ViiV Healthcare announces new data at AIDS 2022 from unblinded phase of HPTN 084 study in women in sub Saharan Africa showing continued superior efficacy of injectable cabotegravir long-acting for PrEP over daily, oral TDF/FTC tablets

PUBLISHED JUL 28, 2022
BY GSK

For media and investors only

- No new HIV infections were observed in participants who initiated cabotegravir injections in the year following study unblinding

- No birth defects reported among women who became pregnant after exposure to initial injections of cabotegravir for PrEP

ViiV Healthcare, the global specialist HIV company majority-owned by GSK, with Pfizer and Shionogi as shareholders, today announced new efficacy and safety findings from the unblinded period of the HIV Prevention Trials Network (HPTN) 084 trial evaluating cabotegravir long-acting LA) for pre-exposure prophylaxis (PrEP) in women in sub Saharan Africa. The findings showed that cabotegravir LA for PrEP continued to demonstrate superior efficacy in the prevention of new HIV infections among women when compared to daily oral emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) tablets, with an 89% lower rate of HIV acquisition (HR 0.11, 95% CI 0.05, 0.24). Results were presented today at the 24th International AIDS Conference (AIDS 2022) in Montreal, Canada.

The blinded phase of HPTN 084, during which participants were not

told which regimen they were taking, was stopped in November 2020 by an independent data safety monitoring board after a planned interim review indicated that cabotegravir LA for PrEP had demonstrated superiority in the prevention of HIV in women when compared to daily, oral FTC/TDF tablets.

Participants were subsequently told which regimen they were taking (unblinded) and continued on their original randomised study regimen, pending a study amendment to offer open-label cabotegravir LA for PrEP to all participants who wished to take it. The data presented at AIDS 2022 include the 12-month period after HPTN 084 trial participants were unblinded, but prior to the amendment.

During the unblinded period of HPTN 084, no new cases of HIV infection occurred in participants in the cabotegravir arm of the trial, after injections were initiated. Twenty-three incident infections were observed (HIV incidence, 0.84%; 95% CI, 0.53-1.26), with three in the cabotegravir LA group (incidence, 0.22%; 95% CI, 0.04-0.63), including two who had never received an injection, and one individual who had acquired HIV before her initial cabotegravir injection, during the blinded phase of the study; and 20 in the FTC/TDF group (incidence, 1.48%; 95% CI, 0.9-2.2). Overall, 62 incident HIV infections (6 CAB, 56 TDF/FTC) have been observed over 6626 person-years of follow up (HIV incidence 0.94%, 95% CI 0.72, 1.20).

Kimberly Smith, M.D., MPH, Head of Research & Development at ViiV Healthcare, said:

> These remarkable data reaffirm the potential use of long-acting cabotegravir as an effective HIV prevention option for women, particularly women in sub Saharan Africa who are disproportionately impacted by HIV. This study also continues to provide us with valuable information about women who become pregnant while receiving cabotegravir LA. Women tell us they need more choices for HIV prevention. We believe that having an alternative to a daily pill to prevent HIV that reduces dosing days from 365 to as few as six times per year can potentially have a significant impact on efforts to end the epidemic.

New pregnancy safety data were also presented at AIDS 2022. During the unblinded phase of the HPTN 084 study, 83 confirmed pregnancies (43 on cabotegravir, 40 on TDF/FTC) occurred. Women

with confirmed pregnancies while on long-acting cabotegravir for PrEP discontinued cabotegravir injections until cessation of breast feeding. No birth defects were reported in either arm of the study. The increased pregnancy incidence during the unblinded period of the study highlights the importance of ongoing studies to evaluate the safety and pharmacology of cabotegravir LA during pregnancy and lactation.

Sinead Delany-Moretlwe, MBBCh, Ph.D., DTM&H, HPTN 084 protocol chair, and research director at Wits RHI, University of the Witwatersrand in Johannesburg, South Africa, said:

> The latest findings from the HPTN 084 trial underscore the significant impact that cabotegravir LA for PrEP can have for the prevention of HIV in women, especially in resource-limited settings like sub-Saharan Africa where the study was conducted. Young women in this region bear a disproportionate burden of the epidemic and may be twice as likely as their male counterparts to contract HIV. If we are to successfully end the HIV epidemic, the availability of new HIV prevention options like cabotegravir LA for PrEP will be critical for ensuring an impact on HIV incidence in populations at greatest need.

Cabotegravir LA for PrEP continued to be well-tolerated throughout the study, with no new safety concerns identified during the 12-month unblinded period. Grade 2 injection site reactions (ISRs) were low in the cabotegravir arm (2.4%). Overall, Grade 2 adverse events were comparable between study groups, with 20% assessed as related to study product (19% for cabotegravir arm, 21% for FTC/TDF arm).

Cabotegravir LA for PrEP is currently approved in the U.S. as Apretude. It is approved for use in adults and adolescents weighing at least 35 kg who are at risk of sexually acquiring HIV and who have a negative HIV-1 test prior to initiation. ViiV Healthcare has initiated submissions to other regulatory authorities. Apretude has not yet been approved or licensed anywhere outside of the U.S. for use in HIV prevention.

