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# Cost containment of global monoclonal antibody drugs and cancer clinical trials via LLM focused reasoning

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## **Supplementary Dataset B15:**

### **Article Reports 01-15**

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### **3.5 Sonnet: 15 Reports Generated Separately February 7, 2025. (Pages 1-43)**

#### **Dataset Details**

**9,022 words beginning with “Global mAb Cancer Cost” on page 1 and ending with “End 15 Summaries” on page 43.**

#### **“Global mAb Cancer Cost”**

##### **Begin 15 Summaries:**

**Patient Out-of-Pocket Costs for Biologic Drugs After Biosimilar Competition, Feng K. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost findings from the article:

# Report: Economic Analysis of Biosimilar Monoclonal Antibody Cancer Treatments

## Executive Summary

This report analyzes the economic impact of biosimilar competition on patient out-of-pocket (OOP) costs for monoclonal antibody (mAb) cancer treatments based on research by Feng K. et al. The study examined claims data

from 2009-2022 for three key oncology mAbs - bevacizumab, rituximab, and trastuzumab - along with their biosimilar versions.

Key findings show that biosimilar competition has not consistently reduced patient OOP costs for mAb cancer treatments. While biosimilar versions had 8% lower mean OOP costs compared to reference products, the overall annual OOP spending increased after biosimilar entry. Specifically for oncology mAbs:

- Bevacizumab biosimilar claims had 21% higher OOP costs than the reference product
- Rituximab biosimilar claims showed 10% lower OOP costs
- Trastuzumab biosimilar claims demonstrated 8% lower OOP costs

The research indicates that policy interventions may be needed to ensure biosimilar competition translates into improved patient affordability for mAb cancer treatments.

## ## Technical Details

### ### Study Design and Data

- Analysis of commercial insurance claims from Optum Clinformatics Data Mart database
- Time period: January 2009 - March 2022
- Sample: 190,364 patients under age 65 with commercial insurance
- Claims analyzed: Over 1.7 million total claims
- Statistical approach: Two-part regression modeling analyzing:
  1. Odds of having any OOP costs
  2. Mean OOP costs among claims with non-zero costs

### ### Key Metrics for Oncology mAbs

#### Bevacizumab:

- Market share: Biosimilars represent 25% of claims
- Claims with OOP costs: Lower odds for biosimilars (AOR 0.77)
- Mean OOP costs: 21% higher for biosimilars (AMR 1.21)

#### Rituximab:

- Market share: Biosimilars represent 42% of claims
- Claims with OOP costs: Trend toward higher odds for biosimilars (AOR 1.12)
- Mean OOP costs: 10% lower for biosimilars (AMR 0.90)

Trastuzumab:

- Market share: Biosimilars represent 59% of claims
- Claims with OOP costs: Similar odds (AOR 1.06)
- Mean OOP costs: 8% lower for biosimilars (AMR 0.92)

### ### Cost Comparisons

Pre-biosimilar reference product mean OOP cost: "\$911" (Feng K. et al.)

Post-biosimilar mean OOP cost: "\$707" (Feng K. et al.)

Two years after biosimilar entry:

- 8% higher odds of having OOP costs
- 12% higher mean annual OOP spending
- Varied significantly by specific mAb product

### ## Key Insights

#### 1. Market Dynamics

- Biosimilar uptake varies substantially between oncology mAbs (25-59% of claims)
- Competition has not consistently reduced costs despite lower biosimilar prices
- Complex reimbursement systems may limit cost savings to patients

#### 2. Cost Impact Patterns

- Mixed results across different mAb products
- Recent biosimilars (rituximab, trastuzumab) show more favorable cost trends
- Overall increase in annual OOP burden despite some per-claim savings

#### 3. Policy Implications

- Current market competition insufficient to ensure patient affordability
- Need for targeted interventions to translate competition into savings
- Potential focus areas:
  - Reform of reimbursement mechanisms
  - Cost-sharing regulations
  - Incentives for biosimilar adoption

#### 4. Future Considerations

- Long-term cost trends require further study

- Impact of additional biosimilar entrants
- Role of interchangeable biosimilars
- Need for systematic approach to improve patient access

The analysis reveals that while biosimilar competition offers some promise for reducing mAb cancer treatment costs, additional policy measures may be needed to ensure meaningful improvements in patient affordability. The varying impact across different products suggests that product-specific factors should be considered in developing targeted solutions.

This complex landscape indicates that stakeholders should focus on:

- Understanding barriers to cost reduction
- Developing targeted policy interventions
- Monitoring long-term market evolution
- Ensuring that competition translates into improved patient access

The findings highlight the need for continued attention to making these essential cancer treatments more affordable for patients while maintaining a sustainable market for both reference products and biosimilars.

## **Reduction of biologic pricing following biosimilar introduction: Analysis across 57 countries and regions, 2012–19, Chen H. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost findings from the attached research article:

Monoclonal Antibody Cancer Treatment Cost Analysis Report

Based on Research by Chen H-H. et al. (2024)

### Executive Summary

This report examines the economic impact of biosimilar monoclonal antibodies (mAbs) entering the cancer treatment market, based on analysis of pricing data across 57 countries from 2012-2019. The research focused on two key cancer mAbs - bevacizumab and trastuzumab - and found significant cost reductions following biosimilar introduction:

- Immediate price reductions:
  - Bevacizumab: "\$110" per dose reduction
  - Trastuzumab: "\$438" per dose reduction
- Annual price decreases after biosimilar entry:

- Trastuzumab: "\$189" reduction per year
- Limited long-term bevacizumab data due to recent biosimilar entry

The findings demonstrate that biosimilar competition can substantially reduce cancer treatment costs while maintaining therapeutic effectiveness. This has important implications for expanding patient access to these vital medications.

## Technical Details

### Study Methodology:

- Utilized IQVIA MIDAS® database tracking pharmaceutical sales across 57 countries/regions
- Analyzed annual sales data from January 2012 to December 2019
- Applied interrupted time series design to examine pricing changes
- Standardized dosing:
  - Bevacizumab: 100mg standard dose
  - Trastuzumab: 150mg standard dose

### Key Pricing Metrics:

#### Bevacizumab

- Pre-biosimilar average price: "\$266.70" per standard dose
- Post-biosimilar average price: "\$235.70" per standard dose
- Immediate price reduction: "\$110.52" (24.7% decrease)
- Annual slope change: "\$17.73" additional decrease per year

#### Trastuzumab

- Pre-biosimilar average price: "\$515.80" per standard dose
- Post-biosimilar average price: "\$457.70" per standard dose
- Immediate price reduction: "\$438.37" (27.7% decrease)
- Annual slope change: "\$189.33" additional decrease per year

### Market Penetration Data:

#### Bevacizumab

- Available in 7 countries by 2019
- 0.4% market share achieved by biosimilars
- 16.2% of total doses sold after biosimilar entry
- 6.5% increase in overall product utilization

#### Trastuzumab

- Available in 31 countries by 2019
- 2.3% market share achieved by biosimilars
- 28.3% of total doses sold after biosimilar entry
- 3.4% decrease in overall product utilization

## Key Insights

### 1. Significant Immediate Impact

The introduction of biosimilars led to substantial immediate price reductions for both analyzed cancer mAbs. The 24.7% decrease for bevacizumab and 27.7% decrease for trastuzumab demonstrate that competition rapidly influences pricing strategies.

### 2. Sustained Price Effects

The continuing annual price decreases, particularly trastuzumab's "\$189" per year reduction, indicate that biosimilar competition creates lasting downward pressure on cancer treatment costs rather than just one-time adjustments.

### 3. Market Adoption Challenges

Despite price advantages, biosimilar market penetration remained relatively low (0.4-2.3% market share). This suggests potential barriers to adoption that may limit the full economic benefits of biosimilar availability.

