High Sensitivity of Human Leukocyte Antigen–B*5701 as a Marker for Immunologically Confirmed Abacavir Hypersensitivity in White and Black Patients

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Background. Although the human leukocyte antigen (HLA)–B*5701 is highly associated with a hypersensitivity reaction (HSR) to abacavir (ABC), variable sensitivities have been reported when clinical data alone have been used to define an ABC HSR. This study evaluated the sensitivity of detection of the HLA-B*5701 allele as a marker of ABC HSRs in both white and black patients, using skin patch testing to supplement clinical diagnosis.

Methods. White and black patients, identified through chart review, were classified as having received a diagnosis of an ABC HSR based on clinical findings only (a clinically suspected ABC HSR) or based on clinical findings and a positive skin patch test result (an immunologically confirmed [IC] ABC HSR). Control subjects were racially matched subjects who tolerated ABC for ⩾12 weeks without experiencing an ABC HSR. Patients and control subjects were tested for the presence of HLA-B*5701. Sensitivity, specificity, and odds ratios for the detection of HLA-B*5701 as a marker for an ABC HSR were calculated for white and black participants.

Results. Forty-two (32.3%) of 130 white patients and 5 (7.2%) of 69 black patients who met the criteria for clinically suspected HSRs had IC HSRs. All 42 white patients with IC HSRs were HLA-B*5701 positive (sensitivity, 100%; odds ratio, 1945; 95% confidence interval, 110–34,352). Among all white patients with clinically suspected HSRs, sensitivity was 44% (57 of 130 patients tested positive for HLA-B*5701); specificity among white control subjects was 96%. Five of 5 black patients with IC HSRs were HLA-B*5701 positive (sensitivity, 100%; odds ratio, 900; 95% confidence interval, 38–21,045). Among black patients with clinically suspected HSRs, the sensitivity was 14% (10 of 69 tested positive for HLA-B*5701); specificity among black control subjects was 99%.

Conclusions. Although IC ABC HSRs are uncommon in black persons, the 100% sensitivity of HLA-B*5701 as a marker for IC ABC HSRs in both US white and black patients suggests similar implications of the association between HLA-B*5701 positivity and risk of ABC HSRs in both races.

The nucleoside reverse-transcriptase inhibitor, abacavir sulfate (ABC), is an effective antiretroviral drug with excellent long-term safety. The major treatment-limiting toxicity of ABC is a hypersensitivity reaction (HSR), which occurs in ~5% of patients [1]. ABC HSRs are typically associated with a combination of ⩾2 symptoms, including generalized malaise, rash, fever, and/or gastrointestinal symptoms. All symptoms typically resolve within several days after discontinuation of ABC therapy but recur more quickly and severely upon rechallenge with the drug. Permanent discontinuation of ABC therapy is mandated for any patient who receives a diagnosis of an HSR.

Although the exact mechanism of ABC HSRs is unknown, an immunogenetic basis is likely (supported by laboratory studies [2] and the rapid and severe rechallenge reactions). Early reports that noted familial

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susceptibility and decreased frequency of ABC HSRs in certain racial groups suggested a genetic basis for the reaction [1, 3]. A strong association has been consistently reported between the HLA-B*5701 allele and ABC HSRs [4–6]. However, studies have shown variable sensitivity of detection of the HLA-B*5701 allele as a marker for HSRs, with much higher sensitivity among white populations than among other racial or ethnic groups. Black populations show lower carriage rates of HLA-B*5701 [5, 7] and a lower incidence of ABC HSRs [1, 8].

Initial studies that evaluated the sensitivity of HLA-B*5701 as a marker for ABC HSRs were based on clinical diagnosis. The overlapping nature of ABC HSR symptoms with the adverse events associated with concurrent antiretroviral therapy (such as efavirenz) and with symptoms of infection and immune restoration disease have confounded accurate clinical diagnosis [1, 9]. In blinded clinical trials, rates of suspected ABC HSRs among subjects not receiving ABC therapy have varied from 2% to 7% [10–14]. Because correct identification of phenotype is critical to accurately estimate sensitivity, previous retrospective studies that used clinical diagnosis alone to detect the phenotype involved in cases of ABC HSRs have shown low sensitivity HLA-B*5701 screening, particularly among black patients; this is likely because of the overshadowing of immunologically mediated HSRs by false-positive clinical diagnoses.

