Precision Medicine

Theory and Practice

MEDICAL
A DICTIONARY WITH AUTHORITATIVE SPELLINGS AND DEFINITIONS IS A PAR
RESOURCE IN MEDICINE, WHERE A MISSPELLING OR MISUNDERSTANDING CAN HAVE
PEOPLE UNDER CARE.

Webinar Content

- Definition of Precision Medicine
- How it works
- Evolution of the technology
- Current use of the technology
- Development pipeline
- Financial and practical issues that employers face

Background

The Technology: Definitions, Technologies, and History

What is Precision Medicine?

According to the Precision Medicine Initiative, precision medicine is "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person."

What Does this Mean?

In the real world, There is a spectrum of strategies and technologies included in this healthcare domain:

- Tailoring program support to an individual's family history, health status, and lifestyle is generally called "**Personalized Medicine**". Examples include Population Health Management and biometric screening programs.
- In the medical community, **Precision Medicine** implies genetic profiling to select from existing therapies, or genetic engineering to produce new biologic treatments tailored to an individual's (or a cancer's) specific gene profile.
- The cost implications of Personalized Medicine are low. For Precision Medicine, they are staggering! **Most of the action is in cancer care.**

The Impact of Precision Medicine

Precision Medicine is a truly disruptive technology.

- It has profound implications for individuals with a number of diseases that had few effective treatment options in the past. It's societal value is enormous.
- From a healthcare perspective, it is dramatically changing the way health risks are defined, diseases are diagnosed and classified, and how they are treated.
- Most importantly, it is now and will increasingly stress our system of financing health care. The very high and unpredictable costs of some of these emerging treatments has transformed risk projection.

Mapping the Human Genome

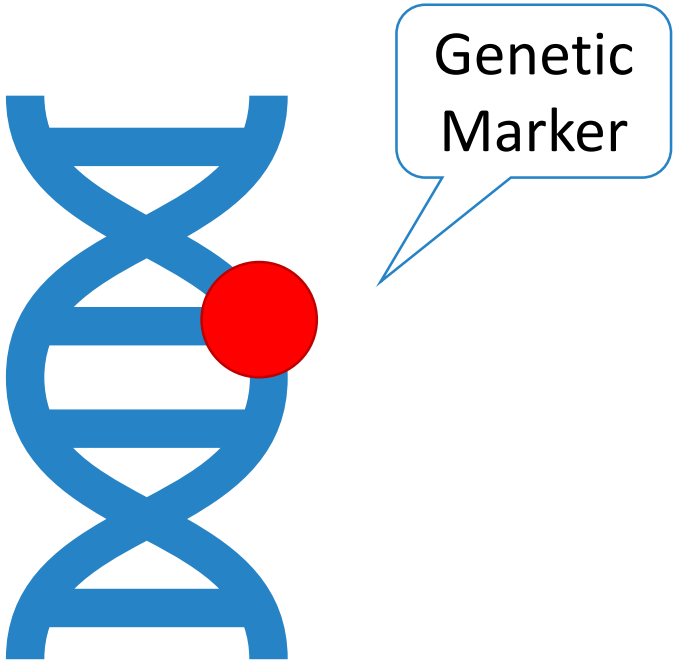
The pivotal event that enabled Precision Medicine was the completion of the 15 year long International Human Genome Project in 2003. The project mapped all 300 billion genes in human DNA. With the sequence in hand, the next steps were:

- to identify the genetic variants that increase the risk for diseases like breast cancer or elevated cholesterol;
- To identify specific genes associated with important diseases like cystic fibrosis or bipolar disorder; and,
- To develop technology to determine the genetic profile of a specific individual's cancer cells.

