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

Short Title: A study to learn about the effect of fostemsavir in adults with HIV-1 resistant to multiple antiretroviral medicines.

Full Scientific Title: A multi-arm, phase 3, randomised, placebo-controlled, double-blind clinical trial to investigate the efficacy and safety of fostemsavir in heavily treatment-experienced subjects infected with multi-drug resistant HIV-1 (BRIGHTE study).

ViiV Healthcare Study Number: 205888

Who sponsored this study?

ViiV Healthcare (the study was originally sponsored by Bristol Myers Squibb)
GSK Clinical Support Help Desk
Website: clinicalsupporthd.gsk.com/contact.html
Email: GSKClinicalSupportHD@gsk.com

General information about the clinical study

When was this study done?

The study started in February 2015. Enrolment was closed, but the study was ongoing when this summary was finalised. The results presented in this summary include data collected up to August 2018.

What was the main objective of this study?

Human immunodeficiency virus type 1 (HIV-1) damages the body's defence system (immune system). This weakens the body's ability to fight infections and increases the risk of developing diseases.

Doctors monitor the amount of HIV-1 in the body (viral load) by measuring HIV-1 RNA levels in the blood. Antiretroviral medicines treat HIV-1 infection by controlling the viral load. Researchers consider that these medicines work well if the participants' viral load reduces and remains undetectable (less than 40 copies per millilitre [c/mL]).

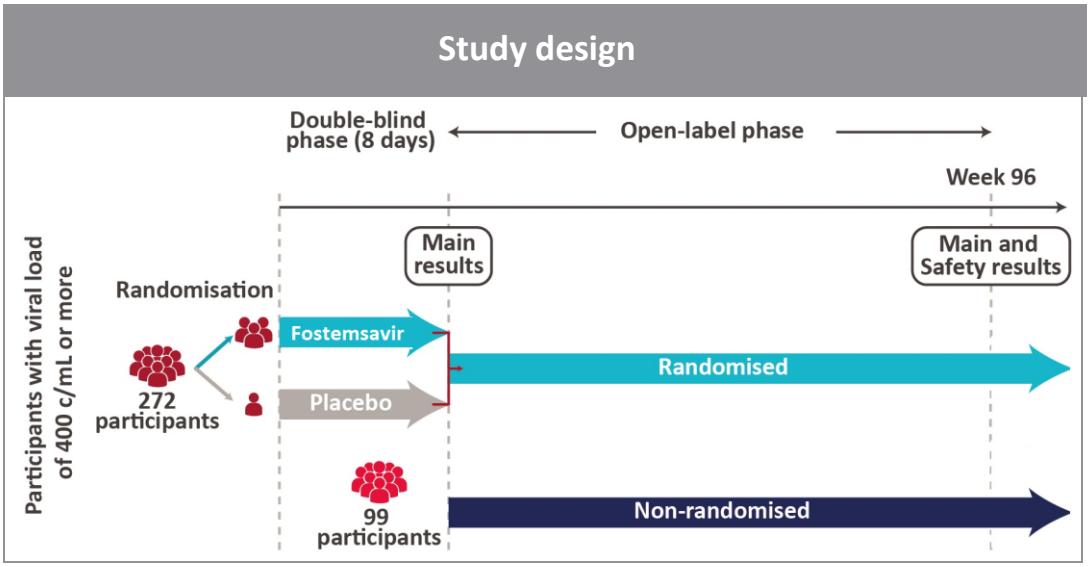
Another test of the effect of HIV-1 on the immune system is CD4+ T cell count. T cells are white blood cells that fight infection. Adults with poorly controlled HIV-1 have low CD4+ T cell counts.

Adults with HIV-1 resistant to multiple antiretroviral medicines and failing their current treatment (viral load of 400 c/mL or more) took part in this study.

Researchers wanted to see how well fostemsavir works in these participants when added to their current failing treatment for 8 days. Researchers also assessed how well fostemsavir works when given long-term with an optimised treatment regimen. This regimen was a combination of medicines chosen by the study doctor based on participant's treatment history and laboratory test results. They also assessed the safety of fostemsavir.

