

To calculate the **Potential Peak Sales** for the combination of nivolumab (Opdivo) and ipilimumab (Yervoy) in the indication of unresectable malignant pleural mesothelioma (MPM) 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 exact patient numbers, pricing, and penetration rates are not provided, I will use reasonable assumptions based on publicly available data, epidemiology, and market research for oncology drugs. I will also outline the methodology so you can adjust assumptions as needed.

Step 1: Key Assumptions and Methodology

1. **Indication:** Unresectable malignant pleural mesothelioma (MPM), a rare cancer with limited treatment options. The combination of nivolumab and ipilimumab is approved as a first-line treatment.

2. **Target Population:**

- MPM has a low incidence, with estimates of ~3,000 new cases per year in the US, ~5,000 in EU5 combined, ~10,000 in China, and ~1,500 in Japan. (Sources: Cancer registries, epidemiology studies).

- Assume 70-80% of cases are unresectable at diagnosis, making them eligible for systemic therapy.

3. **Treated Patients:**

- Not all eligible patients receive treatment due to age, comorbidities, or access issues. Assume 60-70% of eligible patients are treated in developed markets (US, EU5, Japan) and 40-50% in China.

4. **Market Share:**

- Given the 20-30% share of treated patients as per the query, we will use this range to estimate peak sales.

5. **Drug Pricing:**

- Nivolumab and ipilimumab are premium-priced immunotherapies. Annual treatment cost per patient is estimated at ~\$150,000-\$200,000 in the US for the combination (based on typical checkpoint inhibitor costs). Adjust for lower pricing in EU5 (~60-70% of US price), Japan (~70-80% of US price), and China (~30-40% of US price due to pricing controls and negotiations).

6. **Peak Sales Timing:**

- Peak sales are typically reached 5-7 years post-launch after market penetration stabilizes.

Step 2: Estimate Treated Patient Population

Using incidence data and assumptions:

- **US:**

- Incidence: ~3,000 new cases/year.

- Unresectable: 75% → ~2,250 patients.

- Treated: 65% → ~1,460 treated patients/year.

- **EU5:**

- Incidence: ~5,000 new cases/year.

- Unresectable: 75% → ~3,750 patients.

- Treated: 65% → ~2,440 treated patients/year.

- **China:**

- Incidence: ~10,000 new cases/year (higher due to population size and industrial exposure to asbestos).

- Unresectable: 75% → ~7,500 patients.

- Treated: 45% → ~3,375 treated patients/year.

- **Japan:**

- Incidence: ~1,500 new cases/year.

- Unresectable: 75% → ~1,125 patients.

- Treated: 65% → ~730 treated patients/year.

Total Treated Patients Across Geographies:

1,460 (US) + 2,440 (EU5) + 3,375 (China) + 730 (Japan) = **8,005 treated patients/year.**

Step 3: Estimate Potential Peak Sales (20-30% Market Share)

- **Market Share:** Assume 20-30% of treated patients.

- **Patients Treated with Nivolumab + Ipilimumab:**

- At 20% share: $8,005 \times 0.2 = \sim 1,601$ patients.

- At 30% share: $8,005 \times 0.3 = \sim 2,402$ patients.

- **Annual Cost per Patient (Combination Therapy):**

- US: \$175,000 (midpoint of \$150K-\$200K).

- EU5: \$115,000 (~65% of US price).

- Japan: \$130,000 (~75% of US price).

- China: \$60,000 (~35% of US price).

- **Peak Sales Calculation:**

- Distribute patients by geography proportionally to total treated patients:

- US: 18.2% of total (1,460/8,005).

- EU5: 30.5% (2,440/8,005).

- China: 42.2% (3,375/8,005).

- Japan: 9.1% (730/8,005).

At 20% Market Share (1,601 patients):

- US: $1,601 \times 0.182 \times \$175,000 = \sim \$51.0\text{M}.$

- EU5: $1,601 \times 0.305 \times \$115,000 = \sim \$56.2\text{M}.$

- China: $1,601 \times 0.422 \times \$60,000 = \sim\$40.5\text{M}$.
- Japan: $1,601 \times 0.091 \times \$130,000 = \sim\$18.9\text{M}$.
- **Total Peak Sales (20%):** $\$51.0\text{M} + \$56.2\text{M} + \$40.5\text{M} + \$18.9\text{M} = \sim\$166.6\text{M}$.

At 30% Market Share (2,402 patients):

- US: $2,402 \times 0.182 \times \$175,000 = \sim\$76.5\text{M}$.
- EU5: $2,402 \times 0.305 \times \$115,000 = \sim\$84.3\text{M}$.
- China: $2,402 \times 0.422 \times \$60,000 = \sim\$60.8\text{M}$.
- Japan: $2,402 \times 0.091 \times \$130,000 = \sim\$28.4\text{M}$.
- **Total Peak Sales (30%):** $\$76.5\text{M} + \$84.3\text{M} + \$60.8\text{M} + \$28.4\text{M} = \sim\$250.0\text{M}$.

Potential Peak Sales Range: \$166.6M to \$250.0M annually.

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

- Total Treated Patients: 8,005.
- 1% Share = $8,005 \times 0.01 = \sim 80$ patients.
- Value of 1% share by geography:
- US: $80 \times 0.182 \times \$175,000 = \sim\2.55M .
- EU5: $80 \times 0.305 \times \$115,000 = \sim\2.81M .
- China: $80 \times 0.422 \times \$60,000 = \sim\2.03M .
- Japan: $80 \times 0.091 \times \$130,000 = \sim\0.95M .
- **Total \$ Value of 1% Share:** $\$2.55\text{M} + \$2.81\text{M} + \$2.03\text{M} + \$0.95\text{M} = \sim\$8.34\text{M}$.

Final Answer:

- **Potential Peak Sales** for nivolumab + ipilimumab in unresectable malignant pleural mesothelioma (20-30% market share) in the US, EU5, China, and Japan: **\$166.6M to \$250.0M annually**.
- **\$ Value of 1% Share of Treated Patients** in these geographies: **$\sim\$8.34\text{M}$** .

Notes:

- These estimates are sensitive to assumptions about incidence, treatment rates, pricing, and market share. Adjustments can be made if more specific data (e.g., exact patient numbers or local pricing) is available.
- Peak sales may vary based on competition (e.g., other therapies for MPM), reimbursement policies, and market access challenges, especially in China.
- The calculation assumes steady-state annual treatment costs; real-world costs may vary due to treatment duration or discounting.