

Drug Transporter Variants As Predictors Of Cancer Chemotherapy-Induced Toxicity

Introduction

Precision medicine has the potential to improve prediction of ADR risk in patients undergoing cancer chemotherapy. Evidence will be considered for the predictive role of testing for variants in drug influx and efflux transporters in assessing risk of adverse drug reactions.

Methods

Systematic reviews were performed using standard Cochrane Collaboration methodology. Efflux drug transporters, 25 publications comprising three randomised control trials, two retrospective case-controls and 20 clinical observation studies, totalling 3578 patients, were deemed eligible for review.

Results

Of the known efflux drug transporters, we report findings on the ABC members ABCB1, ABCC1, ABCC2, ABCG2, ABCA1, ABCC4 and ABCC5. Meta-analysis showed an decreased risk of irinotecan-induced neutropenia in patients expressing ABCB1 2677G>T/G (odds ratio [OR]: 0.24; 95% CI: 0.1-0.59; p = 0.002) but increased risk for ABCC2 3972T>T (OR: 1.67; 95% CI: 1.01-2.74; p = 0.04). ABCG2 34G>A was associated with a threefold increased risk of irinotecan-induced diarrhoea (95% CI: 1.00-6.24; p = 0.05).

For drug influx transporters, systemic review identified 16 publications concerning 1510 patients, to be eligible for review. Meta-analysis showed east-Asian patients expressing SLCO1B1 521T>C or 1118G>A to have a two- to fourfold increased risk of irinotecan-induced neutropenia but not diarrhea. In American patients, expression of SLC19A1 IVS2(4935) G>A was associated with pemetrexed/gemcitabine-induced grade 3+ leukopenia.

Conclusions

The majority of studies have identified a role for variants in efflux drug transporters in contributing to lung cancer treatment-associated ADRs. However, for implementation of use of these efflux transporter genetic variants as prognostic markers for ADR risk in cancer chemotherapy, future adequately powered a priori studies are needed. Future studies should also look to robust validation of influx transporters SLCO1B1 and SLC19A1 as prognostic markers in the management of lung cancer patients.

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- Introduction
- Methods
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