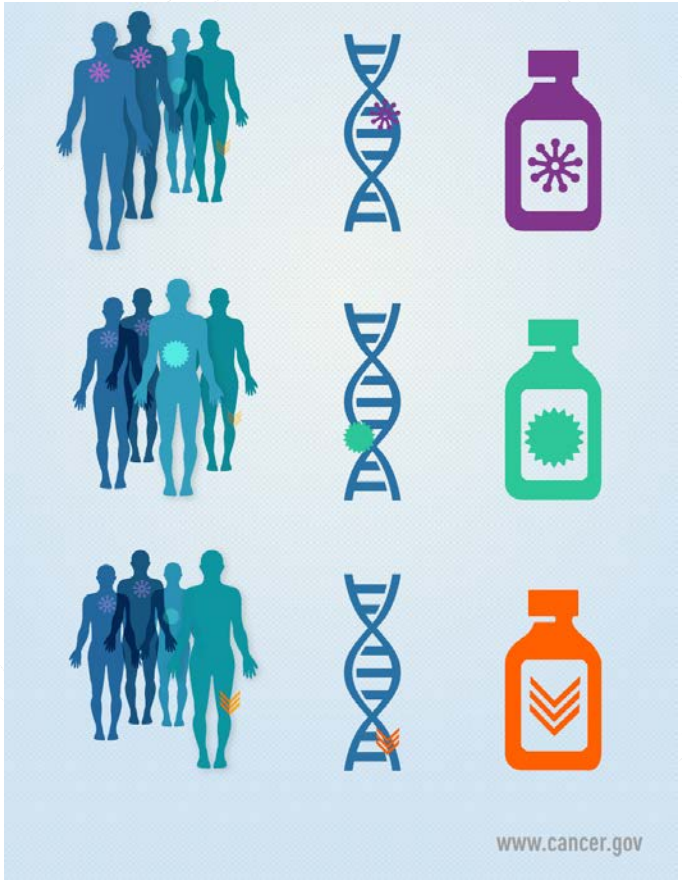


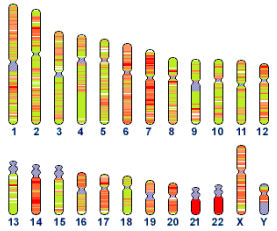
The Clinical Implementation of Precision Medicine

Lincoln Nadauld, MD PhD
Executive Director, Precision Genomics
Intermountain Healthcare

Precision Medicine: An Overview

- **Precision medicine overview**
- Clinical trials in precision oncology
- The evidence
- The future

Precision oncology paradigm



Variants

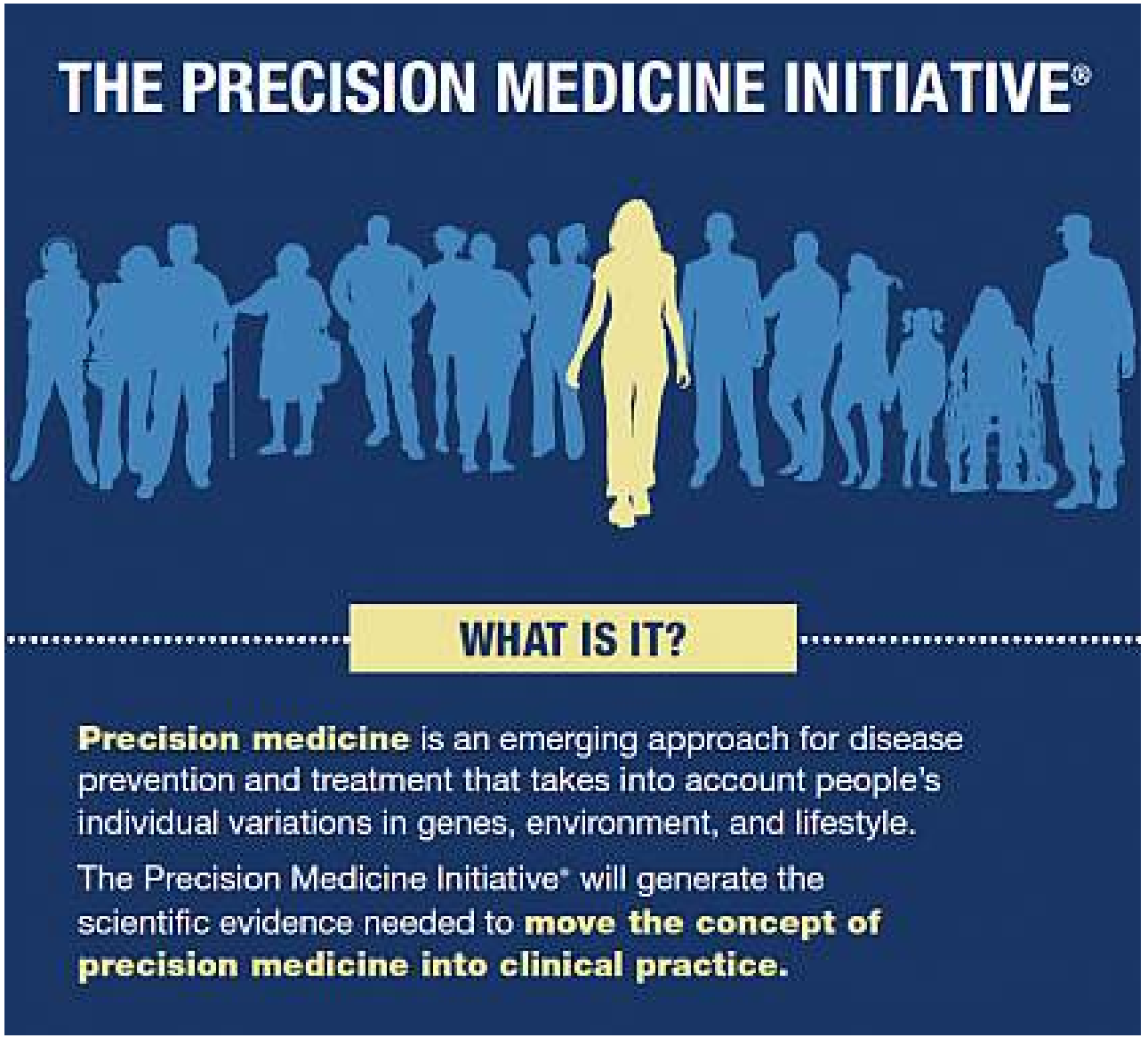
1. HER2 ← drug 1
2. P53
3. MEK1 ← drug 2
4. EGFR ← drug 3
5. FGFR1 ← drug 4

Cancer cell

Genomic analysis

Gene/drug match

Precision Medicine at NIH



WHY NOW?

The **time is right** because of:

Sequencing of the human genome

Improved technologies for biomedical analysis

New tools for using large datasets

Precision oncology journals

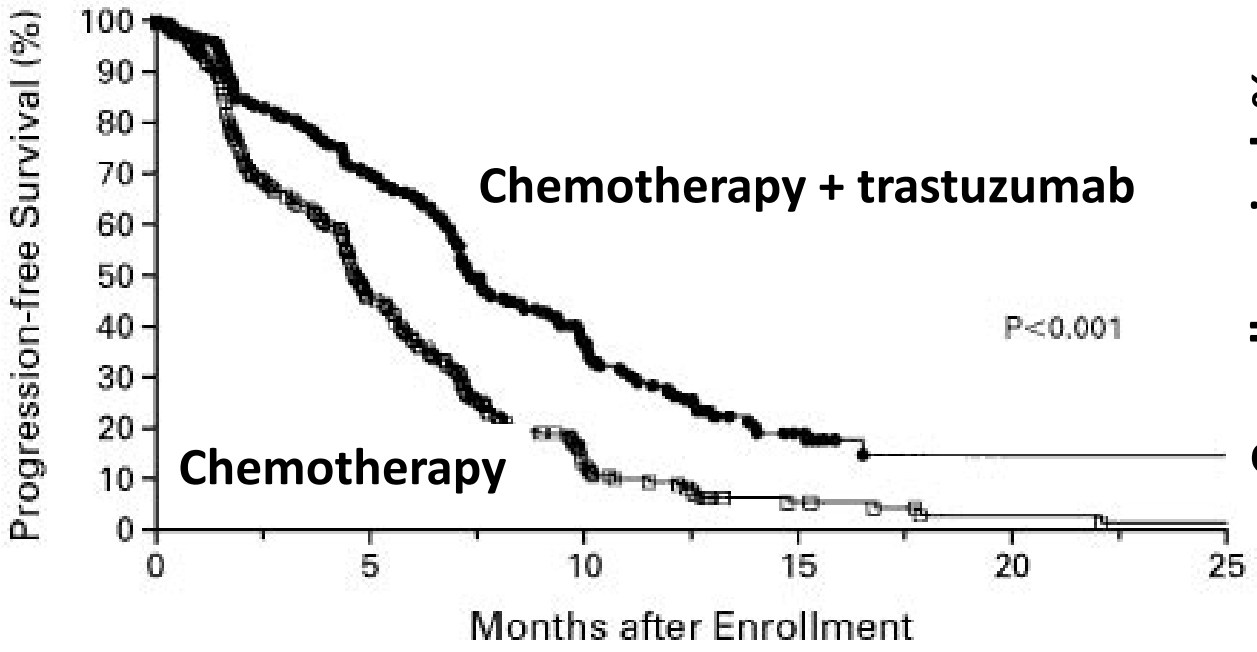
JCO™ | PRECISION ONCOLOGY
An American Society of Clinical Oncology® Journal