Which medicine was studied?

The study was conducted in two parts (phases), as shown in the figure below. Results were collected at the end of the 8-day double-blind phase and at Week 24, Week 48, and Week 96 of the open-label phase.



After Week 96, participants could choose to continue receiving fostemsavir in the study until it was approved and available in their country.

Randomised group

Participants whose current treatment included one or two antiretroviral medicines that could be combined with the study medicine to work against the resistant virus were included in the randomised group.

For the double-blind phase (8 days), these participants were placed in one of the two treatment groups by chance (randomisation). Three times as many participants received fostemsavir compared with placebo.

- Fostemsavir group: Participants received fostemsavir tablets twice daily and continued taking their current failing treatment.
- Placebo group: Participants received placebo (no active medicine) tablets twice daily and continued taking their current failing treatment.

During the double-blind phase, neither the participant nor the study doctor knew which treatment the participant received.

From the start of the open-label phase, all participants who completed the double-blind phase received fostemsavir along with the optimised treatment regimen.

Non-randomised group

Additional participants whose current treatment did not include any antiretroviral medicine that could work against the resistant virus were included in the non-randomised group.

Participants in the non-randomised group received fostemsavir and optimised treatment regimen during the open-label phase.

Participants in both the randomised and non-randomised groups and the study doctor knew which treatment the participant received during the open-label phase.

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.

Men and women with HIV-1 were included in the study if they:

- Were at least 18 years old.
- Had known resistance or intolerance to antiretroviral medicines from at least three different classes.
- Were failing their current antiretroviral treatment and had a viral load of 400 c/mL or more.
- Had no more than two antiretroviral medicines that could work against the resistant virus when combined with the study medicine.

Men and women were excluded from the study if they had:

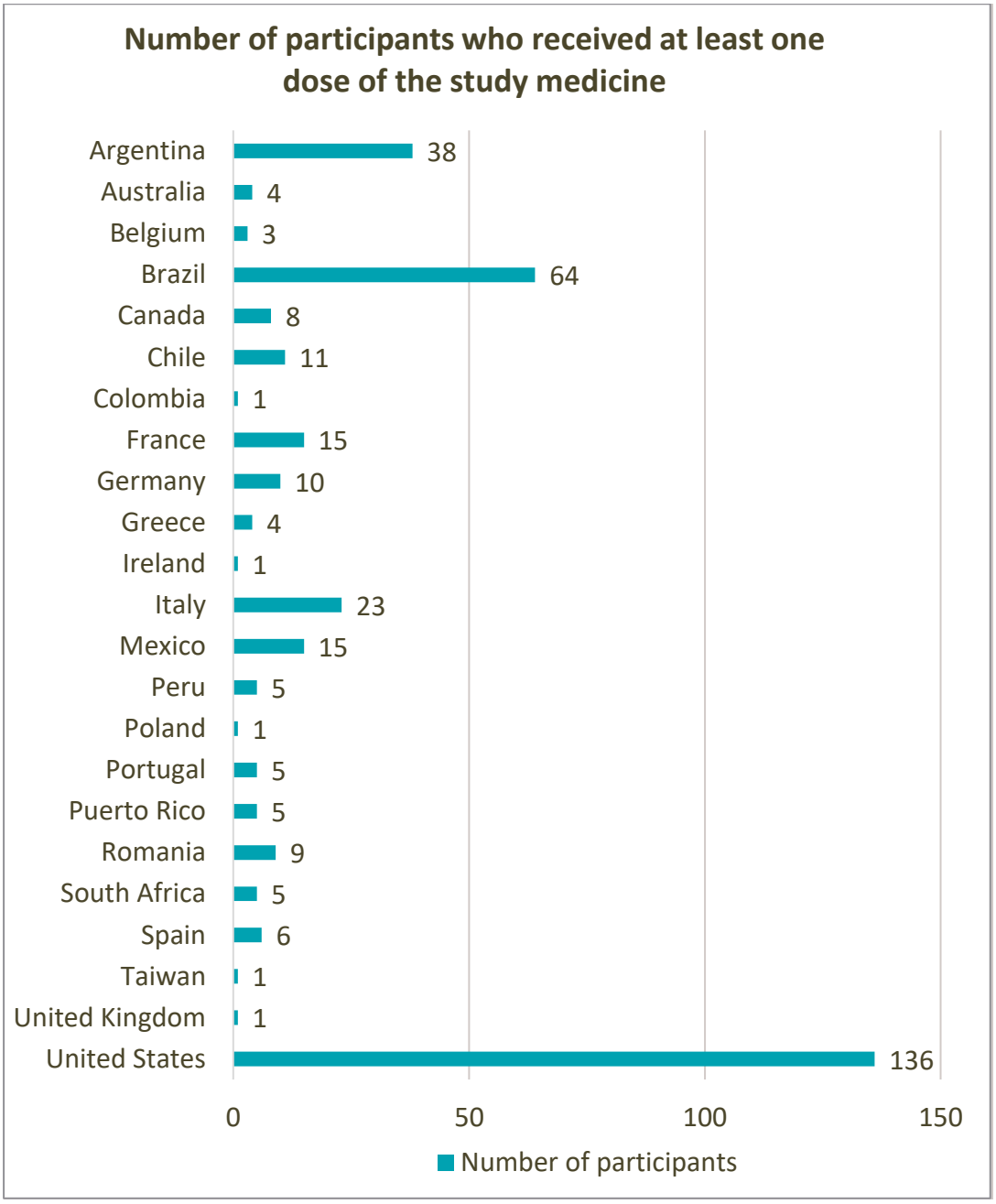
- HIV-2 infection.
- Heart or liver disease.
- Any other disease(s), abnormal blood test results, or taken any medicine(s) that the study doctor thought would affect the results of the study.