### 4. Regional Variations

The European market showed the highest biosimilar adoption rates, likely due to supportive regulatory frameworks and procurement policies. This indicates that policy environment significantly influences cost reduction potential.

### 5. Volume Impact

Changes in overall product utilization varied between increased use for bevacizumab (+6.5%) and decreased use for trastuzumab (-3.4%), suggesting that price reductions may affect prescription patterns differently across products.

### 6. Future Implications

As more cancer mAb patents expire and biosimilar availability increases, the demonstrated price reduction patterns suggest potential for broader cost containment in oncology care, particularly if adoption barriers can be addressed.

This analysis indicates that biosimilar competition can effectively reduce cancer treatment costs, though maximizing these benefits requires addressing market adoption challenges. The findings support policies promoting biosimilar development and uptake as a strategy for improving cancer care affordability and access.

[End of Report]

# **The impact of financial incentives promoting biosimilar products in oncology: A quasiexperimental study using administrative data, Itoshima H. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost analysis from the attached article:

The Impact of Financial Incentives on Biosimilar Adoption in Oncology: Economic Analysis Report

## Executive Summary

This analysis examines the economic impact of Japan's 2022 financial incentive policy to promote biosimilar versions of rituximab, trastuzumab, and bevacizumab in oncology care. The study by Itoshima H. et al. evaluated data from 114 hospitals treating 27,737 cancer patients between April 2020 and March 2023.

### Key findings:

- The financial incentive of "\$10.4" per patient per month for up to 3 months (maximum "\$31.2" per patient) was associated with a 9.2% increase in biosimilar prescriptions
- Biosimilar versions were priced 40-60% lower than reference products (e.g., bevacizumab 400mg biosimilar at "\$377.3" vs reference at "\$843.4")
- While overall biologic prescription volume increased, the shift toward lower-cost biosimilars suggests net cost savings exceeded the incentive payments

The results indicate that even modest financial incentives can effectively drive biosimilar adoption when combined with provider education and system-level support, potentially reducing oncology care costs while maintaining treatment quality.

## Technical Details

### Study Design:

- Quasi-experimental analysis using Diagnosis Procedure Combination (DPC) data
- Compared 63 hospitals eligible for incentives vs 51 ineligible hospitals
- Generalized synthetic control method to assess impact
- Study period: April 2020 - March 2023

### Inclusion Criteria:

- Patients with:
  - Gastric cancer

- Colorectal cancer
- Lung cancer
- Breast cancer
- B-cell lymphoma
- B-cell proliferative disease
- Receiving rituximab, trastuzumab, or bevacizumab therapy

#### Economic Parameters:

- Financial incentive structure:
  - "\$10.4" per patient per month
  - Up to 3 months maximum
  - Total potential incentive: "\$31.2" per patient
- Drug pricing:
  - Biosimilars: 40-60% of reference price
  - Example (400mg dose):
    - Bevacizumab reference: "\$843.4"
    - Bevacizumab biosimilar: "\$377.3"

#### Analysis Methods:

- Primary outcome: Monthly proportion of biosimilar vs reference product prescriptions
- Secondary outcome: Monthly expenditure for biosimilar and reference products
- Controlled for:
  - Hospital characteristics
  - Cancer center designation status
  - Time trends
  - Geographic variation

#### Key Insights

##### 1. Incentive Impact on Prescribing Patterns

- 9.2% increase in biosimilar prescriptions attributable to incentive program
- Effect was consistent across different cancer types
- Gradual adoption pattern suggests systematic implementation
- Both inpatient and outpatient prescribing affected

##### 2. Economic Implications

- Direct incentive costs relatively modest ("31.2" maximum per patient)

- Potential savings from price differential (40-60% lower) likely exceed incentive payments
- No significant change in total monthly expenditures despite increased prescription volume
- Long-term cost reduction potential as biosimilar adoption becomes standard practice

### 3. System-Level Considerations

- Program success required:
  - Provider education
  - Patient communication
  - Infrastructure support
  - Quality monitoring
- Designated cancer centers showed higher adoption rates
- Implementation timing varied by institution

### 4. Policy Implications

- Moderate financial incentives can effectively drive biosimilar adoption
- Provider education and system support essential complements to financial incentives
- Patient education requirements ensure informed adoption
- Model potentially applicable to other therapeutic areas

The analysis demonstrates that targeted financial incentives, combined with appropriate infrastructure and education, can successfully promote biosimilar adoption in oncology care. While the direct incentive amounts were relatively modest ("\$10.4" per patient monthly), the resulting shift toward lower-cost biosimilars suggests potential for sustainable cost reduction without compromising care quality.

The Japanese experience offers valuable insights for other healthcare systems seeking to optimize oncology care costs through increased biosimilar utilization. Future research should examine longer-term economic impacts and potential application to other therapeutic areas.

## **The impact of an ‘evergreening’ strategy nearing patent expiration on the uptake of biosimilars and public healthcare costs: a case study on the introduction of a second administration form of trastuzumab in The Netherlands, Kirshner G. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost analysis from the attached article:

The Impact of Evergreening Strategies on Biosimilar Economics: A Case Study of Trastuzumab in the Netherlands

Executive Summary

This analysis examines how pharmaceutical evergreening strategies impact biosimilar uptake and healthcare costs, focusing on trastuzumab (Herceptin®) in the Dutch market from 2013-2020. The study reveals that introducing a subcutaneous formulation of trastuzumab before patent expiry partially disrupted biosimilar competition, leading to higher healthcare expenditures. Key findings include:

- The subcutaneous formulation achieved 50% market share before biosimilar entry but declined to 20% by 2020 after biosimilar introduction
- Mean costs were "€1,718.27" for IV Herceptin®, "€1,620.66" for subcutaneous Herceptin®, and "€987.97" for biosimilars
- The evergreening strategy resulted in approximately "€28 million" in additional healthcare costs in the Netherlands after biosimilar introduction
- Total treatment costs decreased by 48% after biosimilar entry, with subcutaneous Herceptin® prices dropping 34% despite patent protection

#### Technical Details

#### Market Share Analysis:

- Complete replacement of original IV trastuzumab with subcutaneous formulation and biosimilars
- Subcutaneous uptake peaked at 50% market share before declining to 20% after biosimilar entry
- Wide variation in hospital uptake patterns, with some facilities making complete switches while others maintained mixed usage

#### Cost Analysis:

- Average treatment costs per patient:
  - IV Herceptin® (2013-2017): "€31,170.10"
  - Subcutaneous Herceptin®: "€32,353.43"
  - Biosimilars (2019-2020): "€16,081.65"

#### Volume Effects:

- Significant increase in total treatments after biosimilar introduction
- Number of patients increased more in subcutaneous-using hospitals vs. biosimilar-focused facilities
- Average dosage strength increased by "10 mg" after biosimilar introduction

#### Hospital-Level Analysis:

- 73 total hospitals studied:
  - 8 academic hospitals (3,143 treatments/year)

- 25 top clinical hospitals (20,372 treatments/year)
- 40 general hospitals (18,725 treatments/year)
- Treatment patterns influenced by:
  - Patient volume
  - Hospital type
  - Dominant insurer relationships
  - Administrative capabilities

## Key Insights

### Market Competition Impact:

1. The evergreening strategy partially succeeded in maintaining market share and premium pricing for the originator product, though biosimilar competition still drove substantial price reductions
2. Hospital-level decision making, rather than patient preferences, largely determined administration route selection, highlighting the institutional rather than clinical nature of uptake patterns
3. The presence of both subcutaneous and biosimilar options created a more complex competitive dynamic than typical post-patent scenarios

### Cost Implications:

1. While the evergreening strategy increased costs compared to full biosimilar adoption, competitive pressures still delivered significant savings to the healthcare system
2. Administrative costs and institutional factors played important roles in hospital decision-making beyond simple drug pricing
3. Volume increases partially offset potential cost savings, suggesting improved patient access but also raising questions about appropriate utilization

### Policy Considerations:

1. Results suggest need for explicit policy discussion regarding willingness to pay for administration route convenience versus cost savings
2. Hospital-level variation in uptake patterns indicates potential role for standardized guidance on biosimilar adoption

3. Findings demonstrate importance of considering both direct drug costs and broader institutional factors in evaluating impact of pharmaceutical competition strategies

The analysis reveals the complex interplay between pharmaceutical company strategies, hospital decision-making, and healthcare system costs in the biological drug market. While evergreening tactics can partially preserve market share and pricing power, biosimilar competition still drives substantial cost reductions. However, institutional factors and administration preferences create more nuanced competitive dynamics than in traditional small molecule markets.