npj | Precision Oncology

COLD SPRING HARBOR
Molecular Case Studies
Volume 3 Number 5 September 2017

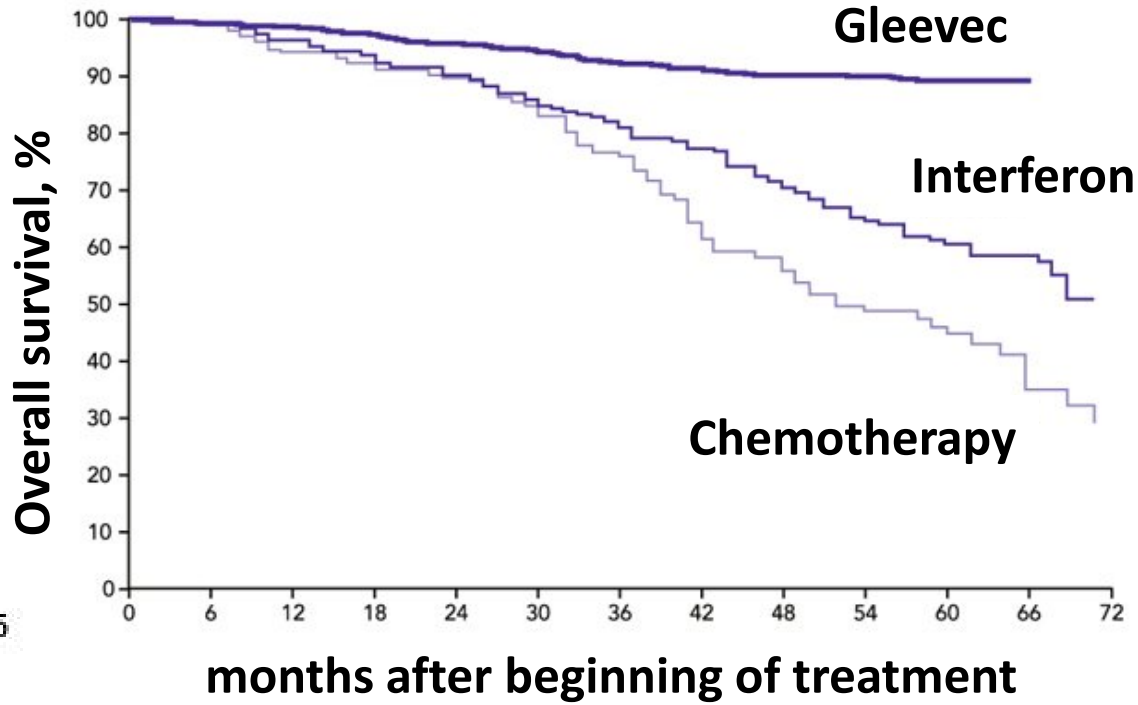
Oncotarget
Advance Online Publications

Precision oncology in practice: we're already doing it



Trastuzumab in HER2+ BC

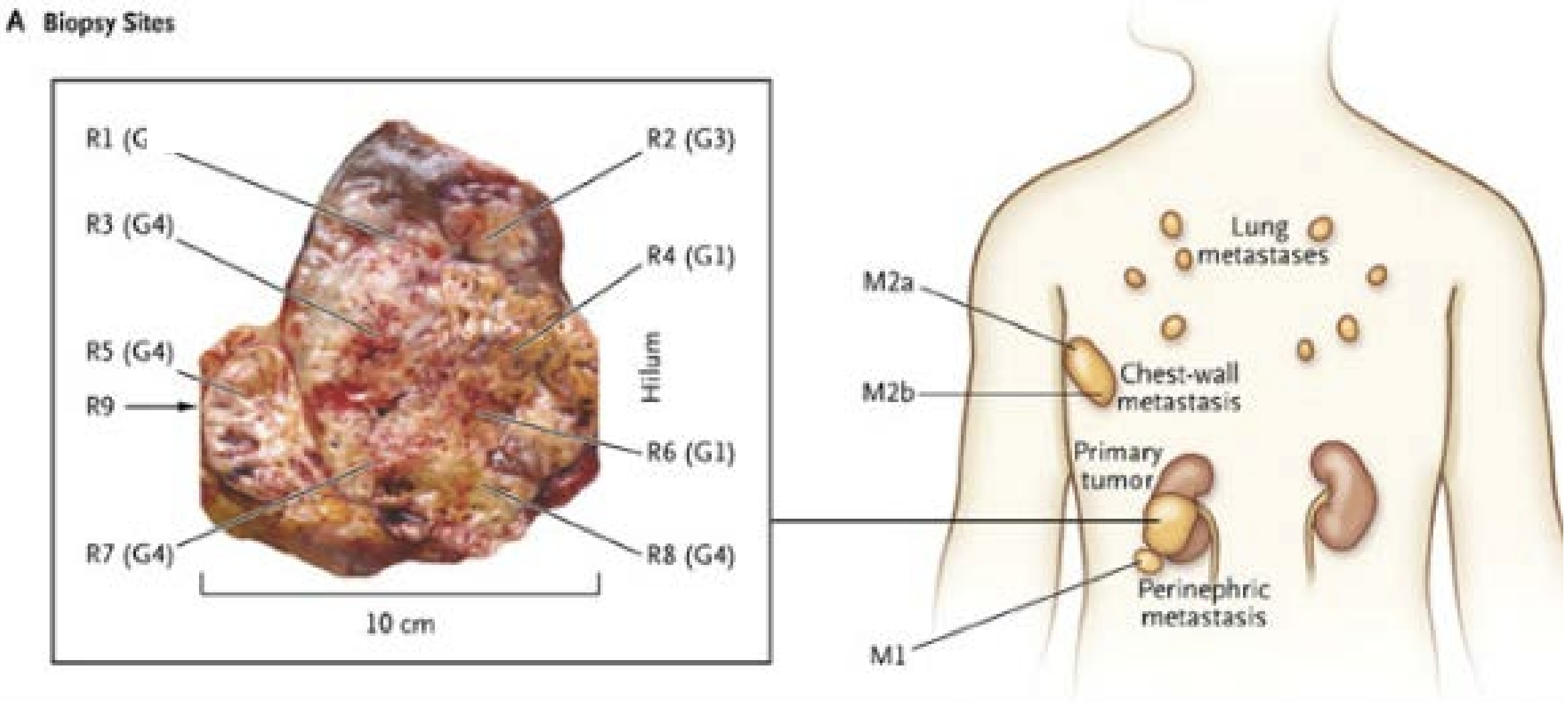
Slamon et al., NEJM. 2001



Imatinib in CML

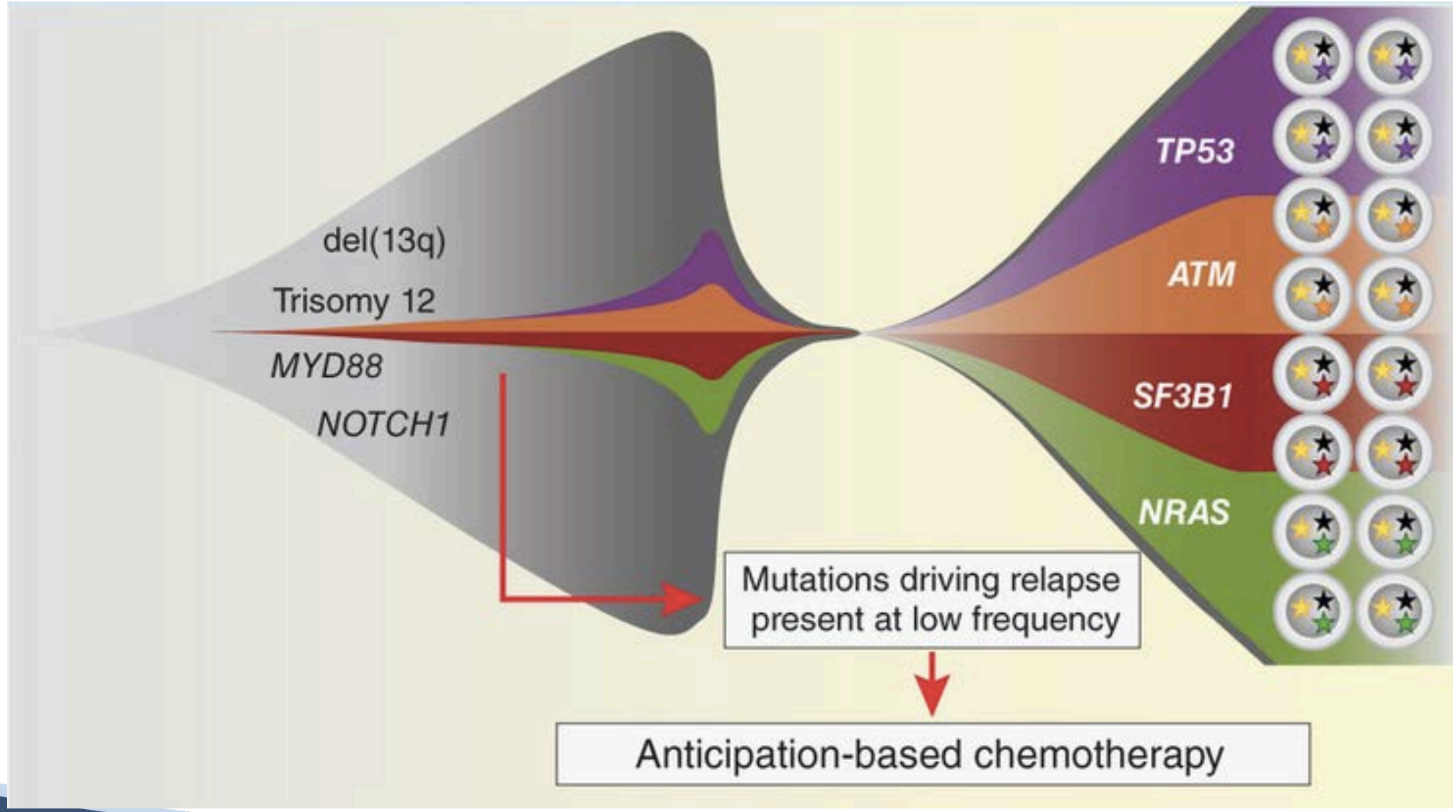
Drucker et al., NEJM. 2006

Challenges in Precision Oncology: Tumor Heterogeneity



Gerlinger, NEJM, 2012

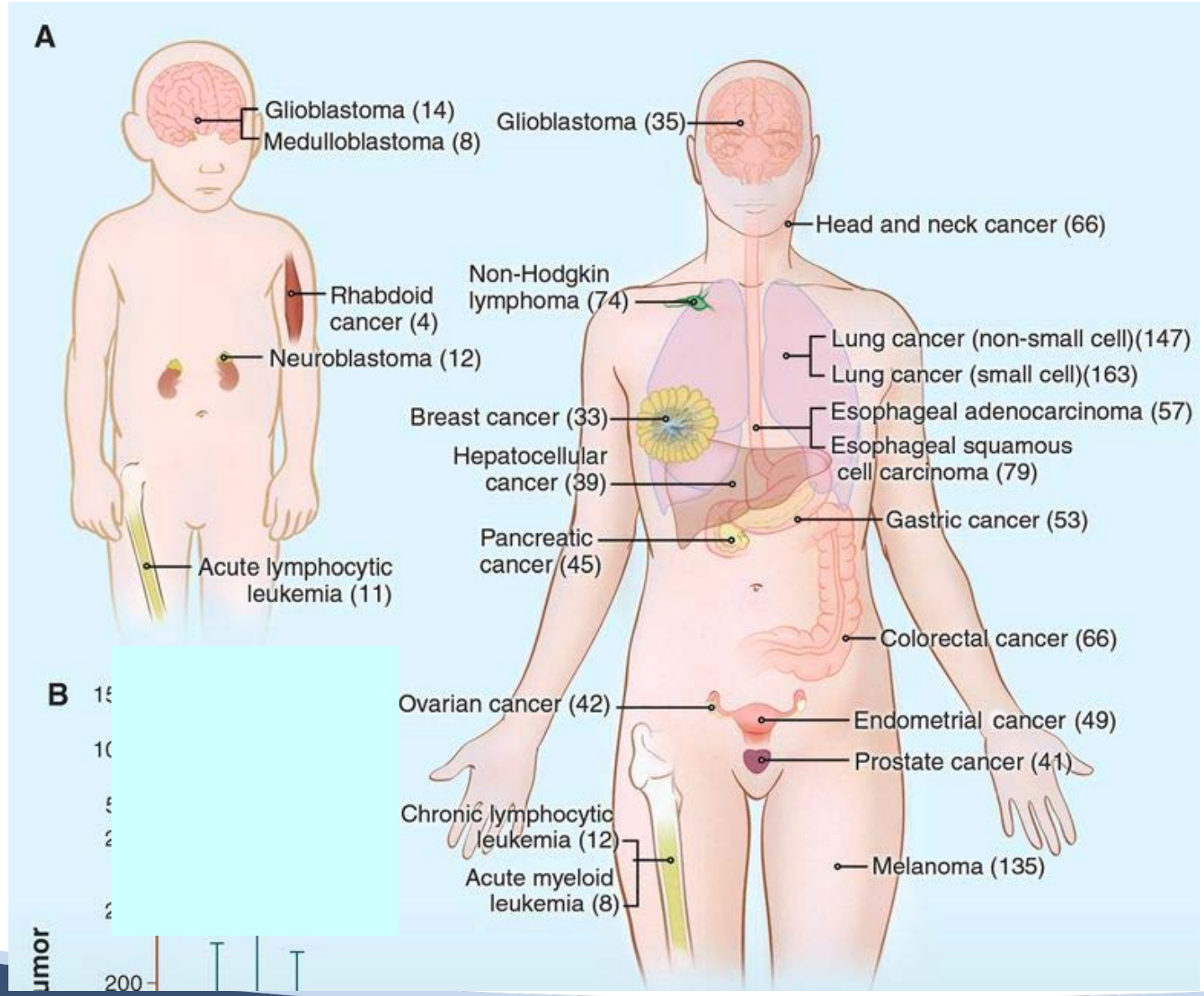
Challenges in precision oncology: Tumor Evolution



Intermountain® Healthcare

