Future MICROBIOLOGY

Plain Language Summary of Publication

Combined bictegravir, emtricitabine and tenofovir alafenamide for treating people with HIV: A plain language summary of the BICSTaR study up to 1 year

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Where can I find the original article on which this summary is based?

You can read the original article called 'Twelve-month effectiveness and safety of bictegravir/emtricitabine/tenofovir alafenamide in people with HIV: Real-world insights from BICSTaR cohorts' for free at: https://onlinelibrary.wiley.com/doi/full/10.1111/hiv.13593

Summary

What is this summary about?
This is a summary of an article about an ongoing study called the BICSTaR study.

The BICSTaR study includes people with HIV (human immunodeficiency virus) who are taking a medicine called bictegravir/emtricitabine/tenofovir alafenamide (shortened to B/F/TAF). B/F/TAF is a single tablet that contains 3 different drugs for the treatment of HIV. The drugs work together to reduce the levels of HIV so that the virus can no longer be detected by a blood test.

How to say (double click sound icon to play sound)...

- **Antiretroviral:** AN-tee-REH-troh-VY-rul
- **Bictegravir:** bik-TEG-ra-vir
- **Emtricitabine:** em-trye-SYE-ta-been
- **Immunodeficiency:** IH-myoo-noh-deh-FIH-shun-see
- **Tenofovir alafenamide:** ten-OF-oh-vir al-a-FEN-a-mide

People taking part in the study are adults with HIV living in Europe, Canada, Israel, Japan, South Korea, Singapore and Taiwan. People take 1 tablet of B/F/TAF once a day. They are either taking B/F/TAF as their first treatment for HIV, or they have switched to B/F/TAF from another HIV treatment.

Researchers looked at how well B/F/TAF worked and how safe it was in people who took B/F/TAF for a year.

What are the key takeaways?
Researchers found that B/F/TAF worked well in almost all people in the study by reducing levels of HIV in the blood. The virus could not be found in the blood of more than 9 out of 10 (94%) people who were taking B/F/TAF as their first HIV medicine and more than 9 out of 10 people (97%) who had taken another HIV medicine before starting B/F/TAF. This is known as having an 'undetectable viral load' and is a major goal for HIV treatment success. Researchers did not find any evidence of HIV developing resistance to B/F/TAF, which might stop B/F/TAF from working properly.

Around 1 out of 10 people (13%) had side effects (any unwanted sign or symptom that people have when taking a medicine that researchers think might be caused by the medicine) that might have

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been caused by B/F/TAF. Most of these side effects were not classified as serious. Less than 1 out of 100 (0.1%) people had serious side effects that might have been caused by B/F/TAF. Only 6 out of 100 people stopped taking B/F/TAF due to side effects caused by B/F/TAF. As a result, more than 9 out of 10 people (95%) took B/F/TAF for at least 1 year.

What were the main conclusions reported by the researchers?
B/F/TAF worked well in people with HIV in this study. Most people (around 9 out of 10) did not have any side effects.

What is the purpose of this PLSP?

The purpose of this plain language summary is to help you to understand the findings from recent research.

The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, and not on the results of a single study.

Who is this article for?

This summary is for people with HIV and their chosen family members or caregivers, healthcare professionals, policy makers, patient advocates and those who help others learn about B/F/TAF as a treatment for HIV.

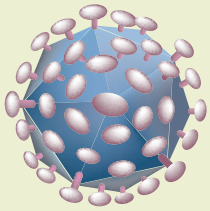
Who sponsored this clinical study?

This study was funded by Gilead Sciences, Inc. (Foster City, CA, USA).

Sponsor: A company or organization that oversees and pays for a clinical research study. The sponsor also collects and analyzes the information that was generated during the study.

What is HIV?

- HIV (human immunodeficiency virus) is a virus that damages the body's immune system (the body's natural defense system) and weakens its ability to fight off infections and diseases.
- Without effective treatment, HIV can be passed to another person through contact with body fluids from a person with HIV. This can include blood, semen, pre-seminal fluid (a fluid that is released from the penis during sexual arousal and before ejaculation), vaginal fluid, rectal fluid, and breast milk.



What is the current treatment for HIV?

