

Creating a System of Precision Oncology Excellence in the Veterans Health Administration

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Disclosures

Michael Kelley

- Research funding from AstraZeneca, Bristol Myers Squibb, Novartis
- Consultant for IBM Japan
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Matthew Rettig

- Research funding from Novartis, Johnson & Johnson, Merck, Astellas, Medivation, Progenics
- Member of speakers bureau for Johnson & Johnson and Bayer
- Consultant for Constellation Pharmaceuticals

Objectives

- Demonstrate knowledge of the paradigm shift in cancer treatment for Veterans through Precision Oncology.
- Describe VA strategy and future vision for cancer treatment through a Precision Oncology System of Excellence.
- Understand and describe the scope of partner affiliations of the VA National Precision Oncology Program to include:
- Explain how the VA-Prostate Cancer Foundation partnership will establish a System of Excellence for Precision Oncology that will:



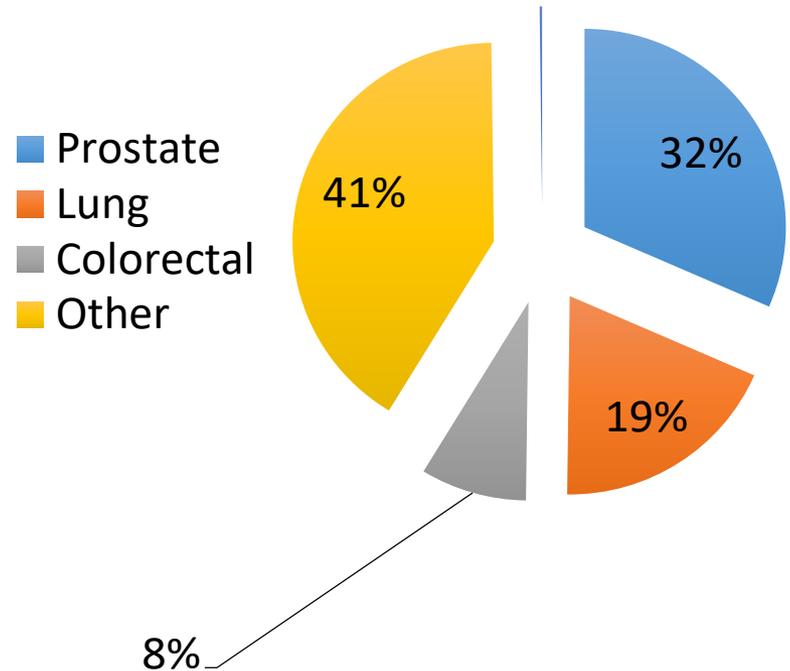
VETERANS HEALTH ADMINISTRATION

VA National Precision Oncology

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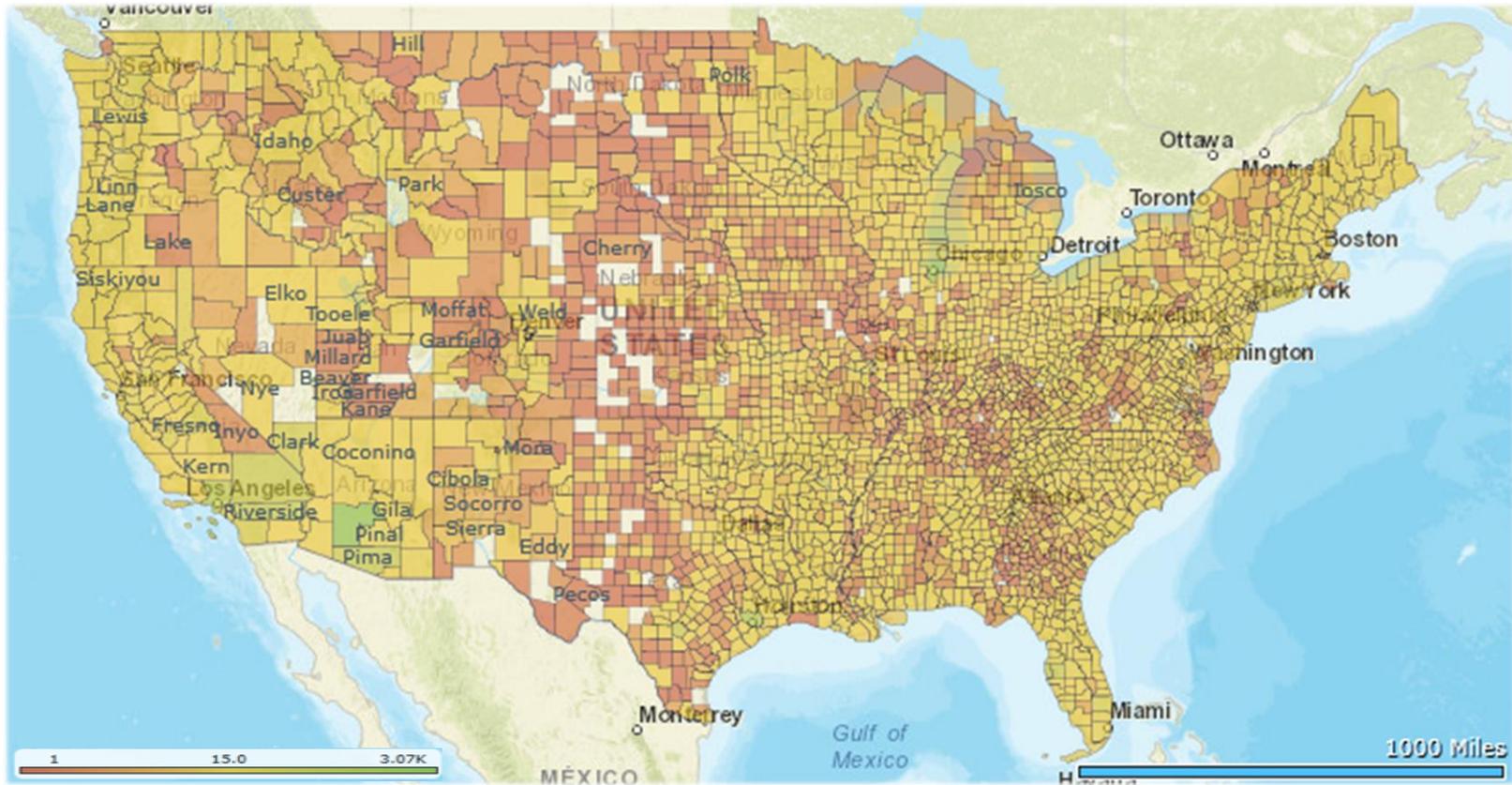
Cancer in VA

- In 2010, 46,166 Veterans in VA were diagnosed with invasive cancer
 - The vast majority (97%) were men
 - The most common non-skin cancers:
 - 19% of these Veterans were black/African American
- VA has a higher cancer incidence rate than the general US population
- 33% live in rural areas (compared to 14% in the general population)