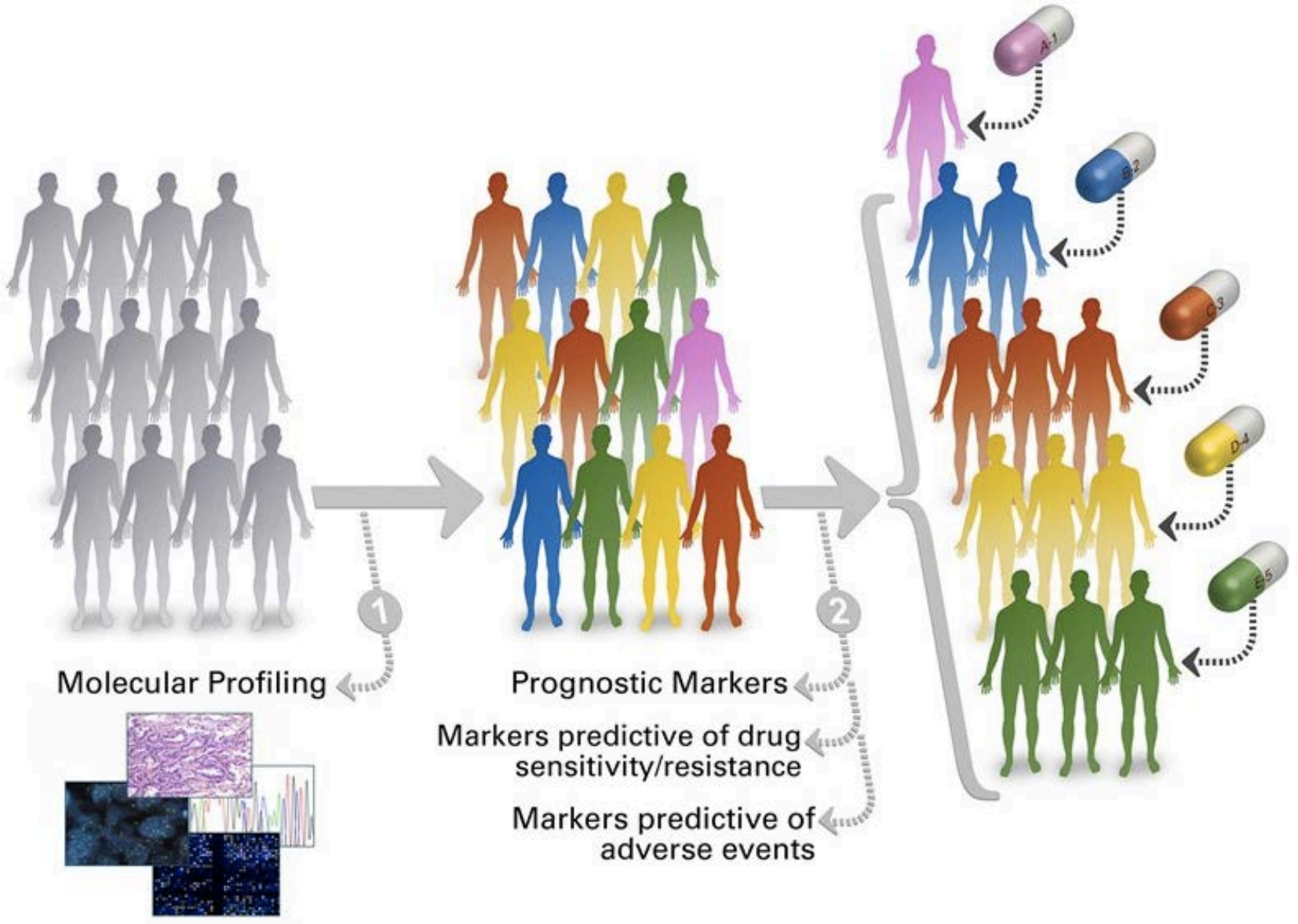
Puente, Nat. Genet., 2013

Challenges in Precision Oncology: Mutation Burden



B. Vogelstein, Science. 2013

Precision oncology in spite of the challenges



mdanderson.org

A typical precision oncology workflow

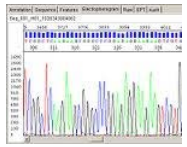
Clinic Day 1

Biopsy or FFPE Day 2-4

Pathology Review Day 5

Sample Prep Day 6

Molecular analysis (NGS) Day 7-8

Bioinformatics  Day 9-11

Molecular Tumor Board Day 12-13

Results and Treatment Day 14-15

Molecular Tumor Board

- Multi-institutional participants
- Experts in Cancer Genomics
- Interpretation of Genomics

