

# Virologic Outcomes of Lamivudine/Dolutegravir in Virologically suppressed persons with Expected or confirmed Resistance to Lamivudine (VOLVER clinical trial-GESIDA 11820).

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## Type selection

## General data

**Abstract category:** Antiretroviral therapy – randomised clinical trials

## Title

## Abstract body

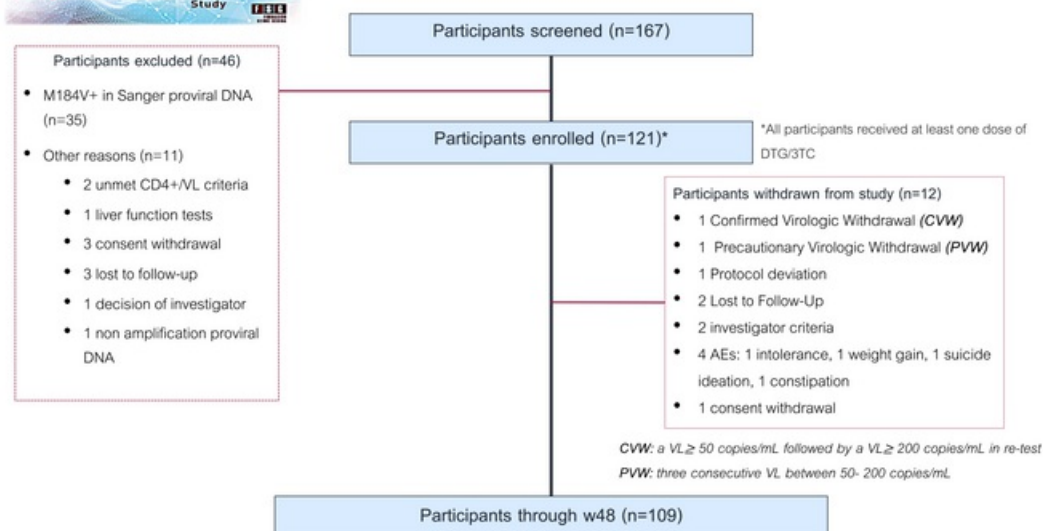
**Purpose:** We investigated the efficacy of dolutegravir/lamivudine as a maintenance treatment for people with HIV and previous lamivudine resistance, not detected in proviral DNA Sanger genotyping.

**Method:** Open-label, single arm, multicentric clinical trial including virologically suppressed participants with historical lamivudine resistance (confirmed by genotypic testing or suspected based on prior virological failure while receiving XTC), no prior integrase resistance and CD4+ >200 cells/mm<sup>3</sup> whose ART was changed to dolutegravir/lamivudine. Participants were eligible if Sanger proviral DNA sequencing at screening did not detect lamivudine resistance mutations. The primary endpoint was the proportion of participants with HIV-1 RNA viral load [VL] ≥50 copies/mL at 48 weeks in the intention-to-treat-exposed (ITT-e) population using the US Food and Drug Administration (FDA) snapshot algorithm. NCT04880785.

**Results:** 121 participants, 114 with historical lamivudine resistance mutations, mean virological suppression of 9 years ( **Figure 1, Table 1 and 2**). At 48 weeks, 4 participants had a VL ≥ 50 copies/mL (3.3%, 95%CI: 0.91%-8.2% FDA-Snapshot ITT-e): 1 confirmed virologic withdrawal (VL ≥ 50 copies/mL followed by a VL ≥ 200 copies/mL in re-test), 1 precautionary virologic withdrawal (3 consecutive VL between 50-200 copies/mL) and 2 excluded for other reasons prior to week 48 with last VL ≥ 50 copies/mL (**Table 3, Figure 2**). Of these 4 participants, plasma population sequencing was successful in 2 at the time of rebound without integrase mutations nor re-emergence of M184V/I or K65R. There were no virologic data for 8 (6.6%) participants: 1 lost to follow-up, 1 protocol deviation, 2 investigator criteria, 3 adverse events, and 1 consent withdrawal. The remaining 109 participants (90.1%, 95%CI: 83%-95%) had VL <50 copies/mL at week 48.