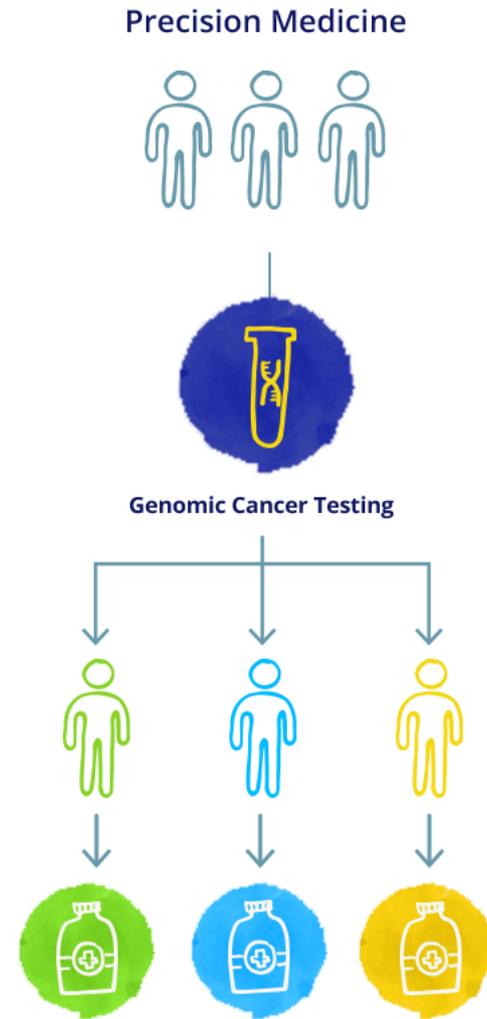
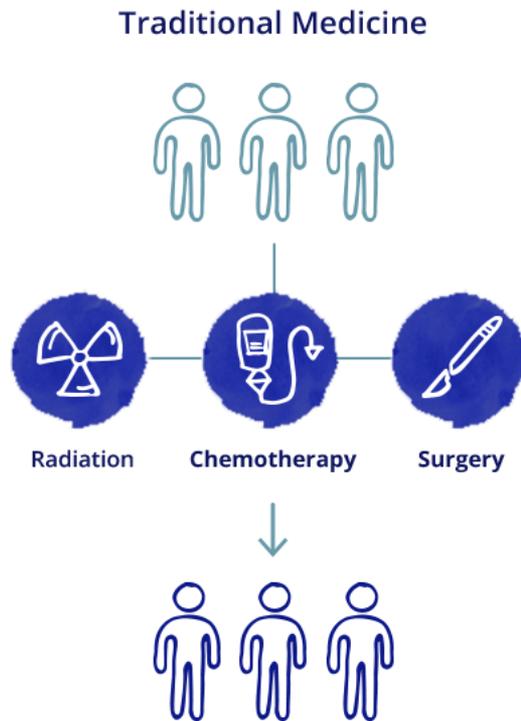
Our Goal

To ensure that all Veterans, no matter where they live, have access to cutting-edge cancer therapy



Geographic distribution of living patients diagnosed since 2000

Transition from Tradition to Precision



What is Precision Oncology?

The right treatment for the right patient at the right time.

Precision oncology:

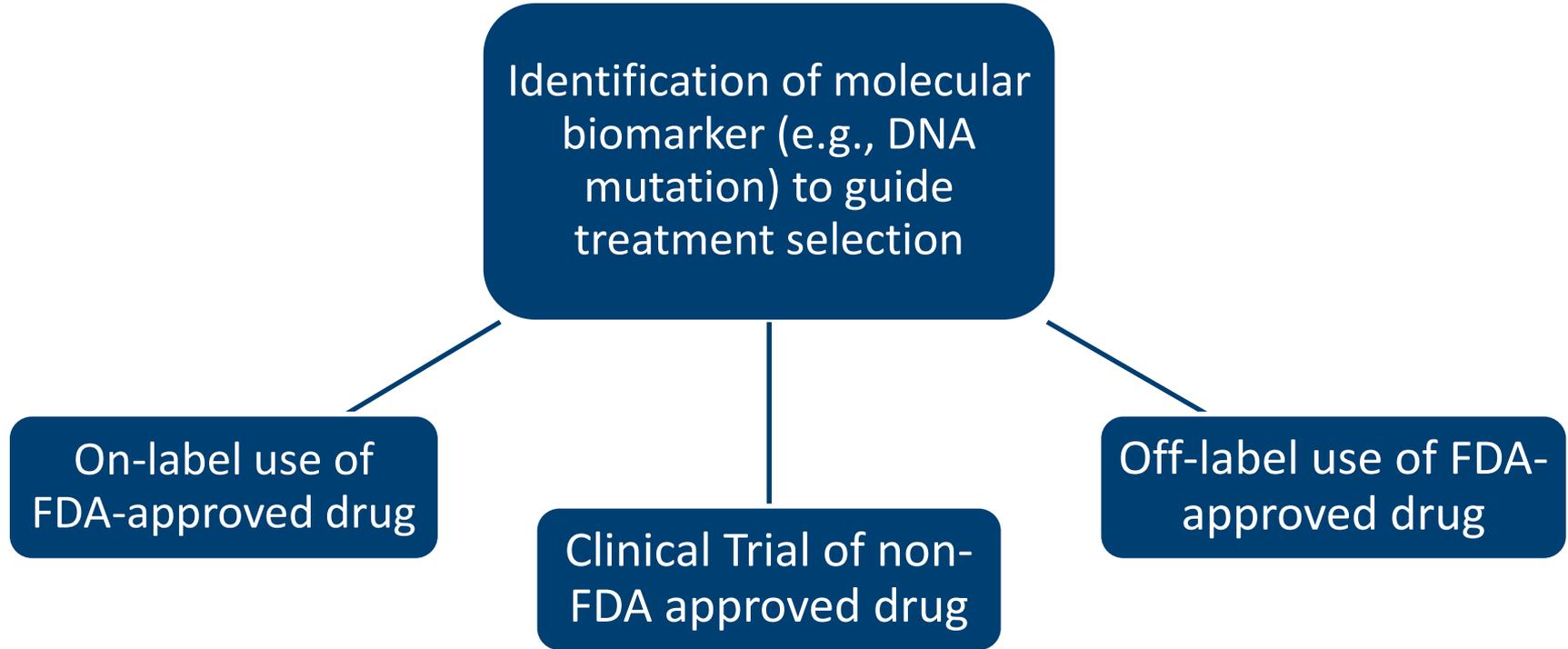
- The evolving understanding of how cancers develop on a molecular level (e.g., DNA mutations and activation of biochemical pathways)
- Development of targeted therapies that reverse cause of cancer
 - Drugs that inhibit activity of proteins that are activated by mutation or gene expression
- Can ultimately lead to better patient outcomes

Research questions we hope to answer:

- Why does one patient do better than another even though they both have the same type of cancer?
- What molecular makeup of tumors make a difference?
- Is the answer contained in their personal genetic mutations?



