

To estimate the **Potential Peak Sales** for retifanlimab-dlwr (Zynyz) in the indication of metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) in the US, EU5 (Germany, France, Italy, Spain, UK), China, and Japan, as well as the **\$ value of 1% share of treated patients** in these geographies, we need to follow a structured approach. Since exact data on patient numbers, pricing, and market penetration may not be publicly available, I will outline the methodology and provide a reasonable estimate based on assumptions and available data on MCC incidence, prevalence, and typical drug pricing for rare cancers.

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## **Step 1: Understanding Merkel Cell Carcinoma (MCC)**

- **Merkel Cell Carcinoma (MCC)** is a rare, aggressive skin cancer often associated with Merkel cell polyomavirus or UV exposure.
- It primarily affects older adults, with higher incidence in regions with high UV exposure.
- The disease often presents as metastatic or recurrent locally advanced at diagnosis, making systemic therapies like retifanlimab-dlwr (a PD-1 inhibitor) a critical treatment option.

## **Step 2: Estimating the Patient Population**

Since MCC is a rare disease, we will estimate the number of eligible patients (metastatic or recurrent locally advanced MCC) using incidence rates and prevalence data.

#### Incidence Rates for MCC (per 100,000 population annually):

- **US:** ~0.7 (based on SEER data, ~2,500 new cases/year).
- **EU5:** ~0.3–0.5 (varies by country, lower UV exposure in some regions; total ~1,500–2,000 new cases/year across EU5).
- **Japan:** ~0.2 (lower incidence due to lower UV exposure and genetic factors; ~200–300 new cases/year).
- **China:** ~0.1–0.2 (limited data, likely lower due to demographics and UV exposure; ~1,000–1,500 new cases/year).

#### Proportion of Metastatic/Recurrent Locally Advanced MCC:

- Approximately **40–50%** of MCC patients present with or progress to metastatic or locally advanced recurrent disease, making them eligible for systemic therapy like retifanlimab-dlwr.

#### Population Estimates (2023):

- US: 330 million
- EU5: ~260 million (Germany: 84M, France: 65M, Italy: 60M, Spain: 47M, UK: 67M)
- China: 1,410 million
- Japan: 125 million

#### Eligible Patient Population (Metastatic/Recurrent MCC):

Using incidence rates and assuming 45% of cases are metastatic/recurrent:

- **US:** 2,500 new cases/year  $\times$  45% = ~1,125 patients/year.
- **EU5:** 1,750 new cases/year  $\times$  45% = ~790 patients/year.
- **Japan:** 250 new cases/year  $\times$  45% = ~110 patients/year.
- **China:** 1,250 new cases/year  $\times$  45% = ~560 patients/year.
- **Total:** ~2,585 patients/year across these geographies.

Note: This is an annual incident population. For peak sales, we may consider a prevalence pool (patients living with the disease over a few years), but since MCC has a poor prognosis, the annual incident population is a reasonable proxy for treatable patients per year.

### **Step 3: Market Share Assumption**

- The problem states a **20–30% share of treated patients**. We'll use the midpoint of **25%** for calculations.
- Not all eligible patients may receive treatment due to access, cost, or clinical factors. We'll assume **80% treatment penetration** among eligible patients.

#### Treated Patients with 25% Market Share:

- **US:**  $1,125 \times 80\% \times 25\% = \sim 225$  patients/year.
- **EU5:**  $790 \times 80\% \times 25\% = \sim 158$  patients/year.
- **Japan:**  $110 \times 80\% \times 25\% = \sim 22$  patients/year.
- **China:**  $560 \times 80\% \times 25\% = \sim 112$  patients/year.
- **Total:** ~517 patients/year.

### **Step 4: Pricing Assumptions**

Retifanlimab-dlwr is a PD-1 inhibitor, and pricing for such immunotherapies in oncology (e.g., pembrolizumab, nivolumab) typically ranges as follows (annual cost per patient):

- **US:** ~\$150,000–\$180,000.
- **EU5:** ~\$100,000–\$130,000 (lower due to price negotiations and healthcare systems).
- **Japan:** ~\$120,000–\$150,000 (similar to EU5 but with specific pricing regulations).
- **China:** ~\$50,000–\$80,000 (lower due to market access programs and generics/biosimilars competition).

For simplicity, we'll use midpoint values:

- US: \$165,000/year
- EU5: \$115,000/year
- Japan: \$135,000/year

- China: \$65,000/year

## **Step 5: Potential Peak Sales Calculation**

Peak sales are calculated as the number of treated patients × annual cost per patient.

- **US:** 225 patients × \$165,000 = **\$37.1 million**.
- **EU5:** 158 patients × \$115,000 = **\$18.2 million**.
- **Japan:** 22 patients × \$135,000 = **\$3.0 million**.
- **China:** 112 patients × \$65,000 = **\$7.3 million**.
- **Total Peak Sales:** **\$65.6 million** annually (at 25% market share).

#### Range for 20–30% Market Share:

- At 20%: ~\$52.5 million.
- At 30%: ~\$78.7 million.

Thus, **Potential Peak Sales** for retifanlimab-dlwr in MCC across these geographies is approximately **\$52–79 million annually**, with a midpoint of **\$65–66 million**.

## **Step 6: \$ Value of 1% Share of Treated Patients**

A 1% market share corresponds to 1% of the treated patient population (80% of eligible patients).

#### Treated Patients (80% of Eligible) for 1% Share:

- **US:**  $1,125 \times 80\% \times 1\% = \sim 9$  patients.
- **EU5:**  $790 \times 80\% \times 1\% = \sim 6.3$  patients.
- **Japan:**  $110 \times 80\% \times 1\% = \sim 0.9$  patients.
- **China:**  $560 \times 80\% \times 1\% = \sim 4.5$  patients.

#### \$ Value of 1% Share:

- **US:** 9 patients × \$165,000 = **\$1.49 million**.
- **EU5:** 6.3 patients × \$115,000 = **\$0.72 million**.
- **Japan:** 0.9 patients × \$135,000 = **\$0.12 million**.
- **China:** 4.5 patients × \$65,000 = **\$0.29 million**.
- **Total \$ Value of 1% Share:** **\$2.62 million**.

## **Final Answer:**

1. **Potential Peak Sales** for retifanlimab-dlwr in MCC (20–30% market share) across the US, EU5, China, and Japan: **\$52–79 million annually** (midpoint ~\$65–66 million at 25% share).

2. **\$ Value of 1% Share of Treated Patients** across these geographies: **\$2.62 million**.

### **Caveats and Notes:**

- These estimates are based on assumptions for incidence, treatment penetration, market share, and pricing. Real-world data may vary due to competition (e.g., other PD-1 inhibitors like pembrolizumab or avelumab, which is already approved for MCC), reimbursement policies, and patient access.
- Peak sales may be influenced by duration of therapy, which could be shorter or longer depending on clinical outcomes (e.g., response rates, progression-free survival).
- China's pricing and market access could vary significantly due to government policies and local competitors.
- These figures are specific to the MCC indication and do not account for potential label expansions to other indications.