Advocating Improved Treatment for DPD Deficient Patients

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What Could Go Wrong?

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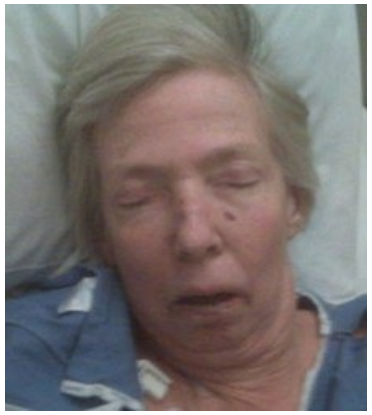
- Diagnosis: Kath a stage III/IV rectal cancer patient at age 60 (2012)
- Treatment plans all included 5-FU chemotherapy -- “fairly well tolerated”
- “If only….
  - Single treatment without pre-screening
  - Early warning signs missed; hospitalization within 9 days – diarrhea/dehydration, neutropenia, mucositis, burn like damage to skin
  - Death after two weeks of hospitalization



Why Does This Happen?

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- A risk considered rare and acceptable in drug labels and treatment guidelines
- “Rare” and acceptable risk?
  - 3-7% of population have a known DPYD variant
  - Variant carriers have ≥ 50% chance of severe toxicity, 3% chance of death
  - Estimate ≥ 1000 deaths/year in US
- Most people are unaware of a deficiency until too late
- It does not need to happen so frequently. Pre-screening/dose adjustment:
  - Is cost effective
  - Saves lives

Advocating to Save Lives

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The Human Cost Of Not Testing Has Brought Us Together

- Single treatment with fluoropyrimidine chemotherapy
- No pre-screening for DPD deficiency
- Severe adverse reactions, suffering, and death

Kathy
Rectal Cancer

Kerrie
Colon Cancer

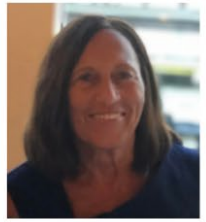
Linda
Rectal Cancer

Jane
Colon Cancer

David
Bile Duct Cancer

Lynn
Colon Cancer

Gerri
Colon Cancer



Carol
Breast Cancer

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Susan
Colon Cancer

Paul
Colon Cancer

Our Mission

To improve the standard of care for cancer patients undergoing fluoropyrimidine chemotherapy (5-FU and/or Capecitabine), through advocacy, education, and research

Connecting:

- Professionals who support testing
- Families of past and current patients
- Patient advocacy organizations

Progress

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- Europe paving the way for patient safety
- Increased willingness in US to discuss testing
  - Precision medicine initiatives
  - President's Cancer Moonshot – "Right treatments for the right patients"
  - ASCO workshop discussion 2022
  - JCO article Sep 2022, Hertz, "Assessment of Clinical Utility of Pre-Treatment Testing…"
- AUDT members earned support for pre-screening in 2021:
  - Institute for Safe Medicine Practices (ISMP)
  - National Community Oncology Dispensing Association (NCODA)
- However, guidelines and drug labels in US still NOT requiring testing

DPYD Test Leaders in US

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Institutes/MDs with at least partial implementation:

- **Dana Farber Cancer Institute, Boston MA**
- Dartmouth Cancer Center, Lebanon NH
- Atrium Health, Charlotte NC
- University of Michigan
- Sanford Imagenetics, South Dakota
- University of Colorado
- Wentworth-Douglass Hospital, Seacoast Cancer Center, Dover NH
- Christ Hospital Health Network, Cincinnati OH
- Yale New Haven Health
- Dr. Rashid, Toledo Clinic Cancer Centers
- Dr. Kasi, Cornell
- Dr. Michael Castro, Los Angeles CA

Implementing within prospective clinical trial:

- University of Pennsylvania Perelman School of Medicine
- University of Chicago
- Moffitt Cancer Center, Tampa FL

Considering test procedures*:

- **Oregon Health Sciences University**
- Cleveland Clinic
- Georgetown University
- St. Elizabeth Hospital of Northern KY
- Intermountain Healthcare, UT
- Fred Hutchinson Cancer Care, Seattle WA

* Based on word of mouth; no public disclosure at this time

Breaking News!

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- FDA replied, Dec 2022, to the Citizens petition of 2020, limiting its response to Xeloda:
  - Denied request to recommend pre-screening for all patients and therapeutic dose monitoring
  - Agreed, however, to revise the following drug label content:
    - Warnings and Precautions: “Consider testing for genetic variants of DPYD prior to initiating Xeloda to reduce risk od serious adverse reactions if the patient’s clinical status permits and based on clinical judgement.”
    - Patient Counseling: changes more explicitly recommend prescribers discuss risk toxicity associated with DPD deficiency and add a recommendation to discuss whether or not testing is appropriate
    - Patient Information: “People with some DPD enzyme may have an increased risk of serious side effect with Xeloda treatment that can sometimes lead to death. Your healthcare provider should talk with you about DPYD testing to look for DPD deficiency.”
    - Add a section on Pharmacogenomics which addresses DPYD and DPD activity

So What is Next?

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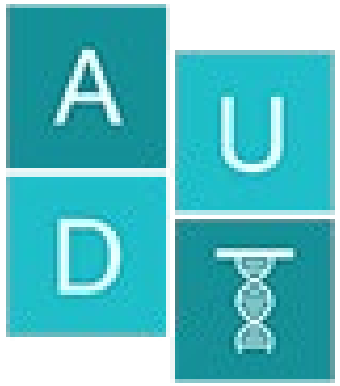
- An increase in demand for DPYD testing resulting from the drug label change
- A demand for a guide to help physicians and patients deal with these changes:
  - Where do oncologists/patients turn for help in the absence of FDA approved DPYD tests?
  - How should physicians treat patients with partial DPD deficiency when the FDA has not determined safe levels of drug use for such patients?



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