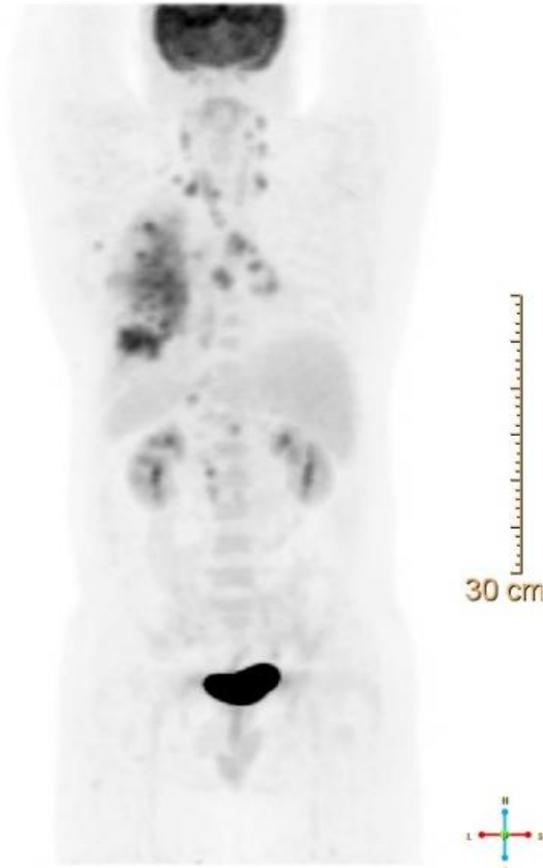
How Precision Oncology Works



VA initial emphasis

- Metastatic prostate cancer
- Lung Cancer

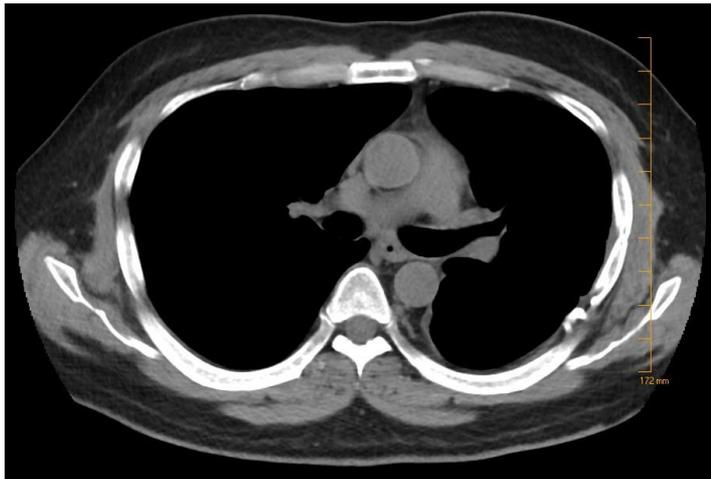
Veteran Case Study



Baseline PET scan, showing widespread metastases

- Army Veteran in his 40s
- Parent of two young children
- Never smoker
- 8 month history of progressive shortness of breath, cough, and weight loss
- Diagnosed with metastatic lung adenocarcinoma in 2016
- Genetic testing for mutations in the EGFR and ALK genes was normal
- Initial treatment with whole brain radiotherapy followed by carboplatin and pemetrexed chemotherapy showed mixed results.

Veteran Case Study



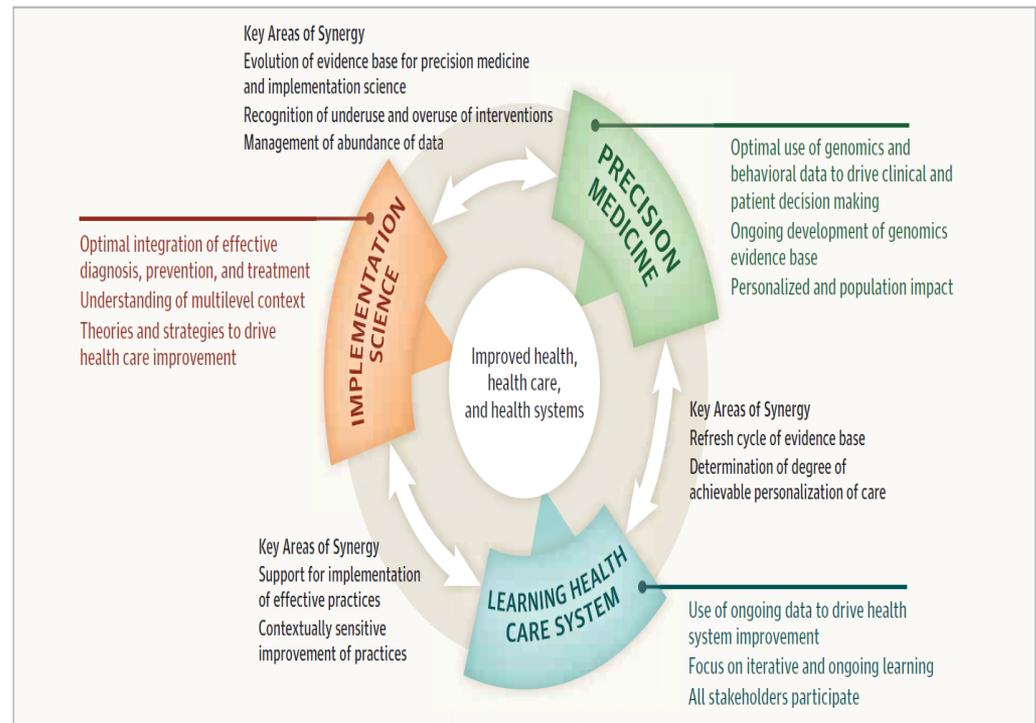
Response to crizotinib between 2 months (top) and 7 months (bottom)

- Next generation sequencing gene panel showed presence of an abnormal fusion between the EML4 and ALK genes, which promotes the cancer
- As a result, in June 2016, chemotherapy was discontinued and oral crizotinib precision therapy was started
- He had an excellent response in all sites and was able to return to work and school
- In July 2017, switched to alectinib for asymptomatic progression in his brain
- In Sept 2019, treated with precision IMRT radiation targeting single brain metastasis as there were no other sites of cancer progression and no cancer-related symptoms.

System of Excellence

- Is Veteran-centric
- Is standardized to adhere to the most up-to-date best practices
- Functions as a high-reliability organization
- Operates at an enterprise-scale, rather than solely a local or regional level
- Innovates and drives innovation
- Precision Medicine
- Implementation Science
- Learning Healthcare System

Figure. Contributions of Implementation Science, Learning Health Care System, and Precision Medicine



Chambers DA, Feero WG, Khoury MJ. Conversion of Implementation Science, Precision Medicine, and the Learning Health Care System, JAMA 2016

VHA National Precision Oncology Program

- Launched in 2016 from regional program whose core service was NGS gene panel DNA sequencing of solid tumor samples
- Standardize molecular testing and analysis across the VA healthcare system
- Define and disseminate Precision Oncology best practices
 - Molecular Oncology Tumor Board
 - Patient-specific consultation service
- Reduce disparities e.g. rural health disparities
- Generate knowledge on effective, and conversely ineffective therapies
- Understand cost and effectiveness of using molecular testing to guide treatment decisions
- Increase opportunities for clinical trial participation
- Completed over 10,000 samples as of November 2019
 - Nearly all VA oncology practices
 - Equal utilization for rural Veterans
 - Results utilized to apply new information (e.g., larotrectinib)
 - Clinical trial eligibility