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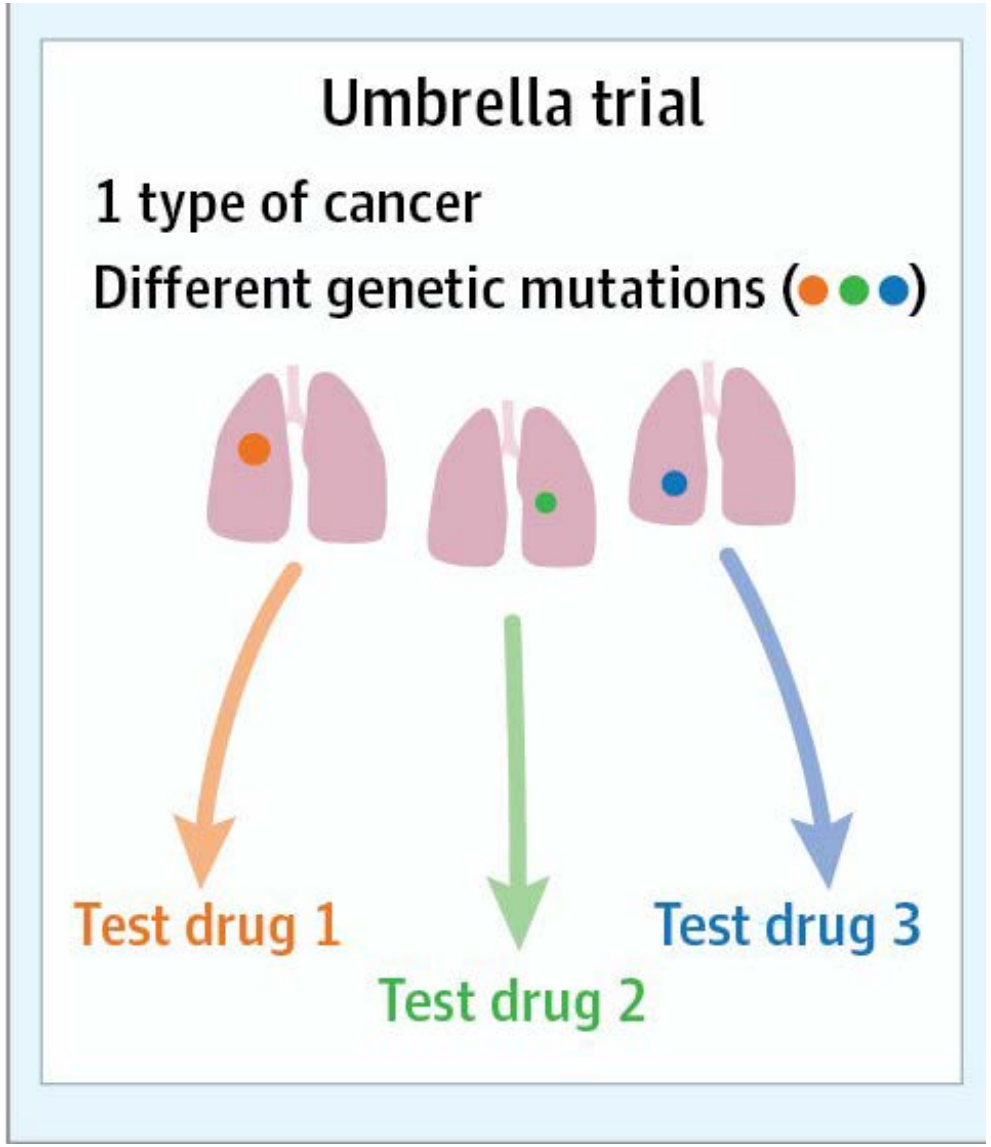
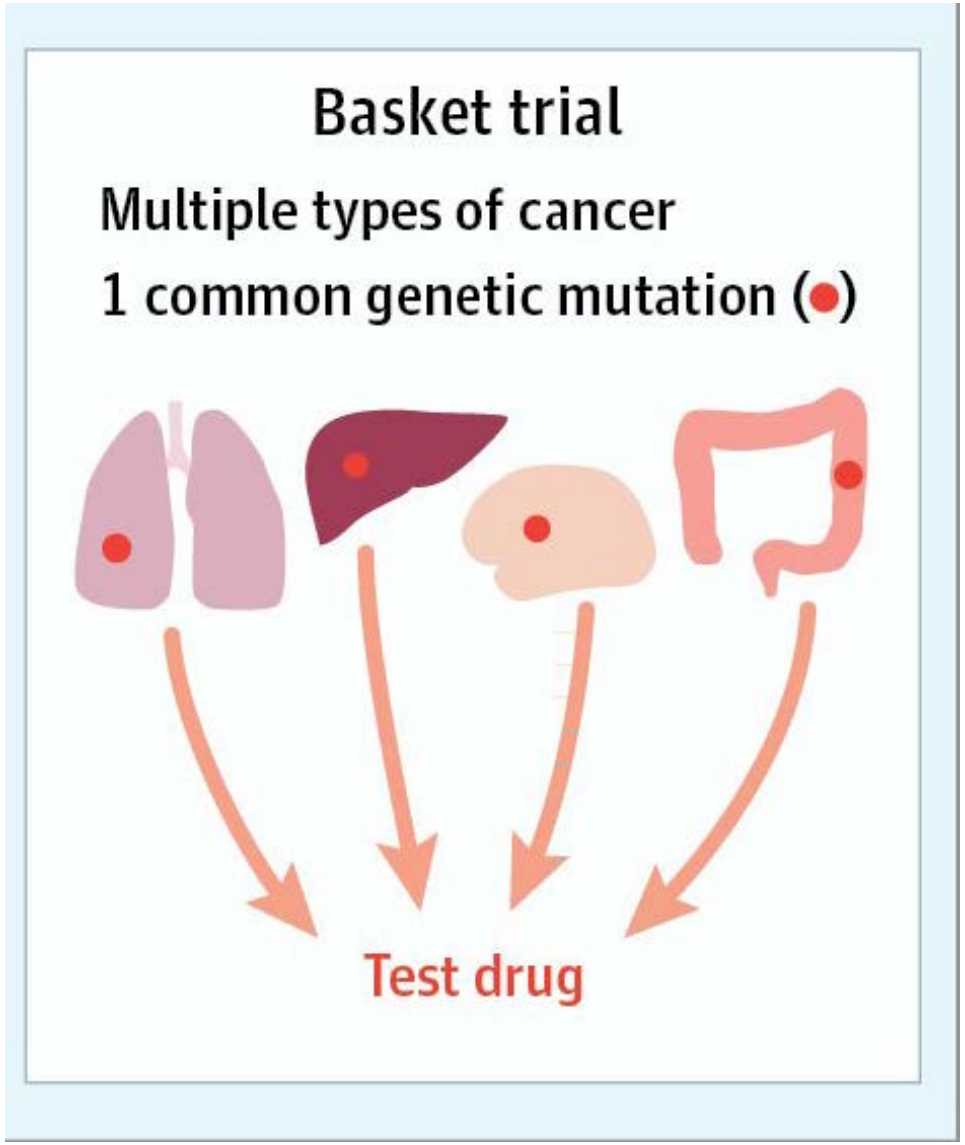
Precision oncology trial designs



Precision oncology trial designs



Precision oncology trials

TAPUR
American Society of Clinical Oncology

NATIONAL CANCER INSTITUTE
NCI-MATCH CLINICAL TRIAL

LUNG-MAP

Precision Medicine: An Overview

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Precision oncology: A meta-analysis

Impact of Precision Medicine in Diverse Cancers: A Meta-Analysis of Phase II Clinical Trials

Maria Schwaederle, Melissa Zhao, J. Jack Lee, Alexander M. Eggermont, Richard L. Schilsky, John Mendelsohn...

Purpose

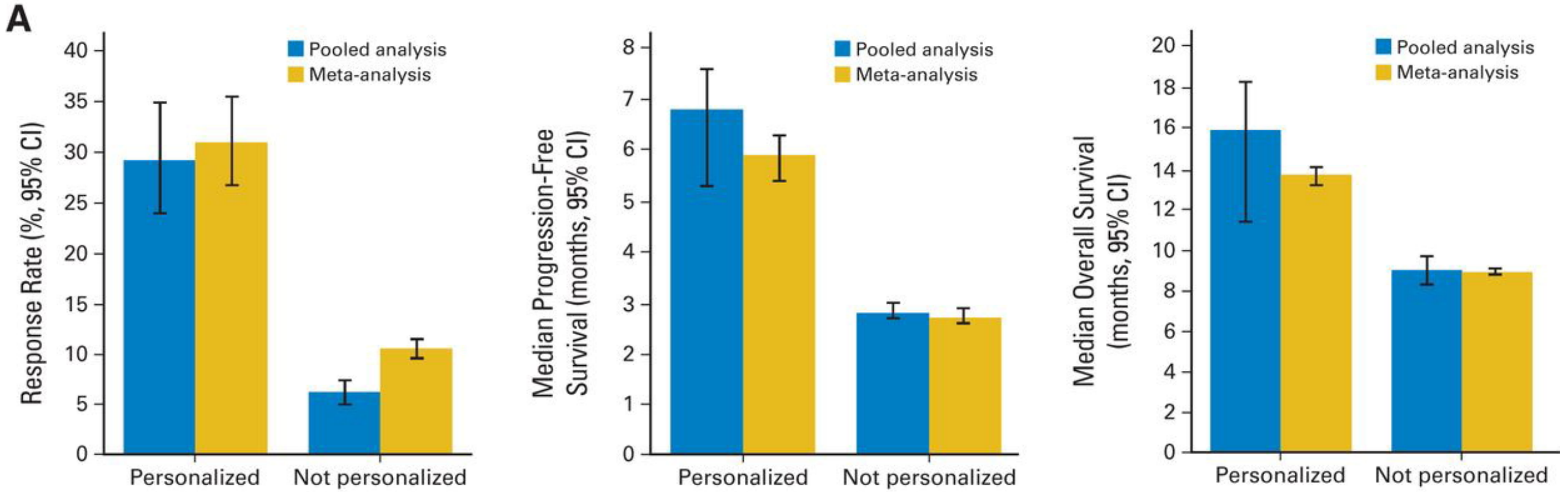
The impact of a personalized cancer treatment strategy (ie, matching patients with drugs based on specific biomarkers) is still a matter of debate.

