Precision Rx-Dx

Patient Leader Education Summit

Precision Medicine: Today and Tomorrow

March 31, 2017

Precision Medicine: Presentation Outline

Agenda

- What is a Precision Medicine
- What is its clinical value
- Overview of what's in place today and what's coming
- What are the barriers for patients?

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What is a Precision Medicine ?

Precision Medicine

The use of biomarker information(ie genetics) obtained through a companion diagnostic test (CDx) to identify subgroups or individual patients more likely to benefit from a particular drug (usually targeted therapy)

Targeted Therapeutic

Targeted therapy blocks the growth of cancer cells by interfering with specific targeted molecules needed for tumour growth, rather than by interfering with all rapidly dividing cells (e.g. with traditional chemotherapy).
The therapies target a protein or enzyme that carries a mutation or other genetic alteration that is specific to cancer cells and not found in normal host tissue.

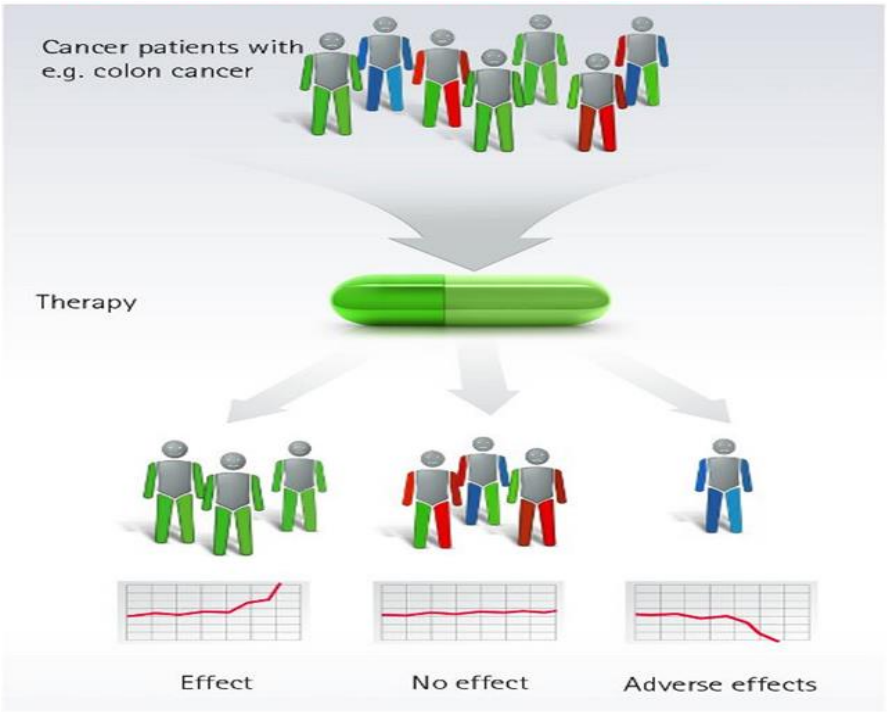
There are targeted therapies for colorectal cancer, head and neck cancer, breast cancer, multiple myeloma, lymphoma, prostate cancer, melanoma and other cancers.[2]

