Cancer Medicines: Value in Context

May 2018
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Overview

- We have made remarkable progress in the fight against the more than 200 diseases we call cancer and current research holds enormous promise to address the great unmet need.

- Too many cancer patients face financial burdens, and these come from a variety of sources including treatment costs, non-medical costs, and insurance benefit design.

- The cost of cancer treatment come from a range of sources including medicines, hospital and ED visits, diagnostics, and physician services.

- The oncology market is working to control spending on cancer medicines and overall treatment costs.

- Reforms are needed to smooth the development path for cancer medicines and promote a delivery system that is increasingly patient-centered and value-based.
1. Advances in Cancer Treatment
Since Peaking in the Early 1990s, Cancer Death Rates Have Declined 26%

Increases in cancer survival are estimated to translate to the avoidance of nearly 2.1 million cancer deaths.

U.S. Death Rates from Cancer Decline Over Time

Since 1975, the chances that a cancer patient will live 5 years or more have increased by 41% across cancers.¹

5-Year Survival Rates Among the Most Common Cancers, 1975-2013²

73% of recent survival gains in cancer are attributable to treatment advances including new medicines.³

Introduction of Novel Cancer Medicines Associated with Survival Increases

Change in Incidence and Survival (2004-2013)
Bubble size – No. of New Drugs with Unique Mechanisms of Action, 2004-2013

Source: QuintilesIMS Institute, "Global Oncology Trends 2017," June 2017.
The continued increase in survival rates is in large part attributable to earlier detection and better treatments.¹

U.S Cancer Survivors Over Time (millions)¹,²,³

Engineered immune T-cells can recognize, zero in on and kill cancer cells.

**CAR-T Therapy Driving Breakthroughs for Cancer Patients**

1. T-cells are isolated from patient.
2. T-cells are engineered to express specific receptors that recognize cancer cells.
3. Modified T-cells are reintroduced to patient.
4. Reengineered T-cells are grown and expanded in culture.
Immunotherapy is Revolutionizing the Treatment of Many Advanced Cancers: Metastatic Melanoma

“No recent cancer advance has been more transformative than immunotherapy.”

- Dr. Julie M. Vose, former President of the American Society of Clinical Oncology

Among teenage girls, widespread use of the quadrivalent human papilloma virus (HPV) vaccine has driven down infection rates by nearly two-thirds.
A greater understanding of the molecular basis of disease has transformed what was once known collectively as “disease of the blood,” into multiple subtypes of leukemias and lymphomas, opening up new treatment approaches.

60 YEARS AGO

“Disease of the Blood”

50 YEARS AGO

Leukemia

Lymphoma

40 YEARS AGO

Chronic Leukemia

Acute Leukemia

Pre-leukemia

Indolent Lymphoma

Aggressive Lymphoma

TODAY

~ 40 Unique Leukemia types identified

~ 50 Unique Lymphoma types identified

5 year survival rates have grown to 70%

There are nearly 340 medicines in development for blood cancers

Since the approval of the first tyrosine kinase inhibitor (TKI) for chronic myeloid leukemia (CML), survival rates have improved dramatically and patients are living close to normal life spans.¹

- Imatinib—the first TKI—was approved in 2001 to treat CML. The transformative impact of this class of medicines had not been completely realized.
- After initial approval, continued research revealed that imatinib had a greater impact when initiated earlier in the progression of the disease.
- Further research also revealed that imatinib was effective in combating other types of cancer.
- Additional TKIs have since been approved for CML and offer alternatives to imatinib.

5-Year Survival Rates for CML Patients Nearly Triple After Introduction of Imatinib²

Prior to Introduction of Imatinib: 31%
After Introduction of Imatinib: 89%

The Role of Personalized Medicines Is Rapidly Growing

Personalized medicines provide effective and efficient care by targeting the right medicine to the right patient.

Oncology Treatment Modalities in Top Pharmaceutical Markets, Share of Sales, 2003-2013

Cancer Treatment Advances Result in Substantial Gains to Society

Between 1988 and 2000:

- **23 million** years of life saved due to cancer treatment advances
- **$1.9 trillion** value of improved cancer treatment to society based on improved productivity, extended life and other factors

2. Innovation in the Cancer Medicine Pipeline
Promise in the Pipeline: More than 1,100 Medicines in Development for Various Cancers

Medicines and Vaccines in Development for Cancer by Tissue of Origin (Selected) – May 2018

“These are exciting times…the pace of discovery and application of new knowledge to patient care is rapidly accelerating.”