- People with HIV are prescribed medicines called antiretroviral therapies.
- When a person with HIV takes their medicine as directed, the medicine stops the virus from making new copies of itself (known as multiplying or replicating). This lowers the amount of HIV in a person's blood (known as the 'viral load').
- The treatment is effective if it lowers the amount of the virus enough that it cannot be found through a special blood test. This is known as having an 'undetectable viral load' or 'viral suppression'.
- Antiretroviral therapies do not cure HIV, but they can help people with HIV to improve how their immune system works, to live longer in good health and to have a better quality of life. With antiretroviral therapies, life expectancy could be similar to that of people without HIV. Having an undetectable viral load means that HIV cannot be passed to another person during sex (known as 'Undetectable equals Untransmittable' or 'U=U').

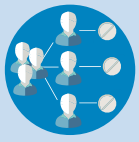
What is B/F/TAF?

- B/F/TAF is a type of antiretroviral therapy that is available in many countries.
- It is taken as a single tablet once a day.
- The tablet contains 3 drugs called bictegravir (B), emtricitabine (F), and tenofovir alafenamide (TAF). Each of these drugs stops HIV from multiplying, but they work in different ways.
- These drugs work best when used together, which is why they are combined in a single B/F/TAF tablet.

How does B/F/TAF work?

- Like other antiretroviral therapies, the 3 drugs in B/F/TAF work together to stop the virus from multiplying.
- Bictegravir (B) interferes with the way the HIV virus makes new copies of itself in the body by blocking a protein called integrase. Emtricitabine (F) works to stop the HIV virus from copying its genetic code into a form that can be inserted into human cells by disrupting the activity of another HIV protein, called reverse transcriptase. Tenofovir alafenamide (TAF) works in a similar way to emtricitabine.
- Together, these drugs help stop HIV from infecting new cells and lower the amount of HIV in the blood.
- When there is a lower amount of HIV in the blood, the immune system can work better. This means a lower chance of developing illnesses related to HIV infection and immunodeficiency (weakened immune system).

Why was the study carried out?



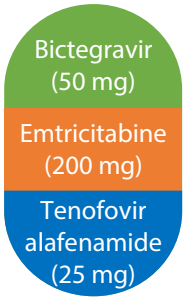
- Before a new medicine is approved by government authorities and can be prescribed, it is tested in clinical trials.
  - ➜ These trials look at how well the medicine works and how safe it is. Clinical trials include a selected group of people and are performed in a very 'controlled' environment with lots of checks and observations. They are designed to answer specific medical questions. Because of this, they do not always show how people take their medicine in real life. Clinical trials often leave out people with other illnesses, elderly people, or people who take other medicines.
- So, once a medicine is approved for use by the government authorities, researchers often do more studies.
  - ➜ These studies try to find out more about how the medicine works when it is taken by lots of different people as part of their treatment and daily life. This is known as a 'real-world' study.
- B/F/TAF is already approved in many countries. This is because clinical trials have shown that it works well and does not have many side effects. A side effect is any unwanted sign or symptom that people have when taking a medicine that researchers think might be caused by the medicine.
- This study (called the BICSTaR study) is a large real-world study. It will tell healthcare professionals more about how effective and safe B/F/TAF is when people with HIV take it as part of their regular clinical care and daily life. The study is still happening but researchers have focused on the results from people who have taken the medicine for 1 year.

How was the study carried out?

The BICSTaR study program includes 5 ongoing studies with over 2,000 adults living with HIV taking part. The present analysis of the BICSTaR study program includes 1,509 people who joined the study between June 28, 2018, and May 17, 2021. They remained in the study for 24 months (2 years) in most countries, and 60 months (5 years) in a few countries.

The study is ongoing and will be completed when the last person has their final checkup. The current results are based on information collected from hospital files, clinical records, clinic visits, electronic medical records and patient questionnaires up to February 18, 2022.

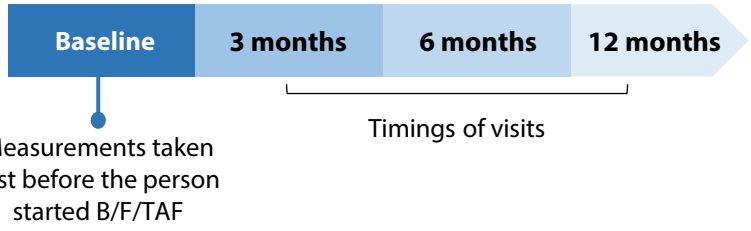
People could join the study if they were prescribed **B/F/TAF** treatment and decided to take part.



