World Health Organization

KSCPT
Korean Society for Clinical Pharmacology & Therapeutics

Pharmacogenomics and Precision Medicine in the field of HIV/AIDS treatment
- The third WHO Global Patient Safety Challenge: Medication without Harm -

A Journey for medication safety and efficacy

During the drug development process, numerous pre-clinical and clinical trials are regarded as the gold standard of medication SAFETY and EFFICACY. However; they can never screen out every possible adverse drug reactions.

BLACK BOX WARNING

⚠️ **ABACAVIR SULFATE**
Serious, sometimes fatal hypersensitivity reactions (HSR) with multiple organ involvement -- Patients who carry the HLA-B*5701 allele are at high risk for experiencing a hypersensitivity reaction to abacavir.

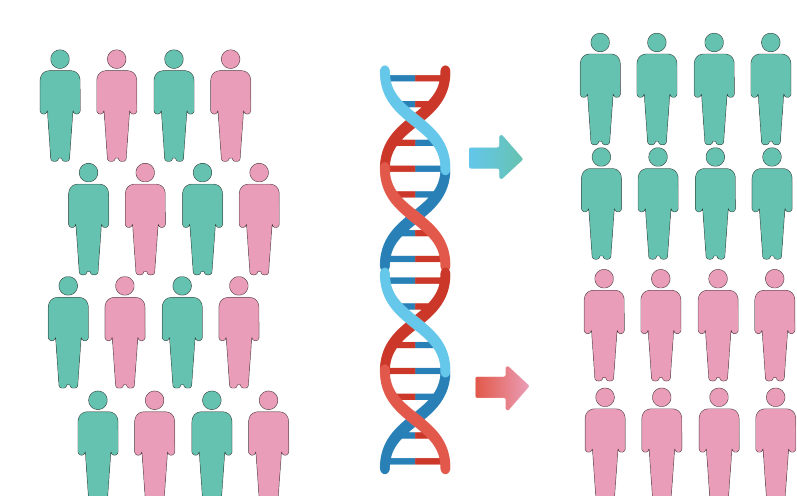### SCARs: Severe cutaneous adverse reactions

◇ DRESS (Drug reaction with eosinophilia and systemic symptoms)
◇ SJS (Stevens-Johnson syndrone)
◇ TEN (Toxic epidermal necrolysis)

