

# Clinical Presentation of Hypersensitivity Reaction to Abacavir (ABC HSR) by HLA-B\*5701 Status

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## Abstract

**OBJECTIVES:** ABC HSR typically presents with multiple symptoms, many with overlapping etiologies. The aim of this analysis was to evaluate clinical presentation of ABC HSR by HLA-B\*5701 status.

**METHODS:** Subjects with clinically-suspected ABC HSR (cases) were identified through chart reviews as a part of study ABC107442 (SHAPE). Cases must have had ABC HSR symptoms in ≥ 2 categories (fever, rash, GI, constitutional) with onset ≤ 6 weeks from initiating ABC. All clinically-suspected ABC HSR cases then underwent ABC skin patch testing (SPT) and HLA-B\*5701 evaluation. Clinical symptoms of ABC HSR were summarized by HLA-B\*5701 status. While Blacks and Whites were analyzed separately in SHAPE, the descriptive results below are combined across race.

### RESULTS:

	HLA-B*5701+ n = 67	HLA-B*5701- n = 131
<b>HSR symptoms, n (%)</b>		
Fever	58 (87)	73 (56)
Rash	41 (61)	70 (53)
GI	42 (63)	88 (67)
Constitutional	57 (85)	96 (73)
Respiratory	17 (25)	34 (26)
<b>Number of symptom categories, n (%)</b>		
None/Missing	3 (4)	2 (2)
One category	0	5 (4)
Two categories	9 (13)	44 (34)
≥ Three categories	55 (82)	80 (61)
<b>Time to onset of symptoms, n (%)</b>		
n	64	119
0 - 21 days	60 (94)	94 (79)
22 - 42 days	4 (6)	13 (11)
> 42 days	0	12 (10)
<b>Median days to onset of first symptom (range)</b>	7 (0 - 34)	7 (0 - 469)
<b>Skin patch test, n (%)</b>		
Positive	47 (70)	0
Negative	20 (30)	127 (97)
Unknown	0	4 (3)
<b>Sensitivity of HLA-B*5701 in SPT+ cases, 95% CI</b>	1.0 (0.92, 1.0)	N/A

**CONCLUSIONS:** Subjects who carry the HLA-B\*5701 allele are more likely than those without the allele to present with fever, and to have three or more categories of ABC HSR symptoms. All HLA-B\*5701+ subjects had onset of ABC HSR within 34 days of starting ABC use. HLA-B\*5701 is a highly sensitive marker for SPT+ ABC HSR; subjects who are HLA-B\*5701- are unlikely to have a positive skin patch test result.

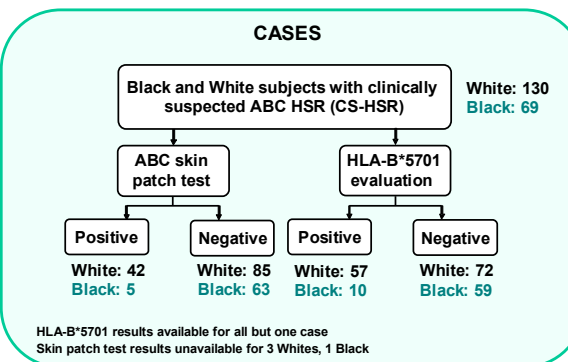
## Introduction

- Presence of the *HLA-B\*5701* allele is strongly associated with the development of hypersensitivity reaction to abacavir.<sup>1, 2</sup>
- Symptom categories typically associated with ABC HSR (fever, rash, GI, constitutional, respiratory) can be non-specific and can decrease diagnostic precision.
- SHAPE was a retrospective case-control study which demonstrated high sensitivity of *HLA-B\*5701* for immunologically-confirmed (skin patch test (SPT) positive) ABC HSR in both Black and White subjects.
- This analysis evaluated the clinical presentation of ABC HSR based on *HLA-B\*5701* status.

## Methods

- ABC HSR cases in SHAPE were identified from clinical practice and must have met specific entry criteria to be included:
  - Clinical symptoms in at least 2 categories (fever, rash, GI, constitutional)
  - Onset of symptoms within 6 weeks of initiating ABC and resolution of one or more symptoms upon discontinuation of ABC.
- All subjects with clinically-suspected ABC HSR underwent ABC skin patch testing and *HLA-B\*5701* evaluation (see Figure 1).