Companion Diagnostic eg. ALK in NSCLC

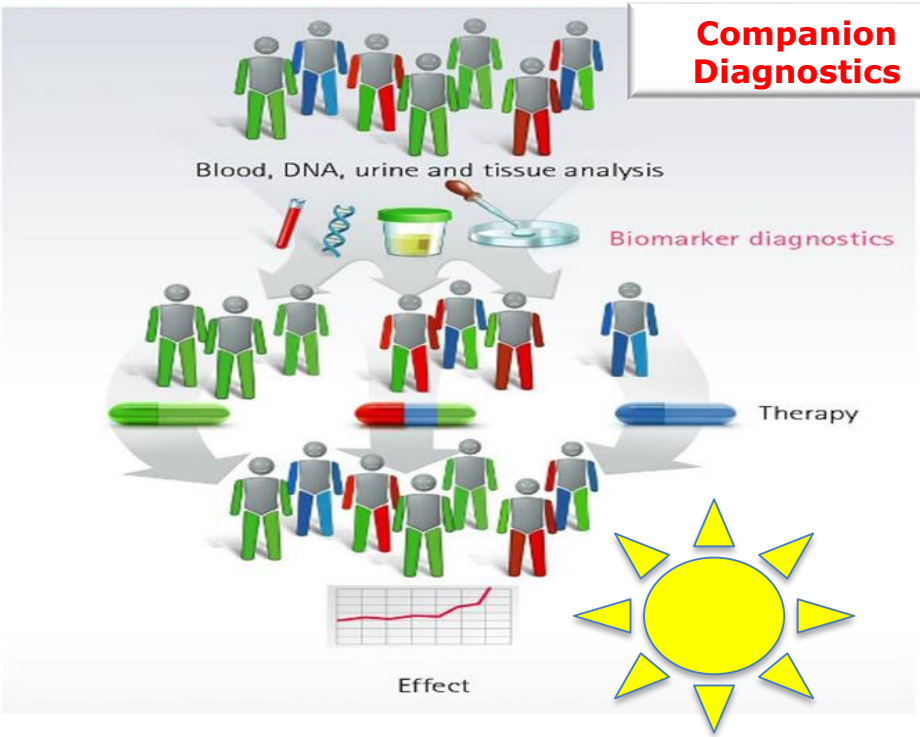
A diagnostic test which provides information that is essential for the safe and effective use of a corresponding drug. The test helps a health care professional determine whether a particular therapeutics' benefits to patients will outweigh any potential serious side effects or risks

Why are Precision Medicines important?

Shifting the healthcare paradigm to higher efficacy & safety



"One Treatment Fits All"

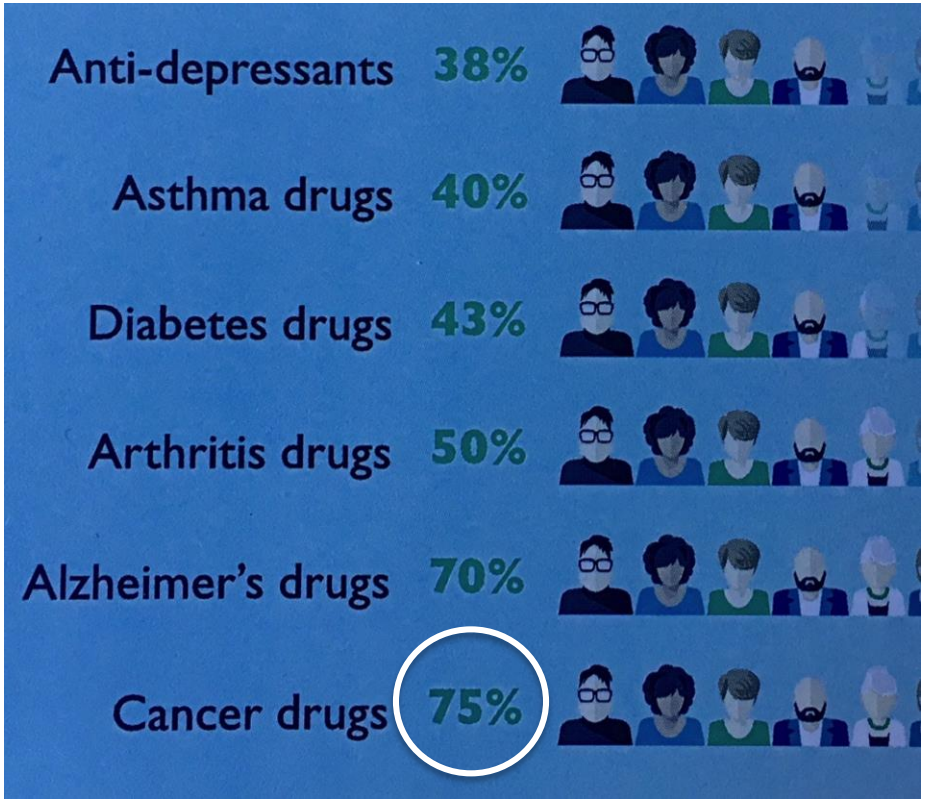


Precision Medicine:
Right **Treatment** –Right **Patient**-
Right **Time**

Benefits of Precision Medicine

Many current therapies do not benefit patients
- Average % of Patient Population for which a particular drug is ineffective

