

To estimate the **Potential Peak Sales** for the drug combination "nivolumab + ipilimumab" in the indication of unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC) 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 make reasonable assumptions based on publicly available data and industry standards.

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

The indication is for adult and pediatric patients (12 years and older) with unresectable or metastatic MSI-H or dMMR colorectal cancer. MSI-H/dMMR mutations occur in approximately 4-5% of metastatic colorectal cancer (mCRC) cases.

### #### Incidence and Prevalence of mCRC

- **US:** Annual incidence of CRC is ~150,000 cases, with ~20% being metastatic at diagnosis (~30,000 mCRC cases). Of these, ~5% are MSI-H/dMMR (~1,500 patients/year).
- **EU5:** Annual incidence of CRC is ~300,000 cases, with ~20% metastatic (~60,000 mCRC cases). Of these, ~5% are MSI-H/dMMR (~3,000 patients/year).
- **China:** Annual incidence of CRC is ~400,000 cases, with ~20% metastatic (~80,000 mCRC cases). Of these, ~5% are MSI-H/dMMR (~4,000 patients/year).
- **Japan:** Annual incidence of CRC is ~150,000 cases, with ~20% metastatic (~30,000 mCRC cases). Of these, ~5% are MSI-H/dMMR (~1,500 patients/year).

### #### Total Eligible Patients (Incident Cases per Year)

- US: ~1,500 patients
- EU5: ~3,000 patients
- China: ~4,000 patients
- Japan: ~1,500 patients
- **Total:** ~10,000 patients/year across these geographies.

### #### Treated Patient Population

Not all eligible patients receive treatment due to factors like access, diagnosis rates, and healthcare system differences. Assuming a treatment rate of 70-80%:

- US: ~1,200 patients
- EU5: ~2,400 patients
- China: ~3,200 patients
- Japan: ~1,200 patients
- **Total Treated Patients:** ~8,000 patients/year.

#### #### Market Share Assumption

The question assumes a 20-30% share of treated patients for nivolumab + ipilimumab. We'll use the midpoint of 25% for calculations.

- US:  $1,200 * 25\% = 300$  patients
- EU5:  $2,400 * 25\% = 600$  patients
- China:  $3,200 * 25\% = 800$  patients
- Japan:  $1,200 * 25\% = 300$  patients
- **Total Patients Treated with nivolumab + ipilimumab:** ~2,000 patients/year.

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### **Step 2: Estimate Annual Treatment Cost**

Nivolumab (Opdivo) and ipilimumab (Yervoy) are expensive immunotherapies. The annual cost varies by region due to pricing differences and healthcare systems.

- **US:** Annual cost of nivolumab + ipilimumab combination therapy is approximately \$250,000–\$300,000 per patient (based on list prices and typical treatment duration for mCRC).
- **EU5:** Pricing is lower due to negotiations and health technology assessments (HTA). Assume ~\$150,000–\$200,000 per patient.
- **Japan:** Pricing is similar to EU5, ~\$150,000–\$200,000 per patient.
- **China:** Pricing is significantly lower due to market access challenges and local pricing policies. Assume ~\$50,000–\$100,000 per patient.

For simplicity, use midpoint estimates:

- US: \$275,000 per patient/year
- EU5: \$175,000 per patient/year
- Japan: \$175,000 per patient/year
- China: \$75,000 per patient/year

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

Peak sales are calculated by multiplying the number of treated patients (at 25% market share) by the annual treatment cost per patient in each geography.

- **US:** 300 patients \* \$275,000 = **\$82.5 million**
- **EU5:** 600 patients \* \$175,000 = **\$105 million**
- **China:** 800 patients \* \$75,000 = **\$60 million**
- **Japan:** 300 patients \* \$175,000 = **\$52.5 million**

- **Total Potential Peak Sales:**  $\$82.5\text{M} + \$105\text{M} + \$60\text{M} + \$52.5\text{M} = \$300 \text{ million/year}$

#### Range for 20-30% Market Share

- At 20% share: Total treated patients = ~1,600 → Peak sales ~**\$240 million/year**

- At 30% share: Total treated patients = ~2,400 → Peak sales ~**\$360 million/year**

- **Peak Sales Range: \$240–\$360 million/year**, with a midpoint of **\$300 million/year**.

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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 ~8,000 total treated patients across geographies, i.e., ~80 patients.

- **US:** 1% of 1,200 = 12 patients \* \$275,000 = **\$3.3 million**

- **EU5:** 1% of 2,400 = 24 patients \* \$175,000 = **\$4.2 million**

- **China:** 1% of 3,200 = 32 patients \* \$75,000 = **\$2.4 million**

- **Japan:** 1% of 1,200 = 12 patients \* \$175,000 = **\$2.1 million**

- **Total \$ Value of 1% Share:**  $\$3.3\text{M} + \$4.2\text{M} + \$2.4\text{M} + \$2.1\text{M} = \$12 \text{ million}$

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## **Final Answer**

1. **Potential Peak Sales for nivolumab + ipilimumab** in the indication of unresectable or metastatic MSI-H/dMMR colorectal cancer (assuming 20-30% market share):

- **Range: \$240 million to \$360 million per year**

- **Midpoint: \$300 million per year**

2. **\$ Value of 1% Share of Treated Patients** across US, EU5, China, and Japan:

- **Total: \$12 million per year**

## **Notes and Caveats**

- These estimates are based on assumptions for patient numbers, treatment rates, market share, and pricing. Real-world data may vary due to competition (e.g., other immunotherapies like pembrolizumab), reimbursement policies, and patient access.

- Peak sales could be influenced by treatment duration (e.g., if patients respond well and remain on therapy longer or shorter than assumed).

- Prevalence (existing patients) could increase the eligible population over time, but incident cases are used here for simplicity.

- Pricing in China is particularly uncertain due to ongoing reforms and potential inclusion in national reimbursement drug lists (NRDL), which could lower costs further.

If you have access to more specific data (e.g., exact patient numbers or pricing), these calculations can be refined accordingly.