Accelerating Technology

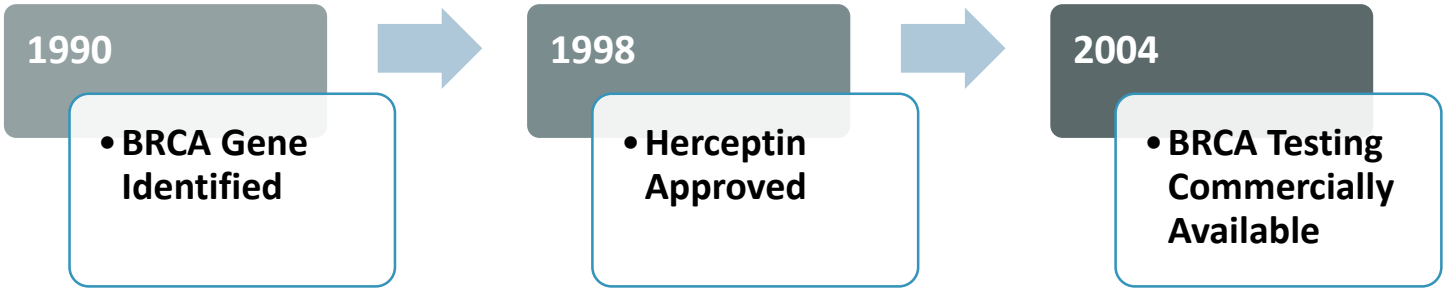
- **Research into identifying clinically useful target genes for diseases or patient-specific cancer cells began in the 1990's.**
- **Drugs design to suppress cancer genes appeared in the late 2000's.**
- **Biologics designed to "kill "cancer cells began entering the market in the late 1990's.**
- **The first two drugs (Kymriah and Lescarta) using CAR T-Cell technology for genetically amplifying a patients immune system's ability to kill cancer cells (leukemia and lymphoma) were FDA approved in 2017.**

Drug Targeting



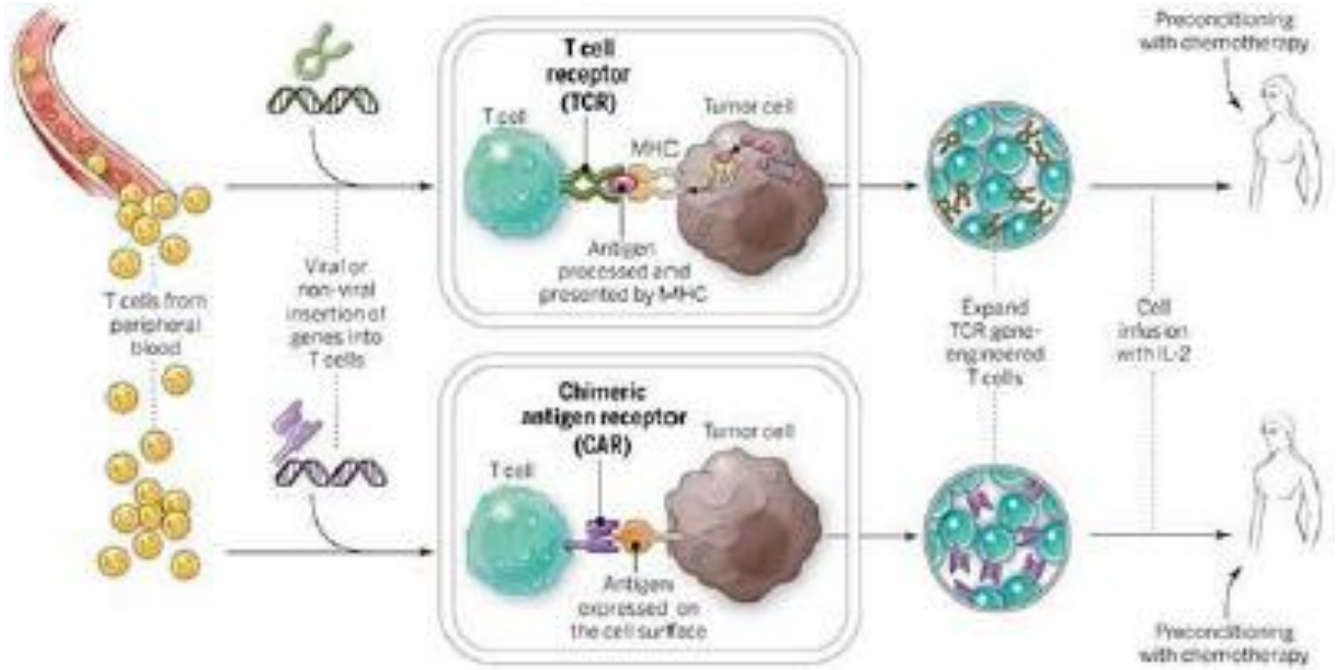
Abnormal genes are identifiable in many diseases (especially cancers). Presence of a genetic marker aids in both drug development and treatment selection.