Skin patch testing has been used successfully as an adjunct to clinical diagnosis to identify patients with immunologically mediated ABC HSRs. These studies have shown a consistently high sensitivity of HLA-B*5701 among patients with a history of ABC HSRs confirmed with skin patch testing but were limited to a primarily white population [2, 15–17]. The aim of the present study (ABC107442/SHAPE) was to assess the sensitivity of HLA-B*5701 as a marker for clinically diagnosed and patch test–confirmed ABC HSRs in black and white patients in the United States.

METHODS

Study design and population. The Study of Hypersensitivity to Abacavir and Pharmacogenetic Evaluation (SHAPE) study was a retrospective case-control study to evaluate the sensitivity and specificity of the HLA-B*5701 allele as a marker for ABC HSRs in the black and white populations in the United States (study ABC107442; clinical trials identifier, NCT00373945). Approvals to conduct this study were obtained from a centralized institutional review board and, where required, from individual site institutional review boards.

Participants were assessed for eligibility through retrospective assessment of information regarding clinical presentation of ABC HSR symptoms, antiretroviral therapy, and date of use of ABC-containing products. Participants were eligible for the study if they were self-identified as either black or white, provided written informed consent for study procedures (including pharmacogenetic research), and had experienced clinically suspected (CS) ABC HSRs consisting of at least 2 major symptoms (fever, rash, or gastrointestinal or constitutional symptoms) with onset date within 6 weeks after initiating ABC therapy. The group of black participants included all of those who identified themselves as "black" and was not restricted to those who were of African American or African descent.

All participants underwent skin patch testing and had a blood sample obtained for pharmacogenetic research. The 2 following case definitions were used in this study: a CS ABC HSR was defined as diagnosis of an ABC HSR based on clinical findings only, and an immunologically confirmed (IC) ABC HSR was defined as diagnosis of an ABC HSR based on clinical findings and a positive skin patch test result.

Racially matched control subjects were retrospectively identified from subjects who had taken ABC for at least 12 weeks while participating in a previous clinical study, had not experienced ABC HSRs, had provided written informed consent, and had a blood sample obtained for pharmacogenetic research. Data were analyzed separately for white and black patients because of the differential sensitivities of HLA-B*5701 screening among white and black patients with ABC HSRs (48% and 8%, respectively) [5].

Skin patch testing. Skin patch tests were prepared and applied in duplicate according to the procedure previously reported by Phillips et al. [15] and were adapted to use 1% and 10% concentrations of ABC and excipient and petrolatum controls. Skin patch testing consisted of applying diluted, nonirritating concentrations of ABC to the surface of the skin of participants who were suspected to have experienced an ABC HSR. A positive cutaneous reaction (erythema, induration, pruritis, and in some cases, vesiculation and blistering) implied immunological confirmation of the original ABC HSR. Patch test kits were standardized, with detailed instruction regarding application and interpretation of the test being distributed from a central site. Test results were read and recorded at 24 and 48 h after application, and photographic images were collected using standard cameras (Kodak EasyShare C530). Statistical analyses were based on patch test results, as determined by site investigators (figure 1).

Pharmacogenetic evaluation. Blood samples were obtained from all participants for HLA-B*5701 detection and were assayed for the presence of HLA-B*5701 using high-resolution DNA-based assay methodologies (Quest Diagnostics).

Statistical analyses. The sample size target of 40 patients with IC HSRs for each race was based on feasibility of recruitment and acceptable precision around the observed point estimate. Using the sample size software package PASS 2005 (NCSS), a sample size of 40 patients with IC HSRs produced a 95% CI with 0.15 precision (one-half of the width of the confidence interval), assuming an observed sensitivity of 0.60.

