Memorial Sloan Kettering
Cancer Center™

Lessons Learned from AACR Project GENIE to Inform Evidence Generation

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DISCLOSURES

Board of Directors of Novartis

Co-founder of ORIC Pharmaceuticals

Co-inventor of enzalutamide and apalutamide

Science advisor: Arsenal, Beigene, Blueprint, Column Group, Foghorn, Housey Pharma, Nextech, KSQ and PMV

Framing Comments

Cancer is a hundreds of smaller diseases - defined by mutations.

Efficient development of precision oncology drugs requires knowledge of clinical outcomes in genomically annotated patients.

GENIE was founded on the principle that this knowledge is pre-competitive, much like basic science, and should be freely accessible for drug development and drug discovery research.

Clinico-genomic data registries require stewardship to ensure responsible use of the data and protection of patient privacy.

TOWARD PRECISION MEDICINE

Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease

Committee on A Framework for Developing a New Taxonomy of Disease

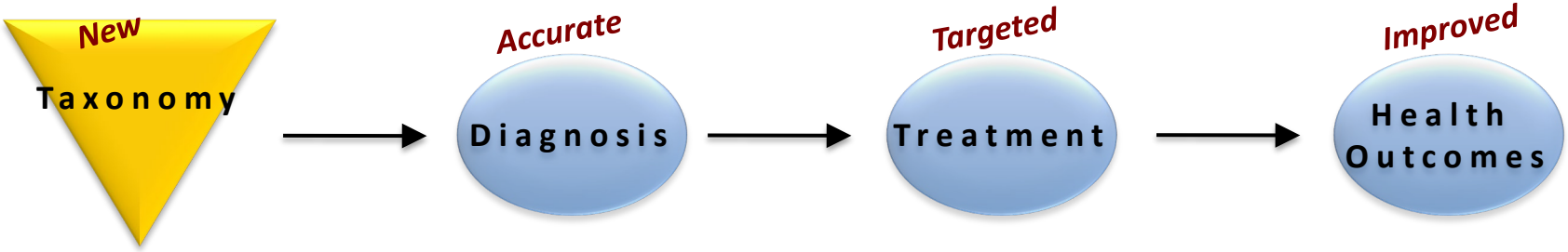
Board of Life Studies
Division on Earth and Life Studies

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

published in 2011

Co-chairs: Susan Desmond Hellman, Charles Sawyers

Guiding Principle



Diagnosis is the foundation of medicine.

Accurately and precisely defining a patient's condition does not assure effective treatment, but it is unequivocally the place to start.

Project GENIE Beginnings

Launched in 2015 with startup capital from AACR

Eight cancer centers with preexisting investment in clinical sequencing infrastructure agreed to aggregate genomic and clinical data.

Harmonized the custom sequencing panels at each center on the backend (through SAGE BioNetworks)

Started with a modest number baseline clinical data elements, including uniform pathologic annotation of tumor type (using OncoTree)