Applied Proteogenomics Organizational Learning and Outcomes (APOLLO) Consortium VA/DoD/NCI

- Biological information flow: DNA -> RNA -> protein
- Research question: how can information from proteins improve cancer care?
- Proteins more complex than DNA & RNA
- Simple protein analyses already utilized (e.g., ER in breast cancer)
- Sophisticated multiplex protein analyses now available and clinically feasible
- The APOLLO collaboration examining questions of biology, prognosis, and treatment
 - Breast, Prostate, Lung, Ovarian cancers
 - Tissue banking
 - Multidimensional clinical information
 - Poised for rapid clinical application



Pharmacogenomics Action for Cancer Survivorship (PHASeR)

- 1 in 3 Veterans is prescribed a medication that is affected by their genetic makeup.
- 90% of Veterans are estimated to have genetic mutations that affect their response to one or more drugs (Chanfreau-Coffinier et al JAMA Network Open 2019).
- Antineoplastic agents impacted, e.g., 5FU in GI cancers
- Partnership between VA and Sanford Health Care in Sioux Falls, SD
 - \$40 million of in-kind germline genetic testing
 - \$10 million to VA for widespread implementation
- DNA testing for common, actionable genetic variants in 8 genes that are known to affect a person's response to a drug
- Outcomes: operational, utilization and impact on prescribing, efficacy, toxicity and cost-efficacy in VHA



Tele-Oncology

- Problem: misalignment of supply of (urban) and demand for (rural) oncologists
- Primary Goal: Improve access to care for Veterans with cancer, including timeliness of cancer care
- VA has well-developed telehealth resources, including national services for radiology, genetic counseling, and Tele-ICU
- Institute Virtual Cancer Center(s) similar to NCI-designated Comprehensive Cancer Center
 - Providers with specialization in patient's cancer type & involved in research
- Improve efficiency and precision of clinical practice
- Initial focus on Medical Oncology in context of multidisciplinary care
- Targeted service areas
 - Smaller VA medical centers
 - Larger VA medical clinics (health care centers)
 - Smaller VA medical clinics (community-based outpatient clinics)
 - Non-VA location, including Community partners and patient's home



A call to action

- Spread the word about VA's Precision Oncology System of Excellence
- Contribute to the Culture of Excellence in VA
 - VA Providers and Staff
 - Medical Education
 - Volunteer for VA
- Partnerships in Core Care Delivery Areas
 - Tumor gene sequencing
 - Molecular Tumor Board
 - Clinical Pathways
 - TeleOncology to rural areas
 - Health Informatics
- Research and Discovery
 - Clinical Research
 - Access to new drugs and diagnostics
 - Funding for clinical trials
 - Health Outcomes & Real-World Data
 - Novel analyses
 - Computing resources

Precision Oncology Program in Prostate Cancer (POPCaP)

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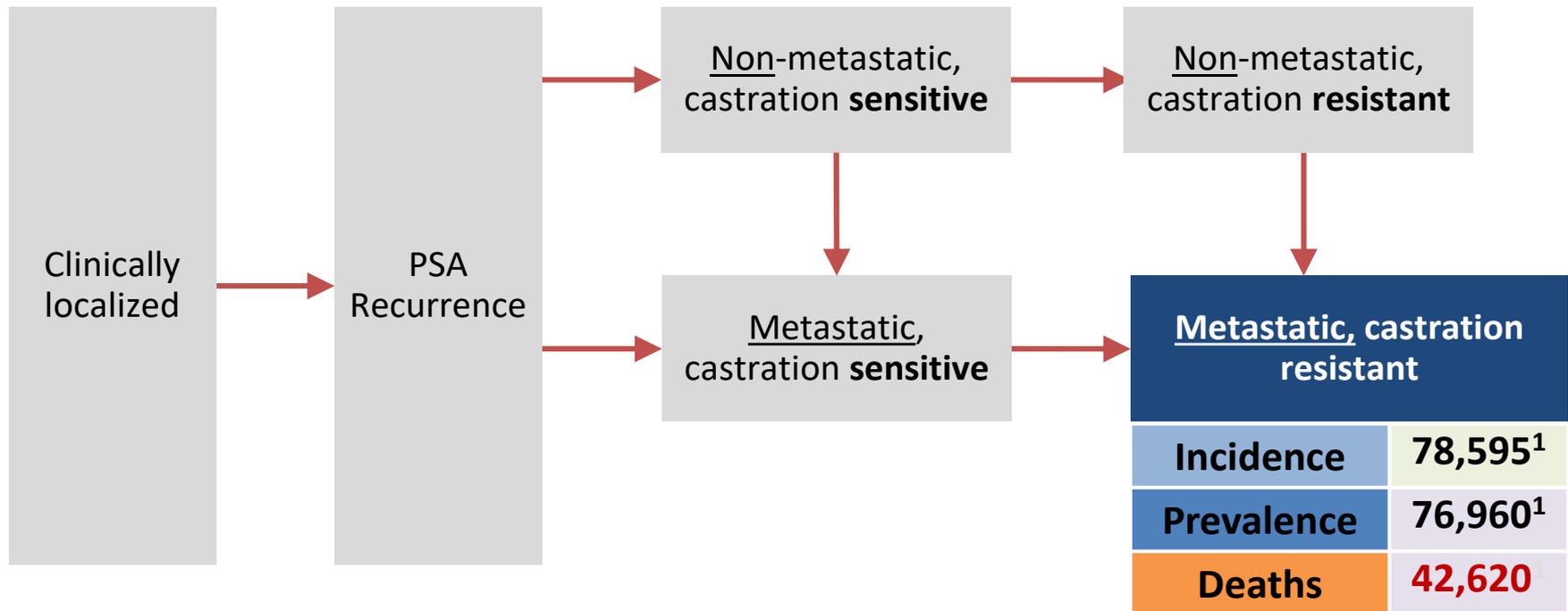
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Facts about prostate cancer



¹Scher et al. *PLOS ONE*. 2015.

Note: Epidemiology data for US only

What is POPCaP

- Precision Oncology Program for Cancer of the Prostate: Goal is to deliver precision oncology to all Veterans with prostate cancer.
- Partnership between VA and Prostate Cancer Foundation (PCF) to create system of excellence for prostate cancer in VA
 - MOU signed by Secretary in November 2016
 - Funding by PCF began in April, 2018 (\$50M over five years)
 - Clinical emphasis on advanced prostate cancer
 - Catalyzed the VHA-supported initiative to create a precision oncology system of excellence, with VHA funding beginning in FY20
- Consists of:
 - Network of VA medical centers with capacity to perform precision oncology
 - Coordinating center
 - Data core



Next Generation Sequencing (NGS) of DNA

- A central premise of POPCaP network is biomarker based management.
- Results of next generating DNA sequencing of all Veterans with metastatic prostate cancer is the seminal biomarker.
 - Germline (DNA from non-cancer cells): **10-12% of patients have hereditary cancer syndrome!!!!**
 - Somatic (DNA from cancer cells)

How do we apply precision oncology to ALL Veterans?

