Tumors and ‘Targets’

SMA CME on the River - 2015
Mark S. Williams, MD, MBA, JD
Began as a multi-disciplinary discussion within a large safety-net health system in a state challenged with poor health and very low household income . . .

Matching Drugs to Tumors

The Promise, the Limitations and the Ethics of Targeted Therapies for Cancer Patients - An Introduction

Medical Ethics Forum, September 2014
Mark S. Williams, MD
Targeted Cancer Therapies - What are They?

Drugs or other substances that block the growth and spread of cancer by interfering with specific molecules ("molecular targets") that are involved in the growth, progression and spread of cancer. Targeted therapies are sometimes called "molecularly targeted drugs," "molecularly targeted therapies," "precision medications," or similar names.

National Cancer Institute, FactSheet, (available at www.cancer.gov/cancertopics/factsheet/Therapy/targeted)
Three Dimensions to the Discussion

How to Fairly Distribute Access to Needed Healthcare Given the Almost Limitless Demand?

Escalating Costs of Healthcare

Complex issue of cancer drug resistance
Targeted Cancer Therapies - Comparison to Chemotherapy

- Act on specific molecular targets whereas most standard chemotherapies act on all rapidly dividing cells

- Deliberately chosen or designed to interact with their target, whereas standard chemotherapies were identified because they kill cells

- Often cytotoxic (block tumor cell proliferation) whereas chemotherapy agents are cytotoxic (kill tumor cells)

National Cancer Institute, FactSheet, (available at www.cancer.gov/cancertopics/factsheet/Therapy/targeted)
Targeted Cancer Therapies - What Types are Available?

- Hormone therapies
- Signal transduction inhibitors
- Gene expression modulators
- Apoptosis inducers
- Angiogenesis inhibitors
- Immunotherapies
- Monoclonal antibodies that deliver toxic modules
- Cancer vaccines
- Gene therapy

National Cancer Institute, FactSheet, (available at www.cancer.gov/cancertopics/factsheet/Therapy/targeted)
Targeted Cancer Therapies - Potential Applications

• AdenoCa of stomach
• Basal cell carcinoma
• Brain cancer
• Breast cancer
• Cervical cancer
• Colorectal cancer
• Head and neck cancer

• GI stromal tumor
• Kaposi sarcoma
• Kidney cancer
• Lung cancer
• Lymphoma
• Many others

National Cancer Institute, FactSheet, (available at www.cancer.gov/cancertopics/factsheet/Therapy/targeted)
• Imatinib - a tyrosine kinase inhibitor
• Invented in late 1990s
• Used in treatment of CML, gastrointestinal stromal tumors, others
• FDA approval in 2001
• Ciba-Geigy (later merged with Sandoz to become Novartis)
• Original researchers honored for “converting a fatal cancer into a manageable chronic condition”

Original costs approximately $30,000/year, then went to $92,000 in 2012
Targeted Cancer Therapies - What are the Limitations?

- Cancer cells can develop resistance
  - target itself may mutate
  - tumor finds new pathway not dependent on target
- May require combinations of treatments (melanoma, metastatic breast cancer, others)
- Identified target’s structure or function may be unusually complex, making drug development difficult

National Cancer Institute, FactSheet, (available at www.cancer.gov/cancertopics/factsheet/Therapy/targeted)
First medicine to treat the underlying cause of Cystic Fibrosis (CF), a rare, genetic disease

Approved for patients with CF ages 6 and older who have at least one copy of the G551D mutation in the CF transmembrane conductance regulator (CTR) gene

- 30,000 CF patients
- 1200 with this genetic defect
Mississippi Medicaid FY2015 Requested Funding by Sources
Total = $5,625,510,068

Federal Funds - $4,090,174,813
General Funds - $983,049,485
Provider Tax - $420,052,225
Other Funds - $132,233,545

Source: Fiscal Year 2015, Budget Presentation, Office of the Governor, Mississippi Division of Medicaid, Sept 2013
Mississippi General Fund Appropriations for Fiscal Year 2014 Budget

Total = $5,050,081,966

Source: Budget, FY 2014, Joint Legislative Committee
State of Mississippi
"These price increases do not reflect the cost of development of drugs or the benefit they provide to the patient . . .