AACR
American Association for Cancer Research
FINDING CURES TOGETHER™

PROJECT GENIE
Genomics Evidence Neoplasia Information Exchange

GENIE TODAY

American Association for Cancer Research
FINDING CURES TOGETHER℠

GENOMICS

- ✓Somatic Tumor DNA
- ▪Germline DNA
- ▪cfDNA
- ▪RNA Seq
- ▪Epigenetics

PHENOMICS

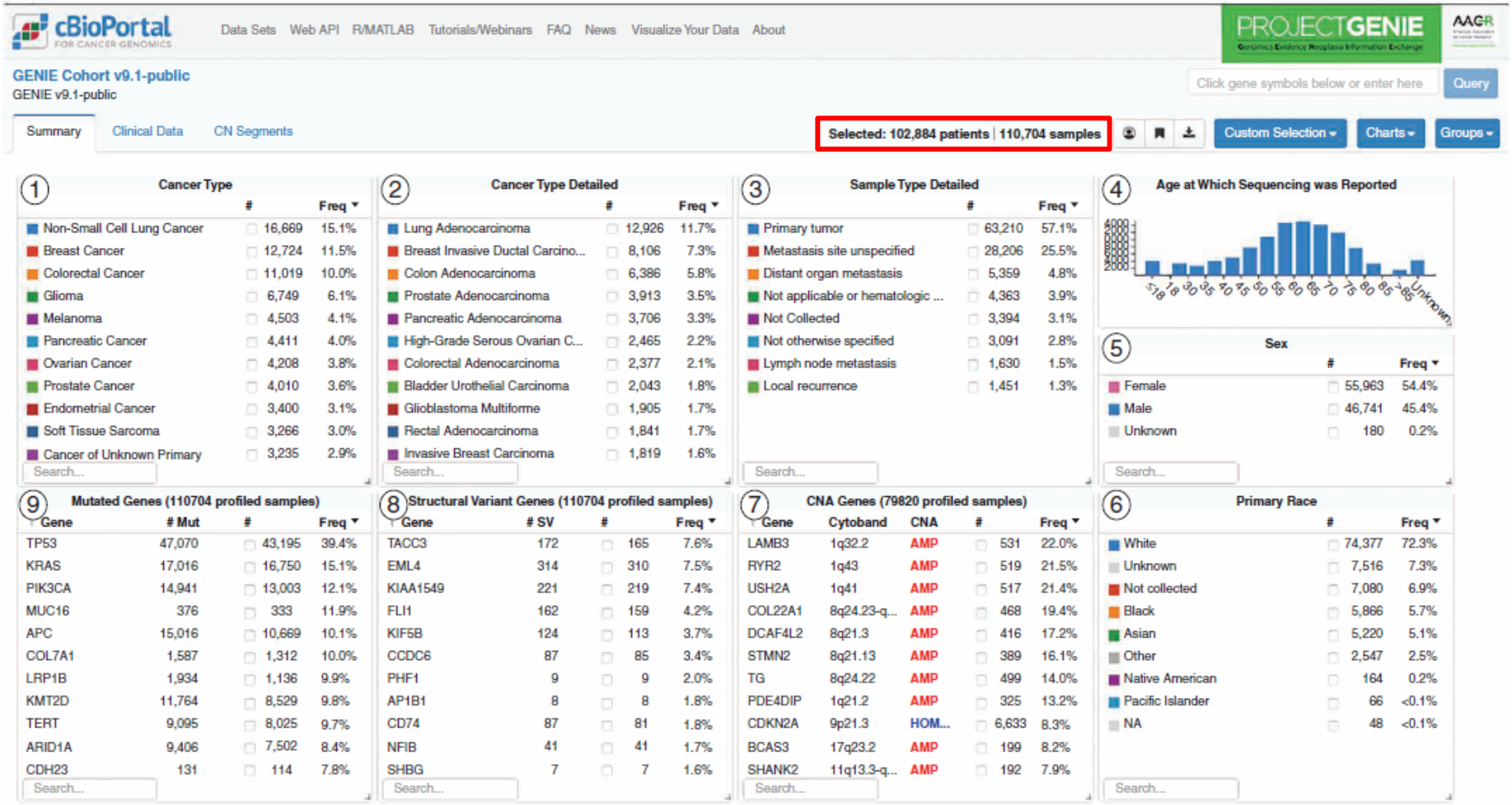
- Tumor type
- Histology
- Demographics
- Vital status
- Medications
- Treatment Outcomes

>148,000 Sequenced Tumors
18 Cancer Centers (expanding to 22)

Data to Drive Discoveries

12,584 registrants; 839 GENIE citations in pubs, abstracts, …

AACR Project GENIE: Open Source Genomic and Clinical Data on >148,000 Patients (and growing)

