Optimizing Oncology Care With Germline Pharmacogenomics:

Case-Based Education for Oncology Practitioners

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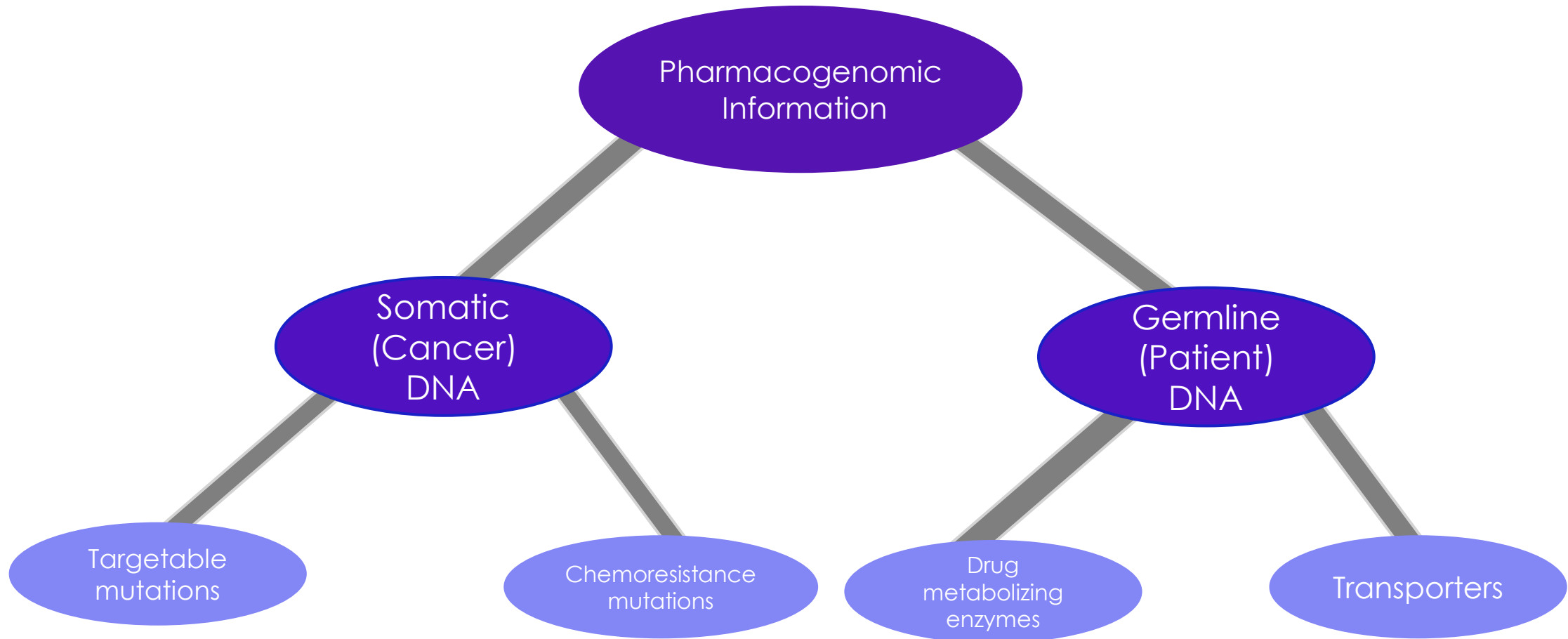
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In oncology, there are at 2 sources of pharmacogenomic information – the tumor and the patient.

Germline pharmacogenomic practice guidelines for chemotherapy and supportive care medications exist.

Chemotherapy

- *TPMT* and *NUDT15:* **6-mercaptopurine and Thioguanine**
- *DPYD:* **5-Fluorouracil and Capecitabine**
- *CYP2D6:* **Tamoxifen**
- *UGT1A1:* **Irinotecan**

Supportive Care

- *CYP2D6:* 5HT3 Inhibitors
- *CYP2C19:* Anti-infectives
- *CYP2C19* and *CYP2D6:* Anti-depressants
- *G6PD:* Rasburicase
- *CYP2D6:* Pain Medications
- *RYR1* and *CACNA1S:* Anesthesia
- *CYP2C19*: Proton Pump Inhibitors

Several regulatory agencies acknowledge the impact of germline pharmacogenomics on chemotherapy.