— Dr. Jose Baselga, Physician-in-Chief, Memorial Sloan Kettering Cancer Center

Sources: PhRMA, Medicines in Development for Cancer, May 2018; American Association for Cancer Research. "Jose Baselga, MD, PhD" http://cancerprogressreport.org/2015/Pages/baselga.aspx
Promise in the Pipeline: More than 200 Immuno-oncology Medicines in Development

Number of Medicines in Development in the United States, May 2017, Selected Classes of Immunotherapy

- Adoptive Cell Therapies: 40
- Bispecific Antibodies: 30
- Checkpoint Modulators: 45
- Cytokines: 23
- Oncolytic Cell Therapies: 14
- Vaccines: 96

“In the past 5 years, immunotherapy has emerged as one of the most exciting new approaches to cancer treatment that has ever entered the clinic.”

- American Association for Cancer Research

Researchers are using novel approaches to attack cancer at the molecular level. An average of 85% of drugs in the oncology pipeline, including 79% in the clinical research phase, have the potential to be first-in-class medicines.

New Approaches to Treating Cancers Represent the Majority of Medicines in the Oncology Pipeline

Biopharmaceutical Companies are Researching New Targeted Cancer Therapies

42% of all medicines are in development to be personalized medicines.

73% of cancer medicines have the potential to be personalized medicines.

The cancer pipeline is ripe with innovative therapeutic options. Emerging combinations of medicines hold particular promise for controlling and killing cancer cells.

**Oncolytic viral therapies** zero in on cancer cells, replicate, and cause them to rupture.

**PARP inhibitors** interrupt cancer’s hyperactive DNA repair systems, thus allowing tumors to be crippled and die.

**CRISPR/Cas9 gene editing** allows researchers to manipulate cancer cell function.

**Immunotherapies** help target and kill cancer cells by unleashing the immune system. (e.g. CAR-T)

“We are in the midst of a sea change in how we are treating cancer. We’re really seeing the fruits of many years of research into what drives cancer and how it interacts with the immune system to defeat it and survive.”

- Dr. Louis Weiner, director of the Georgetown Lombardi Comprehensive Cancer Center

Developing a new cancer medicine is a complex process, fraught with setbacks, but these so called “failures” are not wasted efforts. Researchers learn from them to inform future study.

Cancer Researchers Build on Knowledge Gained from Setbacks to Inform Advances

MELANOMA
• 96 unsuccessful attempts
• 7 new medicines

BRAIN CANCER
• 75 unsuccessful attempts
• 3 new medicines

LUNG CANCER
• 167 unsuccessful attempts
• 10 new medicines

*Setbacks and advances from 1998 to 2014

Lung-MAP: Innovative Clinical Trial Takes New Approach to Cancer Drug Development

Lung-MAP (Lung Cancer Master Protocol) matches patients to specific investigational medicines based on genomics. Shared infrastructure accelerates drug development and increases efficiency.

HOW IT WORKS:

- Patients undergo genomic profiling to identify mutations that may cause squamous cell lung cancer
- Patients are directed to a treatment arm based on their genomic profile
- Patients receive highly targeted therapies and researchers collect data to advance the study of new medicines

THE PARTNERS:

Lung-MAP is a unique public-private partnership between:

- Patient and disease advocacy groups
- Biopharmaceutical companies
- National Cancer Institute
- Foundation for the National Institutes of Health

3. Cancer Patient Spending and Financial Burden
Multiple Factors Contribute to the Financial Burden Faced by Cancer Patients

Top Patient Financial Concerns

<table>
<thead>
<tr>
<th>Non-Medical</th>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gasoline</td>
<td>Diagnostic Tests or Scans</td>
</tr>
<tr>
<td>49%</td>
<td>53%</td>
</tr>
<tr>
<td>Food (Groceries or Dining Out)</td>
<td>Prescription Medicines</td>
</tr>
<tr>
<td>48%</td>
<td>43%</td>
</tr>
<tr>
<td>Over-the-Counter Medicines</td>
<td>Physician Office Visits</td>
</tr>
<tr>
<td>42%</td>
<td>39%</td>
</tr>
<tr>
<td>Special Clothing and/or Wigs</td>
<td>Outpatient Treatments (Incl. Radiation)</td>
</tr>
<tr>
<td>38%</td>
<td>37%</td>
</tr>
<tr>
<td>Car Repairs</td>
<td>Surgery</td>
</tr>
<tr>
<td>23%</td>
<td>36%</td>
</tr>
</tbody>
</table>

A Cancer Diagnosis Impacts Productivity and Employment for Patients and Caregivers

Patients

67% of patients who were employed full-time when diagnosed either stopped working or reduced their work hours.

