

## **Dolutegravir/Lamivudine for Maintenance of Virological Suppression in Persons with Historical Suspected or Confirmed Resistance to Lamivudine: Week 48 Results of a Single-Arm, Open-Label, Multicentre, Phase IIA Clinical Trial**

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### **Abstract**

**Background:** We investigated the efficacy of dolutegravir/lamivudine for maintenance treatment for people with HIV and previous lamivudine resistance.

**Methods:** Open-label, single arm, multicentric clinical trial including virologically suppressed PWH with historical lamivudine resistance (confirmed by genotypic testing or suspected based on clinical history), no integrase resistance and CD4+ >200 cells/mm<sup>3</sup> whose ART was changed to dolutegravir/lamivudine if the M184V/I mutation was not detected in baseline proviral DNA population sequencing. Proviral DNA next-generation sequencing (NGS) was retrospectively performed in baseline samples. Primary endpoint was 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 Food and Drug Administration snapshot algorithm.

**Results:** 121 participants enrolled, 114 with a prior genotype with M184V/I, mean virological suppression of 9 years. 24 (19.8%) had the M184V/I in baseline proviral DNA NGS (>5% threshold). At 48 weeks, 4 participants had a VL ≥50 copies/mL (3.3%, 95% CI: 0.9%-8.2%, FDA-Snapshot ITT-e): 1 confirmed virologic withdrawal, 1 precautionary virologic withdrawal and 2 discontinued from study treatment for other reasons with last VL ≥ 50 copies/mL; none had M184V/I in baseline proviral DNA NGS and there was no emergent integrase resistance. 90.1% participants (109/121) had a VL<50 copies/mL (95% CI: 83.3%-94.8%) and there were no data for 6.6 % (8/121 participants) at 48 weeks.

**Conclusions:** After excluding lamivudine mutations in proviral DNA by population sequencing, dolutegravir/lamivudine effectively maintained virological suppression in PWH with CD4+ >200 cells/mm<sup>3</sup> and history of lamivudine resistance. Notably, no treatment-emergent resistance was observed.

**Keywords:** Dolutegravir; Lamivudine; Proviral DNA; Resistance.