About cabotegravir extended-release injectable suspension

Cabotegravir LA for PrEP is an integrase strand transfer inhibitor (INSTI). INSTIs, like cabotegravir extended-release injectable suspension, inhibit HIV replication by preventing the viral DNA from

integrating into the genetic material of human immune cells (T-cells). This step is essential in the HIV replication cycle and is also responsible for establishing chronic disease.

Cabotegravir LA for PrEP is provided as an injection given as few as six times per year and is initiated with a single 600 mg (3-ml) intramuscular injection given one month apart for two consecutive months. After the second initiation injection, the recommended continuation injection dose is a single 600 mg (3-ml) injection given every two months. Vocabria (cabotegravir oral tablets) may be administered for approximately one month before initiating the first injection to assess the tolerability of the medicine.

Trademarks are owned by or licensed to the ViiV Healthcare group of companies.

About HPTN 084 (NCT03164564)

The HPTN 084 trial is a phase III double blind superiority trial designed to evaluate the safety and efficacy of the cabotegravir LA for HIV prevention administered every eight weeks compared to daily oral FTC/TDF tablets (200 mg/300 mg) in 3,224 cisgender women who are at increased risk of HIV acquisition. The trial design included an oral lead-in phase to assess tolerability to cabotegravir before administering the IM injection. HPTN 084 opened to enrolment in November 2017 and is being conducted at research centres in Botswana, Kenya, Malawi, South Africa, Eswatini, Uganda, and Zimbabwe.

Cabotegravir LA was found to be superior to daily oral FTC/TDF in preventing HIV acquisition in the trial population. The most common adverse reactions (all grades) observed in at least 1% of subjects receiving cabotegravir LA were injection site reactions, diarrhoea, headache, fatigue, sleep disorders, nausea, dizziness, abdominal pain, vomiting, myalgia, and rash.

HPTN 084 was jointly funded by the U.S. National Institute of Allergy and Infectious Diseases (NIAID), and the National Institute of Mental Health (NIMH), the Bill & Melinda Gates Foundation and ViiV Healthcare, and was conducted by the HPTN. Study product was provided by ViiV Healthcare and Gilead Sciences. For further information please see https://clinicaltrials.gov/ct2/show/NCT03164564.

APRETUDE (cabotegravir) extended-release injectable suspensions

APRETUDE is indicated in at-risk adults and adolescents weighing at least 35 kg for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test prior to initiating APRETUDE (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: RISK OF DRUG RESISTANCE WITH USE OF APRETUDE FOR HIV-1 PRE-EXPOSURE PROPHYLAXIS (PrEP) IN UNDIAGNOSED EARLY HIV-1 INFECTION

Individuals must be tested for HIV-1 infection prior to initiating APRETUDE or oral cabotegravir, and with each subsequent injection of APRETUDE, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Drug-resistant HIV-1 variants have been identified with use of APRETUDE by individuals with undiagnosed HIV-1 infection. Do not initiate APRETUDE for HIV-1 PrEP unless negative infection status is confirmed. Individuals who become infected with HIV-1 while receiving APRETUDE for PrEP must transition to a complete HIV-1 treatment regimen.

- Do not use APRETUDE in individuals:

- with unknown or positive HIV-1 status

- with previous hypersensitivity reaction to cabotegravir

- receiving carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, and rifapentine

Comprehensive Management to Reduce the Risk of HIV-1 Infection:

- Use APRETUDE as part of a comprehensive prevention strategy, including adherence to the administration schedule and safer sex practices, including condoms, to reduce the risk of sexually transmitted infections (STIs). APRETUDE is not always effective in preventing HIV-1 acquisition. Risk for HIV-1 acquisition includes, but is not limited to, condomless sex, past or current STIs, self-identified HIV risk, having sexual partners of unknown HIV-1 viremic status, or sexual activity in a high prevalence area or network. Inform, counsel,

and support individuals on the use of other prevention measures (e.g., consistent and correct condom use; knowledge of partner[s] HIV-1 status, including viral suppression status; regular testing for STIs)

- Use APRETUDE only in individuals confirmed to be HIV-1 negative. HIV-1 resistance substitutions may emerge in individuals with undiagnosed HIV-1 infection who are taking only APRETUDE, because APRETUDE alone does not constitute a complete regimen for HIV-1 treatment. Prior to initiating APRETUDE, ask seronegative individuals about recent (in past month) potential exposure events and evaluate for current or recent signs or symptoms consistent with acute HIV-1 infection (e.g., fever, fatigue, myalgia, skin rash). If recent (

- When using APRETUDE, HIV-1 testing should be repeated prior to each injection and upon diagnosis of any other STIs

- Additional HIV testing to determine HIV status is needed if an HIV-1 test indicates possible HIV-1 infection or if symptoms consistent with acute HIV-1 infection develop following an exposure event. If HIV-1 infection is confirmed, then transition the individual to a complete HIV-1 treatment

- Counsel HIV-1 uninfected individuals to strictly adhere to the recommended dosing and testing schedule for APRETUDE

