

# Enhanced HLA-B\*15:02 Screening Before Carbamazepine Therapy in Vietnam: Advancements in Real-Time PCR TaqMan Probe Procedure

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## INTRODUCTION

Carbamazepine (CBZ) is widely used for the treatment of bipolar disorder, seizures, and neuropathic pain. However, its use is associated with serious dermatologic reactions such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), particularly in individuals carrying the HLA-B\*15:02 allele.

Carriers of HLA-B\*15:02 had 12.82 times higher odds of developing SCARs compared to non-carriers in Vietnamese population.

Our study highlights the prevalence of the HLA-B\*15:02 allele in Vietnam, the clinical outcomes of HLA-B\*15:02-positive patients, and the critical need for genotyping as a standard of care by improving a Real-time PCR TaqMan probe procedure using PNA clamping

## METHOD

This prospective multicenter study involved patients aged 18 and older, either starting carbamazepine or diagnosed with serious cutaneous adverse reactions (SCARs). The study analyzed 123 medical records from Hai Phong International Hospital and Hai Phong Psychiatric Hospital from April 2022 to July 2024.

Blood samples were collected and analyzed using a Realtime-PCR technique for HLA-B(15) genotyping with procedure: 1) Design and optimize primers and a TaqMan® probe targeting the HLA-B\*15:02 allele 2. Conduct SYBR® Green-based PCR with previously reported primers, 3) Apply PNA clamping in real-time PCR to enhance the accuracy of HLA-B\*15:02 detection, reducing false positives and validating results with known samples.