Figure 1. SHAPE Study Design for HSR Cases



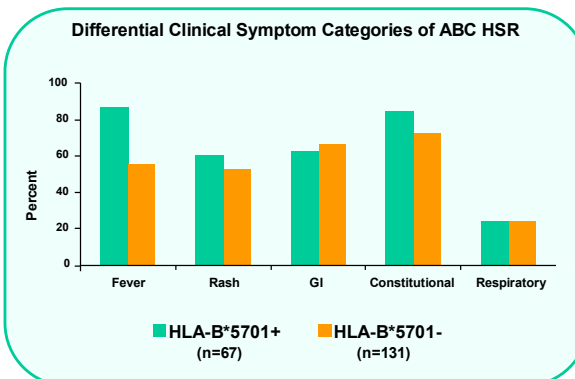
- Primary study results have been previously presented.<sup>3</sup>
  - Descriptive results were summarized by *HLA-B\*5701* status. Because descriptive results were comparable across race, they have been combined for this analysis.
- ## Results
- All cases of immunologically-confirmed ABC HSR were positive for *HLA-B\*5701* (sensitivity = 100% [95% CI: 0.92, 1.0]).
  - *HLA-B\*5701* results were available for all but one White case (SPT negative).

Table 1. Presentation of ABC HSR Symptom Categories and Time to Onset by HLA-B\*5701 Status

	HLA-B*5701+ (n=67)	HLA-B*5701- (n=131)
<b>Number of symptom categories, n (%)</b>		
None/ missing	3 (4)	2 (2)
One category	0	5 (4)
Two categories	9 (13)	44 (34)
Three or more categories	55 (82)	80 (61)
<b>Time to Onset of Symptoms, n (%)</b>	n=64	n=119
0-21 days	60 (94)	94 (79)
22-42 days	4 (6)	13 (11)
>42 days	0	12 (10)

The median time to onset was the same for both the *HLA-B\*5701* positive and negative groups (7 days) with ranges of 0-34 days and 0-469 days, respectively.

Figure 2. Clinical Symptom Categories of ABC HSR by HLA-B\*5701 Status



Subjects who were *HLA-B\*5701* positive reported fever (87% vs 56%) and constitutional (85% vs 73%) symptom categories more often than *HLA-B\*5701* negative subjects as part of ABC HSR clinical presentation (Figure 2). The most common symptoms are presented in Table 2 by time to onset.

Table 2. Presentation of Select Symptoms by Days to Onset

Symptom, n (%)	HLA-B*5701+ n=67	HLA-B*5701- n=131
<b>Fever</b>	n=58	n=66
0-21 days	55 (95)	46 (70)
22-42 days	3 (5)	10 (15)
>42 days	0	10 (15)
<b>Malaise</b>	n=44	n=62
0-21 days	43 (98)	51 (82)
22-42 days	1 (2)	6 (10)
>42 days	0	5 (8)
<b>Myalgia</b>	n=28	n=41
0-21 days	27 (96)	32 (78)
22-42 days	1 (4)	5 (12)
>42 days	0	4 (10)
<b>Fatigue</b>	n=39	n=65
0-21 days	35 (90)	51 (78)
22-42 days	3 (8)	6 (9)
>42 days	1 (3)	8 (12)
<b>Rash</b>	n=41	n=61
0-21 days	36 (88)	50 (82)
22-42 days	5 (12)	4 (7)
>42 days	0	7 (11)

As noted above, fever, malaise, myalgia and fatigue were more commonly reported in subjects who were positive for *HLA-B\*5701* than in those who were not. Rash, however, was reported nearly as often in both groups.

## Discussion

- The current analysis expands upon the original SHAPE analyses by examining differences in clinical presentation by *HLA-B\*5701* status:
  - These differences may be particularly relevant as prospective screening for *HLA-B\*5701* becomes more widespread
  - These data may also help to refine the diagnostic indicators for ABC HSR
- Specific symptoms of fever, malaise, myalgia and fatigue were more commonly reported as ABC HSR in subjects positive for *HLA-B\*5701* than in those not carrying the allele.
- Time to symptom onset within 21 days of ABC initiation was also more common in subjects positive for *HLA-B\*5701*.

## Conclusions

- Subjects carrying the *HLA-B\*5701* allele were more likely than those without the allele to present with fever and constitutional symptoms, and to have ≥ 3 categories of ABC HSR symptoms.
- Most (94%) of *HLA-B\*5701*+ subjects had onset of ABC HSR symptoms within 21 days of initiating ABC therapy
  - The median time to onset of symptoms was the same for subjects in both groups (7 days), however *HLA-B\*5701*+ subjects had a narrow range (0-34 days) compared to *HLA-B\*5701* negative subjects (0-469 days).
- *HLA-B\*5701* was 100% sensitive for SPT+ ABC HSR in this study.

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## References

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