Medication needs Life Cycle Managements

⇨ **Post-marketing survey (pharmacovigilance, PV)** as well as discovering appropriate biomarkers and tools to predict ADRs is required to ensure patient/medication safety.
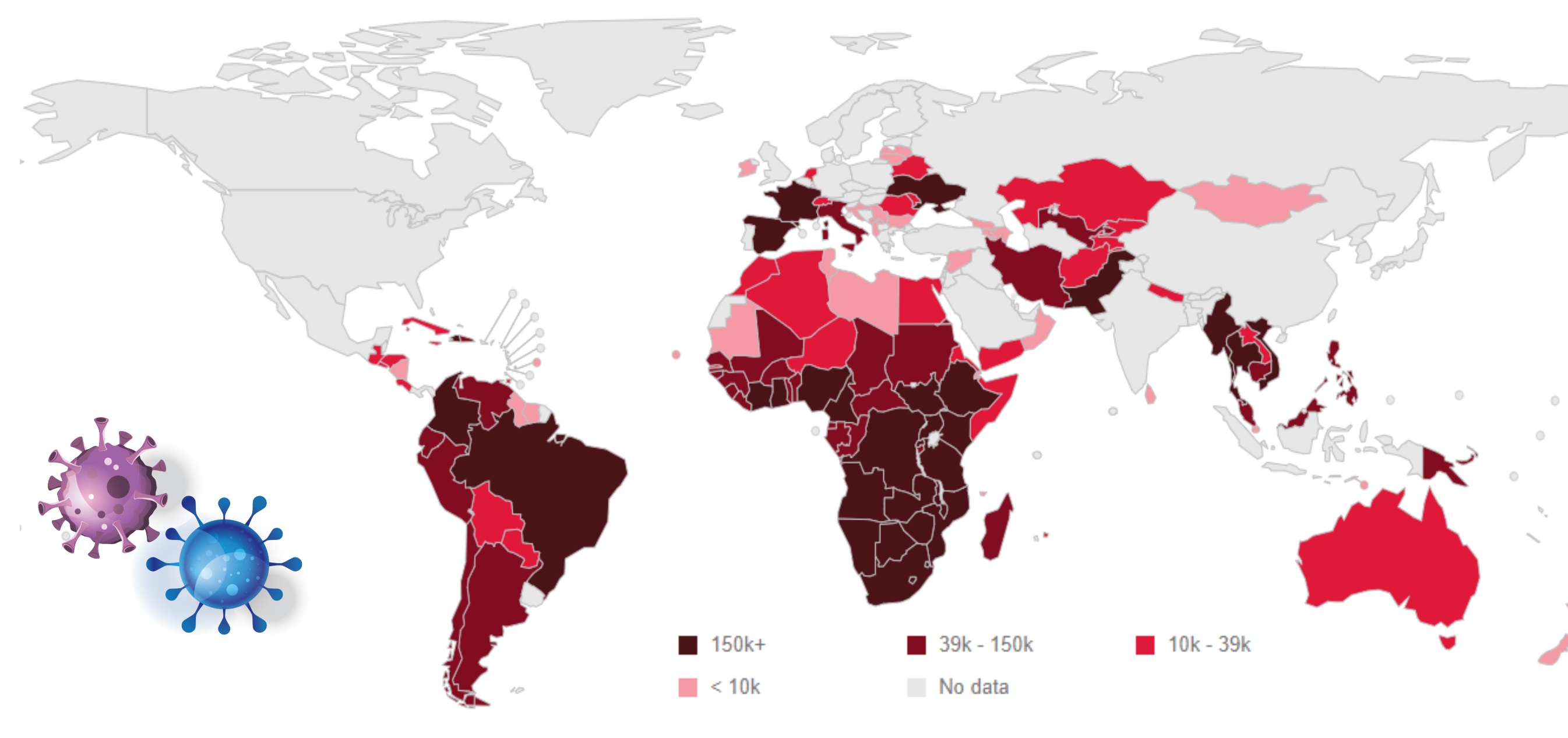
⇨ **Pharmacogenomics (PGx),** the key element of *precision medicine*, has provided biomarkers for more than 200 drugs. Genetic data can prevent medication harms by individualizing medication uses and guiding health professionals to use **"RIGHT medicine for RIGHT patient."**
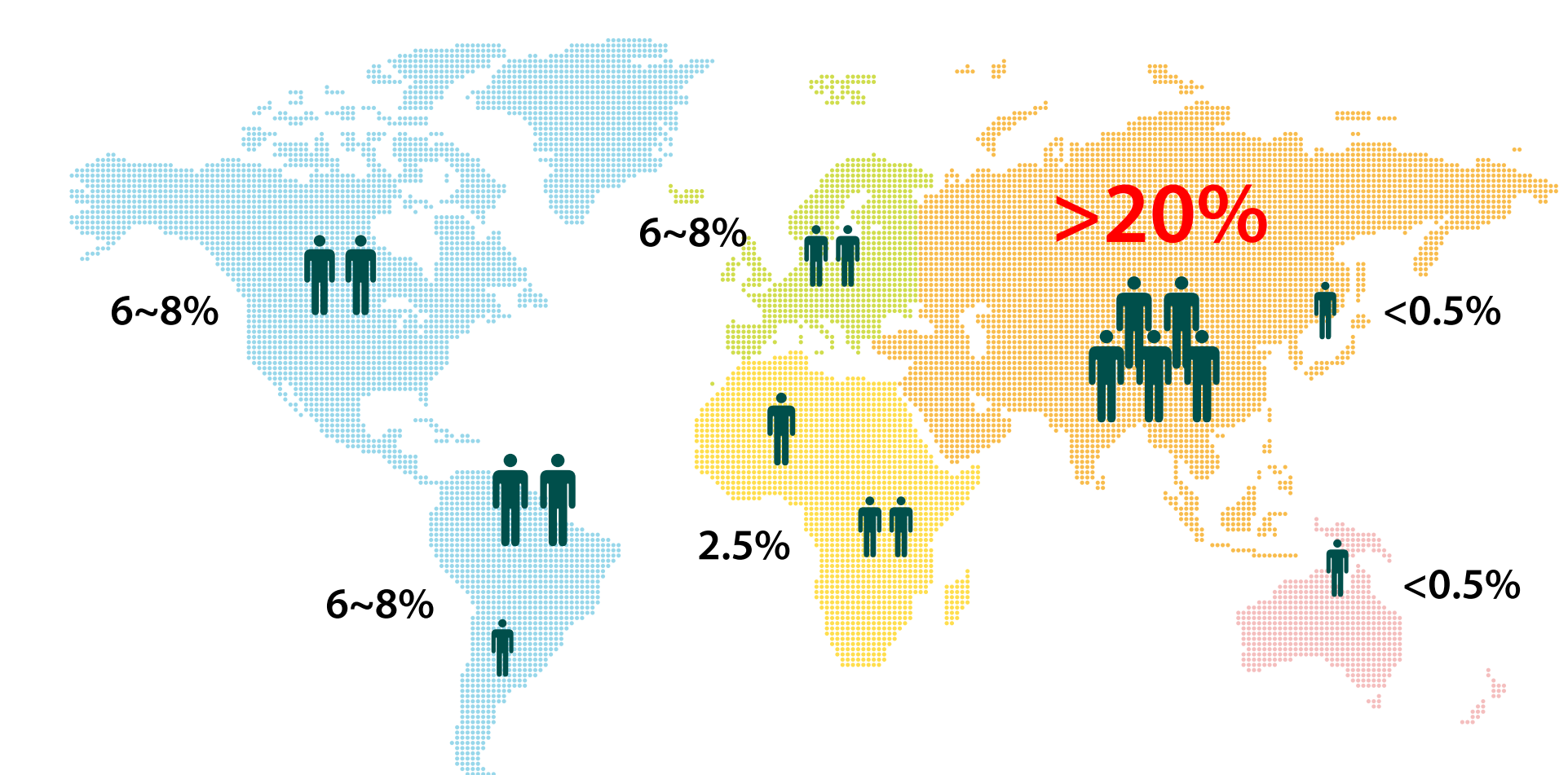
Pharmacogenomics of HIV therapy: The Abacavir Hypersensitivity