An Early Example: The BRCA Gene



- **Women with the BRCA Gene Have a 60% risk of developing breast or ovarian cancer in their lifetime.**
- **If BRCA+, are often choosing to undergo prophylactic mastectomy (Angelina Jolie).**
- **Women with BRCA+ breast cancer are treated with Herceptin ($70,000) per treatment cycle).**
- **Genentech notified hospitals that the drug could only be purchased through it's specialty drug distributors.**
- **Biosimilar approved in U.S. in 2017.**

CAR T Cell Technology



The simple version:

1. The patient's own immune cells are harvested.
2. Viral genes are inserted into these cells to amplify immune function.
3. Millions of cells are grown in the laboratory.
4. The patient is "pre-conditioned" with chemotherapy.
5. The CAR T cells are infused back into the patient.

The Devil is in the Details…

The Good News:

- Biologics and CAR T technologies can treat or cure diseases that previously had few treatment options.
- The biologics and CAR T development pipelines are robust.
- The FDA approval process for "breakthrough" drugs has been accelerated. Drugs are now being approved in twelve to eighteen months.
- Indications for existing drugs are being expanded.

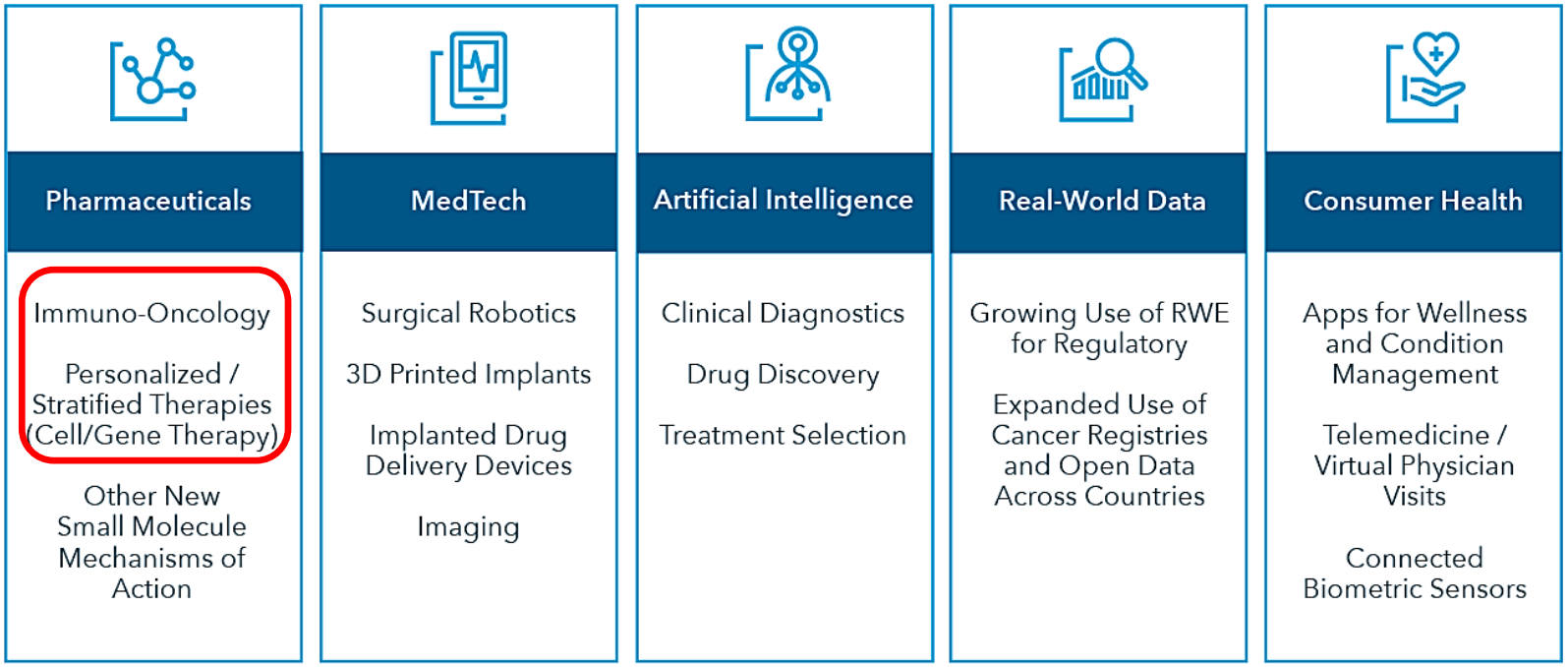
The Bad News:

- The cost. For example, a course of CAR T therapy costs around a million dollars ($600,000 in drug costs and $400,000 for hospital costs). Costs for non-CAR T drugs can also be as high as a million dollars annually (Soliris).
- Manufacturers are restricting distribution channels and resisting calls for lower pricing.

The Market

Technology Adoption and Market Impact

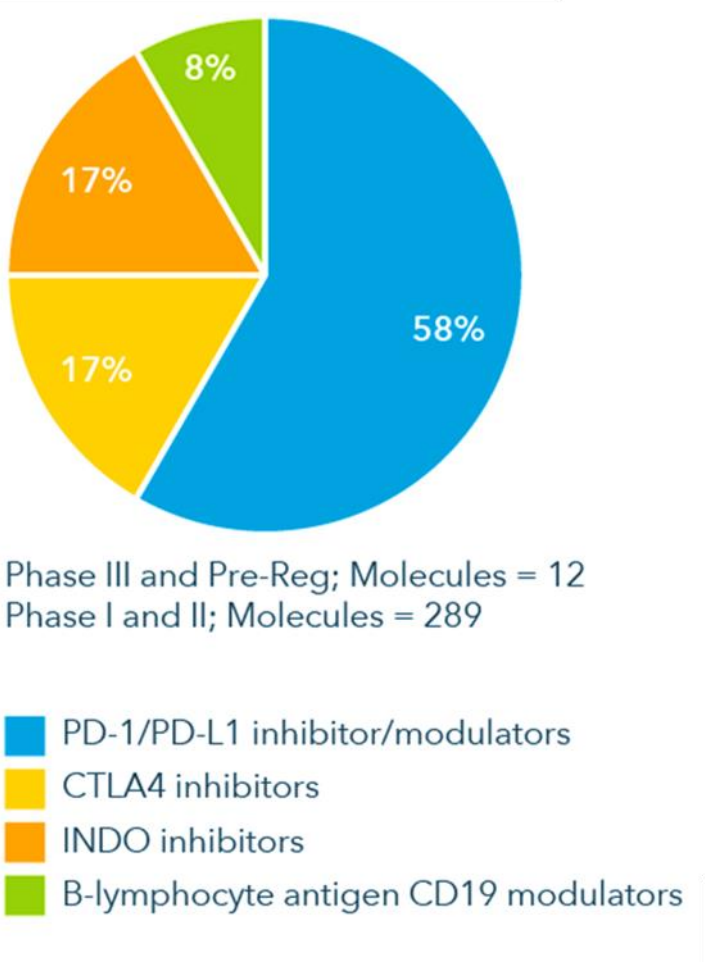
Technology Drivers: Cancer Care