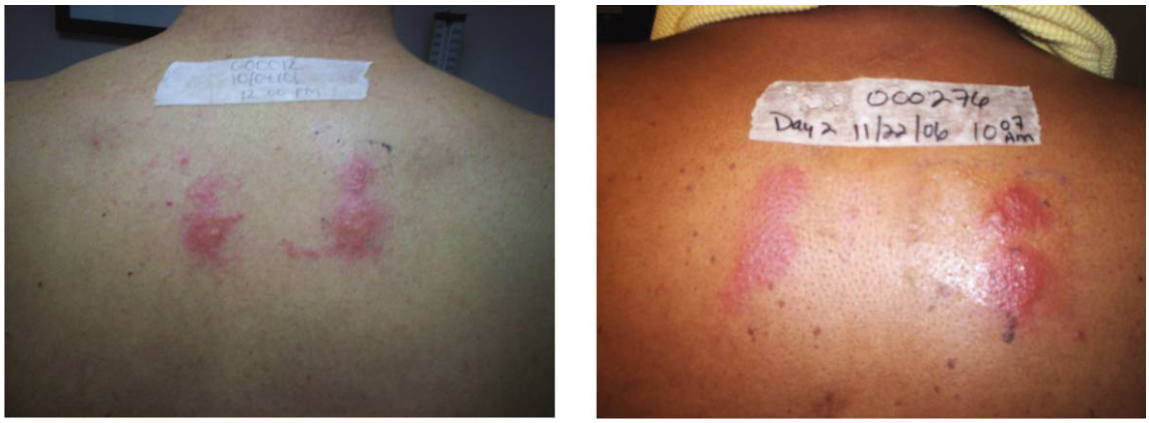

Figure 1. Positive skin patch test results photographed 48 h after patch application for a white patient *(left)* and a black patient *(right)*. In each image, the patch on the left was removed 24 h after application and the patch on the right was removed 48 h after application.

A sample size comprising 80 control subjects would produce a 95% CI with 0.07 precision, assuming an observed specificity of 0.90. Because of the very low carriage frequency of HLA-B*5701 among control subjects, attempts were made to locate up to 200 control subjects for estimating the specificity of HLA-B*5701. Assuming an OR of 5 and the sample sizes proposed for this study, there would be sufficient power (>90%) to test the association of HLA-B*5701 with ABC HSRs among patients and control subjects ($\alpha = 0.05$). The primary objective of this study was to estimate the sensitivity of HLA-B*5701 in white and black patients with IC HSRs. In addition, sensitivities for determination of CS HSRs among white and black patients and specificities among white and black control subjects were calculated. ORs and exact χ^2 tests were used to evaluate the association between the presence of HLA-B*5701 and ABC HSRs. To estimate the ORs and 95% CIs when 1 of the cells contained zero subjects, 0.5 was added to each of the cells before computing [18].

Statistical analyses included all enrolled subjects for whom HLA-B*5701 screening and skin patch testing results were available. A per-protocol analysis was also conducted to exclude subjects who violated any major study criterion. The full analysis results, which closely matched the per-protocol results, are presented. Statistical analyses were conducted using SAS, version 8.2 (SAS Institute).

RESULTS

We identified 130 white patients with CS HSRs, 42 (32%) of whom had a positive skin patch test result. Of 69 black patients with CS HSRs, 5 (7%) had a positive skin patch test result. For 4 patients (3 white and 1 black), valid skin patch test results were not available, generally because the patches did not adhere to the skin, despite attempts at reapplication and change in application site. These patients were excluded from the primary analysis, because it was not possible to classify them as having positive or negative skin patch test results. They were included in the CS HSR analysis but were excluded from the per-protocol analysis. Baseline characteristics, including details of the qualifying ABC HSR event, are described in tables 1 and 2. Demographic characteristics were similar for white patients and control subjects and for black patients and control subjects.

All of the white patients with IC HSRs experienced onset of ABC HSR symptoms within 17 days after starting ABC therapy, and black patients with IC HSRs experienced onset of symptoms within 32 days after initiation of ABC therapy. The majority of patients with IC HSRs (90% of white patients and 100% of black patients) presented with ABC HSR symptoms in ⩾3 categories (table 2). Fever and gastrointestinal symptoms were the most commonly reported symptoms in white and black patients with IC HSRs, respectively.

