This document provides a short summary of this study for a general audience. You can find more information in the scientific summaries of the study. Links to those summaries are provided at the end of this document.

Study names

<u>Short Title</u>: A study to compare a combination of dolutegravir and lamivudine with tenofovir alafenamide-based regimen in adults living with HIV.

<u>Full Scientific Title</u>: A phase III, randomised, multicentre, parallel-group, non-inferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus lamivudine in HIV-1-infected adults who are virologically suppressed (TANGO Study).

ViiV Healthcare Study Number: 204862

Who sponsored this study?

ViiV Healthcare GSK Clinical Support Help Desk Website: <u>clinicalsupporthd.gsk.com/contact.html</u> Email: <u>GSKClinicalSupportHD@gsk.com</u>

General information about the clinical study

When was this study done?

The study started in January 2018 and ended in May 2022 when all participants completed the end of study Week 200 visit.

What was the main objective of this study?

HIV (human immunodeficiency virus type 1) damages the body's defence system (immune system). It weakens the ability to fight infections and increases the risk of developing diseases when not treated effectively. HIV has ribonucleic acid (RNA) as its genetic material. Doctors can check the amount of HIV in the body (viral load) by measuring HIV RNA levels in the blood.

Use of the data and information contained in this Document is unrestricted, provided that it may not be used in applications by others for regulatory approval of a product. While not required, when using these data, we ask that proper credit or attribution of ViiV Healthcare as the source of the data be given. ViiV Healthcare/GSK disclaims liability for all uses of the data by users of this Document, to the fullest extent permitted by applicable law. No trademark, patent, or regulatory/data exclusivity rights held by ViiV Healthcare/GSK are waived, licensed or otherwise affected. HIV medicines control the viral load by preventing HIV from making any more virus. Researchers consider that these medicines are working well if the participants' viral load remains undetectable (less than 50 copies per millilitre of blood [c/mL]). This means levels of HIV measured by tests that are commonly used in clinics are too low to harm the immune system.

Adults living with HIV with an undetectable viral load took part in this study. When this study started, they were being treated with tenofovir alafenamide and at least two more approved HIV medicines. This was their tenofovir alafenamide-based regimen (TBR). Researchers wanted to see how well a combination tablet of dolutegravir (DTG) and lamivudine (3TC) maintained viral loads in these participants compared with continuing TBR. They also studied the safety of these medicines.

Which medicines were studied?

On Day 1, participants were placed in one of the two treatment groups by chance (randomisation):

- Early Switch DTG and 3TC group (two-medicine regimen): Participants switched from TBR to receive DTG and 3TC tablet once daily throughout the study.
- TBR group (three- to four-medicine regimen): Participants continued taking TBR up to week 148.

At Week 148 (about three years), participants with an undetectable viral load (less than 50 c/mL) were switched from TBR to DTG and 3TC referred to as the Late Switch DTG and 3TC group.

• Late Switch DTG and 3TC group: Participants received DTG and 3TC tablet once daily and were followed up to Week 200.

Each participant and his/her study doctor knew which treatment the participant received (open-label study).

After Week 200 (about four years), participants completed the study and continued treatment with locally available DTG and 3TC medicine and were managed as per the standard of care by their doctors.

Which participants took part in this study?

Studies have a list of requirements for participants who can enrol (inclusion criteria) and those who can't (exclusion criteria). For this study, the main inclusion and exclusion criteria are listed below.



Overall, 741 participants received at least one dose of the study medicines. The study included 683 (92%) men and 58 (8%) women. The average age was 41 years. The youngest participant was 18 years old and the oldest participant was 74 years old.

For more detailed information about the participants included in this study, see the scientific results summaries (links to those summaries are provided at the end of this document).

Where was this study done?



Study sites were in 10 countries.

What were the main results of the study?

Study doctors collected blood samples and measured participants' viral loads.

The study compared the number of participants in the two treatment groups, who had a detectable viral load (50 c/mL or more) at Week 48.

One of 369 participants (less than 1%) in the Early Switch DTG and 3TC group and two of 372 participants (less than 1%) in the TBR group had a detectable viral load at Week 48.

At Week 48, there were 24 participants (7%) in each treatment group with no results. These participants had left the study or missed the Week 48 visit.

The study also compared the percentage of participants in the two treatment groups, who had an undetectable viral load (less than 50 c/mL) at Week 48 and Week 144. Results are shown in the figure below.



At Week 148, from the TBR group, all 298 on-going participants were switched to treatment with DTG and 3TC. This group is referred to as the Late Switch group. The remaining 74 participants (20%) had left the study before Week 148. At Week 196, in the Early Switch DTG/3TC group, 83% of participants had an undetectable viral load (less than 50 c/mL) compared to 86% at Week 144.