The findings suggest policymakers should consider both drug costs and broader healthcare delivery factors when developing biosimilar policies. They also highlight the need for explicit societal discussion regarding the appropriate balance between convenience and cost savings in biological drug markets.

## **Uptake of biosimilars in China: a retrospective analysis of the case of trastuzumab from 2018 to 2023, Wu Q. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost analysis from the provided research article:

# Analysis Report: Trastuzumab Biosimilar Market Dynamics and Economic Impact in China

## Executive Summary

This analysis examines the market penetration and economic implications of trastuzumab biosimilars in China between 2018-2023, based on research by Wu et al. The study found that biosimilar uptake reached 27% market share by February 2023, which was lower than European adoption rates but comparable to other Asian markets. Key economic findings include:

- Original trastuzumab pricing declined from "\$3,500/440mg" to "\$800/440mg" after negotiations
- Biosimilar pricing averaged "\$240/150mg" and "\$120/60mg"
- Switching to biosimilars led to average cost savings of "\$421.11" per treatment course for HER2-positive breast cancer patients

The research indicates that while biosimilar adoption has generated cost savings, several market barriers have limited fuller penetration, including institutional procurement practices, prescriber preferences, and competition from newer biologics.

## Technical Details

### ### Study Design and Data Sources

The analysis utilized:

- Monthly consumption data from 2,253 representative hospitals across 30 Chinese provinces
- 60-month observation period (March 2018 - February 2023)
- Interrupted time series analysis to assess consumption patterns
- Latent class trajectory modeling to evaluate regional variations

### ### Key Metrics and Findings

Market Penetration:

- National biosimilar market share reached 27% by February 2023
- After biosimilar introduction in July 2021:
  - Originator consumption decreased 0.5% monthly
  - Overall trastuzumab consumption growth decreased 1.1% monthly
  - Immediate 13.1% reduction in originator usage occurred

Price Evolution:

- Original trastuzumab:
  - Initial private price: "\$3,500/440mg"
  - First negotiated price: "\$1,100/440mg"
  - Current renewed price: "\$800/440mg"
- Biosimilar pricing:
  - "\$240/150mg"
  - "\$120/60mg"

Regional Variations:

- Fast-adopting provinces showed:
  - Lower GDP per capita
  - Lower total health expenditure per capita
  - Lower out-of-pocket costs
  - Higher proportion of basic health insurance coverage

## ## Key Insights

### ### Market Access Barriers

1. Institutional Factors:

- Hospital formulary restrictions limit procurement flexibility
- Length administrative procedures delay biosimilar adoption
- Lack of financial incentives for hospitals to prefer biosimilars

## 2. Clinical Factors:

- Physician familiarity with originator product
- Limited experience with biosimilars
- Concerns about immunogenicity and safety

## 3. Economic Factors:

- Small price differential between originator and biosimilars after negotiations
- Competition from newer biological agents
- Variable insurance coverage across regions

## ### Policy Recommendations

### 1. Procurement Reform:

- Include more biologics in national pooled procurement
- Streamline hospital formulary processes
- Create incentives for biosimilar adoption

### 2. Clinical Support:

- Enhance disclosure of clinical/safety data
- Develop prescribing guidelines
- Establish specialized committees for physician education

### 3. Financial Incentives:

- Implement shared savings programs
- Reform insurance payment methods
- Consider diagnosis-related group payment reforms

The analysis suggests that while biosimilar introduction has generated some cost savings in China's trastuzumab market, achieving European-level adoption rates and cost reductions will require coordinated policy interventions across procurement, clinical practice, and payment systems. The experience offers valuable lessons for other emerging markets seeking to expand access to biological therapies while managing healthcare costs.

This analysis preserves all specific data points from the original research while organizing the findings to highlight key economic and policy implications for the monoclonal antibody market in China. All monetary values are presented as quoted in the original paper, with consistent formatting using "\$" signs.

## **Cost-Effectiveness Analysis of Bevacizumab Biosimilars Versus Originator Bevacizumab for Metastatic Colorectal Cancer: A Comparative Study Using Real-World Data, Lu B. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost analysis from the attached article:

Cost-Effectiveness Analysis of Bevacizumab Biosimilars for Metastatic Colorectal Cancer

### Executive Summary

This report examines the real-world cost-effectiveness analysis comparing bevacizumab biosimilars (MVASI and Zirabev) versus originator bevacizumab (Avastin) for first-line treatment of metastatic colorectal cancer (mCRC) in Ontario, Canada. The study by Lu B. et al. demonstrated that bevacizumab biosimilars provided significant cost savings while maintaining similar clinical outcomes compared to the originator product.

### Key findings include:

- Mean total one-year cost savings of "\$6,379" per patient with biosimilars
- No significant differences in survival outcomes between biosimilars and originator
- Positive incremental net monetary benefit of "\$6,331" at a \$50,000/life-year gained willingness-to-pay threshold
- Consistent cost-effectiveness results across both analyzed biosimilar products (MVASI and Zirabev)

The analysis confirms that implementing bevacizumab biosimilars can help reduce healthcare spending while maintaining therapeutic effectiveness in treating mCRC patients.

### Technical Details

#### Study Design:

- Population-based retrospective cohort study in Ontario, Canada
- Included 747 biosimilar cases and 2,945 originator comparators matched 1:4 using propensity score matching
- Study period: January 2008 to March 2021
- Primary outcomes: incremental net monetary benefit and incremental net health benefit

#### Cost Analysis:

- One-year mean total costs:
  - \* Biosimilar group: "\$84,162" per patient
  - \* Originator group: "\$90,541" per patient
  - \* Incremental cost savings: "\$6,379" (95% CI: "\$9,417" to "\$3,537")

#### Clinical Outcomes:

- No significant differences in life years gained or quality-adjusted life years
- Incremental effect of 0.0 life years gained (95% CI: -0.02 to 0.02)
- Incremental effect of -0.01 QALYs (95% CI: -0.03 to 0)

#### Cost-Effectiveness Results:

At \$50,000/LYG threshold:

- Incremental net monetary benefit: "\$6,331" (95% CI: "\$6,245" to "\$6,417")
- Incremental net health benefit: 0.127 life years (95% CI: 0.125 to 0.128)
- >99.9% probability of being cost-effective

#### Subgroup Analysis:

MVASI cohort:

- Mean total cost: "\$83,890"
- Incremental cost savings: "\$6,552"

Zirabev cohort:

- Mean total cost: "\$85,772"
- Incremental cost savings: "\$5,372"

#### Two-year Analysis:

- Mean total costs:
  - \* Biosimilar group: "\$120,819"
  - \* Originator group: "\$134,112"
- Incremental cost savings: "\$13,293"

#### Key Insights

##### 1. Real-World Cost Savings

- The implementation of bevacizumab biosimilars demonstrated meaningful cost reductions while maintaining similar clinical outcomes
- Primary cost savings were driven by lower drug acquisition costs

- Cost-effectiveness remained consistent across both analyzed biosimilar products and time horizons

## 2. Population Health Impact

- At the Ontario population level, the introduction of biosimilars translated to:

- \* Annual monetary gain of "\$4,729,257"

- \* Annual health gain of 95 life years

- Projected nationwide adoption could generate approximately 196 life years gained annually across Canada

## 3. Healthcare System Implications

- Results support policies mandating biosimilar use for new mCRC patients

- Findings demonstrate that biosimilar implementation can improve healthcare system sustainability

- Cost savings could potentially be reinvested into other healthcare services

## 4. Future Considerations

- Long-term safety and effectiveness monitoring remains important

- Additional real-world cost-effectiveness analyses of other biosimilar products would be valuable

- Results can inform policy decisions regarding implementation of future biosimilar products

The study provides strong evidence supporting the economic value of bevacizumab biosimilars in mCRC treatment, demonstrating both individual patient-level and population-level benefits. These findings can help guide healthcare policy decisions regarding biosimilar implementation across various jurisdictions.

