

Baseline Antiretroviral Resistance Profile and Correlation with Clinical Events in the OPTIMA Trial:

M Holodniy^{1*}, J. Singer², R. Woods², R. Harrigan², S. Brown³, W. Cameron⁴, T. Kyriakides⁵, B. Angus⁶ for OPTIMA Study Team

¹VA Palo Alto HCS, Palo Alto, U.S., ²Canadian HIV Trials Network, Vancouver, Canada, ³Bronx VAMC, New York, U.S., ⁴U Ottawa Hospital, Ottawa, Canada, ⁵West Haven VA CSPCC, West Haven, U.S., ⁶UK MRC, London, U.K.

Background: The OPTIMA trial is an ongoing strategy study for patients with virologic failure and multi-drug resistant (MDR) virus. The trial is a collaboration between the U.S. Department of Veterans Affairs, U.K. MRC and Canadian CIHR.

Methods: Patients (target N=504) with HIV RNA >2,500 copies/mL, CD4 < 300/mm³, on ARV therapy are randomized in a 2 x 2 factorial design to a 3-month antiretroviral (ARV) drug-free period (ARDFP) vs. no ARDFP followed by a new standard ART (≤ 4 ARVs) or MegaART (≥ 5 ARVs) regimen versus no ARDFP (immediate change to new ARV regimen of standard vs. MegaART). The primary endpoint is AIDS or death. Baseline resistance was assessed by virtual phenotype (vP). Cox proportional hazards models were derived to determine whether baseline variables (i.e. CD4 count, pVL, number of prior ARVs used, number of total and class specific resistant ARVs) were associated with clinical endpoints.

Results: 264 patients (98% male, mean age 48) have been enrolled thus far. Mean baseline HIV RNA = 4.79 log₁₀/ml and CD4 = 105 cells/mm³. Prior ARV utilization included > 2 PI (70%), > 2 NNRTI (90%) and > 2 NRTI (99%). Global vP resistance was highly correlated with the total ARV exposure. ARV class specific resistance was highly correlated with the number of prior ARV agents taken in that class. Broad vP resistance to all ARV classes was seen, except for tenofovir (< 10% vP resistance). Of the variables considered, only baseline CD4 count was significantly correlated with death or development of an AIDS event on study.

Conclusions: In this clinically advanced population, the prevalence of ARV resistance is significant and limited treatment options are available. Resistance was highly correlated with prior ARV exposure. However, neither the total number or class specific number of resistant ARVs correlated with clinical outcome. Only baseline CD4 count was a strong predictor of clinical events. We will continue to examine whether in the presence of such significant ARV resistance, benefit is derived from clinical response to standard or MegaART if preceded by ARDFP.