TANGO

96-Week Results

DOVATO is indicated for the treatment of HIV-1 in adults and adolescents above 12 years weighing at least 40 kg, with no known or suspected resistance to the integrase inhibitor class, or lamivudine.

Dovato
dolutegravir/lamivudine

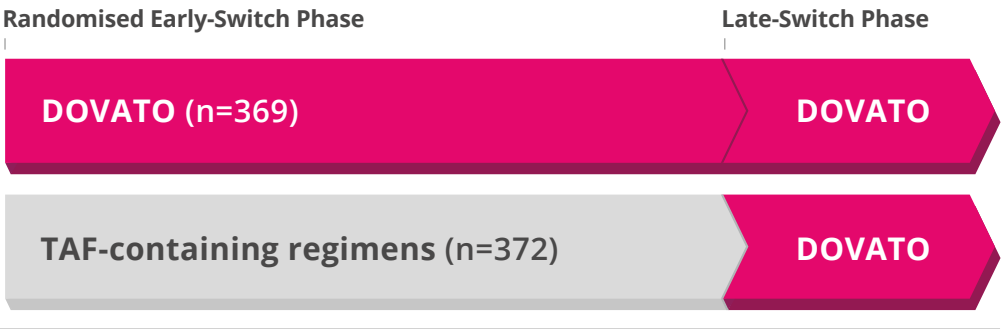
POWER REIMAGINED

AN INNOVATIVE, GUIDELINE-RECOMMENDED REGIMEN FOR YOUR PATIENTS LIVING WITH HIV

DOVATO vs TAF-CONTAINING REGIMENS IN VIROLOGICALLY SUPPRESSED PATIENTS

Phase III, Randomised, Non-Inferiority Trial With More Than 700 Patients[1]

- Virologically suppressed adults with HIV-1 RNA <50 copies/mL for >6 months
- TAF/FTC + PI or INI or NNRTI as initial regimen
- Stable TAF-containing regimen
- No prior virological failure and no documented NRTI or INI resistance
- HBV negative
- CrCL >50mL/min

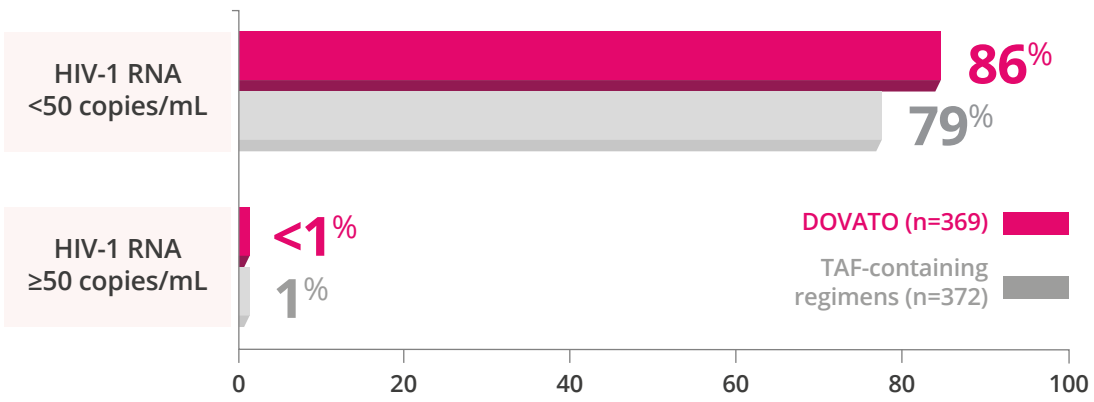


Primary Endpoint:
Proportion of patients with plasma HIV-1 RNA ≥50 copies/mL (by Snapshot algorithm; ITT–E) at 48 weeks