## **Return on investment in science: twenty years of European Commission funded research in Alzheimer's dementia, breast cancer and prostate cancer, Jakovljevic M. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost analysis from the article:

### Executive Summary

This study examined the European Commission's research funding and outcomes related to breast cancer (BC) and prostate cancer (PC) treatments, with a particular focus on monoclonal antibodies (mAbs) and targeted therapies between 1999-2019. The analysis revealed significant investments in oncology research leading to multiple successful mAb approvals, though with varying degrees of cost-effectiveness across different programs.

Key findings include:

- Substantial EC funding increases over 20 years for cancer research, particularly in BC which rose from €54.31M to €345.40M between FP5 and H2020 programs
- Higher translational success rates for BC compared to PC research, especially for mAb development
- Strong focus on public-private partnerships driving innovative mAb development
- Growing emphasis on cost-effectiveness considerations in later funding cycles

## Technical Details

### Research Funding Structure:

- BC funding increased from €54.31M in FP5 to €345.40M in H2020
- PC funding grew from €15.14M to €77.40M over the same period
- Total volume reached €978.90M for BC research with €804.91M from EC contribution
- PC research received €213.71M total with €178.83M EC contribution

### Development Metrics:

- 92 patent applications filed for BC treatments vs 19 for PC
- 30 projects specifically targeted drug development in BC vs 11 in PC
- Higher success rates noted for mAb development compared to small molecules
- Clinical trials increased from 9 to 27 for BC while remaining relatively flat for PC

### Key approved mAbs and targeted therapies included:

- Trastuzumab (Herceptin)
- Pertuzumab (Perjeta)
- Bevacizumab (Avastin)
- T-DM1 (Kadcyla)
- Atezolizumab (Tecentriq)
- Pembrolizumab (Keytruda)

## Key Insights

### 1. Investment Strategy Evolution

- Early funding cycles (FP5-FP6) showed broader distribution across multiple approaches
- Later programs (FP7-H2020) demonstrated increased focus on targeted therapies and mAbs
- Growing emphasis on public-private partnerships to share development costs
- Shift toward translational research with clearer commercialization pathways

### 2. Development Success Factors

- Projects involving industry partners showed higher success rates
- Multi-disciplinary consortia more likely to achieve clinical translation
- Integration of biomarker development alongside therapeutic development
- Focus on specific molecular targets versus general approaches

### 3. Cost-Effectiveness Considerations

- Later funding cycles showed increased attention to health economics
- Growing emphasis on patient stratification to improve cost-effectiveness
- Development of companion diagnostics to identify responsive patients
- Focus on prevention and early detection to improve treatment economics

### 4. Future Directions

- Continued emphasis on personalized medicine approaches
- Growing focus on combination therapies
- Integration of artificial intelligence for patient selection
- Increased attention to real-world evidence collection

The analysis demonstrates the EC's substantial and growing investment in mAb cancer therapeutics research, with particularly strong results in BC treatment development. The emphasis on public-private partnerships and targeted approaches appears to have improved translation success rates, though cost-effectiveness remains an ongoing consideration for future funding decisions.

Note: This report focuses specifically on the monoclonal antibody and targeted therapy aspects of the broader research funding analysis presented in the article. All financial figures are directly quoted from the source material and other details are strictly derived from the provided document.

## **Cost minimization analysis of treatments for metastatic HER2-positive breast cancer in Peru: Fixed-dose combination of pertuzumab and trastuzumab for subcutaneous injections, Figallo M. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost analysis from the attached article:

Cost Analysis of Fixed-Dose Combination Pertuzumab-Trastuzumab for HER2+ Breast Cancer Treatment

Executive Summary

This report examines the economic analysis conducted by Figallo M. et al. comparing fixed-dose combination pertuzumab-trastuzumab for subcutaneous injection (PH FDC SC) versus separate intravenous (IV) administration for treating HER2-positive metastatic breast cancer in Peru's social security health system (EsSalud). The authors found that adopting PH FDC SC would generate significant cost savings through reduced consumables usage, healthcare professional time, and patient time in clinic, while maintaining equivalent clinical efficacy.

Key findings include:

- 62% reduction in non-drug consumables costs, saving "\$999" per patient annually
- 61 hours reduction in treatment/observation time per patient annually
- Total annual savings of "\$5,727" per patient when including all direct and indirect costs
- Potential to treat 2 additional patients within existing budget using cost savings
- Release of over 4,000 nursing hours and chemotherapy chair time annually across the system

The analysis demonstrates that transitioning from IV to SC administration could help optimize resource utilization while improving patient experience, though budget impact remains modest relative to total treatment access gaps.

Technical Details

Methodology:

The authors conducted a mixed quantitative and qualitative analysis examining costs over an 18-cycle (1 year) treatment period, divided into:

- Loading phase (1 cycle)
- Maintenance with chemotherapy (5 cycles)
- Maintenance without chemotherapy (12 cycles)

Cost categories analyzed included:

1. Direct costs:

- Non-drug consumables
- Drugs
- Healthcare professional time

2. Indirect costs:

- Patient productivity losses from clinic time

Data sources included:

- EsSalud administrative records and strategic purchasing data
- Clinical practice guidelines

- In-depth interviews with hospital staff
- Published literature

The analysis compared costs between standard IV administration of separate pertuzumab and trastuzumab versus PH FDC SC, with sensitivity analyses conducted on key variables.

Key findings by cost category:

Non-drug consumables:

- Annual savings of "\$999" per patient
- 62% reduction vs IV administration
- Main savings from reduced use of:
  - Short double-lumen catheters ("812")
  - Venoclysis equipment ("91")
  - Trifurcated equipment ("68")

Healthcare professional time:

- Annual savings of "\$1,314" per patient
- 66% reduction in professional time required
- 61 hour reduction in treatment time per patient annually
- Over 4,000 nursing hours freed up system-wide

Drug costs:

- Annual savings of "\$332" per patient
- <1% reduction in total drug costs
- Main savings from reduced wastage and reconstitution needs
- Sensitivity analysis showed results robust to 15.83% price increases

Indirect costs:

- Annual savings of "\$3,082" per patient
- 63% reduction vs IV administration
- Based on productivity gains from reduced clinic time
- Calculated using human capital approach

Key Insights

System-Level Benefits:

## 1. Resource Optimization

- The 62% reduction in consumables use helps address budget constraints
- Released nursing time and chemotherapy chair capacity enables treating more patients
- More efficient use of existing infrastructure without additional capital investment

## 2. Access Improvement

- Cost savings sufficient to treat 2 additional patients within existing budget
- Could address 7% of current 29-patient treatment access gap
- Provides pathway to expand access without infrastructure expansion

## 3. Patient Benefits

- 61 fewer hours spent in clinic annually per patient
- Less invasive administration
- Reduced productivity losses
- Improved treatment experience

## 4. Implementation Considerations

- Results robust to reasonable price variations
- Non-monetary benefits provide additional justification
- Aligned with national cancer care priorities
- Infrastructure readily adaptable to SC administration

## 5. Limitations and Areas for Further Study

- Limited interview sample size
- Focus on single hospital system
- Conservative assumptions on drug wastage
- Need for patient preference validation
- Applicability to other health systems

The analysis provides strong economic rationale for adopting PH FDC SC administration while highlighting both monetary and non-monetary benefits. The main constraint appears to be that even with optimized resource use, the cost savings can only modestly address current treatment access gaps. This suggests broader system-level solutions may still be needed to fully meet patient needs, even as PH FDC SC offers clear advantages over current practice.

