Abstract

Background: ABC HSR has been associated with the pharmacogenetic marker HLA-B*5701. However, evidence for the clinical utility of screening in patients suspected of ABC hypersensitivity reactions to abacavir is currently lacking. The objective was to determine if ABC HSR affects the incidence of HSR in ABC-naive patients undergoing PGx testing.

Methods: A retrospective case-control study to evaluate the incidence of HSR in ABC-naive patients from the time of PGx testing for HLA-B*5701 and compared to subjects who did not undergo HLA-B*5701 screening.

Results: In the predominantly white population enrolled in PREDICT-1, 5.6% of subjects were positive for HLA-B*5701, and 1.8% had ABC HSR; 7.8% of subjects were positive for HLA-B*5701, and 3.0% had ABC HSR. The sensitivity of HLA-B*5701 screening for ABC HSR was 100%, with a specificity of 96%, yield of 96% for HLA-B*5701 screening, 72.3% for HLA-B*5701 subjects were positive for ABC HSR, and 22.2% of white subjects were positive for ABC HSR. Results from independent validations confirmed the HLA-B*5701 screening results as accurate.

Discussion: In conclusion, the results from this study demonstrate that HLA-B*5701 screening is an effective tool to reduce ABC HSR incidence by detecting ABC HSR patients prior to initiation of therapy.

Introduction

Reasons into the genetics basis of the abacavir hypersensitivity reaction have identified a strong association between the HLA-B*5701 allele and clinical abacavir hypersensitivity.1, 2

Methods

The PREDICT-1, SHAPE and ARIES studies provide the independent cohorts in France, Australia and the UK have also reported similar findings, demonstrating efficient and effective screening practices.

Results

The PREDICT-1 study demonstrated a statistically significant reduction in the incidence of HLA-B*5701-negative ABC HSR (CI: 0.25, 0.62) compared to subjects who did not undergo HLA-B*5701 screening.

Discussion

The SHAPE study, using a case-control design, demonstrated the high sensitivity of HLA-B*5701 screening for ABC HSR to be generalizable across White and Black racial groups, representing the major target populations with the highest and lowest HLA-B*5701 frequencies, respectively, and supporting generalizability of the utility of HLA-B*5701 screening across race.

Conclusions

Screening for HLA-B*5701 among ABC-naive individuals is a standard of care approach to reduce ABC HSR, appropriate clinical management of suspected HSR remains paramount.

References