Overall, 371 participants received at least one dose of the study medicine. The study included 289 men (78%) and 82 women (22%). The average age was 46 years. The youngest participant was 17 years old and the oldest participant was 73 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 23 countries.



What were the main results of the study?

Randomised group - double-blind phase

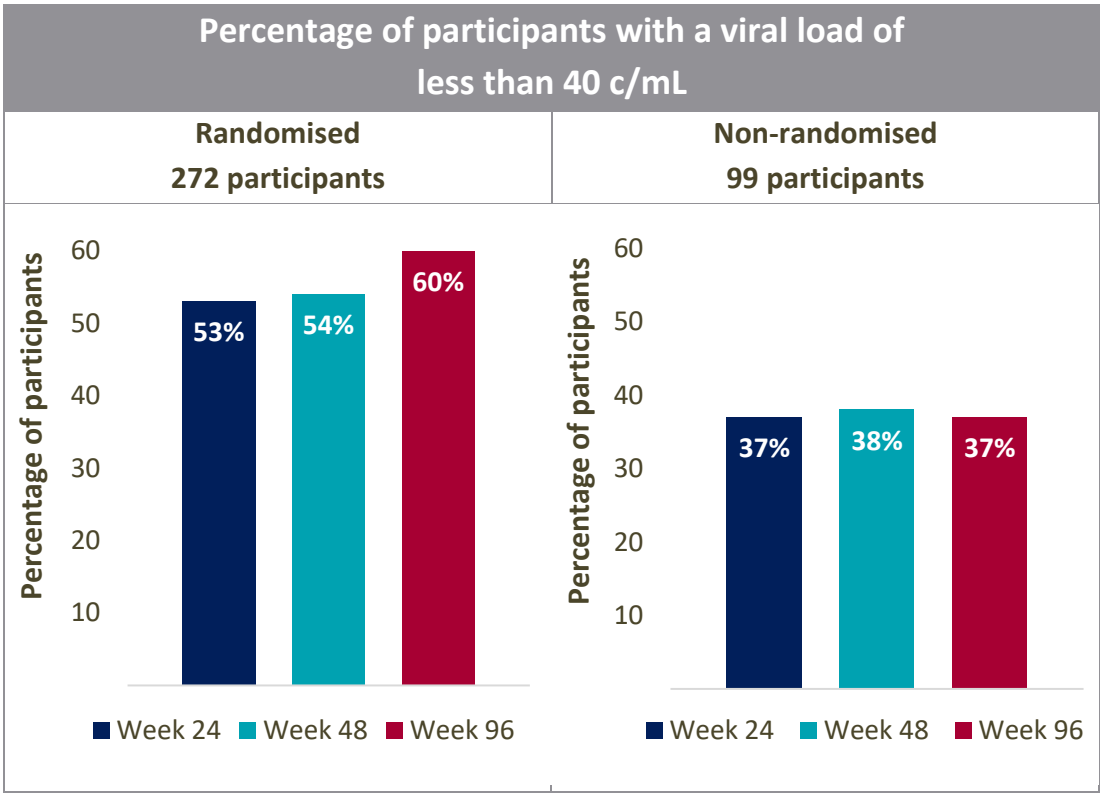
The main objective of the study was to compare the change in viral load in participants who received fostemsavir with those who received placebo during the double-blind phase.