⮞⮞ People living with AIDS - all ages (2019, UNAIDS)

150k+   39k - 150k   10k - 39k   < 10k   No data

⮞⮞ HLA-B*5701 allele frequency

6~8%   6~8%   >20%   <0.5%
6~8%   2.5%   <0.5%

REST OF WORLD

1998 Marketing approval for first ABC product (Ziagen®)

2001 Association of HLA-B*5701 with ABC HSR identified

2008 PREDICT-1 study established the clinical effectiveness of prospective HLA-B*5701 screening
① Clinical validity: Diagnostic accuracy of HLA-B*5701 to detect Abacavir hypersensitivity reaction
② Clinical utility: Prospective HLA-B screening can reduce the incidence of hypersensitivity reaction to abacavir (from 2.7% to 0%, p<0.001).

Positive predictive value	Negative predictive value	Sensitivity	Specificity
47.9%	100%	1.000 (0.852-1.000)	0.967 (0.955-0.980)

2014 Meta-analytic review about the clinical and economic significance of prospective HLA-B*5701 screening
③ Cost effectiveness: Cost per hypersensitivity reaction avoided by conducting prospective HLA-B screening is €214.17 (= $255.6)

Together for Medication Safety, Efficacy, and Cost-Effectiveness

Abacavir (oral solution) price
$412 per year per person

Epzicom® annual worldwide sales
$43,000,000 (2020, Drug Analyst)

US 3.2%
Rest of World 96.8%

Current DNA testing price
$250-500 per test

POCT technology

less than $0.41 per test

Medicine and Pharmacy Clinical healthcare professionals

Technology and Innovation

Government and Regulartory sector

Hyo Yi Choi (College of Pharmacy, Seoul National University)