World Academy of Science, Engineering and Technology
International Journal of Mathematical and Computational Sciences
Vol:14, No:12, 2020

Clinical Impact of Ultra-Deep Versus Sanger Sequencing Detection of Minority Mutations on the HIV-1 Drug Resistance Genotype Interpretations after Virological Failure

Authors : S. Mohamed, D. Gonzalez, C. Sayada, P. Halfon

Abstract : Drug resistance mutations are routinely detected using standard Sanger sequencing, which does not detect minor variants with a frequency below 20%. The impact of detecting minor variants generated by ultra-deep sequencing (UDS) on HIV drug-resistance (DR) interpretations has not yet been studied. Fifty HIV-1 patients who experienced virological failure were included in this retrospective study. The HIV-1 UDS protocol allowed the detection and quantification of HIV-1 protease and reverse transcriptase variants related to genotypes A, B, C, E, F, and G. DeepChek®-HIV simplified DR interpretation software was used to compare Sanger sequencing and UDS. The total time required for the UDS protocol was found to be approximately three times longer than Sanger sequencing with equivalent reagent costs. UDS detected all of the mutations found by population sequencing and identified additional resistance variants in all patients. An analysis of DR revealed a total of 643 and 224 clinically relevant mutations by UDS and Sanger sequencing, respectively. Three resistance mutations with > 20% prevalence were detected solely by UDS: A98S (23%), E138A (21%) and V179I (25%). A significant difference in the DR interpretations for 19 antiretroviral drugs was observed between the UDS and Sanger sequencing methods. Y181C and T215Y were the most frequent mutations associated with interpretation differences. A combination of UDS and DeepChek® software for the interpretation of DR results would help clinicians provide suitable treatments. A cut-off of 1% allowed a better characterisation of the viral population by identifying additional resistance mutations and improving the DR interpretation.

Keywords : HIV-1, ultra-deep sequencing, Sanger sequencing, drug resistance
Conference Title : ICSRD 2020 : International Conference on Scientific Research and Development
Conference Location : Chicago, United States
Conference Dates : December 12-13, 2020