Caregivers

More than 25% of caregivers made extended employment changes.

Out-of-Pocket Costs Are Not Driven by Cancer Drugs

At 6 months post-diagnosis, 60-70% of OOP costs are driven by physician and facility care for commercially insured patients with breast, lung and colorectal cancer on average.

Breast Cancer Patient Out-of-pocket Costs
At 6 Months Following Diagnosis

<table>
<thead>
<tr>
<th>Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer-Related Drugs</td>
<td>22%</td>
</tr>
<tr>
<td>Professional Services</td>
<td>21%</td>
</tr>
<tr>
<td>Facility Services</td>
<td>41%</td>
</tr>
<tr>
<td>Non-Cancer Drugs</td>
<td>8%</td>
</tr>
<tr>
<td>Radiation Therapy</td>
<td>5%</td>
</tr>
<tr>
<td>Hospital Inpatient</td>
<td>4%</td>
</tr>
</tbody>
</table>

Benefit Design Hinders Access to Cancer Medicines in Some New Classes

Some plans place treatments for certain high-cost conditions on the highest drug formulary cost sharing tier.

Percentage of Silver Plans Placing All Drugs per Class on Specialty Tier, 2016

- **Molecular Target Inhibitors***: 23%
- **Antiangiogenics***: 50%

*There are no generic drugs available in this class. All products are single-source.

Source: Avalere Health PlanScape®, a proprietary analysis of exchange plan features, April 2016. This analysis is based on data collected by Managed Markets Insight & Technology, LLC.
High Cost Sharing Leads to Abandonment or Delays in Cancer Treatment

Patients with highest co-pay were 5 times more likely to abandon treatment than the lowest co-pay group

Oral Oncolytic Abandonment Rate by Patient Out-of-Pocket Amount

4. Cancer Costs in Context
Spending on Cancer Medicines Represents About 1% of Overall Health Care Spending

Cancer Medicines as a Portion of Total U.S. Health Care Spending, 2017*

Cancer Medicines
$49.8 Billion1**

Remaining Health Care Spending
$3.49 Trillion2*

* 2017 CMS total National Health Expenditures is a projection
** Cancer drug invoice spending and does not include discounts

Cancer Medicines Represent About 20% of Cancer Spending

Medicare, Actively Treated Cancer Population, 2014

- Cancer Drugs: 18%
- Hospital Inpatient: 34%
- Cancer Surgeries: 21%
- Radiation Oncology: 11%
- Other Out Pt Services: 8%
- Professional Services: 5%

Commercially Insured, Actively Treated Cancer Population, 2014

- Cancer Drugs: 20%
- Hospital Inpatient: 28%
- Cancer Surgeries: 13%
- Radiology: 10%
- Radiation Oncology: 4%
- Other Out Pt Services: 3%
- Professional Services: 2%

Overall Drug Spending Growth Expected to be Moderate as Cancer Progress Continues

Projected Cancer Drug Spending as a Portion of Total Drug Spending, US$ Billions

Projected Total Drug Spending Growth = 2-5% per year

The volume-weighted Average Sales Price (ASP) for cancer drugs administered through Medicare Part B has been growing in line with medical inflation.

* 2016 and 2017 Weighted ASP numbers are projections.

Cancer Treatments Face Growing Competition from Generics and Biosimilars

Oncology Sales at Risk of Reduction Due to Estimated Loss of Exclusivity
(Billions of US Dollars)

Sources: QuintilesIMS Market Prognosis, National Sales Perspectives, QuintilesIMS Institute, Mar 2017. Includes small and large molecules.
Market Drives Rapid Switch to Generic Medicines: Example - Injectable Cancer Medicine Docetaxel

Sales for Docetaxel

Sales (000s)

Market Drives Rapid Switch to Generic Medicines: Example - Injectable Cancer Medicine Gemcitabine

Sales for Gemcitabine

Better Use of Cancer Medicines Can Reduce Health Care Costs

Advanced melanoma patients who were adherent to immunotherapy experienced 10% lower health care costs.