People took B/F/TAF as a single tablet at a dosage of 50 mg/200 mg/25 mg.

At the start of the study, and at all other visits, researchers measured (among other things):

- How much HIV was in people's blood (viral load)
- If people had any unwanted side effects that might be caused by B/F/TAF



How was the effectiveness of B/F/TAF measured?

The **main result** the researchers looked at was the **number of people with an undetectable level of HIV in their blood** at 1 year. An undetectable level meant there was less than 50 copies of the virus per microliter of blood (known as 'viral suppression' or 'undetectable viral load').
Researchers also:

- Looked at how well the immune system was working by counting a type of immune system cell, known as CD4 cells
    - The higher the number of cells, the better the immune system is working
- Counted how many people continued to take B/F/TAF for 1 year

How was the safety of B/F/TAF measured?

Researchers measured the number of people who had any unwanted side effects that might be caused by B/F/TAF

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Who took part in the study?

1,509 people were included in this study. 279 of these people had never taken HIV medicine before (known as 'treatment-naïve'). The other 1,230 people had taken other HIV medicines before the study (known as 'treatment-experienced').

Most people in the study were male and White. People who were treatment-naïve were generally younger and had lower body weight when they started the study than people who were treatment-experienced.

Almost 7 out of 10 people (68%) had at least 1 medical condition in addition to HIV. These included mental health conditions and long-term conditions such as high cholesterol, high blood pressure, and heart disease. About half of people (55%) were taking at least 1 other prescription medicine, such as drugs to treat high blood pressure or to reduce cholesterol levels, as well as their HIV medicine.