The patterns of association between HLA-B*5701 and ABC HSRs are presented in table 3. All of the white patients with IC HSRs were HLA-B*5701 positive (sensitivity, 100%). Among all white patients with CS HSRs, the sensitivity of HLA-B*5701 was 44%. Fifteen white patients with CS HSRs and negative skin patch test results and 8 white control subjects also were HLA-B*5701 positive. The corresponding sensitivities among black patients were 100% for patients with IC HSRs and 14% for patients with CS HSRs. Five black patients with CS HSRs and negative skin patch test results and 2 black control subjects were HLA-B*5701 positive. The specificities of HLA-B*5701 among white and black patients were 96% and 99%, respectively. As indicated by ORs and their 95% CIs (OR for white patients, 1945 [95% CI, 110–34352]; OR for black patients, 900 [95% CI, 38–21045]), the presence of HLA-B*5701 is significantly associated with ABC HSRs, regardless of race and case definition of ABC HSR. The strongest associations were observed in patients with IC HSRs.

There were no serious adverse events that were associated with study procedures, including skin patch testing. Most of

Table 1. Demographic and baseline characteristics of the study population.

Characteristic	White participants				Black participants			
	Patients with ABC HSR				Patients with ABC HSR			
	Positive skin patch test result (n = 42)	Negative skin patch test result (n = 85)	All with CS cases[a] (n = 130)	Control subjects (n = 202)	Positive skin patch test result (n = 5)	Negative skin patch test result (n = 63)	All with CS cases[a] (n = 69)	Control subjects (n = 206)
Age, mean years (range)	44 (23–57)	45 (22–73)	45 (22–73)	41 (19–72)	47 (32–57)	45 (22–76)	45 (22–76)	41 (19–73)
Male sex, %	90	76	82	93	100	57	59	71

NOTE. ABC, abacavir; CS, clinically suspected; HSR, hypersensitivity.

[a] Among patients with CS ABC HSR, 3 white patients and 1 black patient did not have valid skin patch test results. Therefore, the sum of patients who had positive skin patch test results and patients who had negative skin patch test results is not equal to the total number of patients with CS ABC HSR.

the adverse events noted were cutaneous and mild to moderate in severity. A few participants (4 white participants and 5 black participants) reported transient and self-limited constitutional symptoms, such as nausea, fatigue, and myalgias, that were attributed by the site investigator to topical ABC therapy. None of these patients had the patch testing procedure interrupted or discontinued.

DISCUSSION

In this analysis, the sensitivity estimate of HLA-B*5701 as a marker for IC HSRs was 100% for both white and black patients. These results contrast with the lower sensitivities, particularly among black patients, in previous studies that used only a clinical diagnosis to define an ABC HSR (figure 2). Among patients with CS HSRs, the sensitivities of HLA-B*5701 among white patients (44%) and black patients (14%) were similar to those reported elsewhere [5]. The association between IC HSRs and the presence of the HLA-B*5701 allele is striking and further establishes this genetic marker as a potential predictor of an ABC HSR in a clinical context.

Past studies have yielded a range of estimates for the sensitivity of HLA-B*5701 as a predictor of an ABC HSR. One of the possible explanations for the variability in findings is the clinical criteria used in diagnosing ABC HSRs. The frequent concomitant use of efavirenz, which can result in rash and constitutional symptoms early during the course of therapy, likely has increased the reporting of CS HSRs. Historical evidence supports this thesis. Before the more widespread use of efavirenz as part of a potent 3-drug regimen, the initial studies of ABC therapy reported HSR rates of 2%–3% [19]. In contrast, in more recent studies in which ABC therapy has been used in conjunction with efavirenz, the incidence of CS HSRs was 7%–9%, suggesting confounding of the clinical presentation of ABC HSRs. Supporting this notion is the 2%–7% rates of ABC HSRs that have been reported consistently in the non–ABC therapy arms in randomized, double-blinded, controlled studies [10–14].

Similar to our study, other studies that have used skin patch testing to supplement a clinical diagnosis of an ABC HSR have also observed 100% sensitivity of HLA-B*5701 as a marker for IC HSRs [2, 16, 17]. Furthermore, reports have indicated that prospective screening to exclude patients who are HLA-B*5701 positive from receiving ABC therapy results in a decrease in the incidence of ABC HSRs [20–22].