Difference in total healthcare costs by adherence status for advanced melanoma patients

<table>
<thead>
<tr>
<th></th>
<th>Low Adherence</th>
<th>High Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-Cause Costs</td>
<td>$51,991</td>
<td>$41,830</td>
</tr>
<tr>
<td>Melanoma-Related Costs</td>
<td>$48,263</td>
<td>$37,549</td>
</tr>
</tbody>
</table>

5. Evolving Cancer Market Dynamics
Health Plans Make Extensive Use of Prior Authorization in Oncology

Health Plans’ Use of Prior Authorization in Oncology

<table>
<thead>
<tr>
<th>Method</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>76%</td>
</tr>
<tr>
<td>Office Administered</td>
<td>82%</td>
</tr>
</tbody>
</table>

Source: Health Strategies Group Analysis for PhRMA, 2018.
Health Plans Deploy a Range of Tools to Manage Cancer Drug Spending

Current and Anticipated Payer Measures to Manage Oncology Costs (Q1 2017)

- Utilizing one or more value frameworks* in determining reimbursement: 31%
- Using clinical pathways to determine treatment regimens: 35%
- Contracting for preferred first-line therapies: 59%

*Value Frameworks: NCCN Evidence Blocks, ASCO Value Framework, etc.

Source: Zitter Health Insights, Managed Care Oncology Index, 2016.
Non-small cell lung cancer patients treated according to a clinical pathway incurred lower drug and total costs.

12-Month Savings with Lung Cancer Clinical Pathway

OVERALL: -22%
Chemotherapy, biologics: -28%
Radiology: -28%
Radiation Therapy: -23%
Non-chemo infusions, transfusions: -18%
Diagnostics: 5%

Early results from oncology medical homes, bundled payment and specialty ACOs show potential for reducing total cancer costs.

<table>
<thead>
<tr>
<th>Plans Realize Savings via New Payment Models</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-centered medical homes</td>
</tr>
<tr>
<td>Pilot reduced total costs 35% annually</td>
</tr>
<tr>
<td>Episode- or bundled payment</td>
</tr>
<tr>
<td>Pilot reduced total costs of care 34%</td>
</tr>
<tr>
<td>Specialty ACOs</td>
</tr>
<tr>
<td>Reduce drug spending 5%, total spending 2% +</td>
</tr>
</tbody>
</table>

"Notably, all those interviewed suggested that the use of clinical pathways was a driver of financial savings, either through reduced drug spending or indirectly through more appropriate patient treatment."

- Sonal Shah, PharmD, and Greg Reh, *American Journal of Managed Care*
Nearly 200 oncology practices are participating in the Oncology Care Model (OCM) to improve quality and reduce the cost of cancer care in Medicare Part B.

**Market Shift to New Payment Models: CMS’ Oncology Care Model**

- Achieving a performance-based payment: 25%
- Achieving significant savings: 60%
- Implementing Guidelines-Based Care: 100%

Shared risk or outcomes-based contracts (OBCs) between health insurers and manufacturers are becoming more common across diseases, including oncology.

More than 40% of the 65 outcomes-based contracts projected between 2018-2022 are expected to be in oncology.
The rate of commercially insured patients receiving infused chemotherapy in hospitals increased from 6% of transfusions in 2004 to 43% in 2014.

Site of Care Shifts Drive Higher Cancer Costs

Average Drug-Level Spending on Infused Chemotherapy (2004-2014)

Costs per six-month episode of care were 93% higher in the hospital compared to the physician office.

Hospital Consolidation Associated with Increases in Cancer Spending

Spending increases associated with just a 1% increase in the proportion of medical providers affiliated with hospitals and/or health systems.