Methods

We reviewed phase II single-agent studies (570 studies; 32,149 patients) published between January 1, 2010, and December 31, 2012 (PubMed search). Response rate

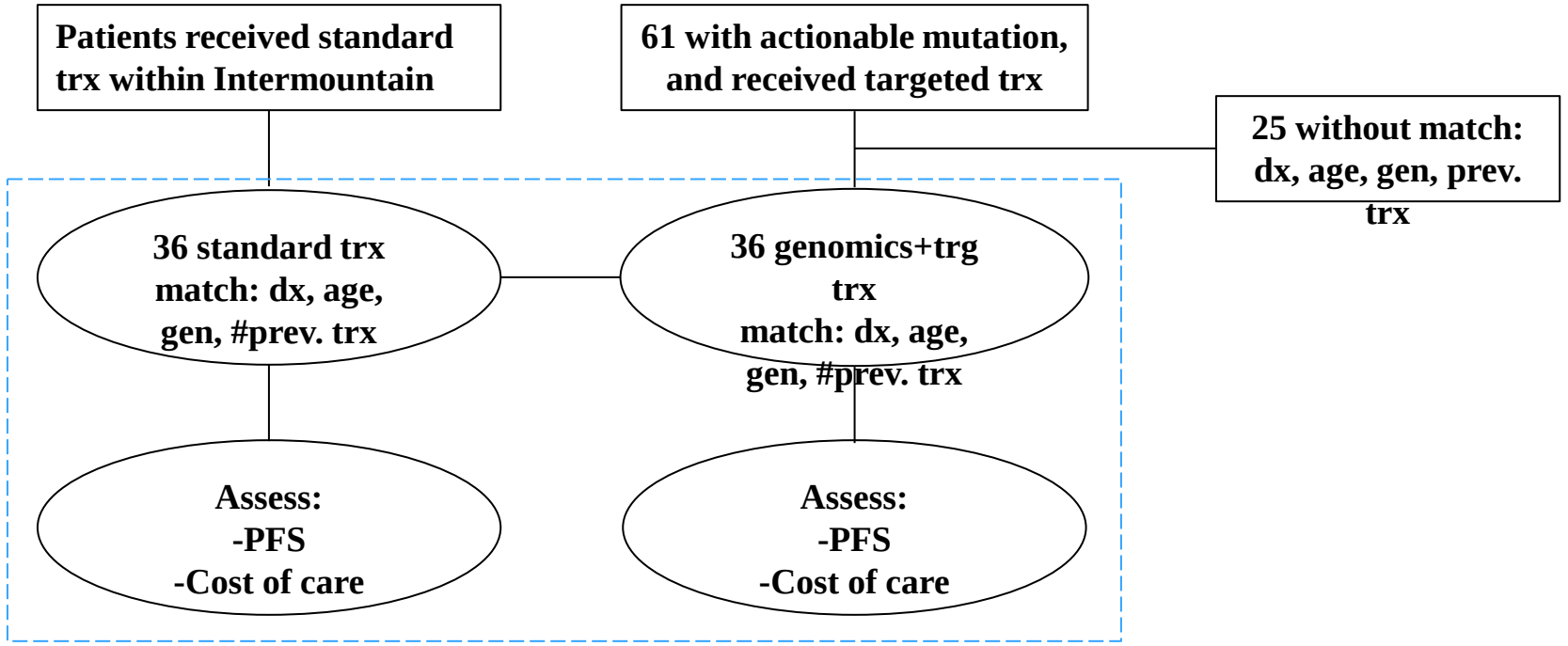
Schwaederle et al., JCO. 2015

Improved PFS with Personalized Medicine



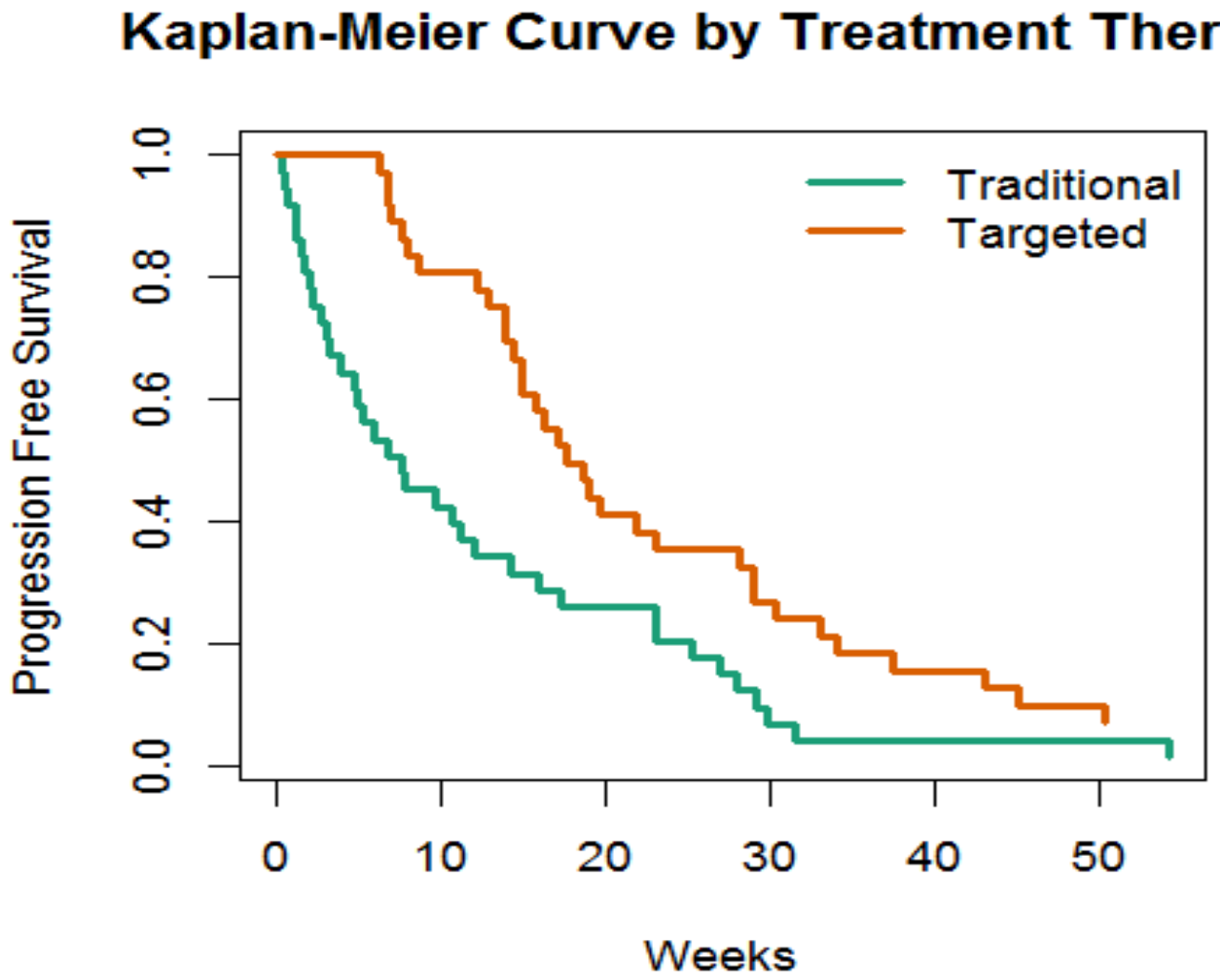
Schwaederle et al., JCO. 2015

Precision Oncology Cohort Study



Haslem et al, JOP, 2016

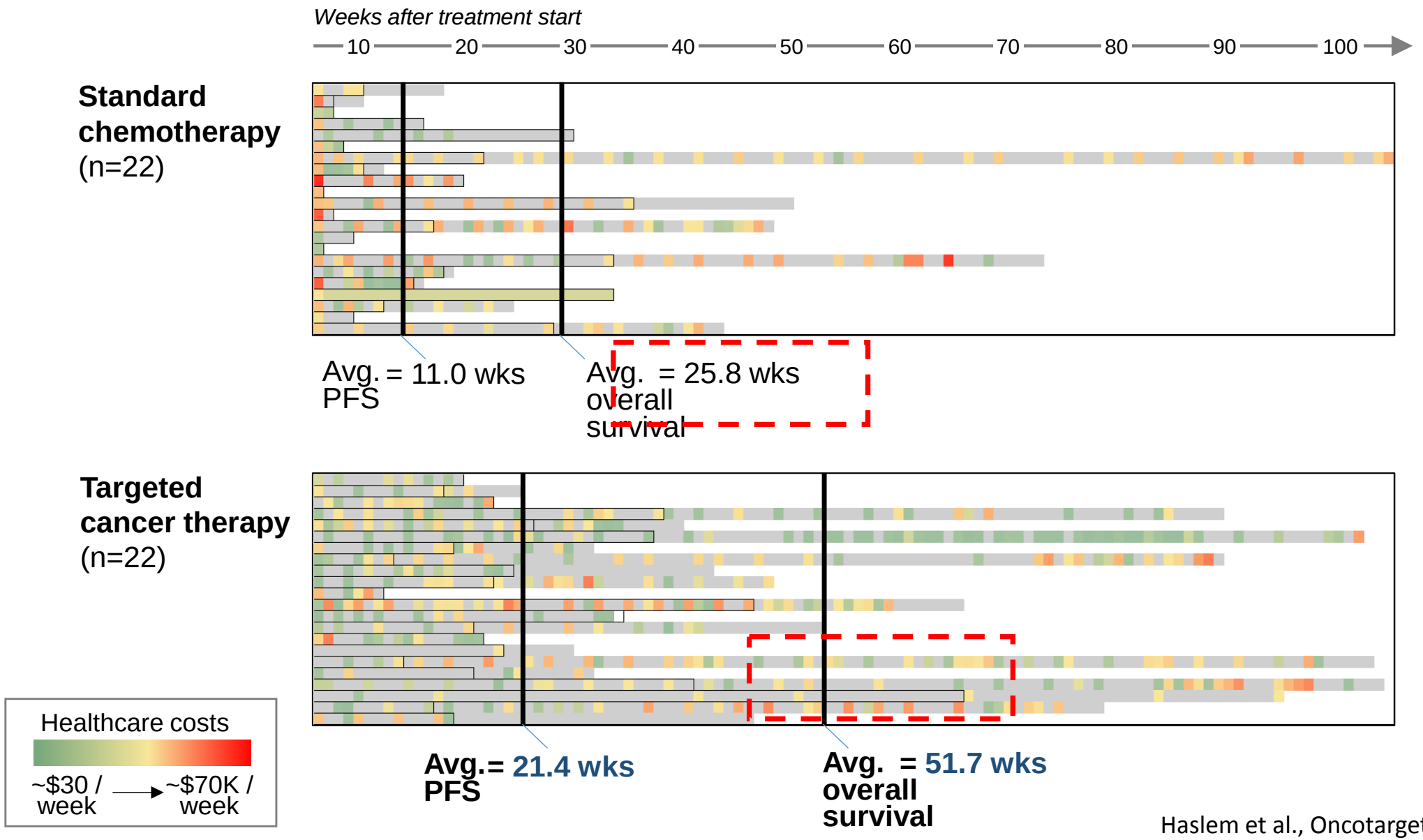
Precision Oncology Outcomes: Improved survival, decreased costs



Progression Free Survival: 23w vs 12w

Haslem, J. Onc. Practice 2016

Precision Oncology: Overall Survival



Haslem et al., Oncotarget. 2018

Precision Oncology Costs