Although patch testing accurately identifies patients who have immunologically mediated ABC HSRs, clinical management accurately identifies individuals who have not developed symptoms of an HSR and, thus, are tolerant of ABC. Therefore, the best estimates of sensitivity of HLA-B*5701 screening for ABC HSRs are provided by patch testing (IC HSRs), and the estimated specificities are provided by clinical evaluation alone. Assuming a 2% carriage frequency of HLA-B*5701 among US black persons and the 100% sensitivity and 99% specificity of HLA-B*5701 observed in the present study, the estimated positive predictive value of screening would be ~50%, and the negative predictive value would be 100%. To illustrate this phenomenon, if a similar population of 100 US black persons was screened, we would expect that 98 persons would be identified as HLA-B*5701 negative and could confidently initiate ABC therapy with very low risk of developing a HSR. Avoidance of ABC therapy for the 2 HLA-B*5701–positive patients would be expected to prevent 1 case of an ABC HSR and would inappropriately deny ABC therapy to 1 patient who would have tolerated the drug. Although this implies that 100 patients would need to be screened to prevent 1 case of immunologically mediated HSRs, it must be borne in mind that 2%–7% of patients have ABC therapy inappropriately stopped because of clinical overdiagnosis of HSRs [10–14], and open genetic screening has been shown to substantially reduce this end point [20–22].

From the perspective of an individual patient, screening reduces the potential anxiety associated with starting ABC therapy. This practice would avoid exposing and sensitizing HLA-B*5701–positive patients to ABC and would facilitate the more accurate diagnosis based on any symptoms that may arise in an HLA-B*5701–negative individual during the first few weeks

Table 2. Description of symptoms for the qualifying abacavir (ABC) hypersensitivity (HSR) event.

Characteristic	White patients with ABC HSR			Black patients with ABC HSR		
	Positive skin patch test result (n = 42)	Negative skin patch test result (n = 85)	All with CS cases[a] (n = 130)	Positive skin patch test result (n = 5)	Negative skin patch test result (n = 63)	All with CS cases[a] (n = 69)
Time from initiation of ABC therapy to onset of symptoms,[b] days						
0–21	42 (100)	61 (80)	106 (88)	4 (80)	44 (77)	49 (78)
22–42	0 (0)	9 (12)	9 (7)	1 (20)	7 (12)	8 (13)
>42[c]	0 (0)	6 (8)	6 (5)	0 (0)	6 (11)	6 (10)
Median (range)	7 (0–17)	6 (0–291)	6 (0–291)	7 (7–32)	8 (0–469)	7 (0–469)
No. of categories of symptoms[d]						
None and/or missing	0 (0)	3 (4)	3 (2)	0 (0)	2 (3)	2 (3)
1	0 (0)	1 (1)	1 (<1)	0 (0)	3 (5)	4 (6)
2	4 (10)	24 (28)	30 (23)	0 (0)	23 (37)	23 (33)
⩾3	38 (90)	57 (67)	96 (74)	5 (100)	35 (56)	40 (58)
Symptom category						
Fever	41 (98)	53 (61)	94 (72)	4 (80)	34 (54)	38 (55)
Rash	27 (64)	51 (60)	78 (60)	3 (60)	30 (48)	34 (49)
Gastrointestinal	25 (60)	55 (65)	83 (64)	5 (100)	43 (68)	48 (70)
Constitutional	39 (93)	65 (76)	107 (82)	4 (80)	43 (68)	47 (68)
Respiratory	13 (31)	26 (31)	40 (31)	1 (20)	11 (17)	12 (17)
Time from diagnosis of HSR to study entry, median days (range)	763 (7–3133)	1326 (8–3550)	1012 (7–3550)	263 (56–2313)	1845 (28–2761)	1718 (28–2761)

NOTE. Data are no. (%) of patients, unless otherwise indicated. CS, clinically suspected.

[a] Among patients with CS ABC HSR, 3 white patients and 1 black patient did not have valid skin patch test results. Therefore, the sum of patients who had positive skin patch test results and patients who had negative skin patch test results is not equal to the total number of patients with CS ABC HSR.

[b] Data are for 42 white patients with positive skin patch test results, 76 white patients with negative skin patch test results, 121 white patients with CS cases, 5 black patients with positive skin patch test results, 57 black patients with negative skin patch test results, and 63 black patients with CS cases.

[c] Patients who experienced onset of ABC HSR >6 weeks after initiating ABC therapy were considered to be protocol violators.