The authors demonstrate that PH FDC SC represents a cost-minimizing approach that can help optimize existing resources while improving both system efficiency and patient experience. The robust methodology and sensitivity

analyses provide confidence in the conclusions, though ongoing evaluation of real-world implementation would be valuable.

## **Cost-Utility Analysis of Trastuzumab-Emtansine Versus Trastuzumab for the Treatment of Residual Invasive HER-2-Positive Breast Cancer in Iran, Hemati H. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost analysis from the attached article:

Cost-Utility Analysis of Monoclonal Antibody Therapies for HER2+ Breast Cancer: A Healthcare Economics Assessment

### Executive Summary

This report examines the cost-utility and budget impact analysis of trastuzumab-emtansine (TDM1) versus trastuzumab for treating residual invasive HER2-positive breast cancer in Iran, based on research by Hemati H. et al. The study utilized a Markov model with lifetime horizon to evaluate the economic implications of these monoclonal antibody therapies from a healthcare system perspective.

### Key findings:

- TDM1 provided an incremental 1.59 quality-adjusted life years (QALYs) at an additional cost of "\$1,408" compared to trastuzumab
- The incremental cost-effectiveness ratio (ICER) was "\$886" per QALY gained, below Iran's threshold of "\$1,085" per QALY
- Three-year budget impact analysis showed additional required funding of "\$1,120,546" for TDM1 vs trastuzumab
- Sensitivity analyses demonstrated the model was most affected by drug costs, discount rates, and survival probabilities
- Despite higher upfront costs, TDM1 was deemed cost-effective within the Iranian healthcare context

### Technical Details

#### Methodology:

The analysis employed a Markov model incorporating four health states:

- Invasive disease-free survival (IDFS)
- Metastatic progression-free (MPF)
- Metastatic progression (MP)

- Death

Key model parameters included:

- Base case patient: 45-year-old women with residual invasive HER2+ breast cancer
- Lifetime horizon with 21-day cycles
- Discount rates: 7% for costs, 3% for utilities
- Healthcare system perspective
- Costs reported in 2021 US dollars

Cost Inputs:

Direct medical costs encompassed:

- Drug acquisition:
  - Trastuzumab 150mg vial: "\$71"
  - Trastuzumab 440mg vial: "\$182"
  - TDM1 vial: "\$180"
  - Docetaxel 20mg vial: "\$8"
  - Docetaxel 80mg vial: "\$31"
- Monitoring costs:
  - Trastuzumab/TDM1: "\$13" per session
  - Docetaxel: "\$6" per session
- Side effect management
- Physician visits
- End-of-life care

Clinical Inputs:

- Treatment efficacy data from published literature
- Transition probabilities between health states
- Side effect probabilities and associated disutilities
- Health state utilities ranging from 0.250-0.826

Key Insights

Cost-Effectiveness Results:

- Total costs:
  - Trastuzumab arm: "\$9,968"

- TDM1 arm: "\$11,376"
- Incremental cost: "\$1,408"
  
- Health outcomes:
  - Trastuzumab: 3.99 QALYs
  - TDM1: 5.58 QALYs
  - Incremental benefit: 1.59 QALYs
  
- ICER of "\$886" per QALY gained falls below Iran's threshold, indicating cost-effectiveness

#### Sensitivity Analysis Findings:

- One-way sensitivity analysis showed model most sensitive to:
  - TDM1 cost (ICER range: "\$215" to "\$1,557")
  - Trastuzumab cost (ICER range: "\$552" to "\$1,220")
  - Discount rates
  - IDFS probability
  
- Probabilistic sensitivity analysis:
  - 88.66% of simulations showed increased effectiveness at higher cost
  - 59.61% fell below cost-effectiveness threshold
  - 11.34% showed TDM1 as cost-saving

#### Budget Impact Considerations:

- Three-year cumulative additional costs:
  - Year 1: "\$195,762"
  - Year 2: "\$578,804"
  - Year 3: "\$1,120,546"
  
- Key factors affecting budget impact:
  - Market uptake assumptions (5%, 10%, 15% over 3 years)
  - Patient population size (1,464 eligible patients in year 1)
  - Annual growth rate of 3% in patient population

The analysis demonstrates that while TDM1 requires higher upfront investment, its superior clinical outcomes make it cost-effective compared to trastuzumab within Iran's healthcare system. The budget impact analysis provides important planning insights for policymakers regarding the additional resources needed to implement TDM1 treatment over a

three-year period. These findings can help inform coverage and reimbursement decisions for monoclonal antibody therapies in HER2+ breast cancer treatment.

## **Subcutaneous versus intravenous administration of Trastuzumab: a minimization cost analysis with real world data from a reference cancer centre in Peru, Otoya I. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost analysis from the attached article:

# Cost Analysis Report: Subcutaneous vs Intravenous Trastuzumab Administration

## Executive Summary

This report analyzes a 2024 cost minimization study by Otoya et al. comparing subcutaneous (SC) versus intravenous (IV) administration of trastuzumab, a monoclonal antibody therapy for HER2-positive breast cancer, at Peru's Instituto Nacional de Enfermedades Neoplásicas (INEN). The analysis demonstrates that SC administration reduces total treatment costs by approximately \$4,071.72 over a full 18-cycle treatment course compared to IV administration. Key cost savings come from reduced drug preparation time, administration time, and resource utilization. The findings align with similar cost analyses from other countries showing economic advantages of SC over IV administration while maintaining comparable clinical efficacy.

## Technical Details

### Study Parameters

- Analysis covers complete 18-cycle treatment course
- Costs calculated in Peruvian Soles (S/.) and converted to USD
- Includes drug costs, materials, supplies, chair time, and personnel costs
- Based on real-world data from INEN pharmacy department

### Drug Formulations & Dosing

- SC trastuzumab: Fixed 600mg dose per cycle
- IV trastuzumab: Weight-based dosing (8mg/kg initial, 6mg/kg maintenance)
- SC requires 1 vial per administration
- IV requires 2 vials for first dose, 1 vial for subsequent doses

### Cost Components Analyzed

1. Drug Costs:

- SC: S/.75,816 (\$20,491)
- IV: S/.82,612 (\$22,327)
- Difference: S/.6,796 (\$1,836) savings with SC

2. Materials for Preparation:

- SC: S/.20.70 (\$5.59)
- IV: S/.399.96 (\$108.10)
- Difference: S/.379.26 (\$102.51) savings with SC

3. Administration Supplies:

- SC: S/.34.02 (\$9.19)
- IV: S/.1,094.40 (\$295.78)
- Difference: S/.1,060.38 (\$286.59) savings with SC

4. Chair Time Costs:

- SC: S/.18.00 (\$4.86)
- IV: S/.702.00 (\$189.73)
- Difference: S/.684.00 (\$184.87) savings with SC

5. Personnel Costs:

- Drug Preparation (Pharmacist):

- SC: S/.0
- IV: S/.693.90 (\$187.54)
- Difference: S/.693.90 savings with SC

- Administration (Nurse):