	Control (N=22)	Targeted (N=22)	Difference
Inpatient	$552	$448	($104)
Outpatient	$2,376	$1,167	($1,209)
ER	$34	$45	$11
Rx drugs	$346	$940	$594
Hospice	$146	$9	($137)
Sequencing	$0	$112	$112
Total/week	**$3,453**	**$2,720**	**($734)**

Haslem and Nadauld, Oncotarget. 2018

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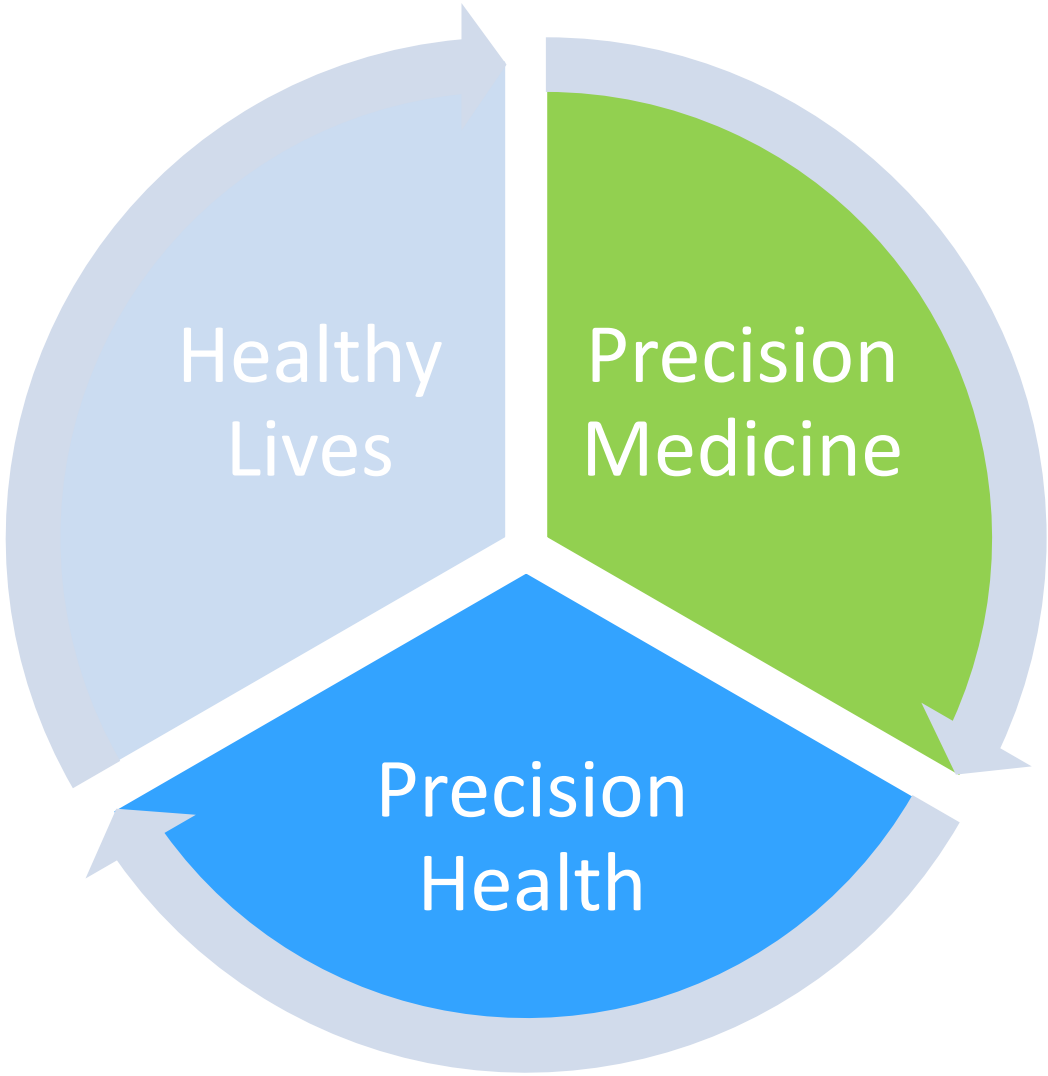
Precision Health

"The vision would be to go beyond Precision Medicine: instead of a frantic race to cure disease after the fact, we can increasingly focus on preventing disease before it strikes. By focusing on health and wellness, we can also have a meaningful impact in reducing healthcare costs…we call this idea Precision Health."