1. Increase number and geographic distribution of POPCaP centers.
2. Leverage EMR and VA informatics infrastructure to identify all patients with prostate cancer
 - Patient demographics: location, age, provider, etc
 - NGS results
 - Does patient have a pathology specimen in VA?
 - Disease specific characteristics
 - Stage
 - Treatment history
3. Increase provider and patient awareness of POPCaP and potential of NGS

1. Increase Number of POPCaP Centers of Excellence

Calendar Year 2019 Map



2. Identify all patients with metastatic prostate cancer: Role of the Data Core

VA Medical Center

- Clinic notes
- Pathology reports
- Radiology reports
- Lab values

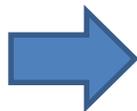


Corporate Data Warehouse (CDW)
Austin, TX

Q: Data Core: How do we Identify All Veterans with Prostate Cancer?

A: Natural Language Processing

'castrate resist',	Semantic Variants
'castrate resistant',	'osseous',
'castraion resistant',	'osteoblastic',
'castrate resistance',	'osteolytic',
'castration resist',	'oligometastatic'
'castrate',	'blastic'
'castrat',	Osseous - Lexical
'castrate naive',	'osseus',
'hormone',	'osseous',
'hormone refractory',	'oseous',
'hormone sensitive',	'oseos',
'hormone sensitive',	'ossious',
'castration - resistant'	'osseious',
	'osseous',
'diffuse',	'osseous',
widespread,	'osseos',
'grossly stable',	'ossous',
'extensive',	'ossoeus',
	'osseuos',
'hx',	Osseoblastic -
'history',	Lexical
'pmh',	'osteblastic',
'pmhx',	'osteoblastic'
'h/o'	



Example Complete Cases Output:

1. Pt with metastatic prostate cancer
2. Hx of prostate ca with mets
3. Diagnosis: Castrate-resistant Metastatic Prostate Cancer
4. Pt w/ osseous metastatic disease
5. Hematological: history of prostate cancer with mets to bone

Diagnosis
Metastatic
Cancer Term
Descriptor
Anatomy
Catrate resistant

Prostate Cancer in VA since the advent of the Electronic Medic Record

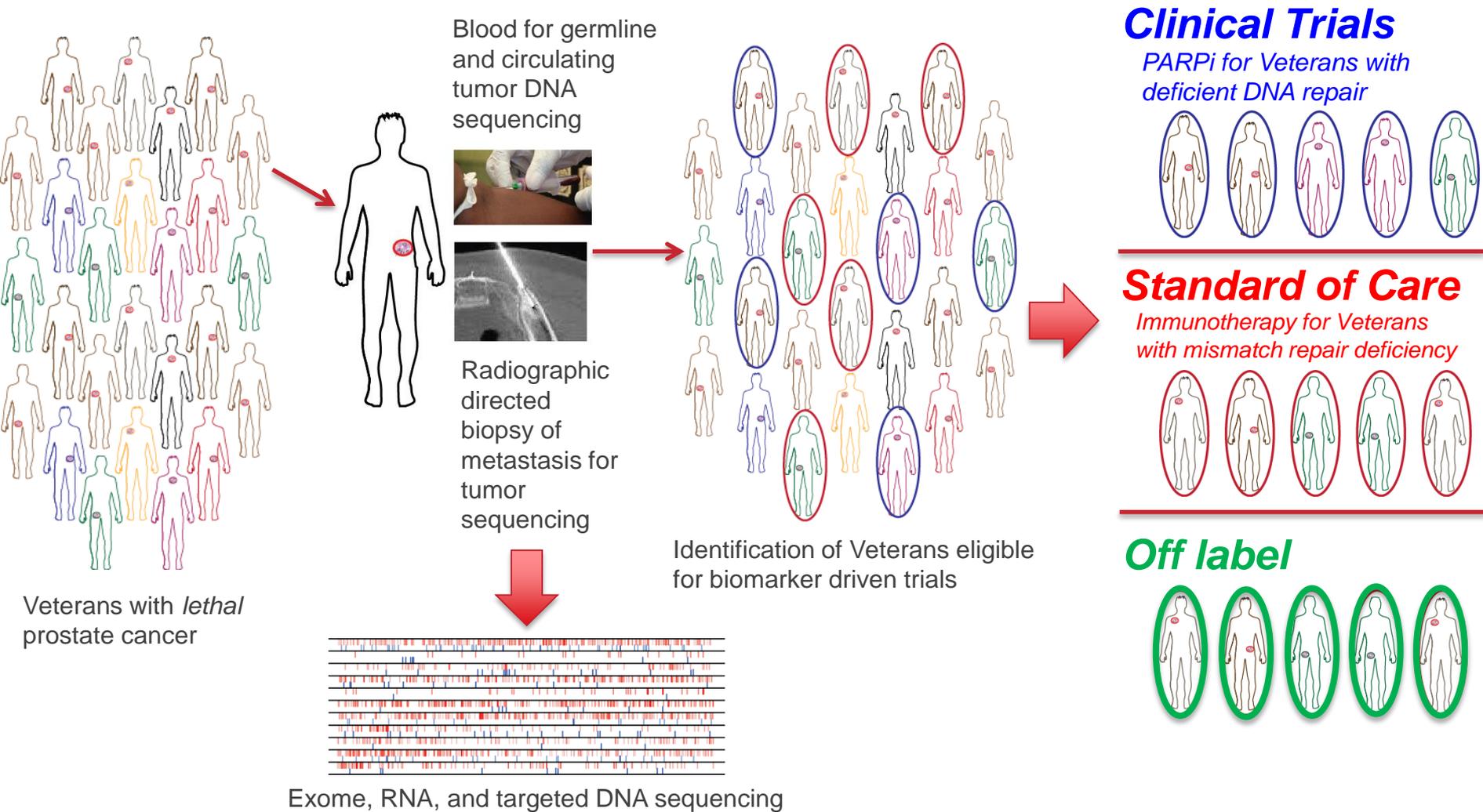
Deceased	Living	Non-metastatic	Metastatic	Living metastatic
592,153	488,984	1,017,915	63,222	16,618