POWERFUL, DURABLE, NON-INFERIOR EFFICACY OUT TO 96 WEEKS VS A TAF-CONTAINING REGIMEN

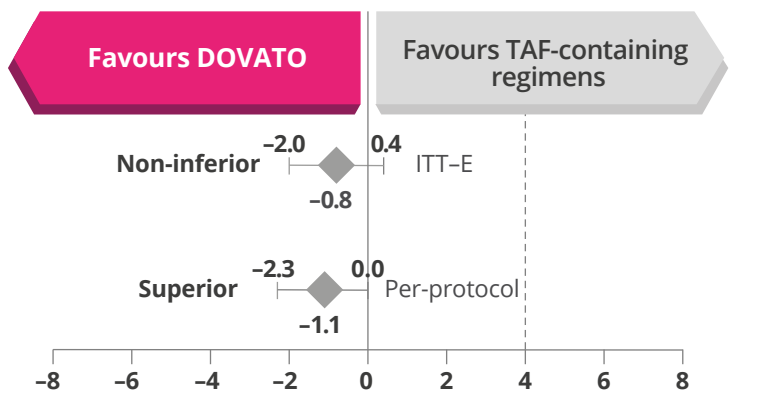
Non-Inferiority Maintained With No Increased Risk of Virological Failure vs TAF-Containing Regimens[1]

Virological Outcomes



ITT–E Snapshot analysis.

Adjust Treatment Difference (95% CI)



Difference in Proportion of Patients With HIV-1 RNA ≥50 copies/mL
Based on a 4% non-inferiority margin

REASSURANCE WITH A HIGH BARRIER TO RESISTANCE

0 **Cases of Resistance-Associated Mutations at 96 Weeks Across Both Arms**

- Confirmed virological withdrawals*: DOVATO 0 vs 3 (<1%) TAF-containing regimens
  - —No INI mutations observed
  - —No NRTI mutations observed (including M184V/I)

TDF, TAF AND ABC FREE

Overall Adverse Events Were Comparable Across Both Arms Out To 96 Weeks[1†]

ANY ADVERSE EVENT

88% DOVATO (n=324/369) — vs — **88%** TAF-containing regimens (n=325/371)

- **Drug-Related AEs, Grade 2 to Grade 5:** DOVATO 6% (21/369) vs TAF-containing regimens 2% (7/371)
- **AEs leading to withdrawal:** DOVATO 6% (21/369) vs TAF-containing regimens 1% (4/371)
  - – For the majority of patients in the DOVATO arm, the introduction of 2 new ARVs may have contributed to the numerical differences in drug-related AEs Grade 2 to Grade 5

Metabolic Parameters at 48 Weeks: Post-Hoc Analysis[2,3]

The TANGO studies did not determine whether the following changes translate to clinical differences:

Insulin Resistance
Overall, significantly fewer patients with insulin resistance* after switching to DOVATO from a TAF-containing regimen. Statistically significant differences for Dovato were observed in the boosted subgroup

Lipids
Overall, significant improvements from baseline in most lipid parameters* in the DOVATO arm vs TAF-containing regimens. Statistically significant differences for Dovato were observed in the boosted subgroup

Weight Gain and Metabolic Syndrome
ACROSS BOTH ARMS:
- A mean weight gain of 0.8kg
- Small increases in metabolic syndrome‡
- Small increases in fasting glucose and HbA_{1c}

Bone and Renal Biomarkers
Minimal changes in bone turnover and renal function biomarkers across both arms

*Defined s homeostatic model assessment of insulin resistance (HOMA-IR) ≥ 2
**The 4 out of 5 lipid parameters were total cholesterol, LDL cholesterol, triglycerides and total cholesterol/HDL cholesterol ratio.
†Longer-term data required to determine clinical impact of switching to DOVATO from TAF-containing regimens.

Dovato
dolutegravir/lamivudine

Prescribing Information

Dovato dolutegravir 50mg/lamivudine 300mg tablets
See Summary of Product Characteristics (SmPC) before prescribing

