NEW FINDINGS

SOLAR, the first head-to-head switch study for CABENUVA vs BIKTARVY

SOLAR is part of the clinical development program for CABENUVA, the only complete, long-acting regimen for HIV-1, dosed once every 2 months.

INDICATION

CABENUVA is indicated as a complete regimen for the treatment of HIV-1 infection in adults and adolescents 12 years of age and older and weighing at least 35 kg to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- Do not use CABENUVA in patients with previous hypersensitivity reaction to cabotegravir or rilpivirine
- Do not use CABENUVA in patients receiving carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, systemic dexamethasone (>1 dose), and St John's wort

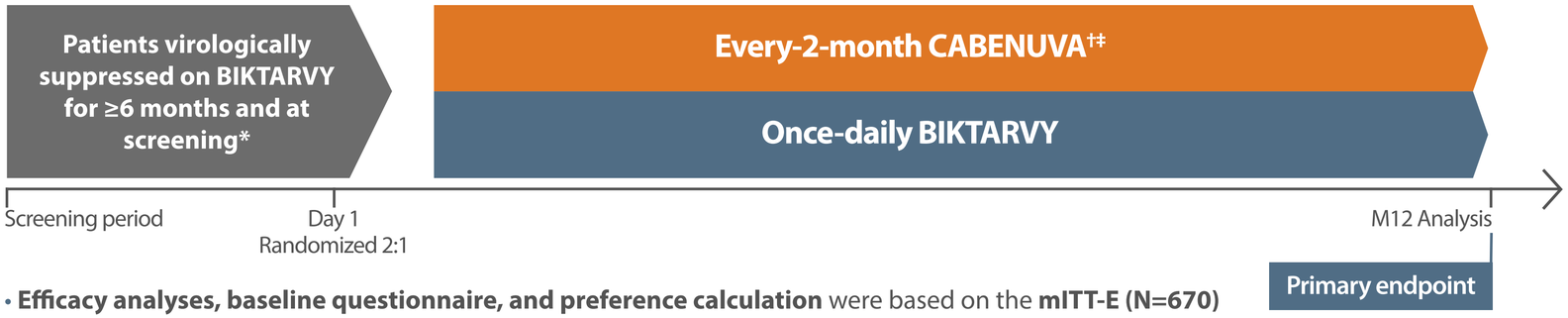
Please see additional Important Safety Information throughout.
Please see accompanying full Prescribing Information for CABENUVA.

CABENUVA
cabotegravir; rilpivirine
extended-release injectable suspensions

ViiV Healthcare

SOLAR is the first head-to-head switch study comparing every-2-month CABENUVA with daily oral BIKTARVY[1,2]

A large phase IIIb, open-label, noninferiority study of virologically suppressed* adults (≥18 years) with HIV-1[1]



- **Efficacy analyses, baseline questionnaire, and preference calculation** were based on the **mITT-E (N=670)** population. After consultation with a blinded external expert, 11 participants at a single study site were excluded from the ITT-E population due to critical findings related to significant and persistent noncompliance to protocol requirements[1]
- **Safety analyses** were based on **ITT-E (N=681)** population[1]

Primary endpoint
- Proportion of patients with HIV-1 RNA ≥50 copies/mL in the Month 12 analysis‡

Secondary endpoint
- Proportion of patients with HIV-1 RNA <50 copies/mL in the Month 12 analysis‡

Key inclusion criteria[2]
- Must be on the uninterrupted, current regimen of BIKTARVY for ≥6 months prior to screening, with an undetectable HIV-1 viral load for ≥6 months prior to screening. BIKTARVY must be the patient's first or second regimen

Exclusion criteria[2,3]
- History of virologic failure
- Known or suspected presence of resistance mutations to the individual components of BIKTARVY or CABENUVA
- HBV infection at screening
- Moderate to severe hepatic impairment
- Women who were pregnant or breastfeeding or planned to become pregnant or breastfeed