FDA

> Initiate a reduced dose of irinotecan for patients homozygous for *UGT1A1* *28.

> Patients with DPD deficiency are at increased risk of severe and even fatal toxicity from fluorouracil or capecitabine.

> Initiate a significantly reduced dose of 6-mercaptopurine for *TPMT* or *NUDT15* poor metabolizers.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Guidelines for Localised Colon Cancer

> Patients should be tested for DPD deficiency prior to starting fluorouracil or capecitabine.

Pfizer. Camptosar (irinotecan) [package insert]. U.S. Food and Drug Administration website. Revised 12/2014.
Spectrum Pharmaceuticals. Fluorouracil [package insert]. U.S. Food and Drug Administration website. Revised 07/2016.
Genentech USA, Inc. Xeloda (capecitabine) [package insert]. U.S. Food and Drug Administration Website. Revised 03/2015.
Statson Pharmaceuticals. Purinethol (mercaptopurine) [package insert]. U.S. Food and Drug Administration Website. Revised 12/2020.

EMA 2020 Guidance Document on DPD Deficiency Screening
Argilés G et al. *Ann Oncol* 2020.

Germline Pharmacogenomics in Oncology Education

Why

- Widespread implementation is limited.
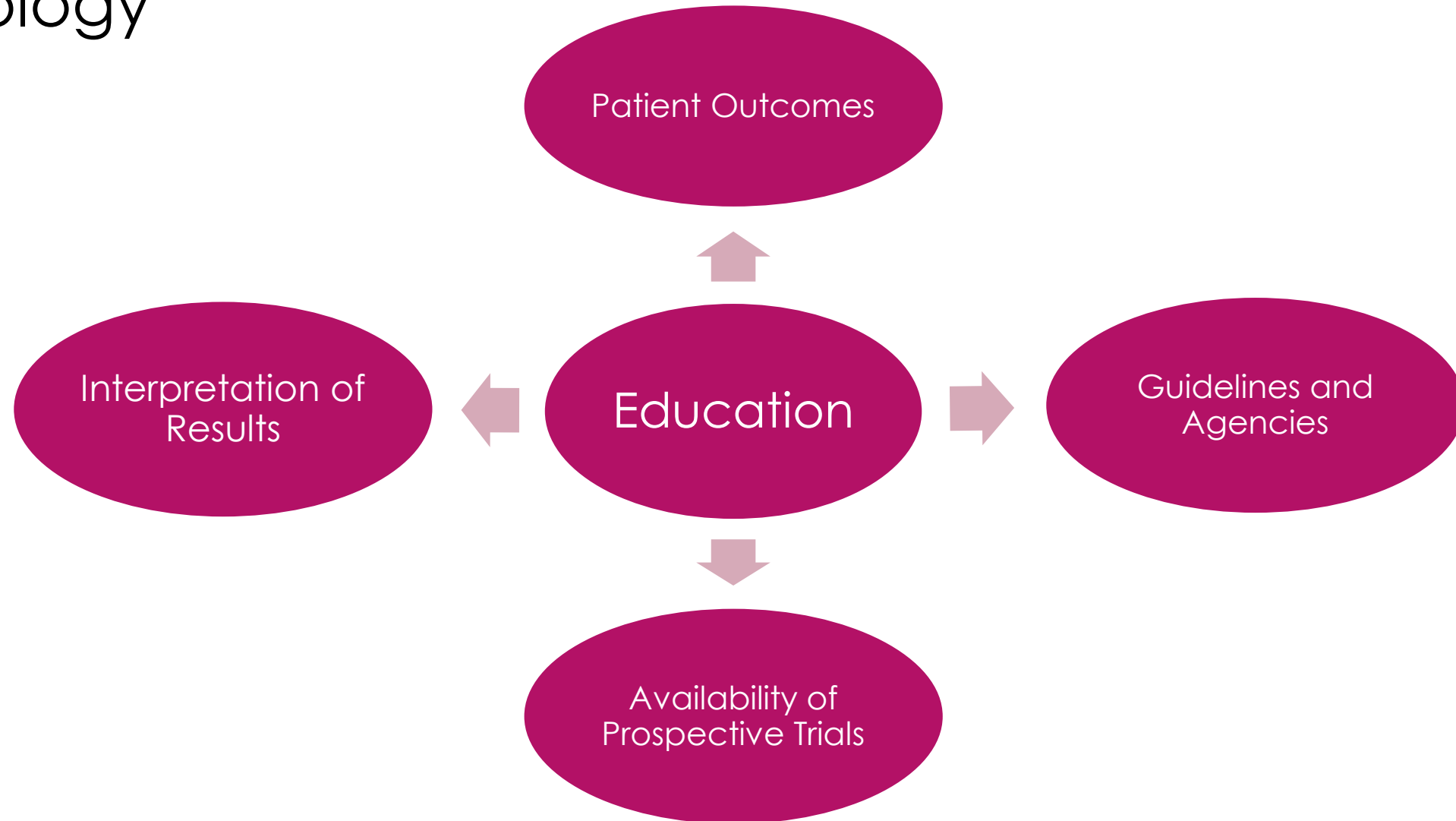
- Lack of education is a barrier.