- SC: S/.732.45 (\$197.96)
- IV: S/.6,168.00 (\$1,667.03)
- Difference: S/.5,435.55 (\$1,469.07) savings with SC

### Time Requirements

1. Drug Preparation:

- SC: 0 minutes
- IV: 270 total minutes (15 min first dose, 255 min subsequent doses)

## 2. Administration:

- SC: 285 total minutes (30 min first dose, 15 min subsequent doses)
- IV: 2,400 total minutes (360 min first dose, 120 min subsequent doses)
- Difference: 2,115 minutes (35.25 hours) saved with SC

## ## Key Insights

### 1. Total Cost Impact

- Overall savings of S/.15,049.09 (\$4,071.72) per treatment course with SC administration
- Represents 16.42% reduction in total treatment costs
- Largest savings from reduced personnel time and administration costs

### 2. Resource Utilization Benefits

- Eliminates drug preparation time
- Reduces chair time by approximately 88%
- Decreases total administration time by 88%
- Frees up facility resources for other patients

### 3. Regional Context

- Results align with analyses from other countries showing SC cost advantages
- Particularly relevant for resource-constrained settings
- Important given high breast cancer burden in Peru
- May improve treatment access through efficiency gains

### 4. Implementation Considerations

- Fixed SC dosing eliminates weight-based calculations
- Reduces complexity and potential dosing errors
- Shorter administration time may improve patient experience
- No compromise in clinical efficacy versus IV administration

The analysis demonstrates clear economic advantages of SC trastuzumab administration while maintaining treatment effectiveness. The findings support broader adoption of SC administration to improve resource utilization and potentially expand access to treatment, particularly in resource-limited settings.

# **Applying a cost-based pricing model for innovative cancer treatments subject to indication expansion: A case study for pembrolizumab and daratumumab, Heine R. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost analysis from the attached article:

Cost Analysis of Monoclonal Antibody Cancer Treatments: A Case Study of Pricing Models  
Research Analysis Report

## Executive Summary

This report analyzes research by Heine et al. examining cost-based pricing (CBP) models for two major cancer monoclonal antibodies - pembrolizumab (Keytruda) and daratumumab (Darzalex). The authors developed and tested pricing models incorporating research & development costs, manufacturing expenses, eligible patient populations, and profit margins to estimate sustainable pricing as indications expand.

### Key findings:

- Calculated cost-based prices were significantly lower than current list prices for pembrolizumab, ranging from "\$52 to \$885" per vial compared to list prices of "\$2,861" in the Netherlands and "\$5,350" in the US
- For daratumumab, cost-based prices ranged from "\$823 to \$31,941" per vial compared to list prices of "\$4,766" in the Netherlands and "\$8,735" in the US
- Patient population size had the largest impact on estimated prices, with smaller initial populations driving higher early prices that decreased as indications expanded
- Manufacturing costs were estimated at "\$55" per gram of antibody in the base case
- A 20% profit margin was used in the base model, with sensitivity analyses testing margins from 0% to 76.5%

The analysis suggests current pricing may exceed cost-justified levels, particularly as indications expand to larger patient populations. The authors recommend implementing time-based or indication-based cost analysis in pricing negotiations.

## Technical Details

### Model Structure and Inputs:

The cost-based pricing model incorporated:

- Initial R&D costs of "\$4.94 billion" for antineoplastic/immunomodulating agents
- Manufacturing costs of "\$55" per gram of monoclonal antibody
- New indication R&D costs of "\$347 million" per indication
- 20% base profit margin

- Eligible patient populations based on cancer incidence in developed regions
- Patent expiry predictions of 2028 for pembrolizumab and 2025 for daratumumab

The model calculated prices using:

1. Cumulative yearly analysis aggregating costs and patient populations annually
2. Cumulative indication analysis examining impact of each new approved use
3. Non-cumulative indication-based pricing analyzing each indication independently

Key assumptions:

- R&D costs included failed trials and 10.5% cost of capital
- Manufacturing costs based on published mAb production estimates
- Patient populations adjusted for treatment eligibility, clinical trial participation, and market share
- Revenue assumed to end at patent expiry
- All costs expressed in 2022 euros and converted to USD

Sensitivity analyses tested:

- R&D costs: "\$3.45-6.64 billion" range
- Manufacturing: "\$33-174" per gram range
- Profit margins: 0-76.5%
- Patent periods
- Indication-based vs. cumulative pricing approaches

Key Insights

1. Pricing Dynamics:

- Initial high prices driven by large R&D costs spread over small patient populations
- Sharp price decreases as indications and eligible populations expanded
- Cumulative pricing approaches resulted in more stable long-term prices compared to indication-specific pricing

2. Cost Drivers:

- Patient population size had largest impact on price estimates
- Initial R&D investment was second most influential factor
- Manufacturing costs had relatively minor impact
- Profit margin selection significantly affected final prices

3. Policy Implications:

- Current pricing may exceed cost-justified levels, particularly for pembrolizumab

- Regular price reviews needed as indications expand
- Consideration of indication-based pricing in markets where feasible
- Potential role for cost-based analysis in price negotiations
- Need for greater transparency in R&D and manufacturing costs

#### 4. Model Limitations:

- Relies on published aggregate R&D cost estimates
- Manufacturing cost estimates have significant uncertainty
- Does not account for all packaging/distribution costs
- Patient population estimates may not reflect actual uptake
- Does not incorporate value-based considerations

#### 5. Recommendations:

- Implement periodic price reviews as indications expand
- Consider indication-based pricing where feasible
- Require greater transparency in cost components
- Use cost analysis as complement to value-based pricing
- Structure agreements to allow price adjustments over time

The analysis suggests current cancer monoclonal antibody pricing may exceed levels justified by costs and reasonable profits, particularly as indications expand to larger patient populations. While the model has limitations, it provides a framework for incorporating cost considerations into pricing discussions. The authors recommend using cost-based analysis as a complement to value-based approaches in price negotiations, with regular reviews as products mature and reach more patients.

The findings highlight opportunities to better align pricing with underlying costs while maintaining incentives for innovation. Greater transparency around R&D and manufacturing costs would enable more refined analysis.

Ultimately, a balanced approach incorporating both cost and value considerations may help optimize pricing for both sustainability and access.

## **Effect of alternative dosing strategies of pembrolizumab and nivolumab on health-care emissions in the Netherlands: a carbon footprint analysis, Malmberg R. et al. 2024**

Here is a 4-page report based on the article:

# # Analysis of Alternative Dosing Strategies for Cancer Monoclonal Antibodies: Environmental and Economic Impact Assessment

## ## Executive Summary

This report analyzes research by Malmberg R. et al. examining the environmental and economic implications of alternative dosing strategies (ADS) for two major cancer immunotherapy monoclonal antibodies (mAbs) - pembrolizumab and nivolumab. The study, conducted at Erasmus University Medical Center in the Netherlands, found that pharmaceutical production accounts for 92.9% of treatment-related carbon emissions. Implementation of ADS could reduce carbon emissions by 21-26% for pembrolizumab and 9-11% for nivolumab while maintaining therapeutic efficacy.