CDx Benefits all healthcare stakeholders



Patients
- Right treatment at the right time

Physicians
- Maximize clinical benefits
- Avoid unnecessary toxicity

Regulators
- Increased efficacy & safety

Payers
- Efficient use of healthcare budgets

Spear Brian B. et al Trend in Molecular Medicine volume 7, Issue 5, 1 May 2001 pgs 2001-2004

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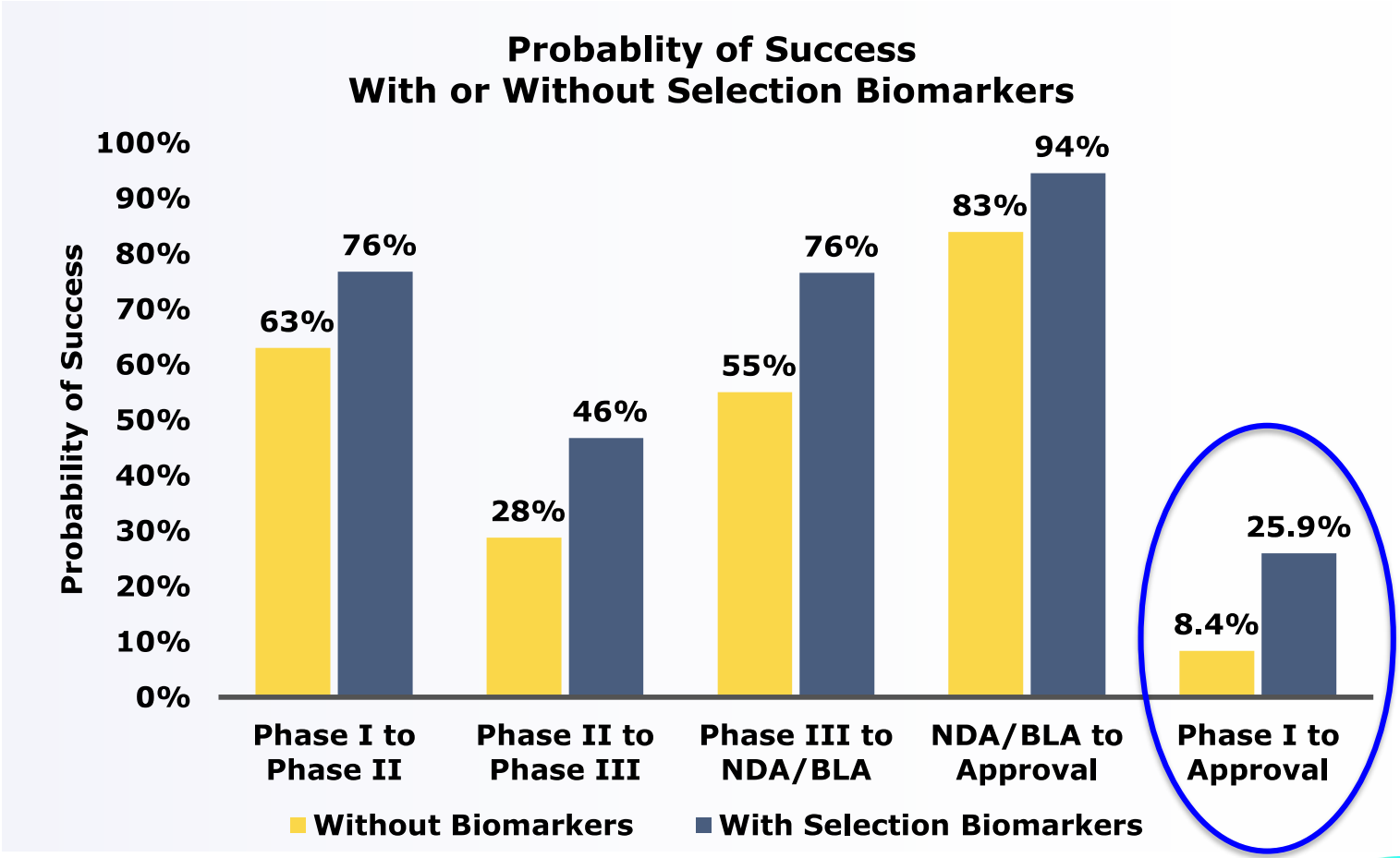