They are simply related to the drug companies' wish to increase profits beyond a reasonable range."

Hagop Kantarjian, MD
Chairman, Leukemia Dept, M.D. Anderson

“A high stakes tale of adventure and intrigue: Barbarians at the Lab”
- The Washington Post
Kadcyla
Roche’s HER2-Positive breast cancer treatment
$94,000 per treatment

Sovaldi
Gilead’s Hepatitis C treatment
$84,000 per treatment

Yervoy
Bristol-Myers Squibb’s melanoma treatment
$100,000 per treatment

“We have this public health mentality that all people have to be cured no matter the cost, and also let the innovators charge whatever they want . . . fine theories independently, but when you combine them together in a finite budget environment, it’s not sustainable”

Matt Salo, Executive Director of the National Association of Medicaid Directors
Do new medical technologies effectively create new medical *needs* (as distinguished in moral terms from mere medical *wants*)?

In 1970, how many people “needed’ bypass surgery? Zero

400,000 CABGs@$124,000 ($50B)

1.3 million coronary angioplasties@$60,000 ($78B)

120,000 ICDs@$134,000

Estimated 200,000 LVADs@$200,000

Just one specialty in medicine!
Oncology - Some Challenges

- 580,000 Americans die from cancer each year
- 1.66 million newly diagnosed each year
- 13.7 million currently identified as “cancer survivors”
- Over 3 million individuals under active treatment in any year
- Cancer most often a disease of those >65 years of age
- Costs largely borne by Medicare, funded by taxes
- Younger patients will likely struggle with paying for needed cancer treatments due to being uninsured or underinsured

“Just Caring”: Can We Afford the Ethical and Economic Costs of Circumventing Cancer Drug Resistance?
LM Fleck, Journal of Personalized Medicine, 2013
Medicare is a growing share of the federal budget

The average per beneficiary inflation

The baby boom generation


NOTE: Medicare Part B covers hospital, nursing home, hospice, and home health services. Medicare Part B covers preventive, diagnostic, and outpatient care. Medicare Part D covers prescription drugs. Expenditures were adjusted for inflation using chained personal consumption expenditure deflator.

Interesting Paradox -

As medical technologies in cardiovascular medicine increase life expectancy, so does the likelihood of getting cancer increase . .
Oncology - Serious Questions, An Example

- In majority of the cases, these drugs yield marginal benefits at very high cost
  - Erbitux® (cetuximab) for non-small cell lung cancer (NSCLC)
  - Median gain in life span is six weeks*
  - Cost is approximately $80,000

A willingness to spend $800,000 to gain an extra year of life

“How Much is Life Worth: Cetuximab, Non-Small Cell Lung Cancer, and the $440 Billion Question”
T Fojo and C Grady, J Natl Cancer Inst, August 2009
• Cancer will affect 1 in 3 individuals over their lifetime
• Out-of-pocket costs increasing to 20% to 30% of total cost
• In 2014, all new US FDA approved cancer drugs were priced above $120,000 per year of use
• Average annual household income is about $52,000

“In Support of a Patient-Led Initiative and Petition to Lower the High Cost of Cancer Drugs”
Mayo Clinic Proceedings, August 2015
‘The prices today are essentially extortion, and people are being taken hostage’

**Recommendations**

- Post-FDA approval review mechanism to propose a fair price based in value
- Allow Medicare to negotiate drug prices
- Evaluate benefits of new treatments
- Allow importation of cancer drugs for personal use
- Pass legislation to prevent drug companies from delaying access to generics
- Reform the patent system (patent “evergreening”)
- Encourage organizations to consider value

“Die Another Day”
L Marsa, Newsweek, July 31, 2015
Oncology - An Economist’ View

A willingness to spend $800,000 to gain an extra year of life

• A prudent use of social resources?
• What if other life-years could be ‘purchased’ at a fraction of that cost by allocating to other health care needs?
• Example - cost of saving one ‘life-year’ for an HIV-positive patient is about $30,000

Why would an economically rational society not make these more reasonable re-allocations of health care resources?

