The ‘Greatest Hits’ of Precision Oncology: the View from the Newsroom

WIN Symposium
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Conflicts of Interest

No conflicts to disclose.
Online news organization founded in 1997

Editorial mission: Cover the scientific and economic ecosystem spurred by the advent of high-throughput genome sequencing.

Our readers are practitioners, not the general public: academic researchers, pharma R&D, diagnostic developers, instrument manufacturers, consultants, etc.

We are journalists. Our job is to ask questions.
NEW YORK (GenomeWeb News) – Pfizer will collaborate with Medco Health Solutions and its United BioSource subsidiary in a research effort based on Pfizer's "precision medicine" approach, which integrates genomic and phenotypic information to help identify patients that may benefit from a new drug.
What are Precision Oncology’s Greatest Hits?
What are Precision Oncology’s Greatest Hits?

gefitinib!  erlotinib!
trastuzumab!  cetuximab!
imatinib!  vemurafenib!
What are Precision Oncology’s Greatest Hits?

1) What exactly do we mean by “Precision Oncology”?

2) What do we consider to be a “hit”?

3) Have there been any hits in Precision Oncology yet?
What are Precision Oncology’s Greatest Hits?

1) *What exactly do we mean by “Precision Oncology”?*

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Stratified Oncology is Not Precision Oncology

**Stratified Oncology**
Using biomarker testing to identify the optimal therapy for a particular tumor type.
- One tissue type
- One marker
- One drug

**Precision Oncology**
Using NGS to identify the best therapy or combination of therapies regardless of the tissue of origin.
- Any tissue type
- Multiple markers
- The “best” drug(s)
**Trastuzumab**

- $7B in revenue in 2017
- About 20% of breast cancer patients are Her2 positive
- American Cancer Society predicts 266K new cases of breast cancer diagnosed in the US in 2018, making more than 50K eligible patients
- Studies have consistently shown that trastuzumab reduces the risk of breast cancer recurrence by about 50 percent and improves survival by about 30 percent.

**Imatinib**

- $2B in 2017 revenue (down from $3.8B in 2016 due to generic entering market)
- About 8,430 new chronic myeloid leukemia cases diagnosed in US in 2018, of which most are eligible for treatment with imatinib due to Phl chromosome
- Often called a “miracle drug” - before Gleevec, only 30% of patients with CML survived for even five years after being diagnosed. With imatinib, that number is now around 90%.

*Sources: Company earnings (revenues); ACS (cancer incidence rates); various (response rates)*
Erlotinib/Gefitinib/Osimertinib

- $2.4B combined revenue in 2017 ($528M erlotinib, $850M gefitinib, $955M osimertinib)
- 199K new cases of NSCLC diagnosed in the US in 2018, of which 10-15% have EGFR mutations, making around 30K eligible patients
- No “miracle drugs” here – incremental improvements in survival with each generation of EGFR-TKIs (18.9 months median PFS for osimertinib vs 10.2 months for erlotinib/gefitinib)

Vemurafenib

- $202M in 2017 revenue
- 91K new cases of melanoma diagnosed in the US in 2018, of which 35-50% have a BRAF mutation (of those, 80-90% have V600E mutation), meaning 25K-41K eligible patients
- 50% response rate for patients who previously had limited treatment options. Milestone for drug/Dx codevelopment.

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How Do We Define Success in Precision Oncology?

- Drug sales?
- Number of patients eligible for treatment?
- Number of patients treated?
- Overall survival, progression-free survival, disease-free survival?
- Complete response, overall response rate?
- Patient quality of life?
- Cost effectiveness?
- Some other measure of value?

Do the same measures of success that we use for stratified oncology apply to precision oncology?