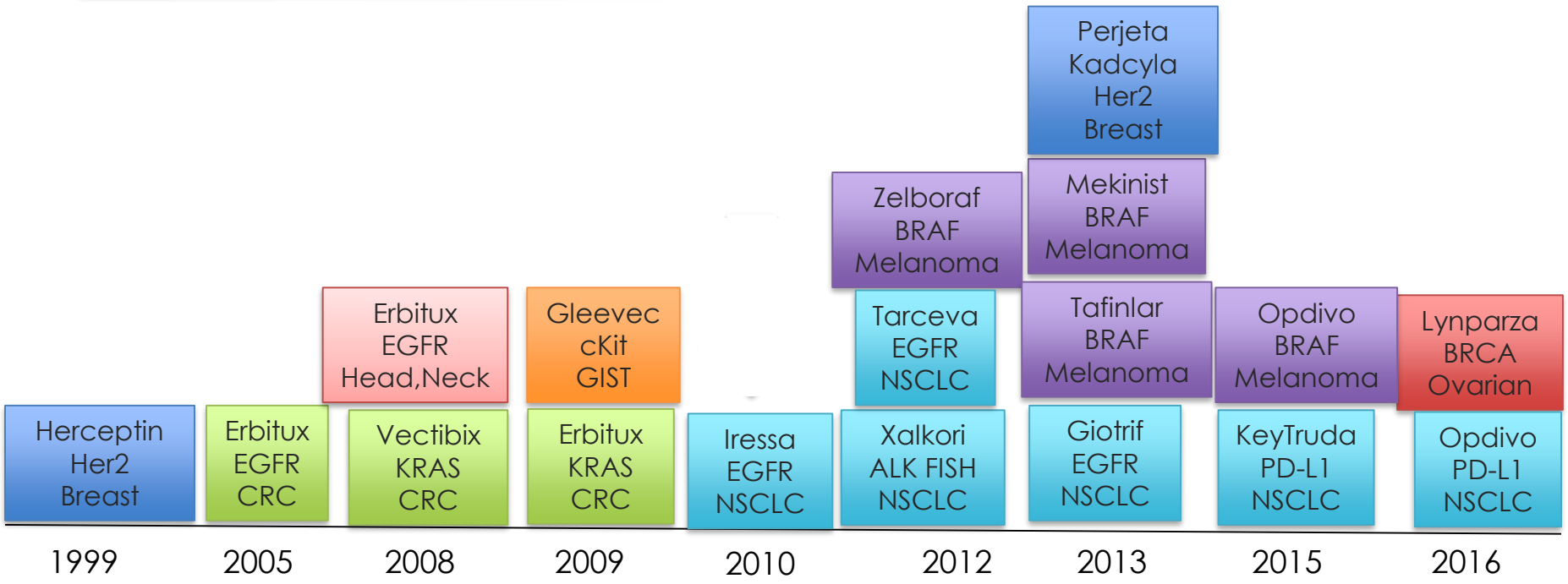
Precision Medicines: Higher success rates, faster approvals



Clinical_Development_Success_Rates_2006-2015_-_BIO.pdf

Approvals of Precision Medicines in Canada
Oncology focused



- Most of these drugs and CDx now reimbursed, although inconsistently across Canada
- Deep Precision Medicine pipelines- 50-70% of new therapies in phII or phIII