Minor, L., *Forbes Tech*. 2016

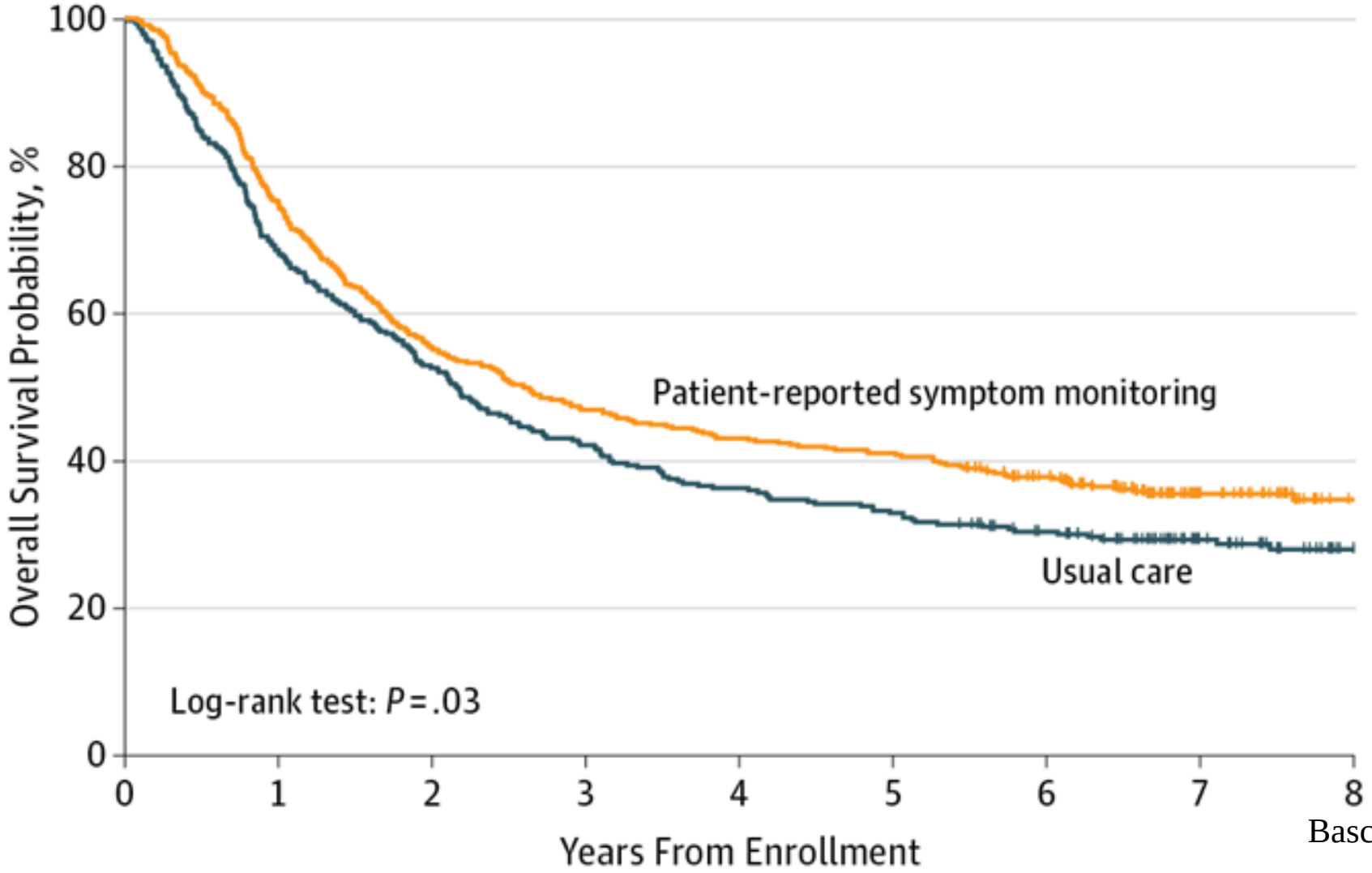
A Virtuous Cycle



Precision Medicine has different forms

Not all precision medicine initiatives require genomics

Precision Medicine: Patient reported outcomes improves survival



Basch et al., *JAMA*. 2017

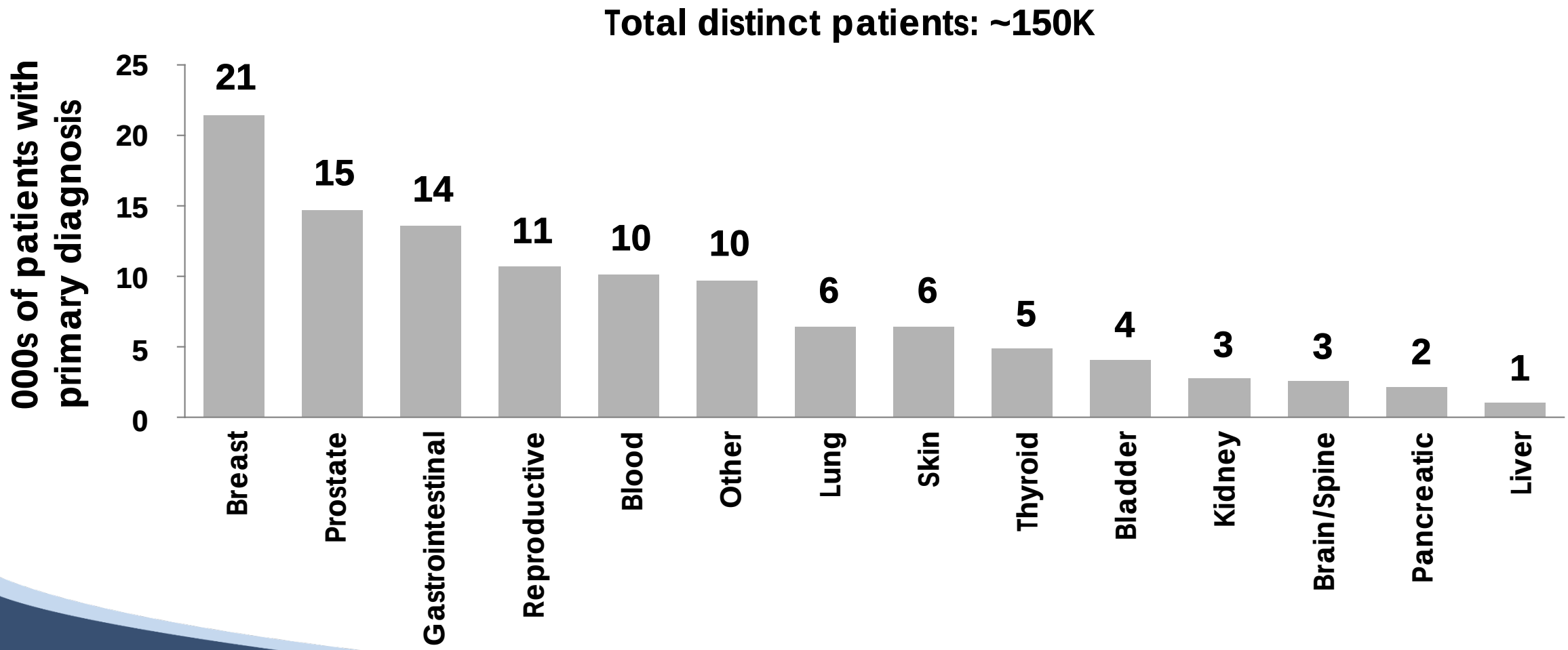
Intermountain Precision Medicine: moving forward

- **Biorepository studies and population genomics**
- Oncology Precision Network (OPeN)
- Intermountain Precision Health

Intermountain Biorepository

- 4.5 million archival samples
- Accumulated from 1975-present
- Longitudinal healthcare outcome data (30yrs)

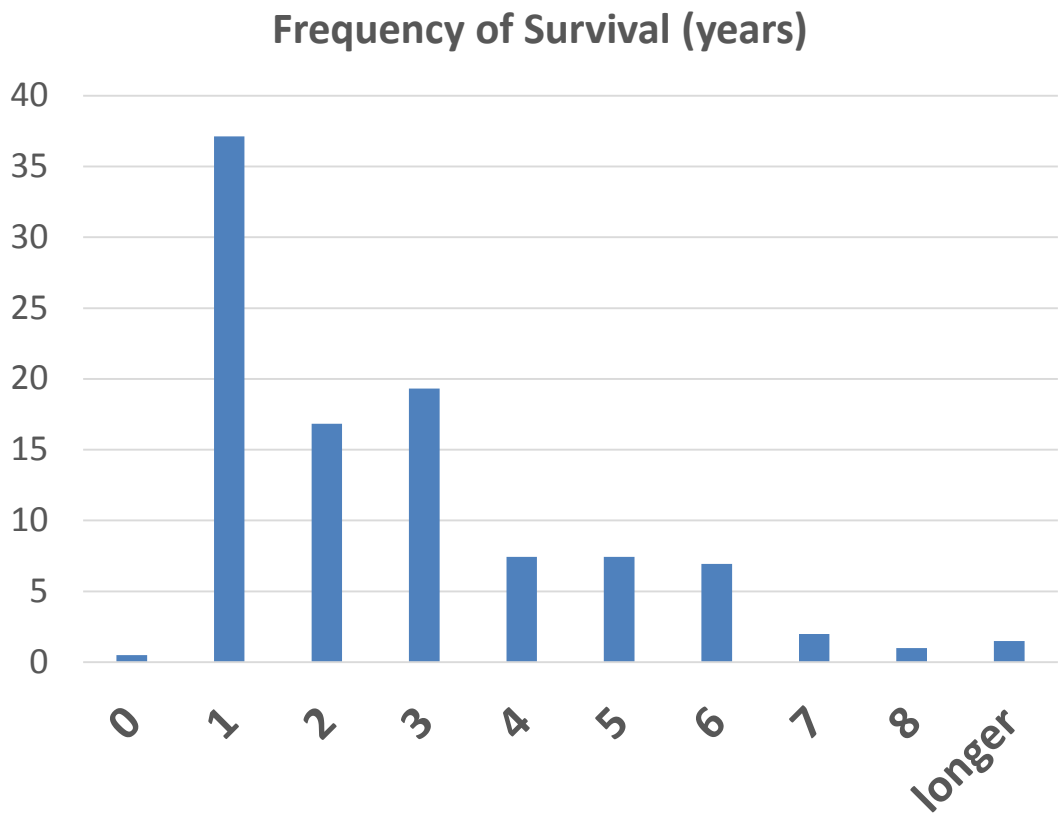
Intermountain biorepository: Oncology



GCB-CRC, Genomics of Colon Cancer

High depth Whole Genome and RNAseq of T/N samples from 150 patients

- Cancer type
  - Stage III colon cancer
  - Adjuvant chemotherapy
  - 23% have survival >5yr
- Genomic endpoints
  - SNV, rearrangements
  - CNV (low-depth as pilot project)
  - Expression, allele specific expression, fusions
- Analysis
  - Markers for survival
  - Landscape of variants
  - Interactions between variant type



Overview: Intermountain Precision Medicine

- Biorepository studies and population genomics
- **Oncology Precision Network (OPeN)**
- Intermountain Precision Genomics

OPeN Participants

Oncology Precision Network

Stanford MEDICINE

Intermountain Healthcare

Healing for life®

PROVIDENCE Health & Services

Henry Ford Health System

Catholic Health Initiatives

Aurora Health Care®

Dignity Health

hoag

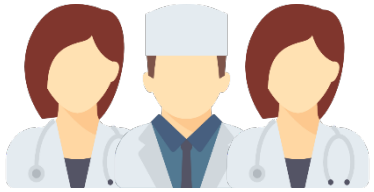
St. Joseph Health

Banner Health®

Anticipated Reach of OPeN

136,000

New Cancer Cases Per Year



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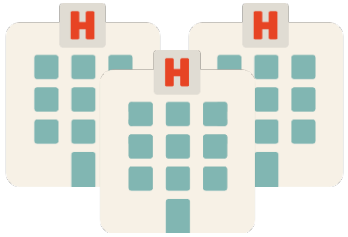
Oncologists



