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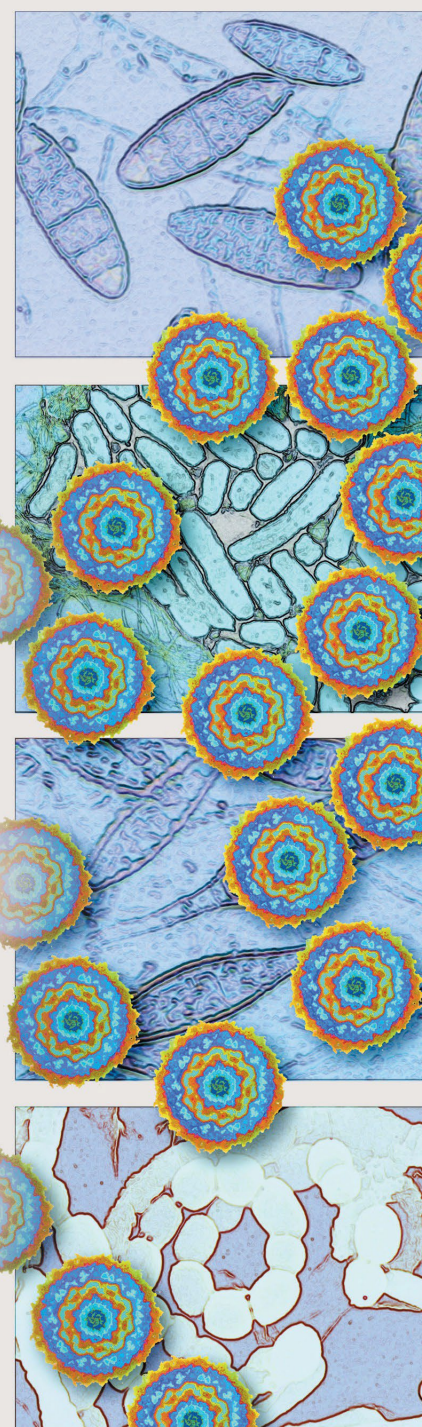
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**CO-02. LONG-TERM EFFICACY AND SAFETY OF DOLUTEGRAVIR/LAMIVUDINE IN VIROLOGICALLY SUPPRESSED PERSONS WITH HIV AND HISTORY OF RESISTANCE TO LAMIVUDINE: WEEK-96 RESULTS OF VOLVER TRIAL-GESIDA 11820**

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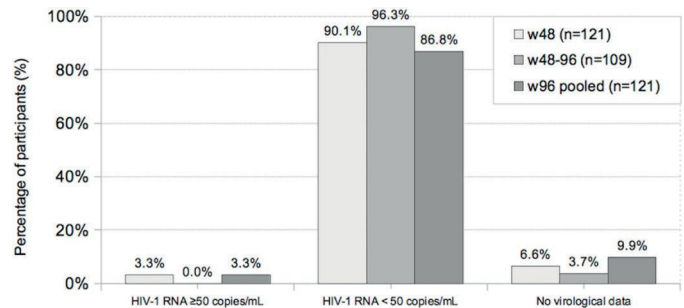
**Introduction:** VOLVER trial demonstrated at 48 weeks that dolutegravir/lamivudine maintained virological suppression in people with HIV and historical confirmed or suspected lamivudine resistance after excluding lamivudine mutations in proviral-DNA by population sequencing. No treatment-emergent resistance was observed. We present week-96 results.

**Methods:** Single-arm, multicentric trial. Participants were virologically suppressed at baseline and proviral-DNA Sanger sequencing at screening did not detect lamivudine-resistance mutations. Proviral-DNA next-generation-sequencing (NGS) was retrospectively performed in baseline samples. The efficacy endpoint was the proportion of participants with HIV-1 RNA viral load [VL]  $\geq$  50 copies/mL at 96-weeks in the intention-to-treat exposed (ITT-e) population using the US Food and Drug Administration (FDA) snapshot algorithm.

Safety and tolerability outcomes were treatment-emergent resistance, incidence of adverse events and treatment discontinuations. NCT04880785.

**Results:** 121 participants, 114 with a prior plasma genotype with M184V/I and 23 (19%) with M184V/I in baseline proviral-DNA NGS ( $>$  5% threshold). At 48 weeks, 4/121 participants had VL  $\geq$  50 copies/mL, with no evidence of integrase mutations nor re-emergence of M184V/I or K65R; 8 (6.6%) participants discontinued the study for other reasons. Between week 48 and 96, there were no new virological failures among the 109 remaining participants including 21 with M184V/I ( $>$  5%) in baseline proviral-DNA NGS ( $>$  5% threshold). At 48 weeks, 4/121 participants had VL  $\geq$  50 copies/mL, with no evidence of integrase mutations nor re-emergence of M184V/I or K65R; 8 (6.6%) participants discontinued the study for other reasons. Between week 48 and 96, there were no new virological failures among the 109 remaining participants including 21 with M184V/I ( $>$  5%) in baseline proviral-DNA NGS. Overall, the proportion of participants with HIV-1 RNA VL  $\geq$  50 copies/mL through 96 weeks was 4/121 (3.3%, 95%CI: 0.9-8.2%) (Fig.). No new resistance genotyping tests were performed per-protocol. Between 48w and 96w there were 4 (3.7%) additional discontinuations: 1 treatment-unrelated death (progression of baseline condition COPD), 1 protocol deviation (HBsAg+ although HBV-DNA undetectable), 1 consent withdrawal and 1 loss of follow-up. There were no new discontinuations related to adverse events. At 96 weeks, the proportion of participants with VL  $<$  50 copies/mL was 86.8% (105/121; 95%CI: 79.4-92.2).

	All (n = 121)
HIV-1 RNA $<$ 50 copies/mL	105 (86.8%)
HIV-1 RNA $\geq$ 50 copies/mL	4 (3.3%)
HIV-1 RNA $\geq$ 50 copies/mL in week 96 window	0 (0%)
Discontinuation due to lack of efficacy <sup>1</sup>	2 (1.7%)
Discontinuation for other reasons and last available HIV-1 RNA $\geq$ 50 copies/mL <sup>2</sup>	2 (1.7%)
<b>No virologic data at week 96</b>	<b>12 (9.9%)</b>
Discontinuation due to an adverse event	3 (2.5%)
Discontinuation for other reasons and last available HIV-1 RNA $<$ 50 copies/mL <sup>3</sup>	9 (7.4%)



**Conclusions:** After excluding lamivudine mutations in proviral-DNA by population sequencing, dolutegravir/lamivudine effectively maintained virological suppression after two years of follow-up in participants with history of lamivudine resistance. Notably, no treatment-emergent resistance was observed. Virological efficacy was not affected by detection of M184V/I in proviral-DNA using NGS.