[d] Symptom categories included fever, rash, gastrointestinal symptoms, and constitutional symptoms. Patients with missing and/or no symptoms either did not have documented evidence of ABC HSR or had symptoms that could not be placed in any of the 4 symptom categories; patients with only 1 symptom were considered to be protocol violators.

of antiretroviral therapy. From the clinician's point of view, it is the ease, level of reimbursement, availability, and turnaround time of accurate testing that also determine the local cost-benefit ratio and uptake of testing. Once testing is introduced, it will be difficult to deny access to screening on the basis of self- or clinician-identified race. Therefore, consideration of the balance between number of patients tested and the total number of prevented cases of HSRs is of less relevance to physicians than it is to those who fund laboratory testing.

Although a positive skin patch test result is a reliable indicator of immunologically mediated HSRs, a negative patch test result does not completely exclude immunologically mediated HSRs. Our study identified 15 white patients and 5 black patients with CS HSRs who were HLA-B*5701 positive and had negative skin patch test results. Although some patients may be HLA-B*5701 positive and ABC tolerant, false-negative skin patch test results due to host or operator factors cannot be ruled out in these cases. This lack of perfect analytical sensitivity of skin patch testing among HLA-B*5701–positive patients with CS ABC HSRs indicates that skin patch testing should not be used as a clinical tool for excluding a HSR diagnosis for purposes of ABC rechallenge.

Despite a large number of participating sites (57 sites) and extension of the enrollment period, only 69 black participants met the inclusion criteria for CS HSRs. Of those, only 5 patients (7%) had IC HSRs—far fewer than the 40 black patients with IC HSRs that were planned for this study. Exploring the robustness of these findings with only 5 black patients who had IC ABC HSRs indicates a relatively small probability (33%) of observing 5 HLA-B*5701–positive patients among 5 patients with IC HSRs if the true probability had been 80%. Even though there were only 5 black patients with IC HSRs, the association between IC HSRs and the presence of HLA-B*5701 was strong enough that the lower limit of the 95% CI was well above 1. If only 4 of the 5 black patients with IC HSRs were HLA-B*5701 positive, the OR would have been 408 (95% CI, 21–20,123). If only 1 of the 5 black patients with IC HSRs were HLA-B*5701 positive, the OR would have decreased to 26 (95% CI, 0.3–555). These exploratory results support the robustness of the original findings. Even though the number of black

Table 3. Results of pharmacogenetic analyses.

Analysis	White participants				Black participants			
	Patients with ABC HSR				Patients with ABC HSR			
	Positive skin patch test result (n = 42)	Negative skin patch test result (n = 85)	All with CS cases[a] (n = 130)	Control subjects (n = 202)	Positive skin patch test result (n = 5)	Negative skin patch test result (n = 63)	All with CS cases[a] (n = 69)	Control subjects (n = 206)
No. HLA-B*5701 screening results available	42	84[b]	129	202	5	63	69	206
No. of results indicating presence of HLA-B*5701	42 (100)	15 (18)	57 (44)	8 (4)	5 (100)	5 (8)	10 (14)	2 (<1)
Sensitivity, % (95% CI)	100 (92–100)	…	44 (35–53)	NA	100 (48–100)	…	14 (7–25)	NA
Specificity, % (95% CI)	NA	…	NA	96 (92–98)	NA	…	NA	99 (97–100)
OR (95% CI)	1945 (110–34,352)	…	19 (8–48)	Reference	900 (38–21045)	…	17 (4–164)	Reference

NOTE. ABC, abacavir; CS, clinically suspected; HSR, hypersensitivity; NA, not applicable.

[a] Among patients with CS ABC HSR, 3 white patients and 1 black patient did not have valid skin patch test results. Therefore, the sum of patients who had positive skin patch test results and patients who had negative skin patch test results is not equal to the total number of patients with CI ABC HSR.

[b] The blood sample obtained from 1 patient was not processed correctly, and a second sample was unattainable; thus, the HLA-B*5701 screening result was not available for this 1 patient.

patients was small, the strength of the association between HLA-B*5701 and IC HSRs (demonstrated by the 100% sensitivity and high OR in the black cohort) suggests that the association is likely to be generalizable.