PPV of NLP algorithm for identifying metastatic prostate cancer = 0.975

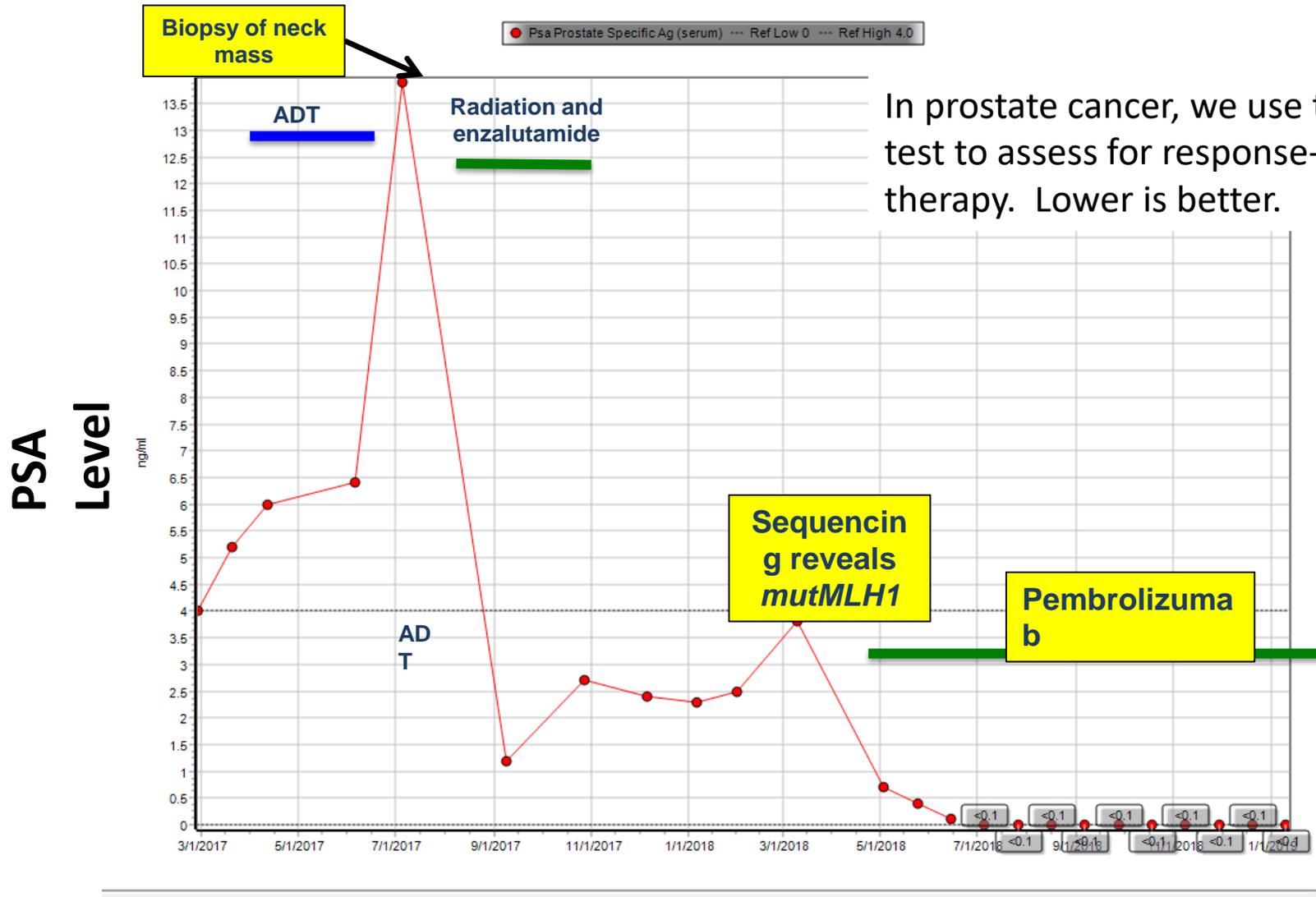
3. Increase Provider and Patient Awareness

- Use data core to identify biomarker positive patients with metastatic prostate cancer.
- Increase geographic distribution of POPCaP centers
- Provide travel support for Veterans to seek precision oncology clinical trials at nearest POPCaP Center
- Increase awareness
 - Provider awareness
 - Patient awareness
- Ongoing education

What are the specific clinical strategies to deliver precision oncology?