At Week 196, for the Late Switch DTG/3TC group (1 year follow-up post-switch: Weeks 148 to 196), 93% of participants had an undetectable viral load (less than 50 c/mL). This result is consistent with the results during the first year of the Early Switch DTG/3TC group (Day 1 to Week 48).

More information about the study results is available in the scientific results summaries (links to those summaries are provided at the end of this document).

What were the side effects?

Medical problems (adverse events) can happen to people when they receive a medicine. Study doctors record these events. A summary of these events can be found in the scientific results summaries (links to those summaries are provided at the end of this document).

If the study doctor thinks that the event was caused by the study medicine, they record this as a possible side effect (also called adverse reaction).

In this summary, side effects refer to those events that the study doctor thinks may have been caused by the study medicines. The side effects in this summary may be new (unexpected) and different to the expected side effects mentioned in the Informed Consent for this study or other documents related to the study medicines.

The side effects in this summary have been reported from Day 1 to Week196. One participant who was randomised to the TBR group did not take tenofovir alafenamide. Side effects for this participant are not reported in this summary.

Serious side effects

Serious side effects were reported by one participant (less than 1%) in the Early Switch DTG and 3TC group, one participant (less than 1%) in the TBR group and by one participant (less than 1%) in the Late Switch group. The participant in the Early Switch DTG and 3TC group had higher than normal levels of a liver protein in the blood. The participant in the TBR group had swelling under the skin. The participant in the Late Switch group had an allergic reaction.

Non-serious side effects

Non-serious side effects are side effects that do not result in death, hospitalisation or disability. These were reported by 55 participants (15%) in the Early Switch DTG and 3TC group over 4 years (Day 1 to Week 196), 17 participants (5%) in the TBR group over 3 years (through Week 144) and by 29 participants (10%) in the Late Switch group over 1 year (Week 148 to Week 196). The table below shows the non-serious side effects that were reported by 1% or more of participants in any treatment group.

Number of participants (percent) with non-serious side effects reported by 1% or more of participants in any treatment group.					
	Early Switch DTG and	TBR	Late Switch DTG and		
	3TC 369	371	ЗТС		
	participants	participants	298 participants		
	(Week 196)	(Week 144)	(Week 196)		
Weight - increase	6 (2%)	6 (2%)	0		
Sleeplessness	6 (2%)	0	3 (1%)		

Nausea	5 (1%)	2 (less than 1%)	1 (less than 1%)
Diarrhoea	4 (1%)	3 (less than 1%)	5 (2%)
Anxiety	4 (1%)	1 (less than 1%)	1 (less than 1%)
Tiredness	3 (less than 1%)	0	3 (1%)
Abnormal weight gain	4 (1%)	0	2 (less than 1%)
Headache	2 (less than 1%)	0	5 (2%)

How has this study helped participants and researchers?

The study showed that participants who switched to a combination tablet of DTG and 3TC had a similar response in maintaining an undetectable viral load compared with participants who continued taking TBR.

The side effects reported in this study were as expected. Initially more participants in the DTG and 3TC group reported side effects compared with those in the TBR group. This could be because participants in the TBR group continued receiving their current medicines and were stable for several months before starting the study, while those in the DTG and 3TC group had started new medicines. Participants in the Late Switch group had similar side effects to those observed in the Early Switch group.

This was a phase III study. Phase III studies collect information about how well new medicines work and how safe they are. The results help government regulators decide whether to approve new medicines for their country.

Are there plans for further studies?

Other studies of DTG and 3TC in adults living with HIV have been completed. Some are ongoing or planned.

Where can I find more information about this study?

Clinical studies have unique study numbers that are included in publications and other information about the study. The unique study numbers associated with this study are shown below with internet links to scientific summaries.

The scientific summaries include more details about the requirements for study enrolment, the study visit schedule, results from other outcomes, and more detailed information about adverse events.

Organisation and Website	Study Number
European Medicines Agency (www.clinicaltrialsregister.eu)	<u>2015-004401-17</u> 1
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	<u>NCT03446573</u> ²

Your doctor or healthcare provider can help you understand more about this study and the results. Speak to your doctor about the treatment options available in your country. You should not make changes to your care based on the results of this or any single study. Keep taking your current treatment unless instructed by your doctor.

We would like to thank the participants who made this study possible. The results of this study will help answer scientific questions about treating adults living with HIV. The content for this document was finalised by ViiV Healthcare on 13 December 2022. The information in this summary does not include additional information available after this date.

¹<u>https://www.clinicaltrialsregister.eu/ctr-search/search?query=2015-004401-17</u> ²<u>https://clinicaltrials.gov/ct2/show/NCT03446573</u>