

693 Impact of Archived Minority Populations With M184V/I on DTG/3TC for Maintenance of Viral Suppression

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Background: There is limited evidence on the utility of proviral DNA sequencing to guide treatment changes in virologically suppressed persons with HIV (PWH) and prior virologic failures. VOLVER clinical trial aimed to evaluate if proviral DNA could assist in switching to dolutegravir/lamivudine (DTG/3TC) in PWH with history of 3TC resistance.

Methods: Open-label single-arm multicentric clinical trial of virologically suppressed PWH with past 3TC resistance. Participants switched to DTG/3TC if population sequencing of proviral DNA at baseline did not detect the M184V/I mutation. Proviral DNA next-generation sequencing (NGS) was performed from baseline samples. Primary endpoint was proportion of participants with HIV-1 RNA viral load (VL) ≥ 50 copies/mL at 48 weeks (intention-to-treat-exposed, FDA snapshot). NCT04880785.

Results: 121 participants with a mean virological suppression of 9 years switched to DTG/3TC. 109 participants (90.1%, 95%CI: 83%-95%) had a VL < 50 copies/mL at week 48, 12 premature discontinuations (4 with VL ≥ 50 copies/mL). Baseline proviral DNA NGS (using a $> 5\%$ detection threshold) data is available for 106 participants: 21 (19.8%) had M184V/I (184V: 18, 184I: 3; mean frequency 28%, range: 8-51%), 1 had K65R, 4 had thymidine analogue-associated mutations (TAMs), and 3 had other nucleoside associated mutations (NAMs) – no participant had both M184V/I and TAMs. Outcomes at 48 weeks of the 21 participants with M184V/I were: all had VL < 50 copies/mL, even though 2 (9.5%) withdrew prematurely due to adverse events. Among participants who withdrew the study with VL ≥ 50 copies/mL with baseline NGS data (3/4), none had M184V/I by NGS at baseline, including 2 who discontinued due to protocol virologic withdrawal criteria (one had NAMs 67G and 70E at baseline in NGS). At virologic withdrawal the only amplifiable sample (139 copies/mL) showed no emerging integrase resistance and the M184V with a 17% frequency by NGS in plasma RNA. After baseline, 10/103 participants with NGS data and VL < 50 copies/mL at week 48 had a transient viral rebound: 1/21 with 184V/I (4.8%), 0/8 with other mutations and 9/74 without mutations (12.2%).

Conclusion: In this clinical trial of DTG/3TC for maintenance of virological suppression detecting M184V/I in proviral DNA with NGS at baseline did not predict virologic outcomes. Our results question the use of proviral DNA NGS to guide switches to DTG/3TC in PWH with a history of lamivudine resistance.