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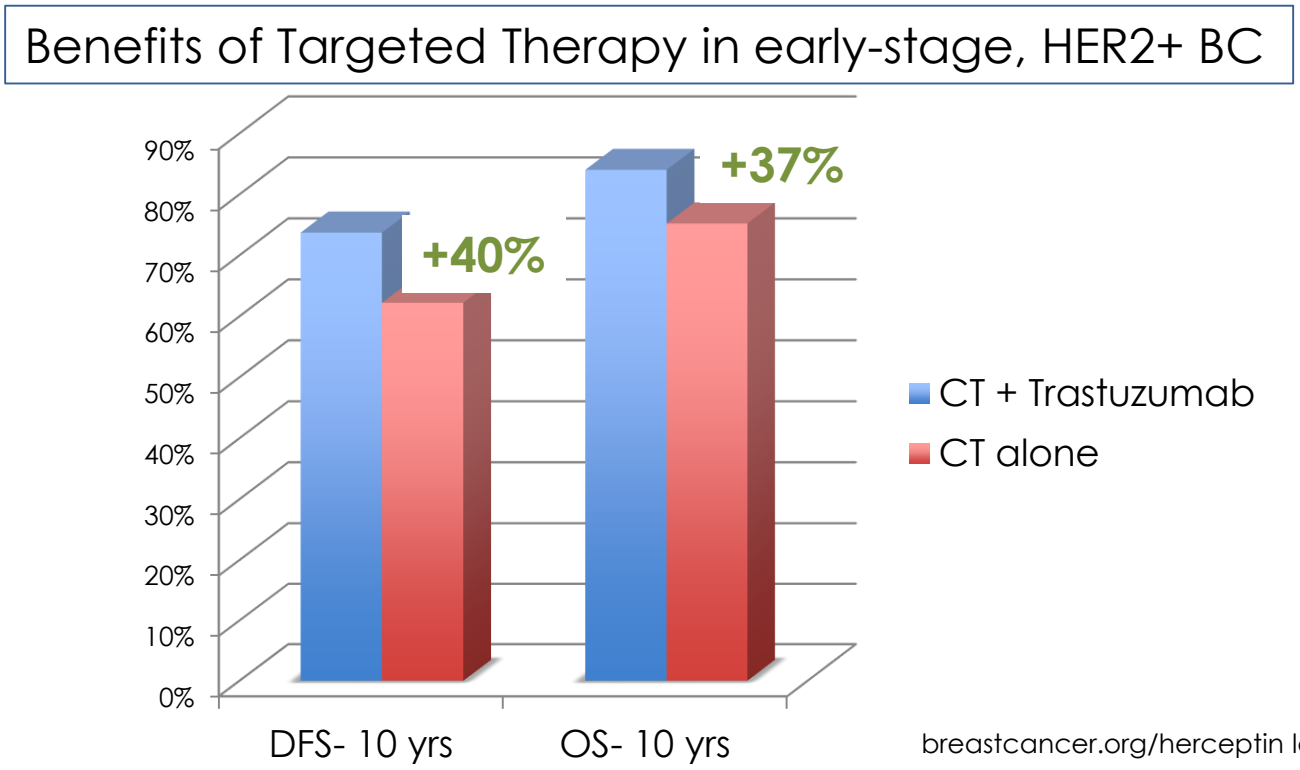
HER2 and Herceptin demonstrate the value for Patients

Herceptin (Trastuzumab) : HER2-positive breast cancer (BC)

- HER2 +ve BC make too much HER2 protein: sits on the cancer cell surface and receives signals that tell the cancer to grow and spread
- About 25% of breast cancers are HER2+ : tend to be more aggressive and harder to treat than HER2 -ve breast cancers