How can the community move from a drug-centric model of success to one that is more process-focused?
Challenge: Defining Success in the ‘Long Tail’

- Patients treated: n = 50K
- Patients treated: n = 40K
- Patients treated: n = 20K
- Patients treated: n = 1K
- Patients treated: n = 500
- Patients treated: n = 1

- Drug/marker options: KRAS, EGFR, ERBB2, BRAF
- Rare markers
“To the best of our knowledge, discussions on value-based genomics, for which we define as the value of genomic profiling in cancer care through the current availability of NGS platforms, are relatively novel and limited compared to the growing discussions on value-based medicine focused on cancer drugs themselves.”
A Retrospective Analysis of Precision Medicine Outcomes in Patients With Advanced Cancer Reveals Improved Progression-Free Survival Without Increased Health Care Costs


Intermountain Healthcare, Saint George and Salt Lake City; University of Utah School of Medicine, Salt Lake City, UT; Duke University School of Medicine, Durham, NC; and Stanford University School of Medicine, Stanford, CA

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Disclosures provided by the authors are available with this article at jop.ascpubs.org.

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QUESTION ASKED: What are the clinical outcomes and health care–associated costs in patients with advanced cancer who receive precision cancer medicine?

SUMMARY ANSWER: Patients who received precision cancer medicine experienced an improved progression-free survival (PFS; 22.9 weeks) compared with historical controls (12.0 weeks) who received standard treatments. The improved PFS was not associated with increased health care–associated costs.

WHAT WE DID: We conducted a matched cohort study of 72 patients with metastatic cancer of diverse subtypes. We analyzed the outcomes of 36 patients who received genomic testing and targeted therapy (precision cancer medicine) compared with 36 historical control patients who received standard chemotherapy (n = 29) or best supportive care (n = 7).

WHAT WE FOUND: The mean PFS was 22.9 weeks for the precision medicine group and
A Busy Year for Precision Oncology News

“Don't mistake activity with achievement.”
— John Wooden, basketball coach

The patients included those with rare cancer types, along with individuals who had relapsed on as many as 16 prior therapies, Tsipresiou noted. Just 28 percent of the individuals had not been treated previously. The most common cancer types represented in the group included gastrointestinal, gynecological, breast, and lung cancers as well as melanoma.

The researchers unearthed one or more targetable mutations in 1,307 cases, or nearly 35 percent of the cases considered. Of those, more than half of the individuals — 711 cases — received matched targeted therapy, while the remaining 596 individuals got non-molecularly matched therapies.

In the molecularly matched arm of the study, the team saw an objective response rate of 16.2 percent, and another 18.7 percent of cases with stable

The research was published online in the journal *Cancer* on July 14. It is the latest in a series of studies illustrating the potential of precision medicine in cancer treatment.

The study was supported by the National Cancer Institute and the American Society for Clinical Oncology.
Challenge: The Promise of Precision Oncology

There will never be one cure for cancer.

There will be millions.

That's because every person's cancer is unique. At Memorial Sloan Kettering, we've developed a new genome sequencing test that can analyze a tumor to find its genetic weaknesses. This and other advancements in technology help us customize tailor care for our patients, changing how the world treats cancer one person at a time.

Learn more at MSKCC.org/MOReSCIENCE.

MORE SCIENCE. LESS FEAR.

Memorial Sloan Kettering Cancer Center

We're not just fighting cancer. Now we're outsmarting it.
“I saw a brief TV program about a clinical trial called Precision Oncology, that you are currently practicing where a patient who had tumors all over the body had taken 2 pills every day for a week and the tumors disappeared. We are desperately seeking other medical help for my father, hoping and praying that you would review his latest reports and let me know if you think you’re clinical trial will be effective?”
“We have to be careful not to allow or propagate the perception that ‘precision oncology’ has reached a point where such benefits can be offered with any reasonable likelihood or frequency. Molecular profiling of tumors using NGS assays will open up some options for some people, but many and in fact, most patients with solid tumors will not be meaningfully benefited by NGS at this time.”
Challenge: Anecdotal Success Stories

'Three words helped me ’Sequence me’

"I didn’t like that," said Bryce, an avid hunter, when he first heard the term "sequencing".

"That was a pretty stinky word," he added.

To Bryce, a 44-year-old hunter, the word "sequencing" had a negative connotation. He had been to a doctor in spring 2014, and he just couldn’t take another step.

"Halfway through the run, I just fell down and collapse was surreal," he said.

That was the day Bryce learned he had prostate cancer.