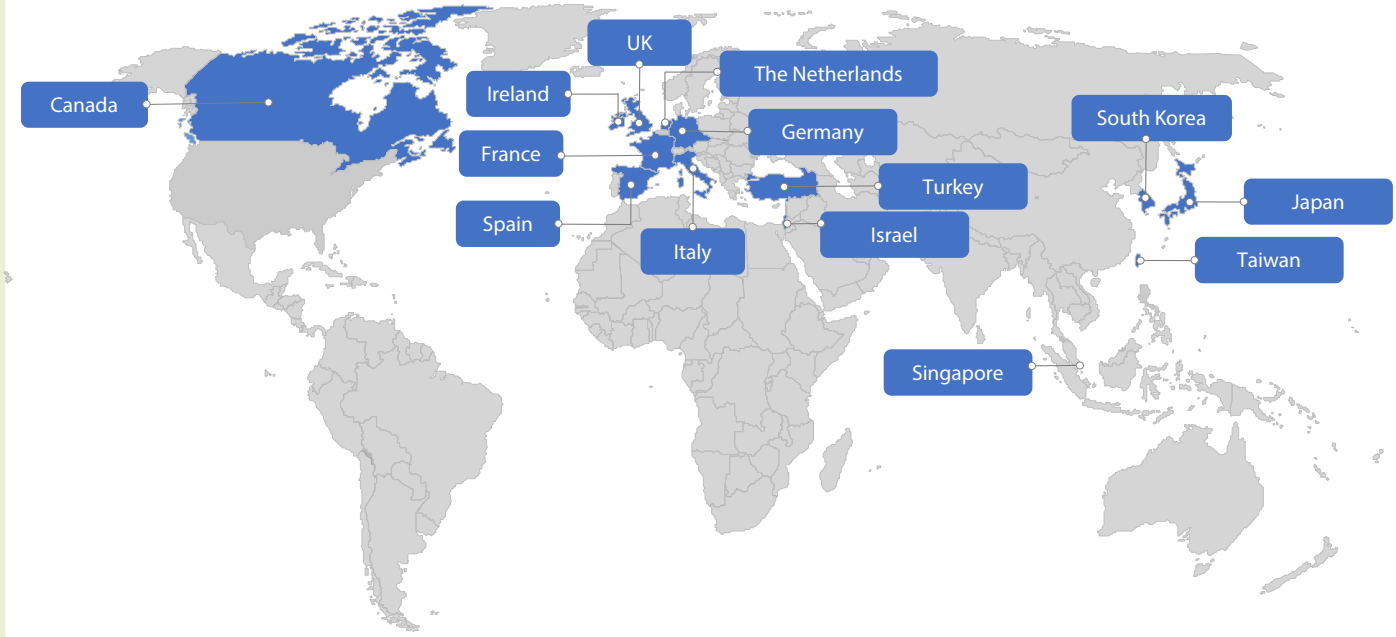
People with HIV took part in the study

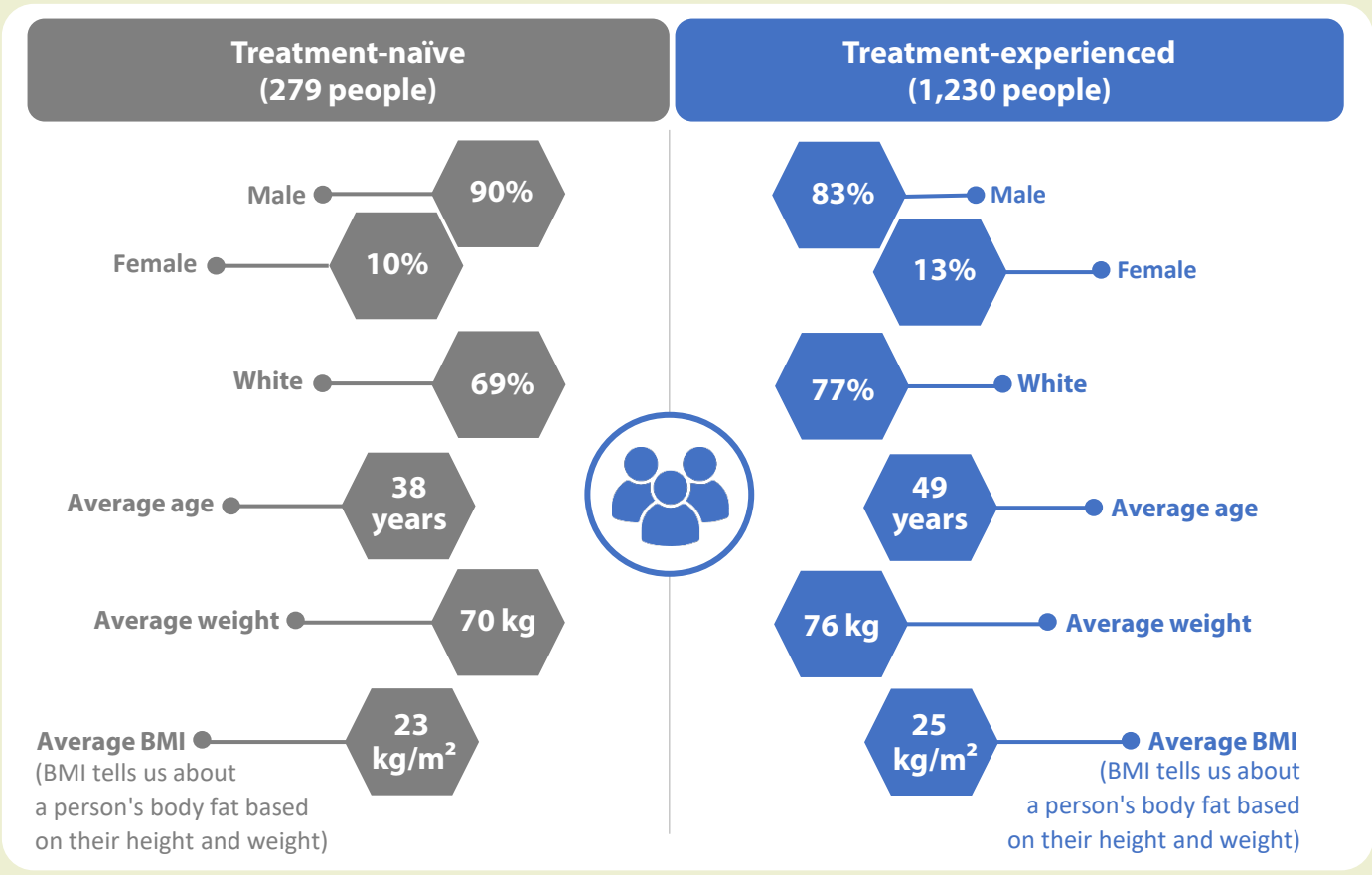
Some people had already taken HIV medicine before the study (**'treatment-experienced'**) and some had never taken HIV medicine before (**'treatment-naïve'**)