Source: IQVIA Real World and Analytics Solutions, Mar 2018

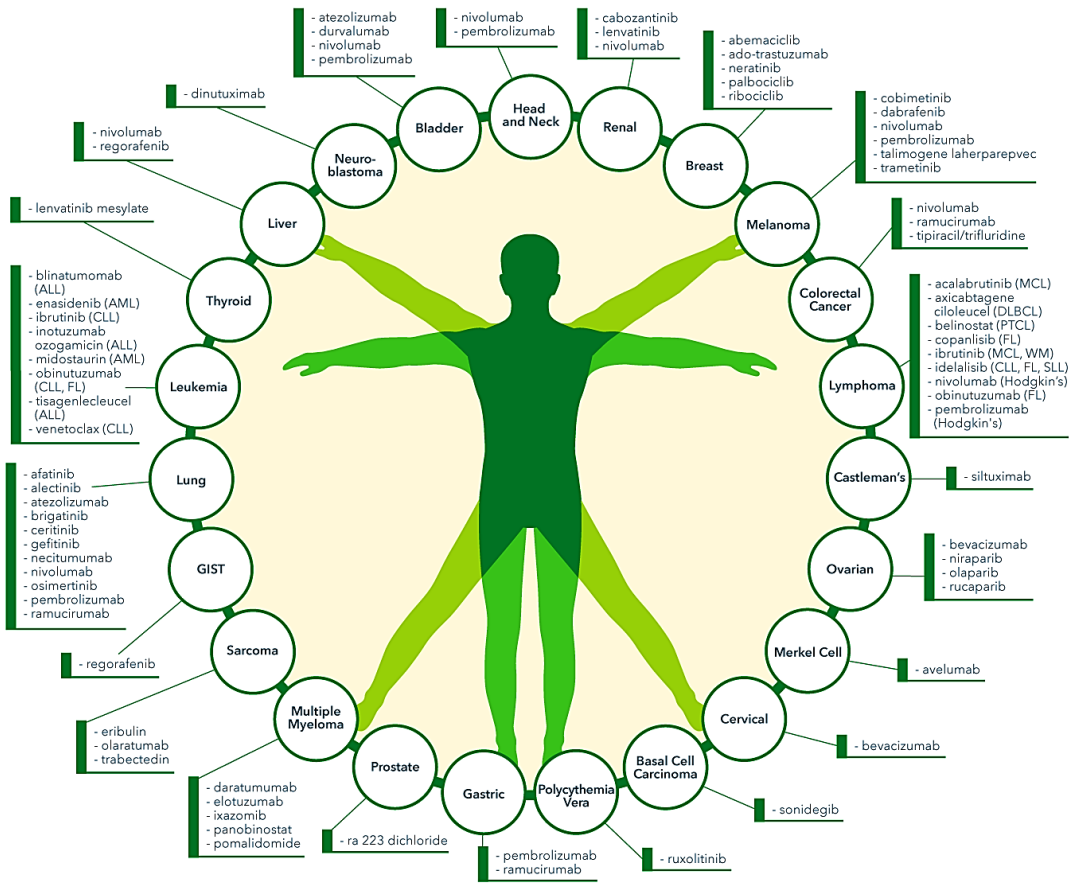
Report: Global Oncology Trends 2018: Innovation, Expansion and Disruption. IQVIA Institute for Human Data Science, May 2018

The Biologics Oncology Pipeline.



There were 301 cancer biologics in the development pipeline in 2017. The majority of them are in early trial phases implying that biologic releases will accelerate.