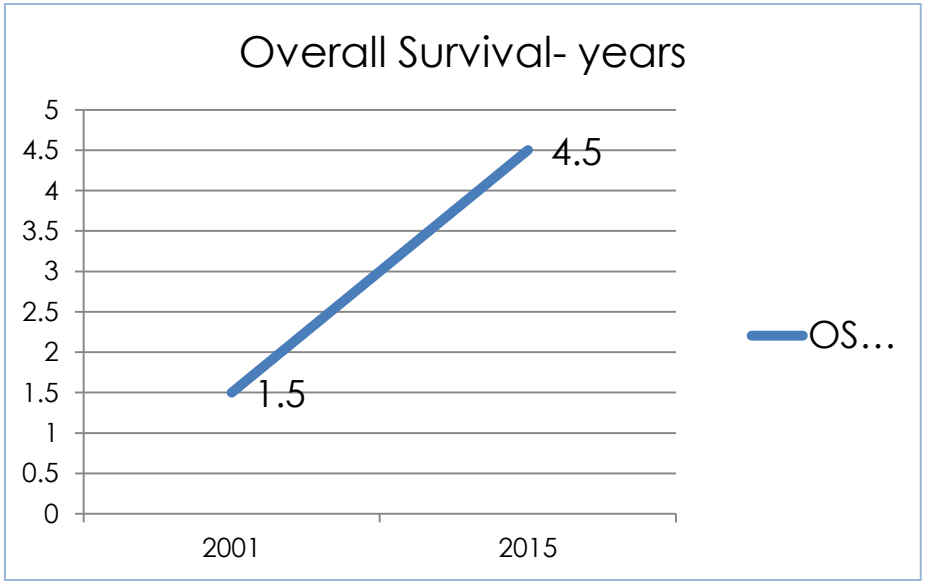


breastcancer.org/herceptin long-lasting benefits 28.10.14

More Precision Medicine Examples

HER2 Directed Therapies in Metastatic BC

- Triple combination



Mendes *et al Breast Cancer Research (2015) 17:140*

BRAF Directed Therapies in Melanoma

The BRAF gene codes for a kinase targeted by selective inhibitors such as vemurafenib

Impact in BRAF+ patients:

Tumour Size ↓ 50%

PFS ↑ 40-60%

Butts et al *Curr Oncol*, Vol. 20, pp. e475-483

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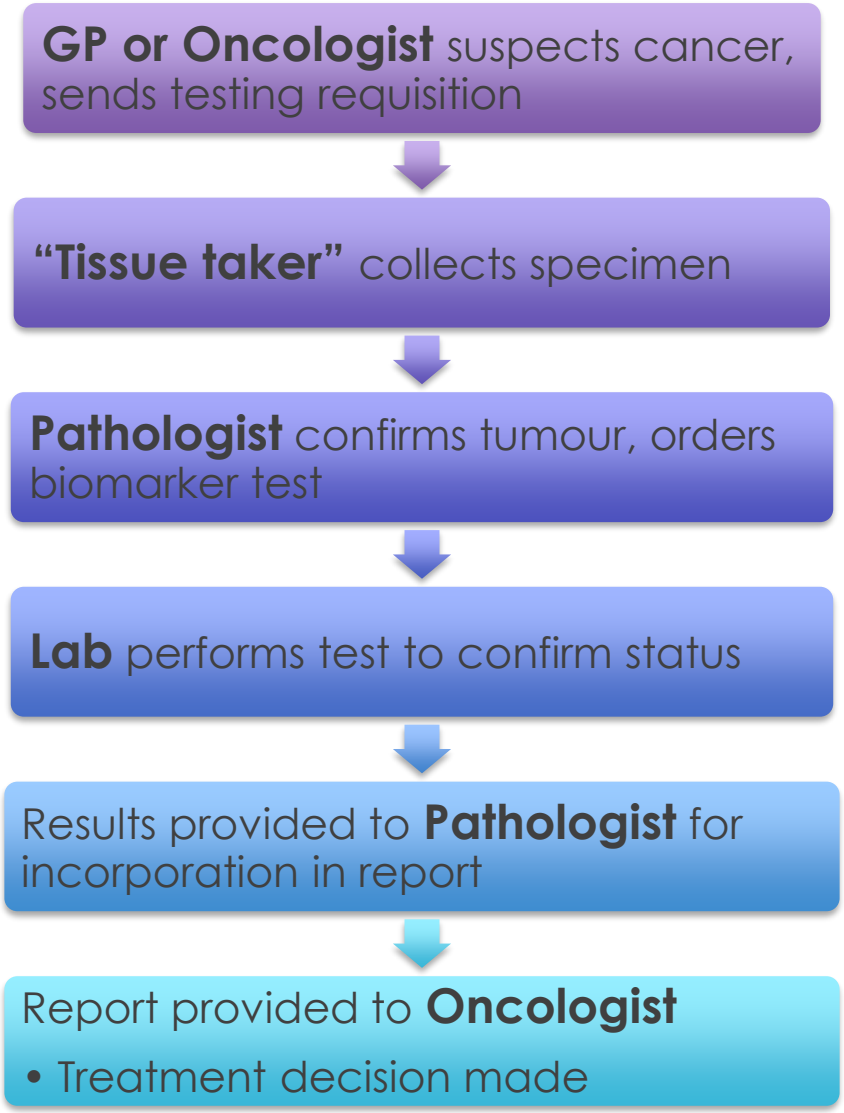
The Clinical Process is Multidisciplinary