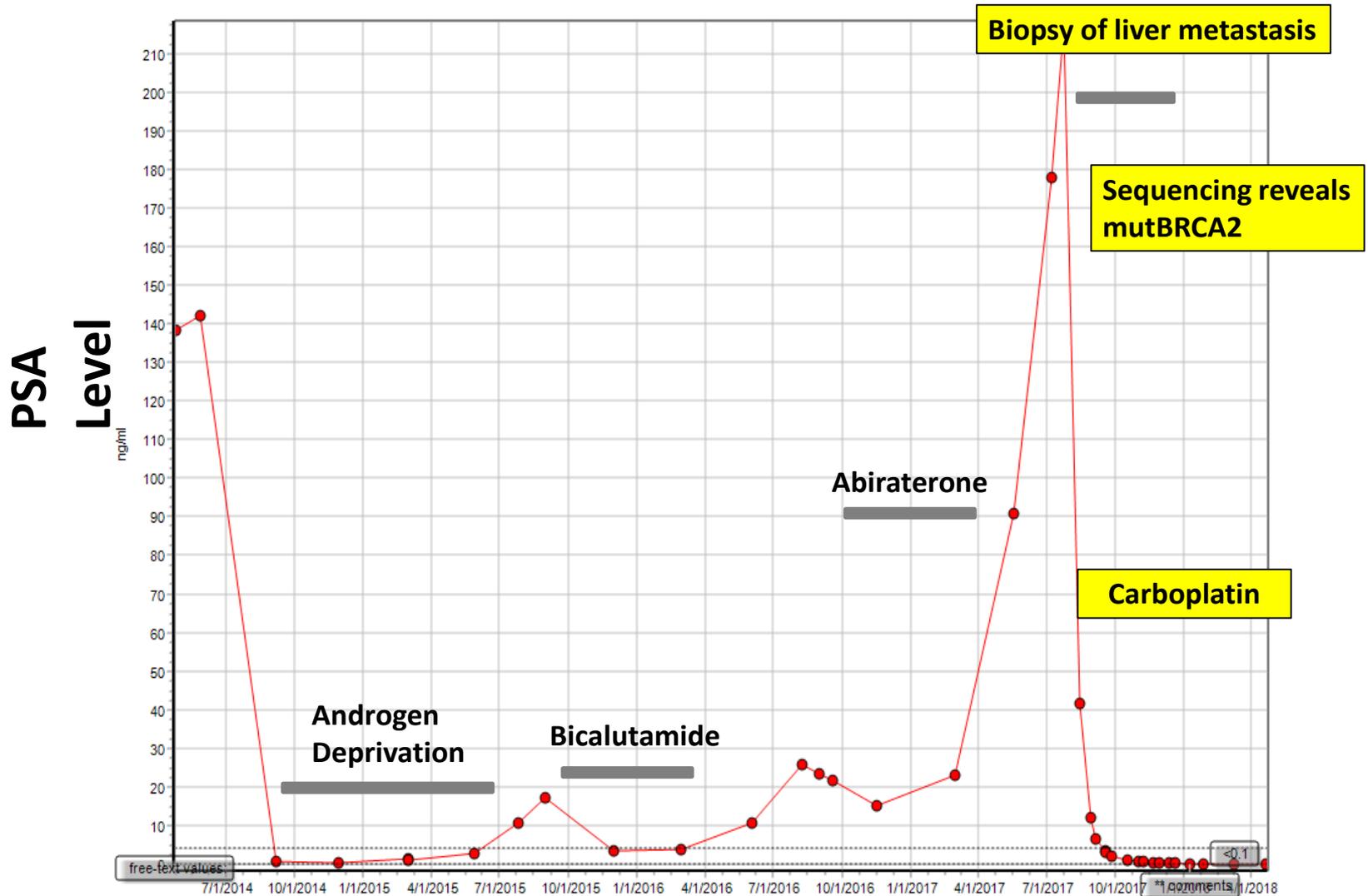


1. Standard of Care Therapy

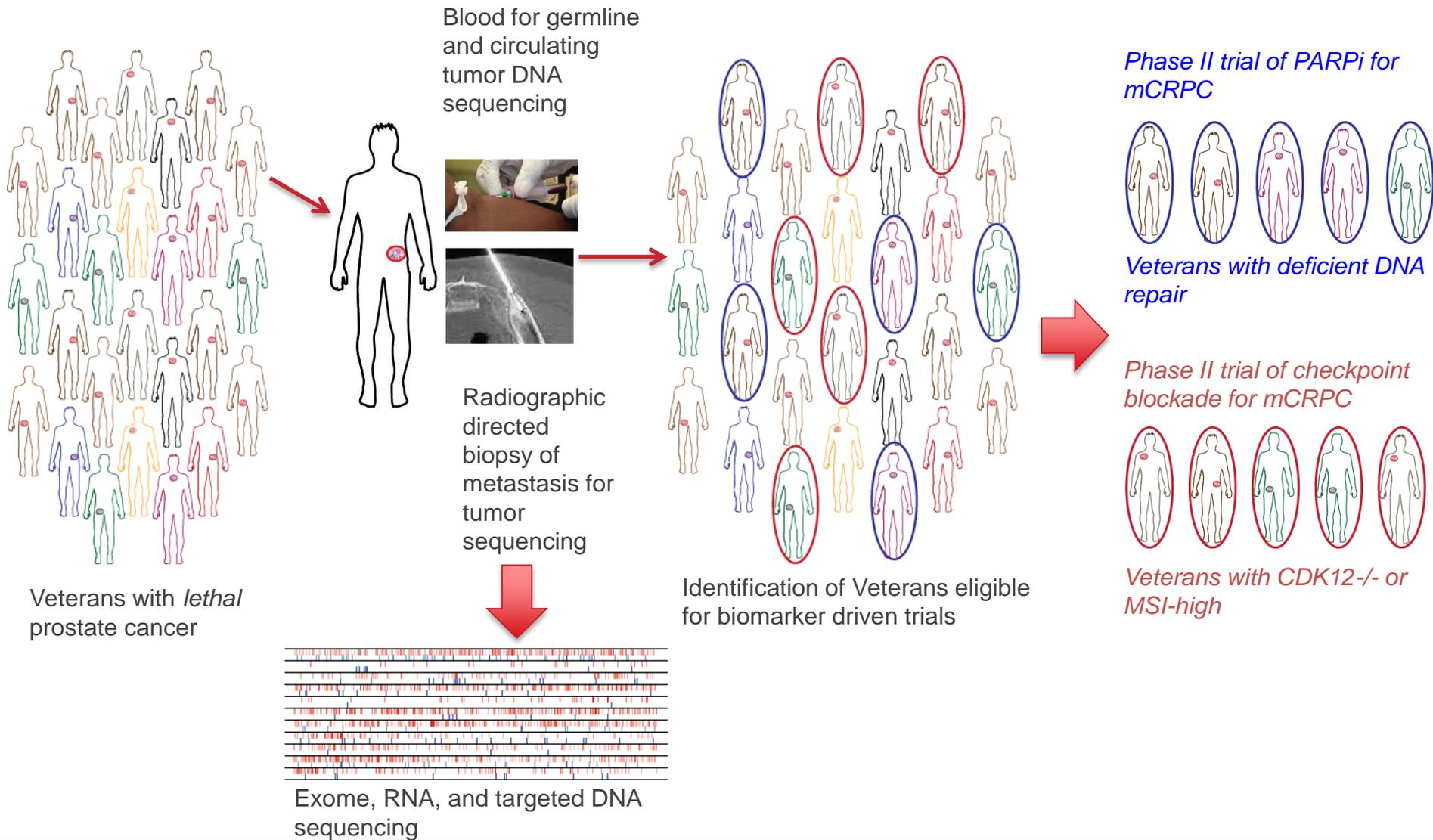


In prostate cancer, we use the PSA test to assess for response-to-therapy. Lower is better.