Who

- Oncology clinicians

  (Physicians, Nurse Practitioners, Physician Assistants, Pharmacists)

What

- Online interactive modules

- Case-based

Lau-Min KS, Varughese LA et al. *BMC Cancer* 2022

Survey Responses Regarding Barriers to Pharmacogenomic Implementation in Oncology

Lau-Min KS, Varughese LA et al. *BMC Cancer* 2022

1: Pharmacogenomics in Oncology

Objectives:

1. Identify the two sources of clinically actionable pharmacogenomic information in patients with cancer.

2. Recognize the role and impact of germline pharmacogenomics in oncology.

1: Pharmacogenomics in Oncology

2: The Pharmacogenomics Toolbox

Objectives:

1. Define pharmacogenomics terms.

2. Recognize limitations of pharmacogenomic testing.

3. Identify resources for the application of pharmacogenomic information to patient care.

4. Assign a phenotype from a patient's genotype.

1: Pharmacogenomics in Oncology

2: The Pharmacogenomics Toolbox

3: Utilizing Germline Pharmacogenomics to Personalize Chemotherapy

Objectives:

1. Describe the mechanism and impact of pharmacogenomics on the safety and efficacy of fluoropyrimidines, 6-mercaptopurine, and tamoxifen.

2. Determine appropriate dosing of chemotherapy agents based on a patient's pharmacogenomic information.

1: Pharmacogenomics in Oncology

2: The Pharmacogenomics Toolbox

3: Utilizing Germline Pharmacogenomics to Personalize Chemotherapy

4: Utilizing Germline Pharmacogenomics to Personalize Supportive Care

Objective:

Determine appropriate dosing and selection of supportive care medications based on a patient's pharmacogenomic information.

1: Pharmacogenomics in Oncology

2: The Pharmacogenomics Toolbox

3: Utilizing Germline Pharmacogenomics to Personalize Chemotherapy

4: Utilizing Germline Pharmacogenomics to Personalize Supportive Care

5: Putting It All Together: Optimizing a Patient's Care Plan with Pharmacogenomics

Given a patient's pharmacogenomic test results, optimize the dosing and selection of chemotherapy and supportive care medications.

Genotype → Phenotype → Therapeutic Recommendation

Examples of Cases

A 55 year old male is diagnosed with colorectal cancer. The physician wants to start FOLFOX therapy. His cancer is resectable, and he will undergo general anesthesia for its removal.

- ► *DPYD* and 5-fluorouracil
- ► *RYR1/CACNA1S* and inhaled anesthetics
- ► *CYP2D6* and opioids

A pre-menopausal woman is diagnosed with ER+ breast cancer and is prescribed tamoxifen. She struggles with nausea and vomiting and depression.

- ► *CYP2D6* and tamoxifen
- ► *CYP2D6* and anti-emetics
- ► *CYP2D6/CYP2C19* and selective serotonin reuptake inhibitors

A 3 year old male patient with acute lymphoblastic leukemia (ALL) presents with tumor lysis syndrome. He is started on ALL-directed therapy, including 6-mercaptopurine.

- ► *TPMT/NUDT15* and 6-mercaptopurine
- ► *G6PD* and rasburicase
- ► *CYP2C19* and voriconazole

Next Steps

Module Development
- Complete and review the content for the 5 modules

Platform Evaluation
- Evaluate the functionality of the online platform

Dissemination
- Host online for CE credit
- Oncology Society Meetings

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