*Suppression defined as plasma HIV-1 RNA <50 copies/mL. A single prior INSTI-based regimen was allowed for reasons other than treatment failure (HIV-1 RNA ≥400 copies/mL).[2]
†Patients randomized to CABENUVA were given the option of 1-month oral lead-in (OLI) or to start long-acting IM CABENUVA directly (SWI). OLI regimen consisted of 30-mg cabotegravir and 25-mg rilpivirine once daily given for 1 month; on last day of the OLI period, patients received 2 sets of initiation CABENUVA injections 1 month apart followed by every-2-month injections thereafter. ‡Month 12 (OLI and BIKTARVY) and Month 11 (SWI).[2]
HBV=hepatitis B virus; IM=intramuscular; INSTI=integrase strand transfer inhibitor; ITT-E=intent-to-treat exposed; mITT-E=modified intent-to-treat exposed; M=month; SWI=starting with injections.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions:

- Hypersensitivity reactions, including cases of drug reaction with eosinophilia and systemic symptoms (DRESS), have been reported during postmarketing experience with rilpivirine-containing regimens. While some skin reactions were accompanied by constitutional symptoms such as fever, other skin reactions were associated with organ dysfunctions, including elevations in hepatic serum biochemistries
- Serious or severe hypersensitivity reactions have been reported in association with other integrase inhibitors and could occur with CABENUVA
- Discontinue CABENUVA immediately if signs or symptoms of hypersensitivity reactions develop. Clinical status, including liver transaminases, should be monitored and appropriate therapy initiated. Cabotegravir and rilpivirine oral lead-in may be used to help identify patients who may be at risk of a hypersensitivity reaction

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cabotegravir; rilpivirine
extended-release injectable suspensions

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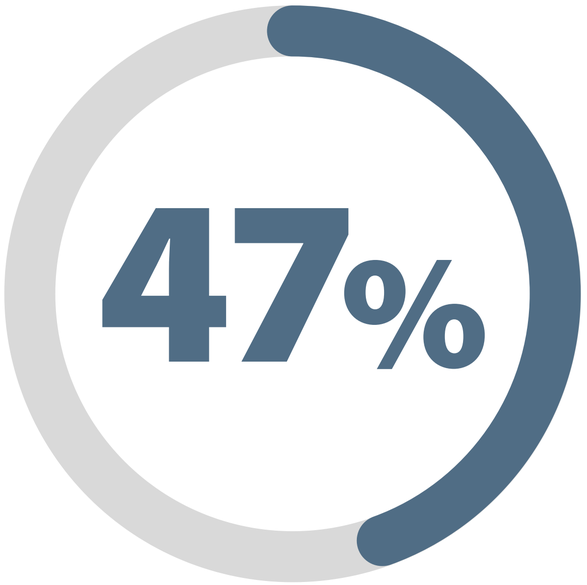
Patients entering SOLAR on BIKTARVY revealed challenges with taking daily oral therapy at baseline[1,2]



On Day 1 (exploratory endpoint), all patients in SOLAR (N=670; mITT-E) responded to three baseline questions about their previous experience on a daily oral therapy.

47% of patients in SOLAR reported experiencing at least one of the following challenges always or often[2*]:

- Worried about people **unintentionally discovering their HIV status**
- Worried about **forgetting to take their HIV medication**
- Felt that taking their HIV medication was an **uncomfortable reminder of their HIV status**

80% of patients in SOLAR reported experiencing one of these same challenges sometimes, often, or always[2*]

These results are descriptive in nature and should not be used to infer clinical significance.

*Patients were asked each of the following questions: "How often are you worried people may unintentionally discover your HIV status because of your current HIV treatment?;" "How often are you worried about forgetting to take your HIV medication?;" and "How often is taking your HIV medication an uncomfortable reminder of your HIV status?" Patients who responded "sometimes," "often," or "always" to any of these questions were counted one time for the endpoints above.[2]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Post-Injection Reactions:

- Serious post-injection reactions (reported in less than 1% of subjects) were reported within minutes after the injection of rilpivirine, including dyspnea, bronchospasm, agitation, abdominal cramping, rash/urticaria, dizziness, flushing, sweating, oral numbness, changes in blood pressure, and pain (e.g., back and chest). These events may have been associated with accidental intravenous administration and began to resolve within a few minutes after the injection
- Carefully follow the Instructions for Use when preparing and administering CABENUVA. The suspensions should be injected slowly via intramuscular injection and avoid accidental intravenous administration. Observe patients briefly (approximately 10 minutes) after the injection. If a post-injection reaction occurs, monitor and treat as clinically indicated