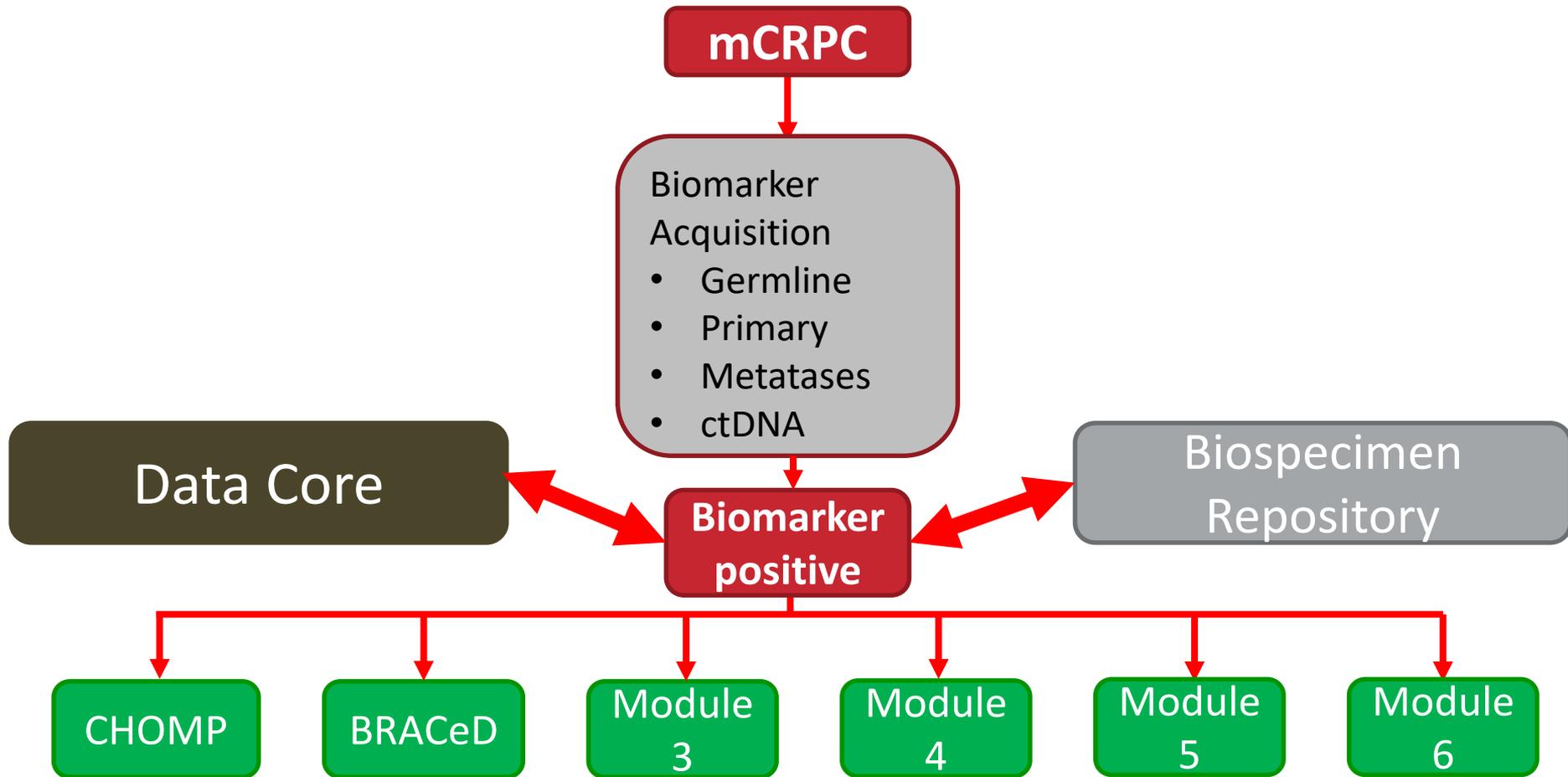
2. Off Label Use of FDA Approved Drug



3. Biomarker driven clinical trial



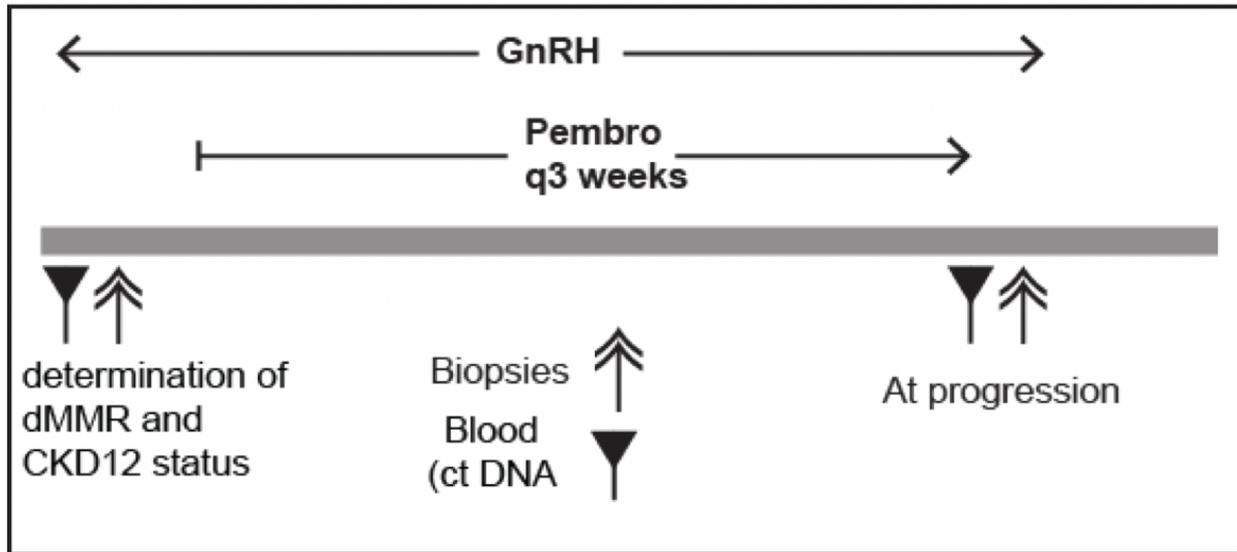
Prostate cancer Analysis for Therapy Choice (PATCH)



A single-arm, open-label, phase II study of Checkpoint inhibitors in men with progressive Metastatic castrate resistant Prostate cancer characterized by a mismatch repair deficiency or biallelic *CDK12* inactivation (CHOMP)

Biomarker =

1. Mismatch Repair Deficiency
2. *CDK12* inactivation



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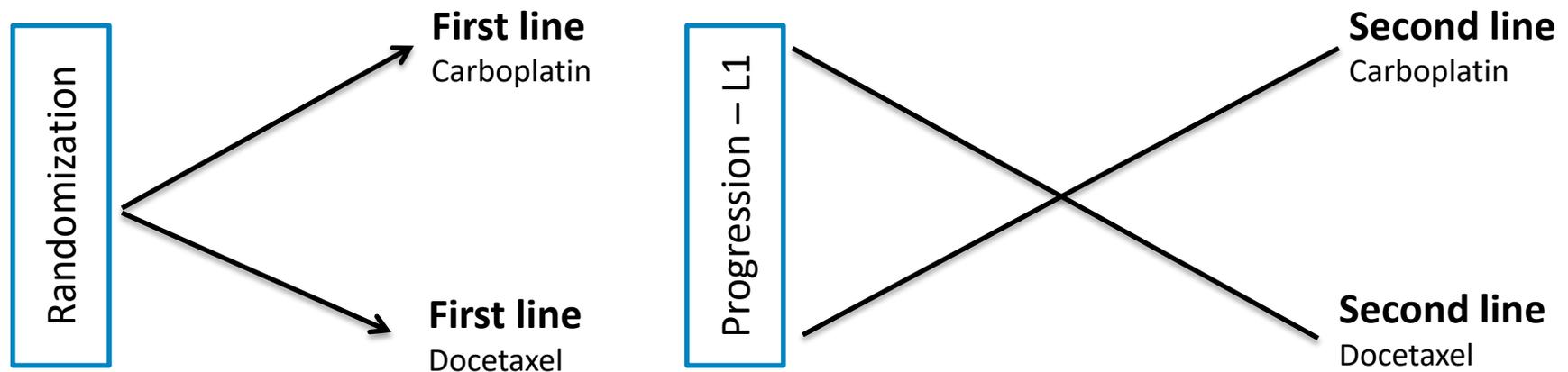


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BRACeD: BRcA deficient prostate cancer treated with Carboplatin or Docetaxel

Biomarker = Homologous Recombination Deficiency (HRD) = mutations in:

- *BRCA1*
- *BRCA2*
- *PALB2*



Transforming the VA: Sustaining POPCaP by Building on and Expanding Expertise

- Prime Example = Jesse Brown VA (Chicago):
 - Initiated Next Generation Sequencing and have identified multiple patients whose treatment plan has been radically modified based on the presence of actionable mutations in nearly half of patients who have undergone sequencing to date.
 - Recruited dedicated GU oncologist.
 - Initiating clinical trials through the POPCaP network.
 - Interface/partner with academic affiliate (Northwestern)
- Planning for a sustainable program.
 - Recruiting and supporting young investigators.
 - VA Career Development Award Program
 - PCF Young Investigator Award program.
- Ongoing education:
 - Virtual Molecular Oncology Tumor Board
 - AVAHO
 - Clinical pathways

A call to action

- Spread the word about POPCaP
 - Discuss with patients and colleagues
- If you provide oncology care, perform NGS on appropriate patients
- Refer patients to POPCaP network centers
- Pharma is encouraged to collaborate
 - Drugs: FDA approved and pipeline
 - Funding of investigator initiated clinical trials
- VA, DOD, NCI
 - Continue to support and expand support for precision oncology.

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