“Just Caring”: Can We Afford the Ethical and Economic Costs of Circumventing Cancer Drug Resistance?
LM Fleck, Journal of Personalized Medicine, 2013
Why would an economically rational society not make these more reasonable re-allocations of health care resources?

- These therapies being offered to patients faced with a likely terminal outcome, no other options
- Greater social value attached to “last chance” therapies
- Sometimes vocalized but often silently affirmed that in our society human life is “priceless”
- It is unseemly to make an *explicit* social decision to deny someone a life-prolonging therapy merely because it may cost too much money

“we seem quite tolerant of less visible implicit ways of denying individuals access to expensive life-prolonging care”

“Just Caring”: Can We Afford the Ethical and Economic Costs of Circumventing Cancer Drug Resistance?
LM Fleck, Journal of Personalized Medicine, 2013
“The American Society of Clinical Oncology is very concerned about the escalating cost of cancer care . . . the unsustainable increase (expected to rise to $175B per annum in 2020 - a 40% increase from 2010) is the result of:

- an increasing demand for cancer services due to aging and lifestyle factors
- continued growth of new interventions and treatments without pricing, relative to value

Patients and their families often face crippling expenses during . . . one of the most difficult times in their lives”

ASCO’s Initiative to Define Value in Cancer Care
RL Schilsky, Chief Medical Officer, ASCO, August 2014
“Value” in Cancer Care

“Defined by more than cost - it includes the clinical outcomes patients can expect from any specific treatment regimen, as well as consideration of costs and side effects.

The overall value of care reflects the benefits in quality and quantity of life gained against the physical, emotional and financial costs of medical intervention.”

ASCO’s Initiative to Define Value in Cancer Care
RL Schilsky, Chief Medical Officer, ASCO, August 2014
In a 2003 article, Joseph Gallo looked at a survey of 765 doctors and found that 64% had created an advanced directive (versus 20% of the general public).
Is it an issue of ‘rationing’
or
Is it an issue of what is ‘rational’?
?
“We have a choice: do we use science to help us reach consensus on what we are willing to pay for new therapies and innovation, or do we leave individual patients to wrestle with the skyrocketing costs of cancer care and treatment determined by their ability to pay?”

JL Malin, Journal of Clinical Oncology, 2010

IBM Watson’s Startling Cancer Coup

For the early part of its existence, IBM’s Watson supercomputer was a bit of a carnival act. It could perform feats of computational magic, win on Jeopardy, and whip up crazy burrito recipes at SXSW. But Watson is designed to become IBM’s money-making, Big Data platform, earning its keep across a variety of industries. In New York, the company announced that a Watson-enabled group of researchers was able to speed the process of discovery to uncover new targets for cancer research.

A Graceful Death -
Being comfortable and in control, having a sense of closure, making the most of relationships and having family involved in care.
Cameras and Film or Images?  Railroads or Transportation?

Health Care or Health?
Most Americans are concerned about health care costs

Getting rid of ‘waste and efficiency’ will not be sufficient to control costs

Emerging and desired new health care technologies are the real drivers of escalating costs

We must identify marginally beneficial health care that costs much more than the benefits are worth

*What is necessary is a collective social choice that reflects what the deliberative process judged to be a fair and reasonable trade-off*
“What makes various health care rationing judgments presumptively just is that they are public or transparent; they are impartially created and enacted; they are freely and rationally self-imposed.

A rational democratic deliberative process suitably inclusive and representative of all who would be affected by such judgments will satisfy those conditions”
Thank You
Questions?

Mark Williams, MD

Right Care, Right Time, Every Time, Without Harm
(And at the Right Cost)