## METHOD

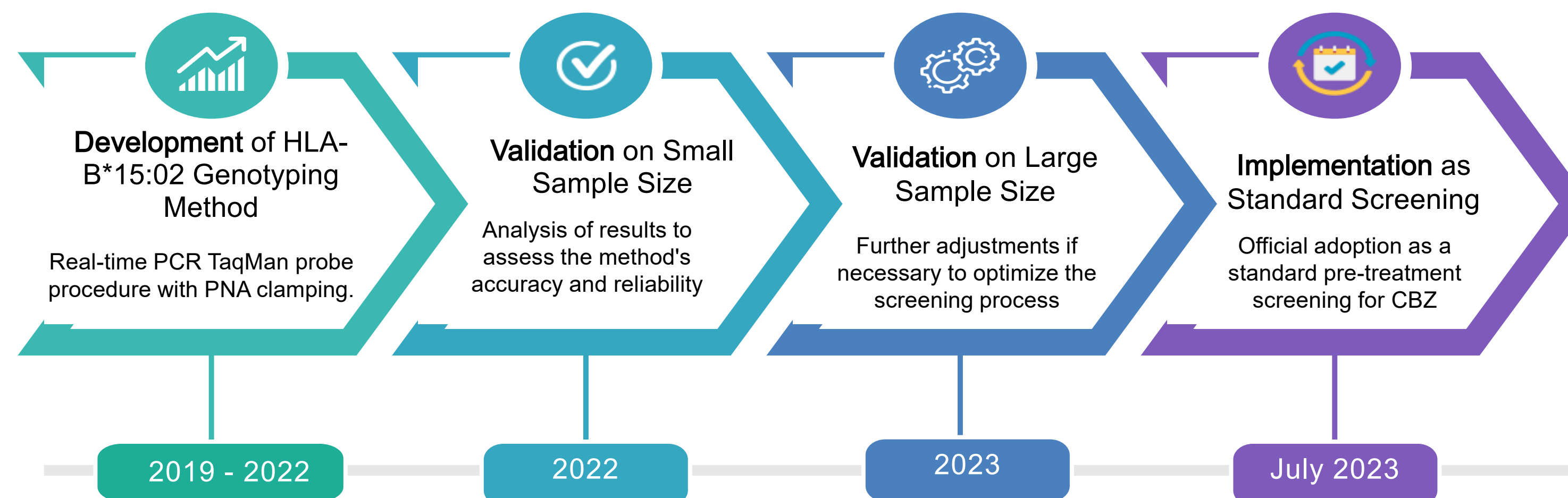


Figure 1: Study Process

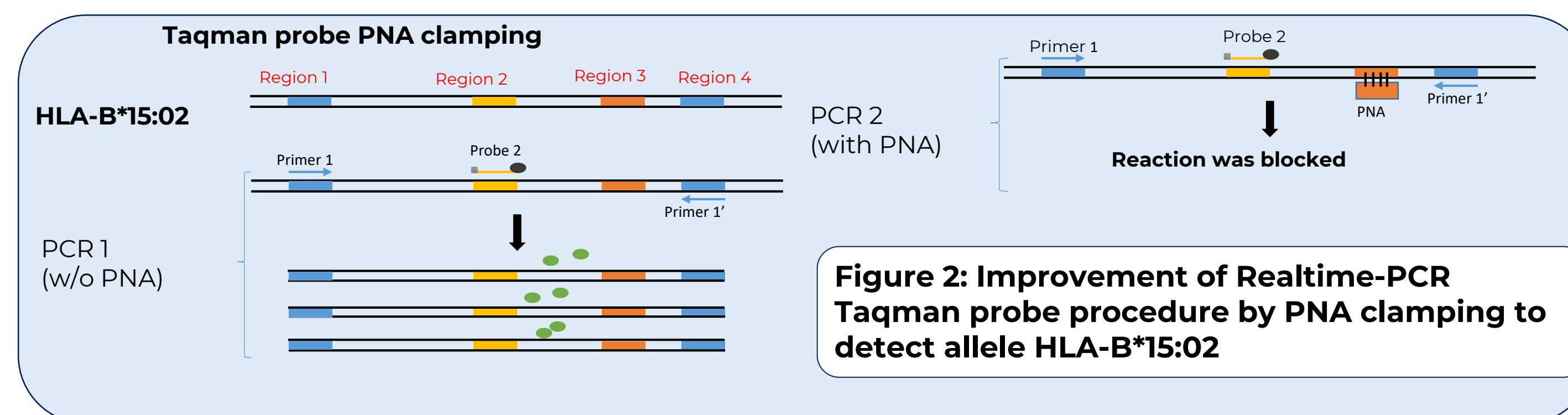


Figure 2: Improvement of Realtime-PCR Taqman probe procedure by PNA clamping to detect allele HLA-B\*15:02