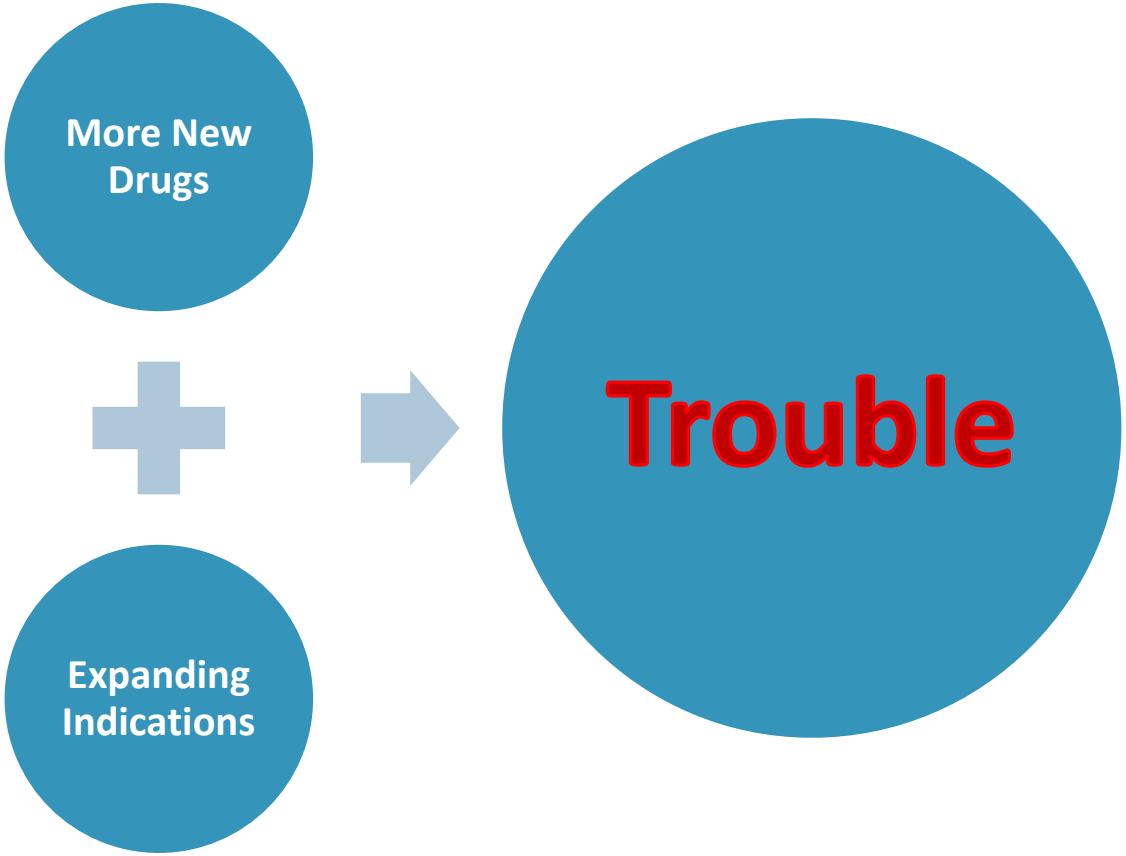
Expanding Indications



Source: IQVIA, ARK R&D Intelligence, Apr 2018; IQVIA Institute, Apr 2018

There were approvals for more than fifty cancers in 2017.

The Potential Disaster…



Risk Mitigation

- The synergy of expanding indications for existing drugs and accelerating new drug releases will result in double digit therapeutic class cost increases for the foreseeable future.
- There are two categories of risk:
- First, there will be an increasing number of members requiring long-term or lifelong treatment with expensive biologics. Forward costs for these members are predictable and represent an annual fixed cost for the plan.
- Second, the “struck by lightning effect” stemming from the appearance of a member requiring CAR T or a similar treatment. It is impossible to forecast this risk.

Risk No Good Answers…

The group market and risk-bearing entities in it are not structured to deal with these emerging volatile and extraordinary costs.

The risk is highest for small self-funded groups (stop-loss lasers and renewals). Fully-insured groups will experience major renewal increases, but do not run the risk of lasers.

What are the options?

- Establishing a long-term relationship with a stop-loss carrier may help.
- Increasing member contribution by changing drug copays and coinsurance is not realistic.
- Manufacturers patient subsidy programs (coupons or grants) cannot be relied upon.
- International drug programs can be effective, but generally only work for oral drugs.