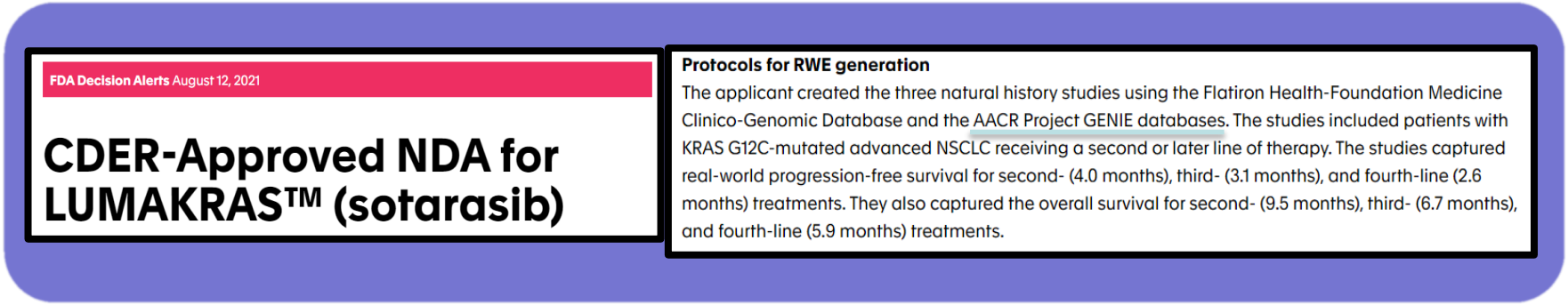


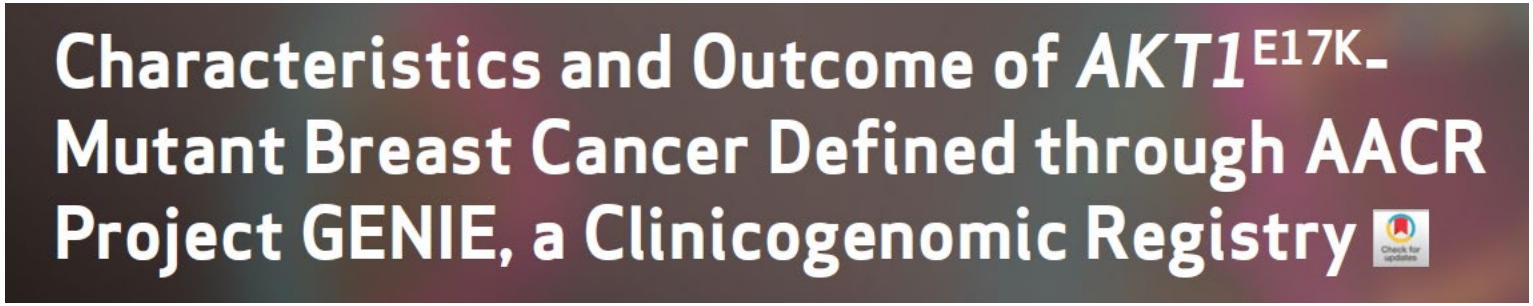
Pugh et al Cancer Discovery 2022

A few GENIE-driven vignettes…

1. Synthetic control cohorts for rare genotype populations

-RAS G12C mutant lung cancer (used in registration package for sotarasib)
-AKT mutant breast cancer
-many others…





Smyth et al Cancer Discov 2020; Scharpf RB et al Cancer Res 2022

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1. Synthetic control cohorts for rare genotype populations

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-many others…

2. Explore race and ethnicity differences in cancer genotypes

-tumor mutation burden
-cancer with unknown drivers

How to improve generalizability of clinico-genomic disease registries?

1. Broaden representation of non-European ethnicities in registries
   - -GENIE is adding four new sites to help address this gap
   - -initiating collaborations with other partners with diverse populations

2. Determine genetic ancestry from sequencing panel data
   - -comparisons with self reported race
   - -opportunities for admixture analysis

3. Address barriers for inclusion of individuals of non-European ancestry
   - -overcome infrastructure needed for informed consent
   - -build trust

Jung C et al, Responsible Open Source Data Sharing for Precision Oncology.
In: A New Deal for Cancer: Lessons from a 50 Year War., 2021.