People were from Europe (France, Germany, Ireland, Italy, The Netherlands, Spain, Turkey, UK), Canada, Israel, Japan, South Korea, Singapore and Taiwan

People were able to take part if they were:

- Diagnosed as having HIV
- Adults (aged 18 years and above in all countries, except Taiwan and Japan, where people had to be at least 21 and 20 years, respectively)



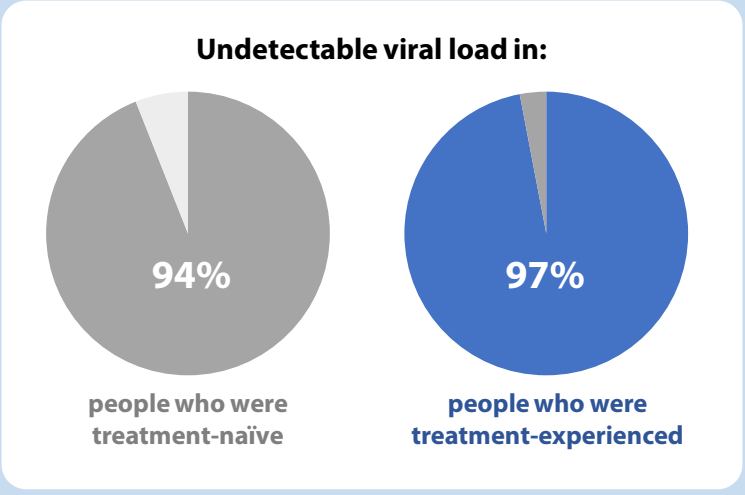


What were the main results of the study?

How effective was B/F/TAF at suppressing the viral load in the blood?

More than 9 out of 10 people, whether treatment-naïve or treatment-experienced, had an undetectable viral load after 1 year.

The researchers separated treatment-naïve and treatment-experienced people into more groups based on sex (men versus women), age (people aged less than 50 years versus people aged 50 years or more), and race (Black people versus other races). They wanted to see if any of these characteristics affected how well B/F/TAF worked. B/F/TAF was shown to work well in all the groups. At least 9 out of 10 people in all groups had undetectable viral load.



Researchers also looked at how well B/F/TAF worked in people who had a late diagnosis of HIV, meaning that they already had advanced disease when they were diagnosed and so had a more weakened immune system at the start of the study. More than 8 out of 10 people (86%) with a very weakened immune system had undetectable viral load at 1 year. More than 9 out of 10 people (96%) with a stronger immune system had undetectable viral load after 1 year.

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How effective was B/F/TAF at improving or maintaining the immune system?

White blood cells are part of the body's immune system. They help fight infection and other diseases. CD4 cells are a type of white blood cell. People with HIV that have not been treated might have a low number of CD4 cells (a weakened immune system). One of the goals of HIV treatment is to get the number of CD4 cells (the 'cell count') back to a healthy level (normally more than 500 cells counted in each microliter of blood).

At the start of the study, treatment-naïve people had an average of 377 CD4 cells in each microliter of blood. This is lower than the normal 500 cells, meaning their immune system was weakened. After 1 year, the number of CD4 cells increased by around 214 cells in each microliter of blood, meaning they were back up to normal levels.

Most treatment-experienced people already had healthy levels of CD4 cells at the start of the study because of the HIV medicine they had already received. After 1 year, the levels of CD4 cells in treatment-experienced people increased by around 13 cells in each microliter of blood.

What were the most common side effects?

Researchers watched closely for side effects during the study. A side effect is considered serious when it is life-threatening, causes lasting problems, or the person needs hospital care.

Only 2 people had serious side effects that researchers thought might have been caused by B/F/TAF. Both people had episodes of depression (1 severe case and 1 life-threatening case). According to the researchers, both people recovered.

10 people who took part in the study died during the 1-year period. Researchers did not think any of these deaths were caused by B/F/TAF.