Today, Allison Schablein looks like a healthy 8-year-old, recently finishing her dance class and looking forward to summer. But this little girl from New Hampshire has overcome a type of cancer that is often fatal for children.

At age 4, Allison started telling her parents that she had headaches.
Beware the Anecdote

Many still shudder at the fiasco that unfolded in the 1980s and 1990s, when doctors started giving women with breast cancer extremely high doses of chemotherapy and radiation on the theory that more must be better. The doctors did not systematically collect data; instead, they reported patient anecdotes claiming success.
Beware the Anecdote

Doctors Said Immunotherapy Would Not Cure Her Cancer. They Were Wrong.
Anecdote or N of One?

patients treated

stratified oncology

n = 50K

n = 40K

n = 20K

precision oncology

n = 1K

n = 500

n = 1

drug/marker options

KRAS  EGFR  ERBB2  BRAF

rare markers
The Precision Oncology Funnel

- Patient Eligibility
- Tissue/Sample Eligibility
- Sequencing Platform/Strategy
- Variant Analysis Pipeline
- Drug Matching Criteria
- Access to Matched Drugs
- Response
Molecularly targeted therapy based on tumour molecular profiling versus conventional therapy for advanced cancer (SHIVA): a multicentre, open-label, proof-of-concept, randomised, controlled phase 2 trial

Dr Christophe Le Tourneau, MD, Prof Jean-Pierre Delord, MD, Prof Anthony Gonçalves, MD, Céline Gavoille, MD, Coraline Dubot, MD, Nicolas Isambert, MD, Prof Mario Campone, MD, Olivier Trédan, MD, Marie-Ange Massiani, MD, Cécile Mauborgne, MSc, Sebastien Armanet, MSc, Nicolas Servant, PhD, Ivan Blièche, PhD, Virginie Bernard, PhD, David Gentien, PhD, Pascal Jezequel, MD, Valéry Attignon, PhD, Sandrine Boyault, PhD, Anne Vincent-Salomon, MD, Vincent Servois, MD, Marie-Paule Sablin, MD, Maud Kamal, PhD, Xavier Paoletti, PhD for the SHIVA investigators

Published: 02 September 2015
Match Rate Mismatch

**IMPACT**
3,743 patients enrolled
1,307 (35%) with one or more targetable mutations
711 (19%) cases received matched targeted therapy

**NCI-MATCH**
6,397 registered for screening
5,560 successful lab testing
992 (18% of tested, 15% of total) "matched" to one of 30 arms
689 (69% of “matched,” 12% of tested, 11% of total) assigned to a treatment — described as “enrollment” rate

**WINThER**
303 consented
158 (52%) received treatment recommendations
124 (40%) treated
107 (35%) “evaluable” treated patients

*Source: data presented at ASCO 2018*
## Increasing Complexity for Oncologists

### 2006

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<tr>
<th>Histological Testing</th>
<th>First Line</th>
<th>Second Line</th>
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<td>EGFR+ve</td>
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- **Indicates segments requiring histological testing**
- **Indicates segments requiring biomarker testing**

Source: IQVIA Global Oncology Trends 2017
### Increasing Complexity for Oncologists

#### 2016

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<td>Chemotherapy</td>
<td>Nab paclitaxel</td>
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*Indicates segments requiring histological testing
**Indicates segments requiring biomarker testing

Source: IQVIA Global Oncology Trends 2017
Challenge: Oncologist Adoption and Perception

USE OF PERSONALIZED MEDICINE SCREENING/TESTING TECHNIQUES

% of respondents, N=200. Q: “What extent do you typically use the following tests in your practice? Enter % of patients.”