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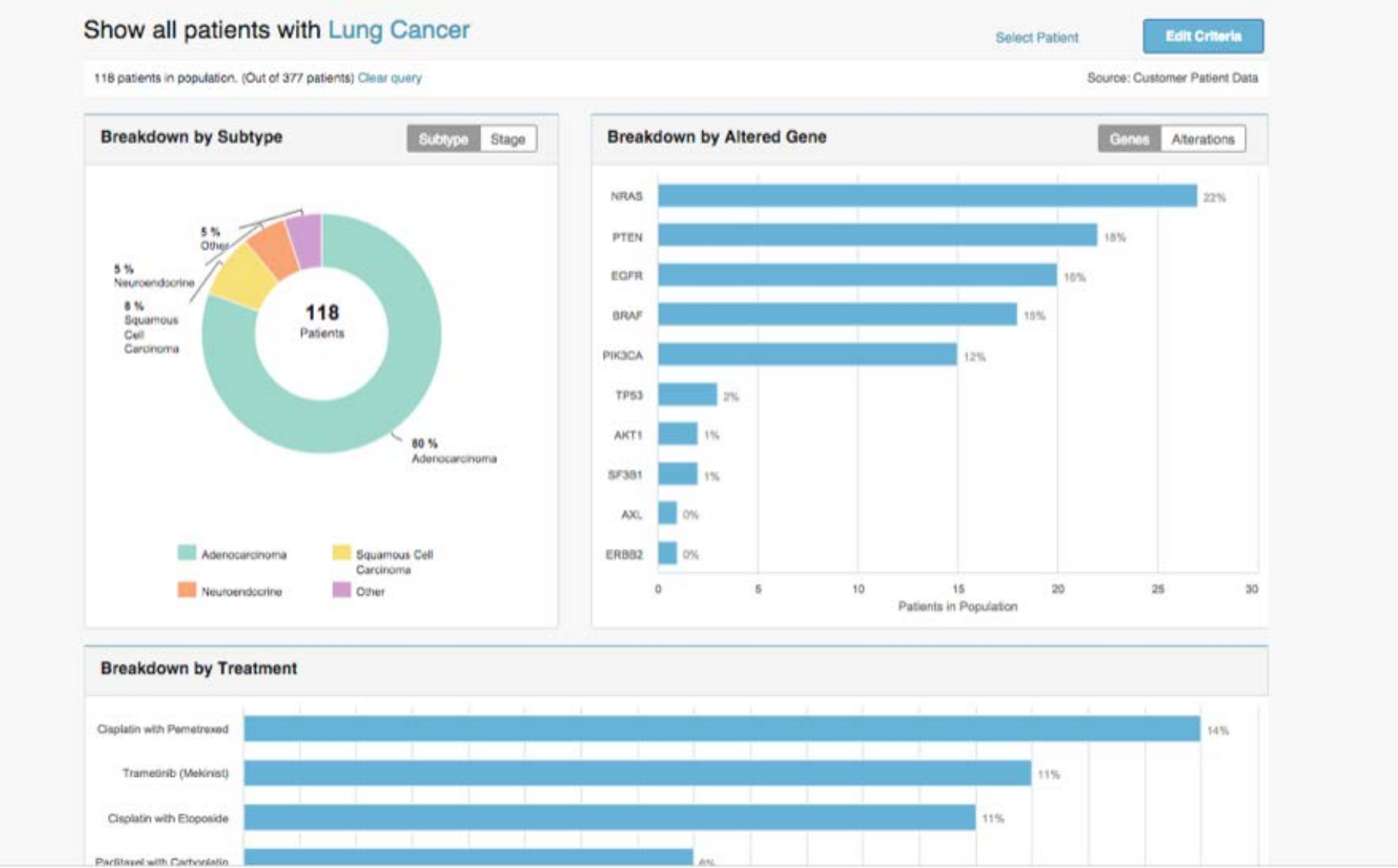
Hospitals

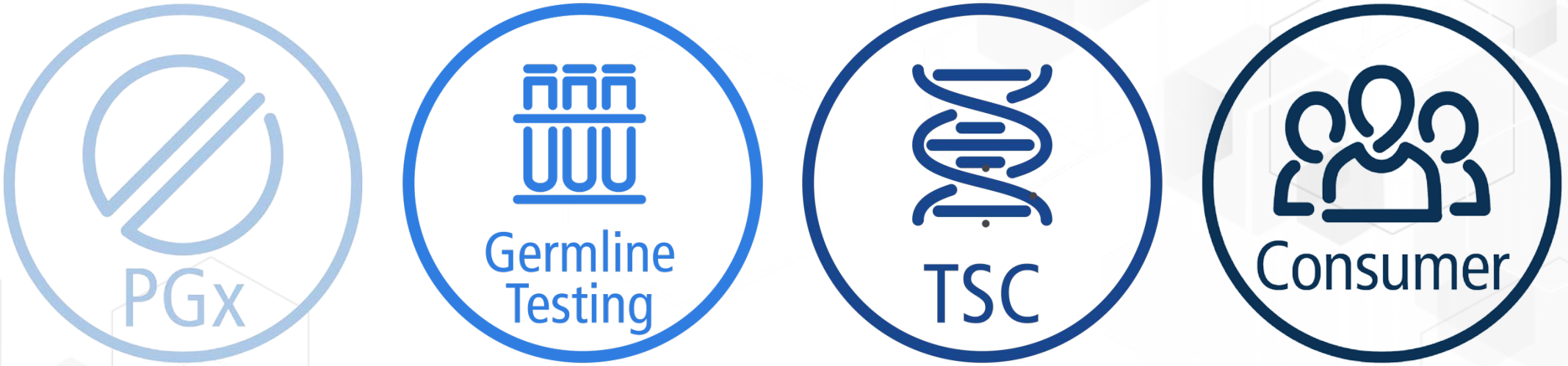
Search data by clinical or molecular characteristics



Overview: Intermountain Precision Medicine

- Precision medicine cohort study
- Biorepository studies and population genomics
- Oncology Precision Network (OPeN)
- **Intermountain Precision Genomics**

Vision: “To become the most genetically advanced healthcare system in the world.”

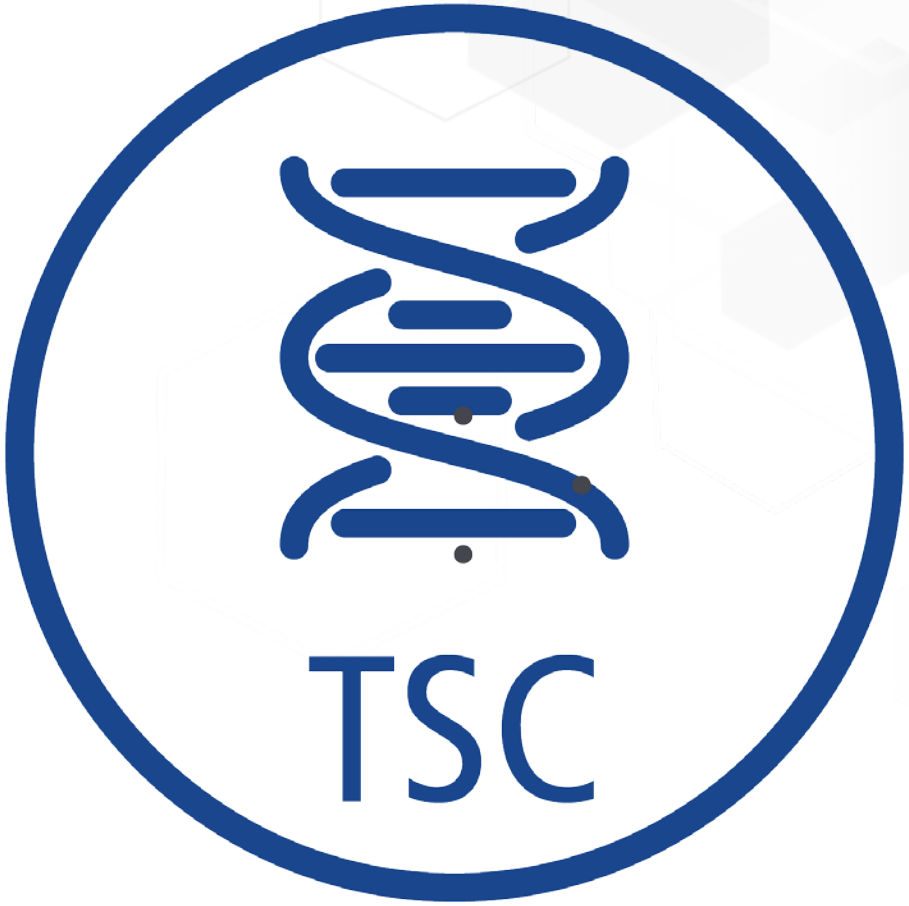


Goal: Implement Pharmacogenomic testing in the primary care setting

Pharmacogenomics

Goal: Implement inherited risk allele testing in primary care

Goal: Provide genome services for internal and external customers



Translational Science Center

Goal: Direct to consumer genomics