The most common side effects researchers thought were caused by B/F/TAF

Weight gain
3 out of 100 people (3%)

Headache
1 out of 100 people (1%)

Nausea
(feeling sick)
1 out of 100 people (1%)

Depression
1 out of 100 people (1%)

Fatigue
(extreme tiredness or lack of energy)
1 out of 100 people (1%)

Some people had changes in their weight. For people who are treatment-naïve, starting treatment for HIV can be linked with weight gain, which may mean that they are returning to a healthier weight. In this study, treatment-naïve individuals gained around 3 kg (7 lbs) over the year whereas treatment-experienced individuals gained around 1 kg (2 lbs) over the year, in line with gains expected in the general population.

How many people were still taking B/F/TAF at 1 year?

It is important that people with HIV receive lifelong treatment so that their viral load remains undetectable. In this real-world study, more than 9 out of 10 treatment-naïve and treatment-experienced people were still taking B/F/TAF after 1 year.

Why did people stop taking B/F/TAF in the study?

Some people had side effects related to B/F/TAF, which meant they stopped taking it. This happened in 4 out of 100 treatment-naïve people and 6 out of 100 treatment-experienced people. Other people stopped taking B/F/TAF because they chose to, or because their healthcare professional decided it would be best for them to stop (both less than 1 out of 100 people).

Was there any drug resistance to B/F/TAF?

If the level of HIV in the blood (viral load) stays high even when a person is taking HIV treatment, it may mean that the virus has become resistant to some anti-HIV drugs. This resistance may cause the HIV treatment to stop working properly. Researchers did not find any evidence of resistance to B/F/TAF in this study.

How satisfied with treatment were people taking B/F/TAF?

When, after 12 months of taking B/F/TAF, people were asked to rate how satisfied they were with B/F/TAF compared with their previous medication, they scored it at an average of 25 out of a maximum score of 30. This means that people taking B/F/TAF were more satisfied with B/F/TAF than with their previous medication.

What do the results of this study mean?

Most people with HIV who took B/F/TAF had an 'undetectable viral load' at 1 year. As this was a real-world study, a lot of people in the study had other medical conditions. It was reassuring for researchers to see that a lot of different people had an undetectable viral load.

A low number of people experienced side effects that researchers thought might be caused by B/F/TAF. Most people were still taking B/F/TAF after 1 year.

Overall, the results showed that B/F/TAF worked well and was well tolerated over 1 year in a large population of diverse people with HIV. These results are similar to those from clinical trials, and they support the use of B/F/TAF by people with HIV.

People with HIV should talk to their healthcare professional if they have any questions about B/F/TAF or other HIV medicines.

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Where can readers find more information on this study?

Details of the original study

This plain language summary is based on the original article titled: 'Twelve-month effectiveness and safety of bictegravir/emtricitabine/tenofovir alafenamide in people with HIV: Real-world insights from BICSTaR cohorts' published in the journal *HIV Medicine*. Original publication citation: Esser et al. *HIV Med.* 2024;25:440-453. doi: 10.1111/hiv.13593

You can read the full article, which is free to access, at: https://onlinelibrary.wiley.com/doi/full/10.1111/hiv.13593

Further details about the study

The main part of the BICSTaR study started on June 25, 2018, and ended on December 20, 2023.

You can find more information on the BICSTaR study on the official ClinicalTrials.gov website

- Canada cohort (NCT03580668): https://clinicaltrials.gov/study/NCT03580668
- Israel cohort: (NCT04009057): https://clinicaltrials.gov/study/NCT04009057

The European cohort (EUPAS22185) is registered in the Heads of Medicines Agencies and European Medicines Agency (HMA-EMA) Catalogue of real-world data studies. Asian and Japanese cohorts are registered as studies GS-TW-380-5727 and GS-JP-380-5605.

The main part of the BICSTaR study has now completed, but participants in Germany, France, and Canada were offered an opportunity to participate for an additional 3 years.

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Author contributions

SE, AI, IL, AD'AM, JSL, BvW, KT, MB, C-EL, OAA, and OR contributed to study accrual, clinical care, and data recording; DT, MH, AM, MB, TC, LD'A, and RH contributed to trial management, data collection, and data analysis or interpretation; DT, MH, and RH contributed to study design. All authors reviewed and critically revised the summary, approved the final draft, and agree to be accountable for the summary's accuracy and integrity.

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Competing interests disclosure

The authors have no competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript.

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