Inclusion criteria for the trial were stringent with respect to timing (occurrence of symptoms <6 weeks after initiation of ABC therapy) and symptoms (≥2 categories consistent with HSRs). Despite the criteria, some participants were enrolled who did not meet the inclusion criteria. Because these violations were discovered only after monitoring of the site and because the study period was brief (only 3 days), these participants were included in the analysis despite the violation of entry criteria. It is interesting that none of the 12 patients with symptoms presenting after 6 weeks and none of the 9 subjects with <2 categories of symptoms had IC HSRs. The criteria established for entry were based on evaluation of risk factor analyses [1]; the criteria, if observed, can help to differentiate HSRs from events involving similar symptoms.

Recent observational studies employing screening for HLA-B*5701 have shown a reduction in the rates of ABC HSRs [20–22] and all-cause ABC therapy discontinuation, suggesting that screening can promote more-informed treatment of patients

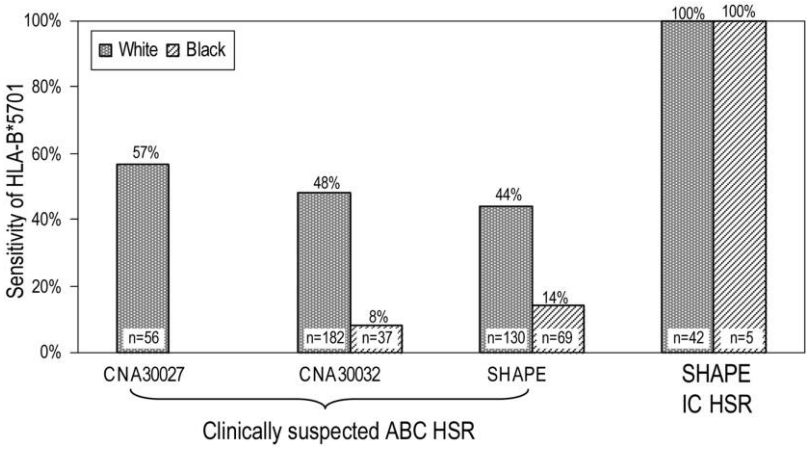

Figure 2. Sensitivity of HLA-B*5701 screening as determined by past studies and the Study of Hypersensitivity to Abacavir and Pharmacogenetic Evaluation (SHAPE) study, in which abacavir (ABC) hypersensitivity (HSR) was defined on the basis of a clinical diagnosis alone, and in only the SHAPE study, in which ABC HSR was also defined on the basis of immunological confirmation (IC HSR). Numbers in parentheses indicate number of cases of ABC HSR. CNA30027 and CNA30032 were retrospective case-control studies. Of the 1041 participants included in the CNA30032 study, a random subset of 541 participants was used for the calculation of sensitivity of HLA-B*5701 screening. Similar to the SHAPE study, patients in the CNA30027 and CNA30032 studies had to have had documented evidence of ABC HSR (consisting of symptoms in ≥2 categories).

[21]. A large prospective study, PREDICT-1, was statistically powered to determine the association between HLA-B*5701 and ABC HSRs in a white population [23]. Because of the lower frequency of the allele among black populations (frequency, ≤2.5%), a powered, prospective study aimed at studying the association between HLA-B*5701 and ABC HSRs in a black population is not feasible. The retrospective case-control study design of the SHAPE study allowed us to identify the strong association between the presence of HLA-B*5701 and IC ABC HSRs in a black population.

In summary, the SHAPE study complements the results provided by prospective studies by providing new and critical information that the HLA-B*5701 allele is important for identifying persons at highest risk of developing ABC HSRs among both white and black populations. These findings, in conjunction with robust laboratory assay results and quality assurance programs, have significant implications for the use of HLA-B*5701 screening in clinical settings worldwide, so that pretherapy assessment of the presence of the allele could be used to identify persons who may be at the highest risk of developing ABC HSRs and to facilitate safer treatment decisions based on this knowledge [24–27]. Because of the more expanded experience with adverse drug reactions, such as anemia, neutropenia, and mitochondrial toxicities, associated with the alternative nucleoside analogues currently in common use in resource-poor settings, other safe options will be needed [28–31]. These findings support the generalizability of HLA-B*5701 screening for the prevention of ABC HSRs in US white and black populations.

STUDY OF HYPERSENSITIVITY TO ABACAVIR AND PHARMACOGENETIC EVALUATION STUDY TEAM

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