

To estimate the **Potential Peak Sales** for bevacizumab (Avastin) in the indication of unresectable or metastatic hepatocellular carcinoma (HCC) in the US, EU5 (Germany, France, 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 such as exact patient numbers, pricing, and market penetration may not be fully available, I will outline the methodology and make reasonable assumptions based on publicly available information and market trends.

Bevacizumab is used in combination with atezolizumab (Tecentriq) for first-line treatment of unresectable or metastatic HCC, as approved by the FDA in May 2020. This analysis focuses on this specific indication.

Step 1: Define Key Parameters

1. **Target Patient Population:** Number of patients with unresectable or metastatic HCC who are eligible for first-line systemic therapy in each geography.
2. **Treatment Rate:** Percentage of eligible patients who receive systemic therapy.
3. **Market Share:** Assuming a 20% to 30% share of treated patients for bevacizumab in combination with atezolizumab.
4. **Annual Cost of Therapy:** Cost of bevacizumab per patient per year, which varies by region due to pricing differences.
5. **Peak Sales:** Estimated maximum annual sales at full market penetration, typically achieved 5-7 years after launch.

Step 2: Estimate Target Patient Population

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer. Incidence and prevalence vary significantly by region due to differences in risk factors such as hepatitis B/C prevalence and alcohol consumption. Below are rough estimates of incident cases of HCC per year and the proportion of unresectable or metastatic cases (advanced stage, eligible for systemic therapy).

- US:

- Annual HCC incidence: ~40,000 cases (based on American Cancer Society data).
- Unresectable/metastatic (advanced stage): ~60-70% of cases (~25,000-28,000 patients).
- First-line systemic therapy eligible: ~80% of advanced cases (~20,000-22,000 patients).

- EU5 (Germany, France, Italy, Spain, UK):

- Annual HCC incidence: ~50,000 cases (combined, based on GLOBOCAN and regional data).
- Unresectable/metastatic: ~60-70% (~30,000-35,000 patients).
- First-line systemic therapy eligible: ~80% (~24,000-28,000 patients).

- China:

- Annual HCC incidence: ~400,000 cases (highest globally due to hepatitis B prevalence, per GLOBOCAN).

- Unresectable/metastatic: ~60-70% (~240,000-280,000 patients).
- First-line systemic therapy eligible: ~60% (lower due to access issues) (~144,000-168,000 patients).
- **Japan:**
 - Annual HCC incidence: ~40,000 cases (high due to hepatitis C prevalence).
 - Unresectable/metastatic: ~60-70% (~24,000-28,000 patients).
 - First-line systemic therapy eligible: ~80% (~19,000-22,000 patients).

Step 3: Estimate Treated Patients (Treatment Rate)

Not all eligible patients receive systemic therapy due to access, cost, or clinical factors. Assuming a treatment rate of 70-80% for the US, EU5, and Japan, and 50-60% for China due to access and affordability constraints:

- **US:** ~14,000-17,600 treated patients.
- **EU5:** ~16,800-22,400 treated patients.
- **China:** ~72,000-100,800 treated patients.
- **Japan:** ~13,300-17,600 treated patients.
- **Total:** ~116,100-158,400 treated patients across these geographies.

Step 4: Estimate Market Share for Bevacizumab + Atezolizumab

Assuming a 20% to 30% share of treated patients for bevacizumab in combination with atezolizumab (based on competition from other therapies like sorafenib, lenvatinib, and emerging immunotherapies):

- **US:** 2,800-5,280 patients (20-30% of 14,000-17,600).
- **EU5:** 3,360-6,720 patients (20-30% of 16,800-22,400).
- **China:** 14,400-30,240 patients (20-30% of 72,000-100,800).
- **Japan:** 2,660-5,280 patients (20-30% of 13,300-17,600).
- **Total:** 23,220-47,520 patients.

Step 5: Estimate Annual Cost of Bevacizumab Therapy

Bevacizumab pricing varies significantly by region due to healthcare systems, negotiations, and generics/biosimilars (e.g., Mvasi in the US and EU). The cost also depends on dosage and treatment duration (often 1 year or until progression). Below are approximate annual costs per patient (based on historical data and biosimilar impact as of 2023):

- **US:** ~\$100,000-120,000 per patient per year (pre-biosimilar list price; discounted post-biosimilar).
- **EU5:** ~\$50,000-70,000 per patient per year (varies by country, lower due to negotiations and biosimilars).
- **China:** ~\$20,000-30,000 per patient per year (lower pricing due to market dynamics and biosimilars).
- **Japan:** ~\$60,000-80,000 per patient per year (similar to EU5 but with specific pricing controls).

Step 6: Calculate Potential Peak Sales

Using the mid-range of patient numbers and costs for simplicity:

- **US:** 4,040 patients (midpoint of 2,800-5,280) \times \$110,000 = **~\$444 million.**
- **EU5:** 5,040 patients (midpoint of 3,360-6,720) \times \$60,000 = **~\$302 million.**
- **China:** 22,320 patients (midpoint of 14,400-30,240) \times \$25,000 = **~\$558 million.**
- **Japan:** 3,970 patients (midpoint of 2,660-5,280) \times \$70,000 = **~\$278 million.**
- **Total Peak Sales:** ~\$444M (US) + \$302M (EU5) + \$558M (China) + \$278M (Japan) = **~\$1.58 billion** (mid-range estimate).

Range for Peak Sales (20% to 30% share):

- At 20% share: ~\$1.1-1.2 billion.
- At 30% share: ~\$1.9-2.0 billion.

Step 7: Calculate \$ Value of 1% Share of Treated Patients

Total treated patients (midpoint): ~137,250 (from Step 3 total range of 116,100-158,400).

- 1% of treated patients = 1,372.5 patients.

Using the same per-patient cost estimates:

- **US:** 1% of 15,800 (midpoint) = 158 patients \times \$110,000 = **~\$17.4 million.**
- **EU5:** 1% of 19,600 (midpoint) = 196 patients \times \$60,000 = **~\$11.8 million.**
- **China:** 1% of 86,400 (midpoint) = 864 patients \times \$25,000 = **~\$21.6 million.**
- **Japan:** 1% of 15,450 (midpoint) = 154.5 patients \times \$70,000 = **~\$10.8 million.**
- **Total \$ Value of 1% Share:** ~\$17.4M (US) + \$11.8M (EU5) + \$21.6M (China) + \$10.8M (Japan) = **~\$61.6 million.**

Final Answer:

- Potential Peak Sales for Bevacizumab in HCC Indication (20-30% share):

- US: ~\$310M-\$580M (midpoint ~\$444M).
- EU5: ~\$200M-\$400M (midpoint ~\$302M).
- China: ~\$360M-\$760M (midpoint ~\$558M).
- Japan: ~\$190M-\$370M (midpoint ~\$278M).
- **Total:** ~\$1.1B-\$2.0B (midpoint ~\$1.58B).

- \$ Value of 1% Share of Treated Patients:

- US: ~\$17.4M.

- EU5: ~\$11.8M.
- China: ~\$21.6M.
- Japan: ~\$10.8M.
- **Total:** ~\$61.6M.

Notes:

- These estimates are based on assumptions and publicly available data as of 2023. Real-world figures may differ due to pricing negotiations, biosimilar competition, reimbursement policies, and evolving treatment landscapes (e.g., new therapies for HCC).
- Peak sales may be lower if biosimilar penetration increases or if competing therapies (e.g., TKIs, other immunotherapies) capture more market share.
- China's large patient pool drives significant sales potential despite lower per-patient costs.