SUPPLEMENTAL DIGITAL CONTENT 3

Stanford Genotypic Susceptibility Scoring

Stanford genotypic susceptibility score (S-GSS) was calculated for antiretroviral drugs in the initial optimized background therapy (OBT) based on the Stanford University HIV Drug Resistance Database (HIVdb; available at https://hivdb.stanford.edu/hivdb/by-mutations/) to reflect the genetic susceptibility of a retroviral population hosted by a participant to the drugs in that participant's initial OBT. The HIVdb provides Integrated Genotypic Resistance Interpretation System to assess genotypic sensitivity to each drug [1]. The HIVdb is an expert system that accepts user-submitted HIV-1 *pol* sequences and returns inferred levels of resistance to 24 FDA-approved antiretroviral drugs. Each drug resistance mutation is assigned a drug penalty score. The total penalty score for each drug in the OBT is derived by adding together the scores for each mutation (and combination of mutations) associated with resistance to that drug. One of 5 levels of inferred drug resistance/sensitivity is then assigned based on the total penalty score, and a Stanford genetic susceptibility rating (S-GSR) is assigned per the table below. The S-GSS for the OBT was the sum of S-GSR for all the antiretroviral drugs in the OBT.

Total penalty score	Sensitivity level	S-GSR
<10	Susceptible	1
10 to <15	Potential low-level resistance	0.75
15 to <30	Low-level resistance	0.5
30 to <60	Intermediate resistance	0.25
≥60	High-level resistance	0

Reference

1. Tang MW, Liu TF, Shafer RW. The HIVdb system for HIV-1 genotypic resistance interpretation. *Intervirology*. 2012;55(2):98-101.