- FDA-approved companion diagnostic matched to therapy under consideration:
  - 0%: 18%
  - 1-10%: 5%
  - 10-25%: 36%
  - 25-50%: 17%
  - >50%: 25%
  - Mean: 30%

- Laboratory developed tests for a specific biomarker:
  - 0%: 20%
  - 1-10%: 5%
  - 10-25%: 39%
  - 25-50%: 21%
  - >50%: 16%
  - Mean: 24%

- Multigene panel:
  - 0%: 17%
  - 1-10%: 9%
  - 10-25%: 44%
  - 25-50%: 17%
  - >50%: 14%
  - Mean: 21%

- Broad next generation/whole genome-based sequencing:
  - 0%: 30%
  - 1-10%: 15%
  - 10-25%: 35%
  - 25-50%: 10%
  - >50%: 12%
  - Mean: 17%

- Minimal residual disease testing:
  - 0%: 52%
  - 1-10%: 11%
  - 10-25%: 24%
  - 25-50%: 6%
  - >50%: 8%
  - Mean: 11%

- Liquid biopsy:
  - 0%: 46%
  - 1-10%: 19%
  - 10-25%: 22%
  - 25-50%: 9%
  - >50%: 6%
  - Mean: 10%

Source: 2018 Genentech Oncology Trends
Challenge: Oncologist Adoption and Perception

**ONCOLOGIST OPINION ON THE FOLLOWING TYPES OF TESTING ON PATIENT OUTCOMES**

% of respondents, N=200

- Molecular/biomarker testing (e.g., companion diagnostics testing like HER2, KRAS)
  - No impact: 2%
  - Little impact: 5%
  - Moderate impact: 22%
  - Significant impact: 68%

- Molecular approaches for disease monitoring (e.g., liquid biopsy)
  - No impact: 10%
  - Little impact: 29%
  - Moderate impact: 37%
  - Significant impact: 22%

- Whole-genome sequencing
  - No impact: 5%
  - Little impact: 32%
  - Moderate impact: 40%
  - Significant impact: 19%

Source: 2018 Genentech Oncology Trends
Challenge: Oncologist Adoption and Perception

Importance to the Field of Oncology

- Not at all important: 1%
- Slightly important: 5%
- Somewhat important: 23%
- Very important: 44%
- Extremely important: 27%

Marketing of Genomic Testing

- Very underpromoted – its value far exceeds expectations: 0%
- Underpromoted – its value exceeds expectations: 11%
- Appropriately promoted and meets expectations: 33%
- Overpromoted – its value is below expectations: 46%
- Very overpromoted – its value is far below expectations: 9%

Source: West, J. Genomic Testing and Precision Medicine in Cancer Care, Medscape May 2, 2017
### Challenge: Oncologist Adoption and Perception

- **It’s too rare that it provides clinically actionable, evidence-based information**: 31%
- **Not enough tissue**: 18%
- **It’s not cost-effective**: 17%
- **It takes too long**: 17%
- **Other**: 2%
- **None; I don’t have significant concerns**: 16%

*Source: West, J. Genomic Testing and Precision Medicine in Cancer Care, Medscape May 2, 2017*
Patient Advocacy Strategies Evolve as Genomic Advances Change Understanding of Cancer

Sep 07, 2017 | Turna Ray

NEW YORK (GenomeWeb) – Over the past two weeks, a group of patients whose lung tumors are driven by rearrangements in the ALK gene have raised $120,000 that they hope to put toward advancing research for their specific cancer subtype.

"The current state of medical research is not enough to save our lives," said Laura Greco, a stage IV non-small cell lung cancer patient and a member of a support group called ALK Positive. "We have the most skin in the game and we definitely have a different perspective, and one that’s generally lacking in research decisions."
Challenge for the Media: Communicating Success

How do we ensure that stakeholders have all the information they need to honestly evaluate the progress that is being made in the field?

How do we communicate success in relatively simple terms, while avoiding hype?
What is the Optimal Precision Oncology Delivery Model?

- Patient Eligibility
- Tissue/Sample Eligibility
  - Sequencing Platform/Strategy
  - Variant Analysis Pipeline
  - Drug Matching Criteria
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What is the Optimal Precision Oncology Delivery Model?

Fully Integrated Precision Oncology Delivery Framework
What are Precision Oncology’s Greatest Hits?
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WINther?  
My Pathway?  
TAPUr?  
IMPACT?  
Intermountain Precision Genomics?
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Please share your thoughts!
Thank You!

Special Thanks
WIN Symposium Organizers
Turna Ray
Cancer Research Community
Clinical Oncology Community