The research demonstrates significant potential for optimizing mAb dosing to reduce both environmental impact and treatment costs. Key findings include:

- Annual carbon emissions from pembrolizumab and nivolumab treatment at the study center were 445 tons CO<sub>2</sub>e in 2022
- Average emissions per dose were 94 kg CO<sub>2</sub>e
- ADS implementation could reduce emissions by up to 557 kg CO<sub>2</sub>e per patient for pembrolizumab and 400 kg CO<sub>2</sub>e for nivolumab over a 2-year treatment course
- Switching from nivolumab to pembrolizumab with ADS could decrease emissions from 3,226 kg to 1,603 kg CO<sub>2</sub>e per patient treatment course

## ## Technical Details

### ### Study Methodology

The researchers conducted a process-based lifecycle assessment focused on CO<sub>2</sub> equivalent (CO<sub>2</sub>e) emissions from:

- Drug manufacturing
- Hospital energy use
- Pharmaceutical distribution
- Patient/staff travel
- Medical equipment and waste disposal

Data sources included:

- Hospital electronic medical records
- Dutch Hospital Data foundation statistics

- Hospital sustainability reports
- Manufacturer-provided transportation data
- Published literature on mAb production emissions

### ### Alternative Dosing Strategies Analyzed

#### Pembrolizumab:

- Standard: 200mg every 3 weeks or 400mg every 6 weeks
- ADS: Weight-based dosing
  - <65kg: 100mg every 3 weeks or 200mg every 6 weeks
  - 65-90kg: 150mg every 3 weeks or 300mg every 6 weeks
  - $\geq$ 90kg: 400mg every 6 weeks

#### Nivolumab:

- Standard: Fixed doses of 240mg/2 weeks, 360mg/3 weeks, or 480mg/4 weeks
- ADS: Weight-based maximum doses
  - 3mg/kg every 2 weeks (max 240mg)
  - 4.5mg/kg every 3 weeks (max 360mg)
  - 6mg/kg every 4 weeks (max 480mg)

### ### Emissions Analysis Results

For a complete 2-year treatment course:

#### Pembrolizumab fixed dosing:

- Every 3 weeks: 2,141 kg CO<sub>2</sub>e
- Every 6 weeks: 2,038 kg CO<sub>2</sub>e

#### Nivolumab fixed dosing:

- Every 2 weeks: 3,789 kg CO<sub>2</sub>e
- Every 3 weeks: 3,694 kg CO<sub>2</sub>e
- Every 4 weeks: 3,634 kg CO<sub>2</sub>e

#### ADS Implementation Impact:

- Pembrolizumab: 21-26% reduction (428-557 kg CO<sub>2</sub>e)
- Nivolumab: 9-11% reduction (352-400 kg CO<sub>2</sub>e)

## ## Key Insights

### ### Production Impact Dominance

The analysis reveals that pharmaceutical production is the overwhelming driver of emissions, accounting for 92.9% of the total carbon footprint. This suggests that optimizing dosing strategies and improving production efficiency should be primary focuses for reducing environmental impact.

### ### Weight-Based vs Fixed Dosing

The transition from weight-based to fixed dosing, while potentially simplifying administration, has led to higher doses and increased emissions without providing additional therapeutic benefit. The research supports returning to weight-based dosing through ADS implementation to reduce both environmental impact and drug consumption.

### ### Drug Selection Considerations

Pembrolizumab demonstrates better environmental performance compared to nivolumab under the assumption of equal production emissions per kg of active ingredient. This is attributed to:

- Lower weekly dosing requirements
- Greater potential dose reduction through ADS
- More efficient packaging and documentation practices

### ### Future Implications

The research highlights several important considerations for the future of mAb cancer treatments:

#### 1. Production Methods

- Need for more sustainable manufacturing processes
- Potential benefits of transitioning from multi-use to single-use technologies
- Importance of renewable energy in production

#### 2. Regulatory and Policy

- Environmental impact should be considered in drug approval processes
- Policies should not incentivize unnecessarily high fixed doses
- Support needed for ADS implementation

#### 3. Clinical Practice

- Regular assessment of dosing strategies considering both efficacy and environmental impact
- Potential for digital documentation to reduce paper waste
- Importance of optimizing treatment duration

#### 4. Economic Factors

- ADS implementation can reduce both environmental impact and treatment costs
- Need to balance accessibility of cutting-edge treatments with sustainability goals
- Potential cost benefits of switching between equivalent drugs based on environmental performance

The findings demonstrate that implementing ADS for cancer mAbs presents a significant opportunity to reduce both environmental impact and treatment costs while maintaining therapeutic efficacy. As global mAb usage continues to grow, optimizing dosing strategies and production methods will become increasingly important for sustainable healthcare delivery.

## **Cost of illness of breast cancer in low and middle-income countries: a systematic review, Yeong S. et al. 2024**

I apologize, but I notice that the attached article is actually about the cost of illness (COI) of breast cancer in low- and middle-income countries (LMICs). It does not contain analysis specifically about monoclonal antibody cancer costs.

Let me provide a structured report based on the actual content of this systematic review:

# Report: Cost of Illness Analysis for Breast Cancer in Low- and Middle-Income Countries

### ## Executive Summary

This systematic review by Yeong et al. analyzed 12 cost of illness (COI) studies from low- and middle-income countries (LMICs) examining the economic burden of breast cancer. The review found significant variation in direct medical costs ranging from "\$195" to "\$11,866", direct non-medical costs from "\$201" to "\$2,233", and productivity losses from "\$332" to "\$26,390" per patient annually. The authors highlighted that hospitalization and medication costs contributed most significantly to the total direct medical costs. Notably, no studies were identified from low-income countries, with 75% of included studies coming from lower-middle-income countries and 25% from upper-middle-income countries.

### ## Technical Details

#### ### Methodology

- Systematic review of studies from Cochrane, PubMed, Proquest Thesis and Scopus databases
- Inclusion criteria: peer-reviewed COI studies with original data, costs and full texts
- Cost data converted to 2022 USD values using CCEMG-EPPI-Centre cost converter
- Quality assessment using CHEERS 2022 criteria and consensus-based guidelines

### ### Cost Components Analysis

#### Direct Medical Costs:

- Lowest reported: "\$195" (Haiti)
- Highest reported: "\$11,866" (Iran, private hospital setting)
- Public hospital costs in Iran: "\$4,676"
- Medication costs represented 44-78% of direct medical costs in some studies

#### Direct Non-Medical Costs:

- Range: "\$201" to "\$2,233"
- Major components: transportation, accommodation, and food
- Transportation typically represented smaller portion compared to accommodation/food costs

#### Indirect Costs (Productivity Loss):

- Range: "\$332" to "\$26,390"
- Higher productivity losses observed in public hospital settings
- Only two studies reported comprehensive indirect cost data

### ## Key Insights

#### 1. Cost Reporting Quality:

- Many studies lacked sensitivity analysis and discount rates
- Limited reporting of cost disaggregation by cancer stages
- Inconsistent methodology in cost component reporting

#### 2. Healthcare System Impact:

- Direct medical costs with hospitalization represented highest burden
- Significant cost variations between private and public healthcare settings
- Medication costs pose substantial economic burden in developing countries

#### 3. Research Gaps:

- No studies from low-income countries
- Limited data on indirect costs and productivity losses

- Need for standardized cost reporting methodology
- Lack of correlation analysis between cost components and other variables

#### 4. Policy Implications:

- Need for enhanced cost monitoring systems in LMICs
- Importance of early detection programs to reduce treatment costs
- Requirement for better healthcare resource allocation strategies
- Need for standardized COI guidelines specific to breast cancer in LMICs

The review emphasizes the need for more comprehensive COI studies in LMICs with standardized methodology and detailed cost component analysis to better inform healthcare resource allocation and planning.

## **‘Financial fallout’ in the US biopharmaceutical industry: Maximizing shareholder value, regulatory capture, and the consequences for patients, Whitacre R. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost analysis from the attached article:

# Analysis of Financial Impact of Monoclonal Antibody Cancer Therapies

## Four-Page Report Based on Whitacre (2024)

### Executive Summary

This analysis examines the financial implications of monoclonal antibody (mAb) cancer therapies, focusing on cost drivers and access challenges identified in recent research. The study reveals concerning trends in the biopharmaceutical industry where shareholder value maximization and regulatory dynamics have led to substantial cost burdens for patients requiring these life-saving treatments.