Per Person Price of Treatment
- 23%

Per-Person Annual Spending
- 34%

340B Creates Incentives to Shift Delivery of Physician-Administered Cancer Medicines to More Expensive Hospital Settings

<table>
<thead>
<tr>
<th>Year</th>
<th>340B Hospitals</th>
<th>Non-340B Hospitals</th>
<th>Physician Offices</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>11%</td>
<td>17%</td>
<td>73%</td>
</tr>
<tr>
<td>2009</td>
<td>13%</td>
<td>18%</td>
<td>70%</td>
</tr>
<tr>
<td>2010</td>
<td>15%</td>
<td>18%</td>
<td>67%</td>
</tr>
<tr>
<td>2011</td>
<td>19%</td>
<td>17%</td>
<td>64%</td>
</tr>
<tr>
<td>2012</td>
<td>24%</td>
<td>18%</td>
<td>58%</td>
</tr>
<tr>
<td>2013</td>
<td>28%</td>
<td>19%</td>
<td>53%</td>
</tr>
<tr>
<td>2014</td>
<td>32%</td>
<td>19%</td>
<td>50%</td>
</tr>
<tr>
<td>2015</td>
<td>33%</td>
<td>18%</td>
<td>49%</td>
</tr>
</tbody>
</table>

6. US System in Context
US Patients Have Access to Cancer Medicines on Average Two Years Earlier Than Patients in Other Developed Countries

Other developed countries use centralized government price setting and coverage decisions to manage drug spending, resulting in significantly slower access to medicines than in the US.

Average Time Delay Compared to the US in the Approval and Reimbursement of Oncology Medicines from 2010 to 2014

- Germany: 10 months (4 months delay between US approval and country-specific approval; 6 months delay between country approval and reimbursement)
- France: 10 months (7 months delay between US approval and country-specific approval; 3 months delay between country approval and reimbursement)
- UK: 10 months (13 months delay between US approval and country-specific approval; 7 months delay between country approval and reimbursement)
- Italy: 10 months (15 months delay between US approval and country-specific approval; 5 months delay between country approval and reimbursement)
- Spain: 10 months (17 months delay between US approval and country-specific approval; 3 months delay between country approval and reimbursement)
- Australia: 15 months (17 months delay between US approval and country-specific approval; 0 months delay between country approval and reimbursement)
- Taiwan: 22 months (21 months delay between US approval and country-specific approval; 1 month delay between country approval and reimbursement)

US Patients Have Greatest Improvement in Cancer Outcomes

Access to medicines is an important driver of mortality improvements

Source: PhRMA analysis of WHO Mortality Database, May 2018. Note: 2012 data was used because some countries lack newer data.
Health technology assessment (HTA) recommendations across countries show little consistency, highlighting the effect of cultural factors on HTA design and implementation, and that a “one-size-fits-all” approach is not realistic.

In Other Countries, Governments Restrict Access to Cancer Medicines


In the U.K. only 7 government assessments recommended without restrictions.
7. Solutions For Advancing Value in Cancer Care
Smoothing the Path for Development of New Cancer Medicines

Advances in regulatory science are creating efficiencies and enhancing the tools needed to drive innovative cancer drug discovery, development and approval.

**SOLUTIONS for ACCELERATING CANCER PROGRESS**

- **Integrating Patient Perspective**
  - Incorporate patient input & increase patient engagement.

- **Accelerating Qualification & Use of Biomarkers**
  - Increase acceptance of novel outcome measures.

- **Advancing Use of Real-World Evidence**
  - Enable use of both safety & efficacy data in regulatory decision making.

- **Increasing Acceptance of Novel Clinical Trial Designs**
  - Enhance use of adaptive & other flexible study designs.
Biopharmaceutical Companies Advancing Patient-Centered Solutions for Better Value

- Expand Value-Based Contracts
- Strengthen Decision Support Tools
- Improve Use of Medicines
- Develop Quality Measures
- Increase Availability of Evidence on Value

SOLUTIONS for BETTER CANCER CARE
<table>
<thead>
<tr>
<th>Value Based Contracts</th>
<th>Value Frameworks</th>
<th>Quality Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expand value-based contracts by modernizing outdated regulations.</td>
<td>Develop better data and tools to support informed decision-making by patients, physicians and payers.</td>
<td>Close gaps in clinical and patient-focused quality measures.</td>
</tr>
<tr>
<td>&quot;[R]egulatory reforms can address these concerns and encourage more robust competition within the drug market.&quot;</td>
<td>&quot;[E]merging approaches for assessing drug value are welcome…. The frameworks will require refinement, however, before they're ready to be broadly applied.&quot;</td>
<td>&quot;All phases of the cancer care continuum… need new measures.&quot;</td>
</tr>
<tr>
<td>- Scott Gottlieb &amp; Kavita Patel</td>
<td>- Peter Neumann &amp; Joshua Cohen</td>
<td>- National Academy of Medicine</td>
</tr>
</tbody>
</table>