- **US:** \$2.25M-\$4.05M
- **EU5:** \$3M-\$6.3M
- **China:** \$9M-\$18.75M
- **Japan:** \$1.875M-\$3.4125M
- **Total:** **\$16.125M-\$32.5125M**

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## **Notes and Caveats**

- These estimates are based on assumptions for patient population, market penetration, pricing, and treatment duration. Real-world data (e.g., from clinical trial enrollment, market reports, or payer data) would refine these numbers.
- Peak sales may take several years to achieve due to gradual market uptake, reimbursement approvals, and competition.
- Pricing in China is highly variable due to government negotiations and inclusion in the National Reimbursement Drug List (NRDL), which could lower costs further.
- This analysis is specific to the ESCC second-line indication and does not account for other indications for nivolumab, which contribute significantly to its overall revenue.

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