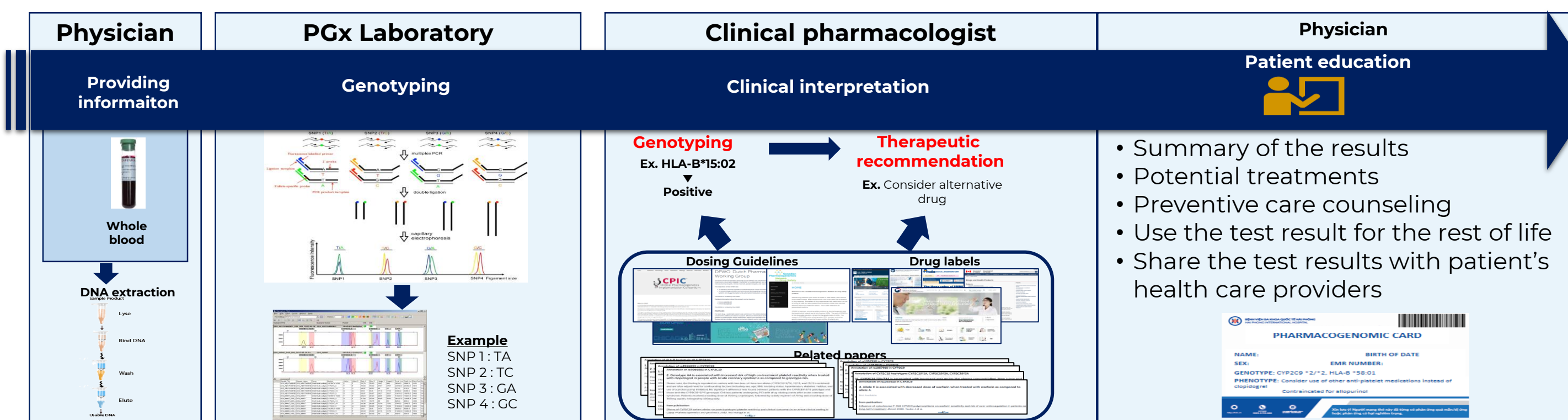


Figure 3: HLA-B\*15:02 screening procedure

## RESULTS

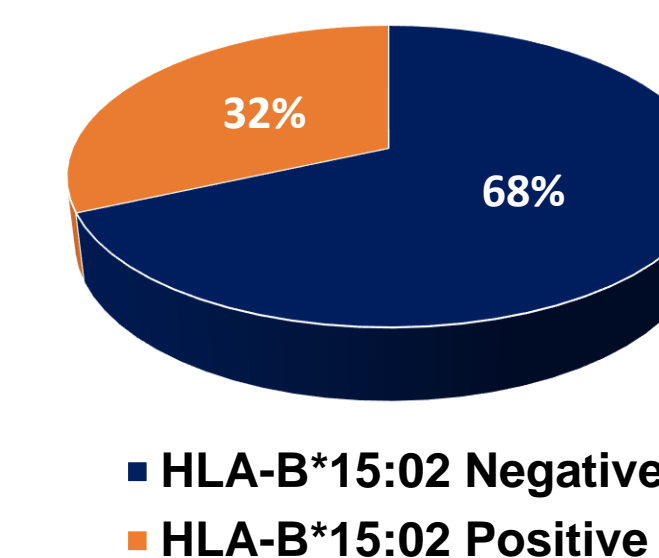
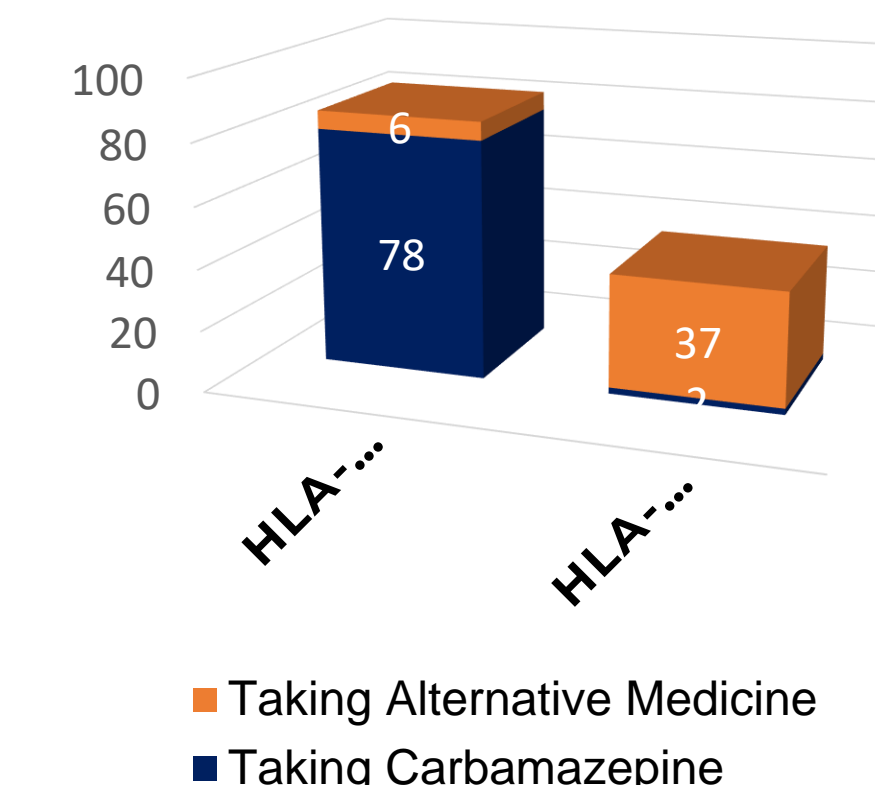


Figure 4: Distribution of HLA-B\*15:02 Genotyping Results (n = 123)

### Prescription Decision After HLA-B\*15:02 Screening

The treatment decisions based on HLA-B\*15:02 screening adhere to FDA and PharmGKB guidelines. Among the 84 patients who tested negative, 78 were prescribed CBZ. Only 2 of the 39 HLA-B\*15:02 positive patients received CBZ due to the urgency of treatment before test results were available, while 37 were given alternative medications.

Figure 5: Decision After Screening (n=123)



### Adverse Events After 2-Month Follow-Up

Among the 78 patients taking CBZ who tested negative for the HLA-B\*15:02 allele, there were no instances of mild cutaneous events or SJS. In contrast, both of the 2 HLA-B\*15:02 positive patients who took CBZ before their screening results were available developed SJS. In a group of 6 patients who used alternative medications, no adverse event were reported. However, a mild cutaneous event occurred in the 37 patients using alternative medicines.

## CONCLUSION

This study successfully developed and optimized real-time PCR methods using TaqMan Probe Procedure to accurately detect the HLA-B\*15:02 allele.

## REFERENCE

M. Whirl-Carrillo<sup>1</sup>, R. Huddart<sup>1</sup>, L. Gong, K. Sangkuhl, C.F. Thorn, R. Whaley and T.E. Klein. "An evidence-based framework for evaluating pharmacogenomics knowledge for personalized medicine." *Clinical Pharmacology & Therapeutics* (2021)