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

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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.

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
- 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

Results

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

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