The participant's viral load change was assessed after eight days of treatment. The results showed that participants who received fostemsavir had a greater average decrease in viral load after eight days of treatment compared with participants who received placebo.

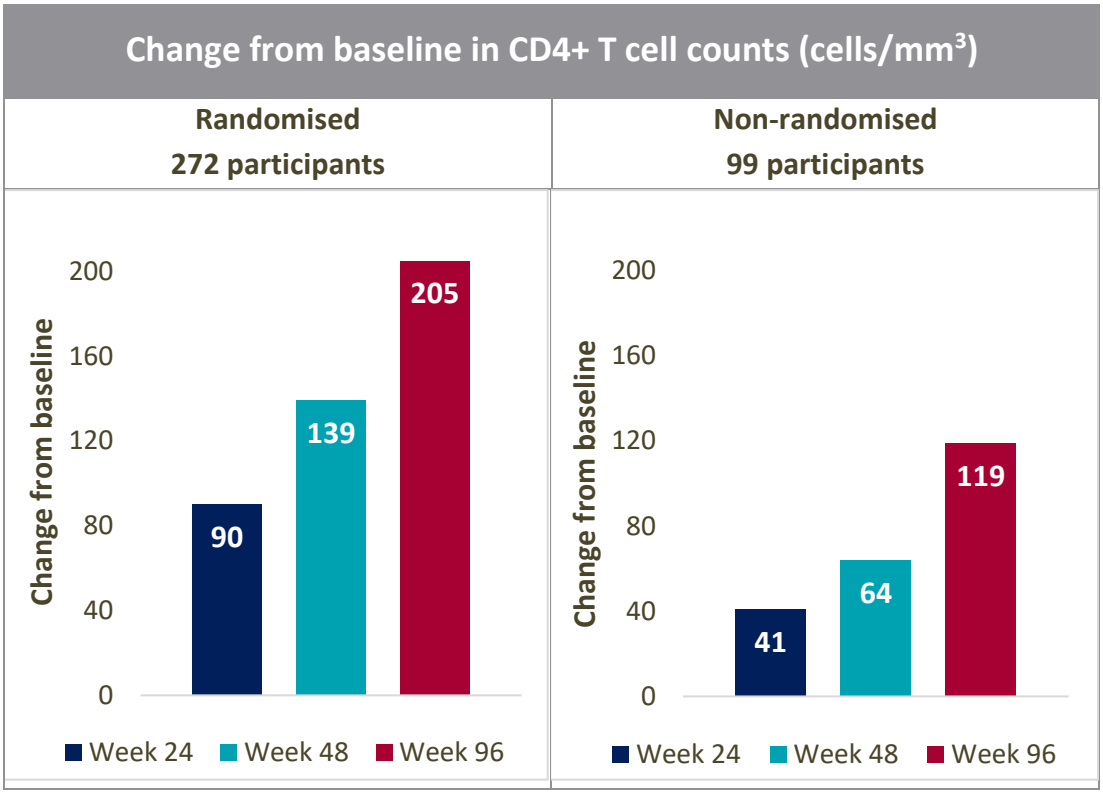
Average change in viral load after eight days of treatment		
	Fostemsavir 201 participants	**Placebo 69 participants**
Average decrease in viral load	0.791 $\log_{10}$ c/mL	0.166 $\log_{10}$ c/mL
Difference	0.625 $\log_{10}$ c/mL	

Randomised and non-randomised groups - open-label phase

Study doctors measured participant's viral load during the open-label phase. The number (percentage) of participants who had an undetectable viral load (less than 40 c/mL) at Week 24, Week 48, and Week 96 in each treatment group was calculated. Results are shown in the figure below.



