Risk of severe toxicity from topical fluoropyrimidine treatment in patients carrying *DPYD* variant alleles.

Javier Granados[1,4], Amy L Pasternak[2], N. Lynn Henry[3], Vaibhav Sahai[3], Daniel L Hertz[2]

[1]University of Michigan Institute for Clinical and Health Research, Ann Arbor, MI; [2]University of Michigan College of Pharmacy, Ann Arbor, MI; [3]University of Michigan Rogel Comprehensive Cancer Center, Ann Arbor, MI; [4]University of Texas at Austin College of Pharmacy, Austin, TX

TEXAS Pharmacy
The University of Texas at Austin College of Pharmacy

COLLEGE OF PHARMACY
UNIVERSITY OF MICHIGAN

ROGEL CANCER CENTER

Background

- Patients carrying variant alleles of *DPYD* that reduce activity of dihydropyrimidine dehydrogenase have high risk of severe toxicity from systemic fluoropyrimidine chemotherapy.
- There is one case report of severe toxicity from topical fluoropyrimidine chemotherapy in a *DPYD* variant carrier, however, the true risk of clinically meaningful toxicity is unknown.

Objective

The objective of this retrospective cohort study was to determine whether patients carrying *DPYD* variant alleles have increased risk of severe toxicity from topical fluoropyrimidine treatment.

Methods

- Cohort: Patients at Michigan Medicine enrolled in Michigan Genomics Initiative, an institutional genetic data repository (n>65,000)
- Received topical fluoropyrimidine treatment
- Carry one of 5 validated *DPYD* variants
- Cycle 1 toxicity graded retrospectively using NCI CTCAE Version 5.0
- Primary Endpoint: grade 3+ toxicity
- Secondary Endpoint: grade 1-2 toxicity

Rates of severe toxicity for patients undergoing topical fluoropyrimidine chemotherapy treatment are extremely low.

Though DPYD variant carriers may have elevated risk for mild toxicity, DPYD genetic testing should be reserved for patients receiving systemic fluoropyrimidine chemotherapy.

Please contact Dan Hertz, PharmD, PhD with any questions: DLHertz@med.umich.edu

MICHR MICHIGAN INSTITUTE FOR CLINICAL & HEALTH RESEARCH
UNIVERSITY OF MICHIGAN

Results

- 201 patients with genetic data received topical fluoropyrimidine treatment
  - 7% carried a *DPYD* variant allele
    - DPD Activity Score=1.5: n=11
    - DPD Activity Score=1.0: n=3
- Cohort Data
  - 79% Actinic keratosis
  - 71% Male
  - 97% White
- Primary Analysis: **Zero (n=0) patients** experienced grade 3+ toxicity
- Nominally increased risk of grade 1-2 toxicity (21.4% [3/14] vs. 10.2% [19/187])
  - Odds ratio = 2.40 (95% CI: 0.10-2.53), p = 0.19

Future Directions

- Update clinical guidelines to recommend *DPYD* testing only for patients receiving systemic fluoropyrimidine therapy
- Patients receiving topical fluoropyrimidine chemotherapy should be monitored for toxicity

Acknowledgements

MICHR Summer Program coordinators for their support in facilitating this project as a student intern.