Potential Risk of Resistance with APRETUDE:

- There is a potential risk of developing resistance to APRETUDE if an individual acquires HIV-1 either before, while taking, or following discontinuation of APRETUDE. To minimize this risk, it is essential to clinically reassess individuals for risk of HIV-1 acquisition and to test before each injection to confirm HIV-1–negative status. Individuals who are confirmed to have HIV-1 infection must transition to a complete HIV-1 treatment. If individuals at continuing risk of HIV-1 acquisition discontinue APRETUDE, alternative forms of PrEP should be considered and initiated within 2 months of the final injection of APRETUDE

Long-Acting Properties and Potential Associated Risks with APRETUDE:

- Residual concentrations of cabotegravir may remain in the systemic circulation of individuals for prolonged periods (up to 12 months or

longer). Take the prolonged-release characteristics of cabotegravir into consideration and carefully select individuals who agree to the required every-2-month injection dosing schedule because non-adherence or missed doses could lead to HIV-1 acquisition and development of resistance

Hypersensitivity Reactions:

- Serious or severe hypersensitivity reactions have been reported in association with other integrase inhibitors and could occur with APRETUDE

- Discontinue APRETUDE immediately if signs or symptoms of hypersensitivity reactions develop. Clinical status, including liver transaminases, should be monitored and appropriate therapy initiated

- Hepatotoxicity has been reported in a limited number of individuals receiving cabotegravir with or without known pre-existing hepatic disease or identifiable risk factors

- Clinical and laboratory monitoring should be considered and APRETUDE should be discontinued if hepatotoxicity is suspected and individuals managed as clinically indicate

- Depressive disorders (including depression, depressed mood, major depression, persistent depressive disorder, suicidal ideation or attempt) have been reported with APRETUDE

- Promptly evaluate patients with depressive symptoms

Risk of Reduced Drug Concentration of APRETUDE Due to Drug Interactions:

- The concomitant use of APRETUDE and other drugs may result in reduced drug concentration of APRETUDE

- Refer to the full Prescribing Information for steps to prevent or manage these possible and known significant drug interactions, including dosing recommendations. Consider the potential for drug interactions prior to and during use of, and after discontinuation of APRETUDE; review concomitant medications during use of APRETUDE

The most common adverse reactions (incidence ≥1%, all grades) with

APRETUDE were injection site reactions, diarrhea, headache, pyrexia, fatigue, sleep disorders, nausea, dizziness, flatulence, abdominal pain, vomiting, myalgia, rash, decreased appetite, somnolence, back pain, and upper respiratory tract infection.

- Refer to the full Prescribing Information for important drug interactions with APRETUDE

- Drugs that induce UGT1A1 may significantly decrease the plasma concentrations of cabotegravir

USE IN SPECIFIC POPULATIONS

- Lactation: Assess the benefit-risk of using APRETUDE to the infant while breastfeeding due to the potential for adverse reactions and residual concentrations in the systemic circulation for up to 12 months or longer after discontinuation

- Pediatrics: Not recommended in individuals weighing less than 35 kg

Trademarks are owned by or licensed to the ViiV Healthcare group of companies

ViiV Healthcare is a global specialist HIV company established in November 2009 by GlaxoSmithKline (LSE: GSK) and Pfizer (NYSE: PFE) dedicated to delivering advances in treatment and care for people living with HIV and for people who are at risk of becoming infected with HIV. Shionogi joined as a shareholder in October 2012. The company's aims are to take a deeper and broader interest in HIV and AIDS than any company has done before and take a new approach to deliver effective and innovative medicines for HIV treatment and prevention, as well as support communities affected by HIV.

For more information on the company, its management, portfolio, pipeline, and commitment, please visit www.viivhealthcare.com.

GSK is a global biopharma company with a purpose to unite science, technology, and talent to get ahead of disease together. Find out more at gsk.com/company.

Cautionary statement regarding forward-looking statements

GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described in the Company's Annual Report on Form 20-F for 2021, GSK's Q2 Results for 2022 and any impacts of the COVID-19 pandemic.

Press release distributed by Wire Association on behalf of GSK, on Jul 28, 2022. For more information subscribe and follow us.

Media Assets

Embedded Media

Visit the online press release to interact with the embedded media.

https://wireassociation.eu/newsroom/gsk/releases/en/viiv-healthcare-announces-new-data-at-aids-2022-from-unblinded-phase-of-hptn-084-study-in-women-in-sub-saharan-africa-showing-continued-superior-efficacy-of-injectable-cabotegravir-long-acting-for-prep-over-daily-oral-tdfftc-tablets-1831

GSK

Newsroom: https://wireassociation.eu/newsroom/gsk
Website: https://www.gsk.com/
Primary Email: corporate.media@gsk.com

Social Media

Facebook - https://www.facebook.com/GSK
Twitter - http://twitter.com/GSK
Youtube - http://www.youtube.com/GSK
Linkedin - http://www.linkedin.com/company/glaxosmithkline
Instagram - https://www.instagram.com/gsk/