

To estimate the **Potential Peak Sales** for dabrafenib (Tafinlar) in combination with trametinib (Mekinist) for pediatric patients with low-grade glioma (LGG) with a BRAF V600E mutation in the US, EU5 (Germany, France, Italy, Spain, UK), China, and Japan, as well as the **\$ value of a 1% share of treated patients**, we need to follow a structured approach. Since specific data on patient numbers, pricing, and market penetration may not be fully available, I will outline the methodology and provide reasonable assumptions based on available information and general market trends. The final numbers are illustrative and should be refined with precise data if available.

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## **Step 1: Define the Indication and Target Population**

- **Indication:** Pediatric patients (1 year and older) with low-grade glioma (LGG) harboring a BRAF V600E mutation who require systemic therapy.
- **Mutation Prevalence:** BRAF V600E mutations are present in approximately 15-20% of pediatric LGG cases (based on literature and studies on gliomas).
- **Geographies:** US, EU5 (Germany, France, Italy, Spain, UK), China, and Japan.

## **Step 2: Estimate the Target Patient Population**

Pediatric LGG is a rare condition, and the number of patients varies by geography. Below are rough estimates of the pediatric LGG population, adjusted for BRAF V600E mutation prevalence (assumed at 20% for simplicity) and the proportion requiring systemic therapy (assumed at 50%, as not all patients may need systemic treatment immediately).

#### Estimated Annual Incidence of Pediatric LGG:

- **US:** ~1,000-1,500 new cases per year (based on brain tumor incidence in children).
- **EU5:** ~1,200-1,800 new cases per year (scaled based on population relative to the US).
- **China:** ~2,000-3,000 new cases per year (higher population, but lower diagnosis rates assumed).
- **Japan:** ~300-500 new cases per year (smaller population, high diagnosis rates).

#### Target Population with BRAF V600E Mutation (20% of cases):

- US: 200-300 patients/year.
- EU5: 240-360 patients/year.
- China: 400-600 patients/year.
- Japan: 60-100 patients/year.

#### Patients Requiring Systemic Therapy (50% of mutation-positive cases):

- US: 100-150 patients/year.
- EU5: 120-180 patients/year.
- China: 200-300 patients/year.
- Japan: 30-50 patients/year.

- **Total:** ~450-680 patients/year across all geographies.

Since LGG is a chronic condition, we also consider **prevalent cases** (patients living with the disease who may require treatment over time). Assuming a 5-year prevalence multiplier (as LGG has a high survival rate), the prevalent pool could be 5x the annual incidence:

- US: 500-750 patients.
- EU5: 600-900 patients.
- China: 1,000-1,500 patients.
- Japan: 150-250 patients.
- **Total Prevalent Pool:** ~2,250-3,400 patients.

### **Step 3: Estimate Market Share of Treated Patients**

- The problem assumes a **20%-30% share of treated patients** for dabrafenib + trametinib.
- Assuming all prevalent patients are eligible for treatment over time, the treated patient pool for dabrafenib + trametinib would be:
  - 20% Share: ~450-680 patients.
  - 30% Share: ~675-1,020 patients.

### **Step 4: Estimate Annual Treatment Cost**

Dabrafenib and trametinib are targeted therapies, and their cost is high. Based on pricing for other indications (e.g., melanoma), the annual cost per patient for the combination therapy is estimated as follows (adjusted for pediatric dosing, which may be lower):

- **US:** ~\$150,000-\$200,000 per patient/year.
- **EU5:** ~\$100,000-\$150,000 per patient/year (lower due to pricing controls).
- **China:** ~\$50,000-\$80,000 per patient/year (significant discounts due to market access challenges).
- **Japan:** ~\$120,000-\$160,000 per patient/year (similar to EU5 but with premium pricing).

For simplicity, let's use the midpoint of these ranges:

- US: \$175,000/year.
- EU5: \$125,000/year.
- China: \$65,000/year.
- Japan: \$140,000/year.

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

Peak sales are calculated as the number of treated patients (based on 20%-30% market share) multiplied by the annual treatment cost per patient. We'll assume peak sales occur when the drug reaches maximum penetration in the prevalent pool.

#### Distribution of Patients by Geography (Roughly Proportional to Population Estimates):

- US: ~25% of total treated patients.
- EU5: ~30% of total treated patients.
- China: ~35% of total treated patients.
- Japan: ~10% of total treated patients.

#### Peak Sales at 20% Market Share (~450-680 treated patients):

- **US:** 113-170 patients  $\times$  \$175,000 = **\$20M-\$30M.**
- **EU5:** 135-204 patients  $\times$  \$125,000 = **\$17M-\$26M.**
- **China:** 158-238 patients  $\times$  \$65,000 = **\$10M-\$15M.**
- **Japan:** 45-68 patients  $\times$  \$140,000 = **\$6M-\$10M.**
- **Total Peak Sales (20% Share): \$53M-\$81M.**

#### Peak Sales at 30% Market Share (~675-1,020 treated patients):

- **US:** 169-255 patients  $\times$  \$175,000 = **\$30M-\$45M.**
- **EU5:** 203-306 patients  $\times$  \$125,000 = **\$25M-\$38M.**
- **China:** 236-357 patients  $\times$  \$65,000 = **\$15M-\$23M.**
- **Japan:** 68-102 patients  $\times$  \$140,000 = **\$10M-\$14M.**
- **Total Peak Sales (30% Share): \$80M-\$120M.**

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

A 1% share of treated patients corresponds to 1% of the prevalent pool (2,250-3,400 patients), i.e., ~23-34 patients.

- **US:** 6-9 patients  $\times$  \$175,000 = **\$1.0M-\$1.6M.**
- **EU5:** 7-10 patients  $\times$  \$125,000 = **\$0.9M-\$1.3M.**
- **China:** 8-12 patients  $\times$  \$65,000 = **\$0.5M-\$0.8M.**
- **Japan:** 2-3 patients  $\times$  \$140,000 = **\$0.3M-\$0.4M.**
- **Total \$ Value of 1% Share: \$2.7M-\$4.1M.**

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## **Final Answer**

- **Potential Peak Sales for Dabrafenib + Trametinib in Pediatric LGG (20%-30% Market Share):**
- **20% Share:** \$53M-\$81M annually across US, EU5, China, and Japan.

- **30% Share:** \$80M-\$120M annually across US, EU5, China, and Japan.

- **\$ Value of 1% Share of Treated Patients:** \$2.7M-\$4.1M annually across US, EU5, China, and Japan.

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## **Notes and Caveats**

1. These estimates are based on assumptions about patient numbers, mutation prevalence, treatment rates, market share, and pricing. Real-world data (e.g., exact incidence, pricing negotiations, or competitor presence) could significantly alter these figures.
2. Peak sales may take several years to achieve due to gradual market penetration, regulatory approvals, and access challenges, especially in China.
3. The combination therapy (dabrafenib + trametinib) is considered together, as the approval is for both drugs used in tandem.
4. If more specific data on patient numbers or pricing becomes available, these calculations can be refined for greater accuracy.

If you have additional data or specific inputs (e.g., exact patient numbers or pricing), I can adjust the analysis accordingly.