Study doctors also measured participant's CD4+ T cell counts, as number of cells per cubic millimetre (cells/mm^3) at baseline (before taking the first dose of the study medicine) and at Week 24, Week 48, and Week 96. The difference in these counts between the visits and baseline was called the change from baseline. Results are shown in the figure below.



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?

Unwanted medical events (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 (adverse reaction). In this summary, side effects refer to those events that the study doctor thinks may have been caused by the study medicine. The side effects in this summary may be different to those in the Informed Consent for this study or other documents related to the study medicine.

Randomised group (study start to Week 96)

The side effects reported by participants who received either fostemsavir or placebo during the double-blind phase and then switched to fostemsavir during the open-label phase were reported together under the randomised group.

Serious side effects

Serious side effects were reported by nine participants (3%) in the randomised group.

Two participants had severe inflammation caused in response to use of antiretroviral therapy. This serious side effect led to the death (fatal side effect) of one participant.

The following serious side effects were reported by one participant each:

- Breakdown of muscle tissue
- Confusion
- Fainting
- Foetal growth restriction
- High blood glucose levels
- Inability of the kidneys to perform their function
- Kidney injury
- Kidney stones
- Liver injury
- Rash

Non-serious side effects

Non-serious side effects were reported by 102 participants (38%) in the randomised group. The table below shows the number of participants (percent) with non-serious side effects that were reported by 3% or more of participants.

Number of participants (percent) with non-serious side effects reported by 3% or more of participants in randomised group	
	Randomised 272 participants
Nausea	26 (10%)
Diarrhoea	12 (4%)
Headache	10 (4%)
Indigestion	8 (3%)

Non-randomised group (from start of open-label phase to Week 96)

Serious side effects

Serious side effects were reported by three participants (3%) in the non-randomised group.

The following serious side effects were reported by one participant each:

- High blood potassium levels
- Inflammation of heart muscles
- Kidney stones
- Severe inflammation in the brain and/or spinal cord caused in response to use of antiretroviral therapy

No fatal side effects were reported by participants in the non-randomised group.

Non-serious side effects

Non-serious side effects were reported by 32 participants (32%) in the non-randomised group. The table below shows the number of participants (percent) with non-serious side effects that were reported by 3% or more of participants.

Number of participants (percent) with non-serious side effects reported by 3% or more of participants in non-randomised group	
	Non-randomised 99 participants
Diarrhoea	6 (6%)
Nausea	6 (6%)
Tiredness	5 (5%)
Vomiting	3 (3%)

How has this study helped participants and researchers?

Adults with HIV-1 resistant to multiple antiretroviral medicines and failing their current treatment took part in this study. The study showed that fostemsavir was better than placebo in decreasing viral load after eight days of treatment.

During the open-label phase, the percentage of participants with an undetectable viral load was maintained. The average CD4+ T cell counts increased over time.

The side effects reported in this study were as expected.

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 make decisions about new medicines for their country.

Are there plans for further studies?

Other studies of fostemsavir in adults with HIV-1 have been conducted and 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 endpoints, and more detailed information about adverse events. When the study is complete, final results will be available in the scientific summaries.

Organisation and Website	Study Number
European Medicines Agency (www.clinicaltrialsregister.eu)	2014-002111-41[1]
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	NCT02362503[2]

Your doctor 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 contributed to this study. The results of this study will help answer scientific questions about treating adults with HIV-1.

The content for this document was finalised by ViiV Healthcare on 17 December 2021. The information in this summary does not include additional information available after this date.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2014-002111-41

[2] https://clinicaltrials.gov/ct2/show/NCT02362503