Indication: HIV-1 in adults & adolescents above 12 years of age weighing ≥40kg, with no known or suspected resistance to the integrase inhibitor class, or lamivudine. **Dosing:** One tablet once daily with or without food. Use an additional 50mg tablet of dolutegravir approximately 12 hours after the dose of Dovato when co-administered with efavirenz, nevirapine, tipranavir/ritonavir, etravirine (without boosted PI), carbamazepine, oxcarbazepine, phenytoin, phenobarbital, St John's Wort or rifampicin. *Elderly*: Limited data in 65+ yrs. Not recommended in patients with creatinine clearance < 50 mL/min. Caution in severe hepatic impairment. **Contraindications:** Hypersensitivity to any ingredient. Co-administration with substrates of OCT-2 with narrow therapeutic windows, such as fampridine. **Special warnings/precautions:** Risk of hypersensitivity reactions. Discontinue dolutegravir and other suspect agents immediately. Risks of osteonecrosis, immune reactivation syndrome. Monitor LFTs in Hepatitis B/C co-infection and ensure effective Hepatitis B therapy. Caution with metformin: monitor renal function and consider metformin dose adjustment. Use with etravirine requires boosted PI or increased dose of dolutegravir. Use with Mg/Al-containing antacids requires dosage separation. Use with calcium, multivitamins or iron also requires dosage separation if not taken at the same time with food. Use with cladribine or emtricitabine not recommended. When possible, avoid chronic co-administration of sorbitol or other osmotic acting alcohols (see SmPC section 4.5). If unavoidable, consider more frequent viral load monitoring. **Pregnancy/ lactation:** The safety and efficacy have not been studied in pregnancy. Women of childbearing potential should be counselled about the potential risk of neural tube defects with dolutegravir (a component of Dovato), including consideration of effective contraceptive measures. If a woman plans pregnancy, the benefits and the risks of continuing treatment with Dovato should be discussed with the patient. If a pregnancy is confirmed in the first trimester while on Dovato, the benefits and risks of continuing Dovato versus switching to another antiretroviral regimen should be discussed with the patient taking the gestational age and the critical time period of neural tube defect development into account. Most neural tube defects occur within the first 4 weeks of embryonic development after conception (approximately 6 weeks after the last menstrual period). Dovato may be used during the second and third trimester of pregnancy when the expected benefit justifies the potential risk to the foetus. Do not breast-feed. **Side effects:** See SmPC for full details. Headache, GI disturbance, insomnia, abnormal dreams, depression, anxiety, dizziness, somnolence, rash, pruritus, alopecia, fatigue, arthralgia, myalgia, hypersensitivity, suicidal ideation or suicide attempt, hepatitis, blood dyscrasias, acute hepatic failure, pancreatitis, angioedema, rhabdomyolysis, lactic acidosis, peripheral neuropathy. Elevations of ALT, AST and CPK. **Basic NHS costs:** £656.26 for 30 tablets. **MA number:** EU/1/19/1370/001. **MA holder:** ViiV Healthcare BV, Van Asch van Wijckstraat 55H, 3811 LP Amersfoort, Netherlands. Further information available from: customercontactuk@gsk.com
Freephone 0800 221 441.

POM

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Adverse events should be reported. For the UK, reporting forms and information can be found at *yellowcard.mhra.gov.uk* or search for **MHRA Yellowcard** in the **Google Play** or **Apple App store**. Adverse events should also be reported to GlaxoSmithKline on 0800 221441.

*Patients met confirmed virological withdrawal criteria if they had 1 assessment with HIV-1 RNA ≥200 copies/mL after Day 1 with an immediately prior HIV-1 RNA ≥50 copies/mL.[1]
‡Defined by the International Diabetes Federation as a combination of risk factors for cardiovascular disease.[4]

References: 1. van Wyk J, Ajana F, Bisshop F, et al. Switching to DTG/3TC fixed-dose combination (FDC) is non-inferior to continuing a TAF-based regimen (TBR) in maintaining virologic suppression through 96 weeks (TANGO study). Presented at: HIV Glasgow 2020; October 5-8, 2020; Virtual. Slides O441. **2.** van Wyk J, Ait-Khaled M, Santos J, et al. Improved metabolic parameters after switching from TAF-based 3-or 4-drug regimen to the 2-drug regimen of DTG/3TC (dolutegravir/lamivudine): the TANGO study. Presented at: International AIDS Conference; July 6-10, 2020; Virtual. Slides OAB0606. **3.** van Wyk J, Ajana F, Bisshop F, et al. Efficacy and safety of switching to dolutegravir/lamivudine fixed-dose 2-drug regimen vs continuing a tenofovir alafenamide–based 3- or 4-drug regimen for maintenance of virologic suppression in adults living with human immunodeficiency virus type 1: Phase 3, randomized, noninferiority TANGO study. *Clin Infect Dis*. 2020. doi:10.1093/cid/ciz1243 **4.** International Diabetes Federation. The IDF consensus worldwide definition of the metabolic syndrome. Published 2006. Updated April 5, 2017. Accessed June 2020. https://www.idf.org/e-library/consensus-statements/60-idfconsensus-worldwide-definitionof-the-metabolic-syndrome.html

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