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Pharmacogenetic Testing to Identify Presence of the *HLA-B*57:01* Biomarker for Abacavir Treatment

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INTRODUCTION

Testing for the *HLA-B*57:01* biomarker is clinically significant to predict the risk of potentially life-threatening hypersensitivity reactions in patients to be treated with the antiretroviral drug abacavir.[1]

Screening for *HLA-B*57:01* is required prior to initiating abacavir therapy and alternative therapy should be prescribed in patients who test positive for the biomarker.[1,2]

AIM

To review and compare genotyping methods for the identification of the *HLA-B*57:01* pharmacogenetic biomarker in relation to abacavir treatment.

METHOD

1. *HLA-B*57:01* genotyping methods were identified from the Clinical Pharmacogenetics Implementation Consortium guidelines supplementary information.[1]

2. A literature search was performed to identify studies describing genotyping for *HLA-B*57:01* with respect to abacavir.

3. The genotyping methods identified were reviewed and compared according to twelve genotyping method characteristics.

Table 1: Characteristics evaluated for each genotyping method

Sensitivity	Specificity
Genomic DNA source	Controls
Reproducibility	Resolution
Time for analysis	Cost per test
Concordance	Robustness
Sample processing	Positive and Negative Predictive Value

RESULTS

- **Fourteen articles (2005-17) describing *HLA-B*57:01* genotyping were reviewed.**
- **Eight genotyping methods were identified: 7 molecular (Sequence-based typing (SBT), Sequence Specific Primer PCR (SSP-PCR), Sequence Specific Probes (SSOP), Allele-Specific PCR, Real-time PCR, Direct PCR, Reverse hybridisation strip assays) and 1 serological (Flow Cytometry).**
- **The 8 methods have high sensitivity (≥99%) and specificity (≥97%) and 100% concordance with reference methods. For all 8 methods single-sample genotyping is not possible.**
- **Four methods allow use of non-invasive genomic DNA sources, 3 methods have integrated controls, turnaround time ranges from 2 to 24 hours and estimated cost/test ranges from €1-35.**

Table 2: Comparison of the eight *HLA-B*57:01* genotyping methods

Genotyping method	Integrated Controls	Genomic DNA source	Time (hours)	Estimated cost/test (€)
SBT	No	Blood	24	30
SSP-PCR	No	Blood /Buccal swab/ saliva	3	30
SSOP	No	Blood	5	35
Allele-Specific PCR	No	Blood	2-4	30
Real-Time PCR	Yes	Blood/Buccal swab/ Saliva	2-8	15
Direct PCR	Yes	Blood Buccal Swab	3	1
Strip Assay	Yes	Blood / Saliva	6	30
Flow Cytometry	No	Blood	24	25-35

CONCLUSION

The genotyping methods reviewed show high sensitivity, specificity and concordance. Possibility of non-invasive testing, availability of integrated controls and on-demand testing are limited. The review highlights the need for development of rapid point-of-care *HLA-B*57:01* genotyping methods to promote use of pharmacogenetic testing in practice to personalise abacavir therapy in the interest of patient safety.

REFERENCES

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2. Lauschke VM, Milani L, Ingelman-Sundberg M. Pharmacogenomic biomarkers for improved drug therapy-recent progress and future developments. AAPS J. 2018;20(1):4.