Key findings include:

- Keytruda (pembrolizumab) generated revenue of "\$17.321 billion" in 2021, with the cost per patient reaching "\$175,000" per year
- Limited Medicare/Medicaid coverage, with CMS spending only "\$326 million" on Keytruda in 2020
- Regulatory incentives and orphan drug designations being leveraged to extend market exclusivity
- Significant patient access barriers due to high costs, leading to increased reliance on private insurance and crowdfunding

The analysis highlights how financial pressures cascade through the pharmaceutical value chain, ultimately impacting patient access and health outcomes.

### ### Technical Details

#### #### Revenue and Pricing Analysis

The study tracked Keytruda's revenue growth:

- 2014: "\$5.5 million"
- 2015: "\$56.6 million"
- 2016: "\$1.402 billion"
- 2017: "\$1.30 billion"
- 2018: "\$7.171 billion"
- 2019: "\$11.084 billion"
- 2020: "\$14.4 billion"
- 2021: "\$17.321 billion"

This dramatic revenue increase corresponded with multiple FDA approvals, expanding from one indication in 2014 to 32 approved indications by 2022.

#### #### Clinical Trial Economics

The research identified cost reduction strategies in clinical trials:

- Phase II trials starting in 2012 averaged 6 years
- By 2018, Phase II trials were reduced to 4 years
- Geographic distribution showed heavy concentration in North America with significant offshoring to lower-cost regions
- Trials were conducted across 63 countries to optimize research costs

#### #### Market Dynamics

Analysis of the top 10 mAbs in 2020 showed annual revenues ranging from "\$4 billion" to "\$19.832 billion". Notable examples include:

- Humira: "\$19.832 billion" global revenue ("\$16.112 billion" US)
- Stelara: "\$7.707 billion" global ("\$5.240 billion" US)
- Opdivo: "\$6.992 billion" global ("\$3.945 billion" US)

#### #### Insurance Coverage Patterns

Centers for Medicare & Medicaid Services (CMS) data revealed limited public coverage:

- 2020 CMS spending of "\$326 million" on Keytruda
- Estimated coverage for fewer than 1,860 patients through public insurance
- Private insurance becoming primary access route with high patient cost-sharing

#### ### Key Insights

##### 1. Business Model Evolution

- Pharmaceutical companies increasingly focus on repurposing existing drugs rather than new development
- Merger and acquisition activities used to acquire drug candidates
- Strategic use of regulatory incentives to extend market exclusivity
- Shift toward treating multiple smaller patient populations under orphan drug designations

##### 2. Access Barriers

- High costs creating significant access challenges for patients
- Limited public insurance coverage pushing burden to private insurance
- Growing reliance on crowdfunding (480 active campaigns identified for Keytruda alone)
- Patient assistance programs having limited reach and strict eligibility requirements

##### 3. Systemic Issues

- Regulatory framework potentially enabling rather than controlling cost increases
- Orphan drug designation system being leveraged for commercial advantage
- Geographic disparities in clinical trial conduct raising ethical concerns
- Financial burden increasingly shifting to patients through various mechanisms

##### 4. Market Implications

- Continued pressure for price increases to maintain shareholder returns
- Limited effectiveness of current regulatory controls
- Growing role of private insurance in determining access
- Emergence of alternative funding mechanisms like crowdfunding

The analysis suggests current market dynamics and regulatory frameworks are contributing to unsustainable cost increases while compromising patient access to essential therapies. The financial model appears to prioritize shareholder returns over accessibility, indicating a need for systematic reform of pricing and access mechanisms.

NOTE: This report focuses solely on economic data from the referenced article and excludes any patient-specific information. All monetary values are quoted directly from the source material.

## **Healthcare Costs and Resource Utilisation of Italian Metastatic Non-Small Cell Lung Cancer Patients, Gentili N. et al. 2024**

Here is a 4-page report analyzing the monoclonal antibody cancer cost analysis from the attached article:

Healthcare Cost Analysis Report: Immunotherapy in Non-Small Cell Lung Cancer

Based on Gentili N. et al. (2024)

### Executive Summary

This analysis examines the economic impact of introducing pembrolizumab immunotherapy as first-line treatment for metastatic non-small cell lung cancer (NSCLC) in Italy. The study compared healthcare costs and resource utilization between three patient groups:

- Mutation-positive patients receiving targeted therapy
- Pre-immunotherapy patients receiving standard chemotherapy
- Post-immunotherapy patients receiving pembrolizumab or chemotherapy

### Key findings:

- First-line pembrolizumab treatment increased mean per-patient costs by EUR 11,497 compared to pre-immunotherapy chemotherapy
- However, monthly costs were similar when accounting for improved survival
- Cancer drug costs were the primary cost driver, representing 65-77% of total costs
- Hospitalization costs increased significantly during later lines of therapy
- Introduction of immunotherapy improved survival from 6.2 to 8.9 months despite higher costs

### Technical Details

#### Study Design:

- Retrospective analysis of 644 metastatic NSCLC patients (2014-2020)
- 125 mutation-positive patients
- 519 mutation-negative/unknown patients
  - 229 pre-immunotherapy (before July 2017)
  - 290 post-immunotherapy (after July 2017)

#### Cost Categories Analyzed:

- Hospitalization
- Cancer therapy (drugs + administration)
- Outpatient procedures
- Hospice care

#### First-Line Treatment Costs:

##### Mutation-positive group:

- Mean total cost per patient: EUR 45,247
- Monthly cost: EUR 3,814
- Drug costs: 76.5% of total

##### Pre-immunotherapy group:

- Mean total cost per patient: EUR 7,804
- Monthly cost: EUR 3,318
- Drug costs: 35.8% of total

##### Post-immunotherapy group:

- Mean total cost per patient: EUR 19,301
- Monthly cost: EUR 3,464
- Drug costs: 64.9% of total

#### Overall Disease Costs:

##### Mutation-positive group:

- Mean total cost: EUR 70,985
- Monthly cost: EUR 3,673
- First-line costs: 63.7% of total

##### Pre-immunotherapy group:

- Mean total cost: EUR 19,649
- Monthly cost: EUR 3,046
- First-line costs: 39.7% of total

##### Post-immunotherapy group:

- Mean total cost: EUR 29,111
- Monthly cost: EUR 3,238
- First-line costs: 66.3% of total

## Healthcare Resource Utilization:

- Low hospitalization rates across groups (0.1-0.3 admissions/month)
- Higher emergency room use in mutation-negative groups
- Similar outpatient visit rates (2.1-2.9 visits/month)
- Increased hospice utilization in later lines of therapy

## Key Insights

### 1. Cost Impact of Immunotherapy

- Introduction of pembrolizumab significantly increased per-patient treatment costs
- However, when normalized for survival time, monthly costs remained relatively stable
- Higher drug costs were partially offset by reduced hospitalization needs
- First-line costs represented a larger portion of total costs in the immunotherapy era

### 2. Value Considerations

- Improved survival (6.2 to 8.9 months) helps justify increased spending
- Monthly cost burden similar despite higher absolute costs
- Reduced hospitalization suggests better disease control
- Quality of life benefits not captured in cost analysis

### 3. Resource Utilization Patterns

- Lower hospitalization rates in mutation-positive patients suggest better outcomes
- Emergency room use higher in mutation-negative groups indicating more complications
- Consistent outpatient visit patterns across treatment approaches
- Increased late-stage resource use regardless of initial therapy

### 4. Healthcare System Implications

- Drug costs now dominant driver of cancer care spending
- Need for balance between access to innovative therapies and sustainability
- Importance of appropriate patient selection for expensive treatments
- Value of real-world evidence in understanding economic impact

The analysis demonstrates that while immunotherapy introduction has increased absolute treatment costs, the survival benefits help justify the additional expenditure when considering monthly cost burden. Healthcare systems must balance access to innovative therapies with sustainable resource allocation.

**“Global mAb Cancer Cost”  
End 15 Summaries**