## Participant disposition



## All (n=121)

|  |                   |
|--|-------------------|
| Sex, Male (%)  | 86 (71.1%)        |
| Age, median (IQR)  | 56.2 (51.8, 59.8) |
| Years since HIV diagnosis, median (IQR)                    | 26.9 (20.7, 30.7) |
| Route of transmission (%)                                  |                   |
| Men who have sex with men                                  | 42 ( 34.7%)       |
| Heterosexual sex   | 36 ( 29.8%)       |
| Intravenous drug use                                       | 35 ( 28.9%)       |
| Blood transfusion  | 1 (0.8%)          |
| Unknown  | 7(5.8%)           |
| Nadir CD4+ count (cells/mm <sup>3</sup> ), median (IQR)    | 180 (71, 270)     |
| Baseline CD4+ count (cells/mm <sup>3</sup> ), median (IQR) | 675 (516, 819)    |

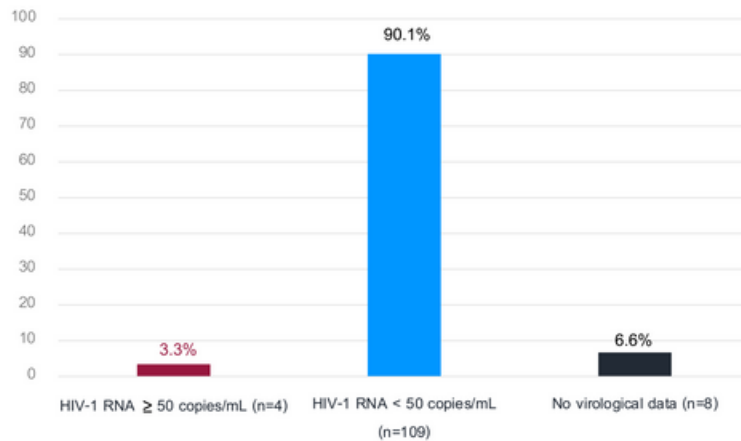
|   |   |
|---|---|
| ART duration (years), median (IQR)              | <b>All (n=121)</b><br>29.4 (17.3, 27.1) |
| Number of previous ART regimens, median (IQR)   | 8 (6, 12)                               |
| Suppressed plasma HIV RNA (years), median (IQR) | 9.2 (3.7, 14.4)                         |
| Baseline ART                                    |   |
| 2 NRTI + 1 NNRTI                                | 3 ( 2.5%)                               |
| 2 NRTI + 1bPI                                   | 27 ( 22.3%)                             |
| 2 NRTI + 1 INSTI                                | 30 ( 24.8%)                             |
| Two-drug regimens                               | 36 ( 29.8%)                             |
| bPI monotherapy                                 | 20 (16.5%)                              |
| Other   | 5 ( 4.1%)                               |

**Table 1.**

| <b>All (n=121)</b>   |                   |
|--|-------------------|
| Confirmed prior 3TC resistance (%)                           | 114 (94.2%)       |
| M184V mutation (%)   | 107 (88.4%)       |
| M184I/undefined (%)  | 7 (5.8%)          |
| Prior K65R mutation (%)                                      | 5 (4.1%)          |
| Suspected prior 3TC resistance (%)                           | 7 (5.8%)          |
| Time since genotype with 3TC resistance (years) median (IQR) | 15.2 (14.9, 15.3) |
| 3TC o FTC at baseline (%)                                    | 66 (54.5%)        |
| Prior exposure to INSTIs (%)                                 | 67 (55.4%)        |
| Prior exposure to DTG (%)                                    | 38 (56.7%)        |

**Table 2.**

### Efficacy at 48 weeks FDA- Snapshot ITT-e



| <b>All (n=121)</b>   |             |
|--|-------------|
| HIV-1 RNA < 50 copies/mL   | 109 (90.1%) |
| HIV-1 RNA ≥50 copies/mL  | 4 (3.3%)    |
| HIV-1 RNA ≥50 copies/mL in W48 window  | 0 (0)       |
| Discontinuation due to Lack of Efficacy                                      | 2 (1.65%)   |
| Discontinuation for other reasons and Last available HIV-1 RNA ≥50 copies/mL | 2 (1.65%)   |
| No virologic data at week 48   | 8 (6.6%)    |
| Discontinuation Due to an Adverse Event                                      | 3 (2.48%)   |
| Discontinuation for other reasons and Last available HIV-1 RNA <50 copies/mL | 5 (4.13%)   |

**Table 3.**

**Conclusions:** After excluding lamivudine mutations in proviral DNA by population sequencing, dolutegravir/lamivudine effectively maintained virological suppression in persons with HIV and prior history of lamivudine resistance. Notably, no treatment-emergent resistance was observed.

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