Multi-disciplinary education regarding the clinical value and workflow is essential



Evolving Test Technology will provide benefits for Patients

Evolution	Benefit for Patients
More mutations identified, defined and linked to treatment	More personalized treatment options available

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Move to Test Panels (such as Next-Gen Sequencing)	More mutations, genes can be tested at the same time speeding time to the "right" treatment

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Development of "Liquid Biopsies" using plasma instead of tissue. These tests will identify circulating tumour DNA and Cells	Invasive tissue biopsy procedures, will be unnecessary and it will be easier (and faster) to monitor mutation changes & (re)occurrence

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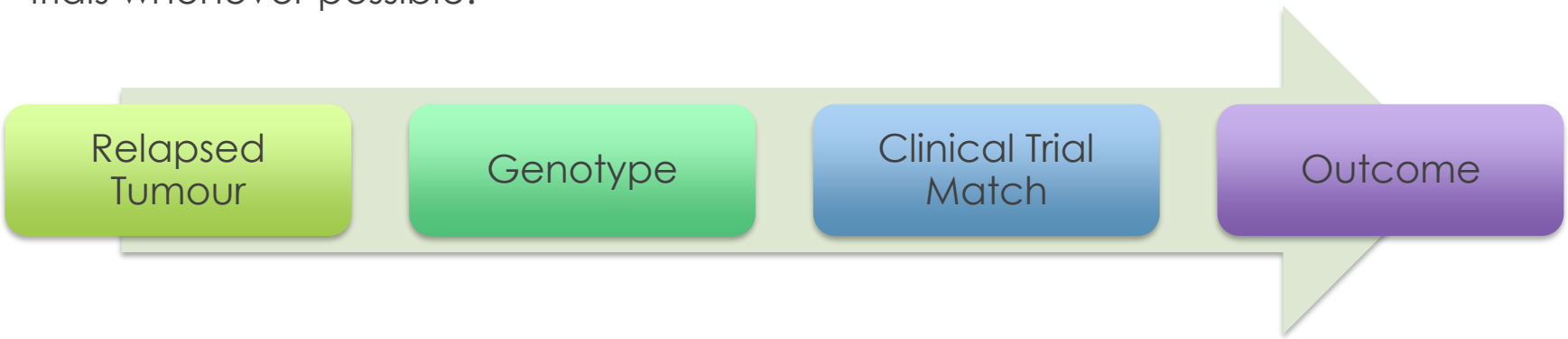
The Future : A Patient's Genotype will direct their Treatment

Main Goal: to decode the genome of an individual patient's cancer and use the information to direct the patient's treatment toward targeted therapy clinical trials whenever possible.



Current examples in Canada:

- The BC Cancer Agency's Personalized Onco-Genomics (POG)
- Mount Sinai Sarcoma Genotyping Program
- PMH IMPACT/COMPACT trial

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Regulation and Reimbursement: Policy Direction

Regulation and Assessment occurs at National and Provincial levels:

- Current "Action" is at the provincial level

Goals

- Concurrent approval of Rx & CDx
- Concurrent reimbursement of Rx & CDx
- Consistent laboratory quality

Challenges

- Independent and variable Rx/CDx review processes
- De-centralized CDx/lab decision-making
- No national laboratory standards

Proposed Solutions

- CADTH has proposed a new assessment process
- Health Canada - Align provinces to a laboratory quality standard

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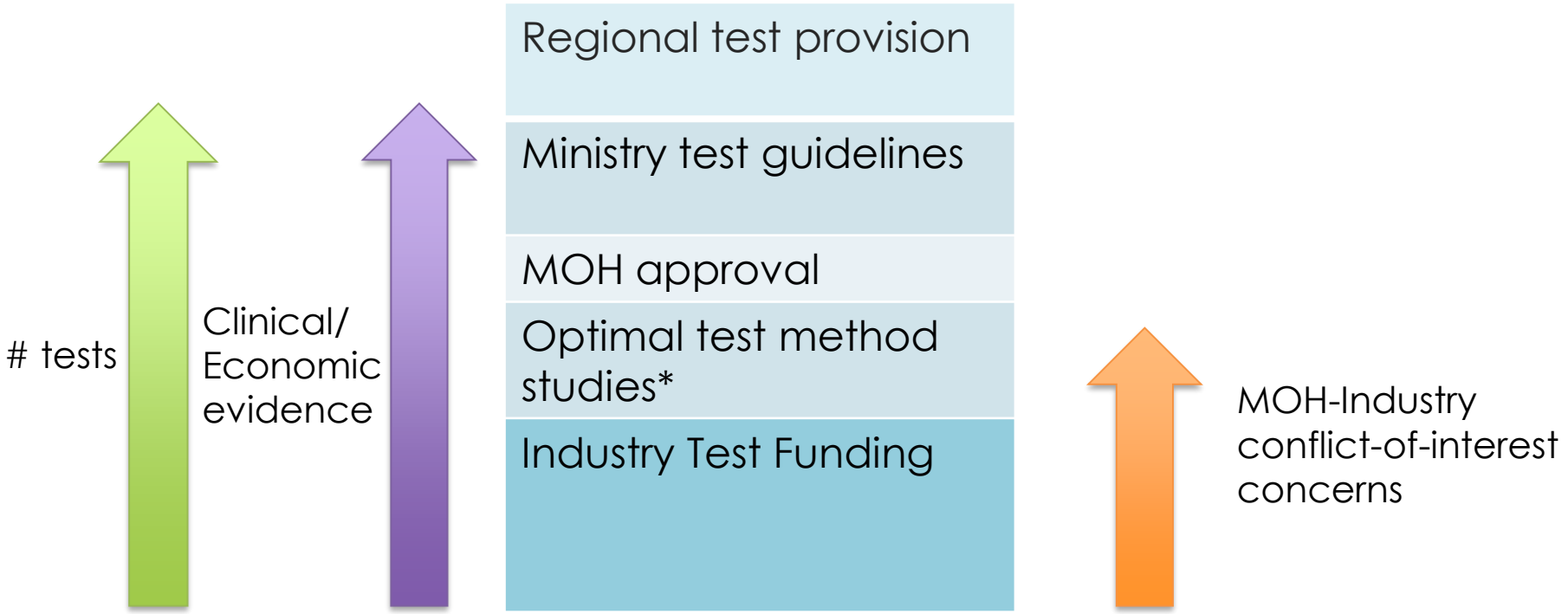
Adoption-Reimbursement of new CDx Tests



*example- Her2

- Every province different; distinct from Rx process
- Review time 8-18 months

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Patient Access Barriers

- Funding for biomarker testing is not aligned (much slower) with drug approval: slows access for patients to new therapies which are dependent on biomarker results
  - Initially funding may be dependent on the Pharmaceutical Industry
  - CADTH (pCODR) is leading an effort to align drug and CDx assessment and reimbursement

- Regulation of CDx is a provincial responsibility and so Regulatory and Reimbursement processes are variable across the country
  - Lab quality thresholds, genetic expertise and test availability varies by province
  - The lack of reimbursement alignment leads to inconsistent availability of the biomarker test and new therapies across Canada.

- Clinician adoption of biomarker testing.
  - 2015- 29% of Canadian NSCLC patients were not sub-typed prior to therapy*
  - Broader education is needed regarding clinical value of Precision Medicine

- Limited patient education resources available

*Abstract at 2015 European Lung Cancer Conference Geneva, Switzerland

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