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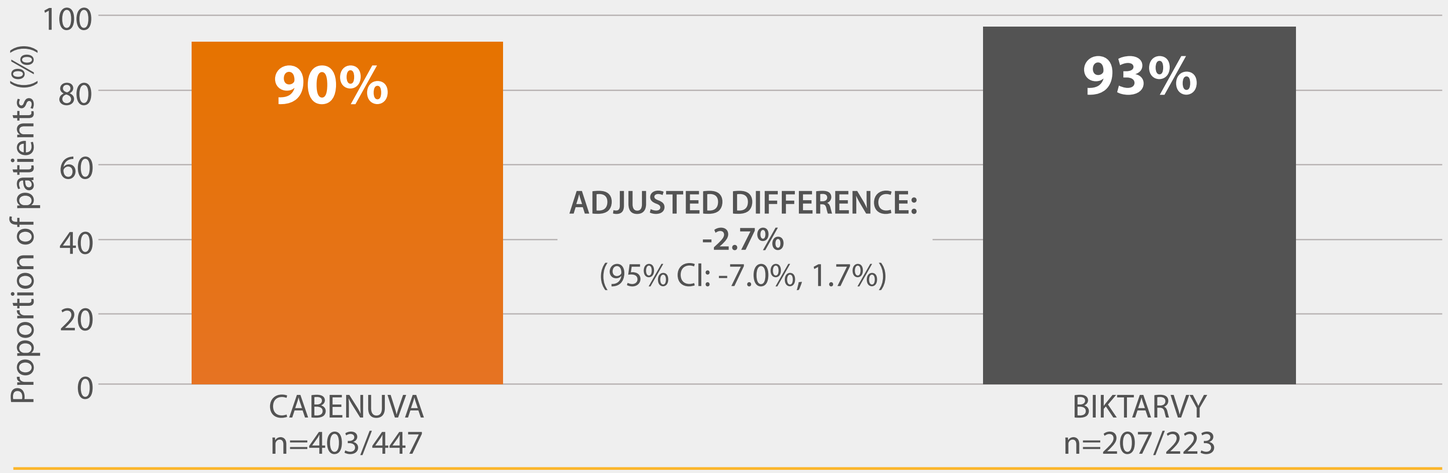
Every-2-month CABENUVA was noninferior to daily oral BIKTARVY[1,2]

The SOLAR primary endpoint was met (HIV-1 RNA ≥50 copies/mL):

- Every-2-month CABENUVA was noninferior* to BIKTARVY at Month 12 analysis (mITT-E: 1% [5/447] vs <1% [1/223], respectively, adjusted difference = 0.7 [95% CI -0.7 to 2.0]). Noninferiority would be shown if upper bound of the 95% CI for the treatment difference was <4%.[1,2]

The SOLAR secondary endpoint was met: plasma HIV-1 RNA <50 copies/mL at Month 12 analysis

(Noninferiority would be shown if lower bound of the 95% CI for the treatment difference was > -12%)



CI=confidence interval.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hepatotoxicity:

- Hepatotoxicity has been reported in patients receiving cabotegravir or rilpivirine with or without known pre-existing hepatic disease or identifiable risk factors
- Patients with underlying liver disease or marked elevations in transaminases prior to treatment may be at increased risk for worsening or development of transaminase elevations
- Monitoring of liver chemistries is recommended and treatment with CABENUVA should be discontinued if hepatotoxicity is suspected

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SOLAR: Confirmed virologic failures were seen in 2 patients receiving CABENUVA (in mITT-E)[1,2]

Confirmed Virologic Failure* Through Month 12 Analysis

2 of 447 CABENUVA patients	**0.4%**	**VS**	**0 of 223 BIKTARVY patients**	**0%**

Patients who met the CVF criteria were tested for emergent INSTI (cabotegravir) or NNRTI (rilpivirine) substitutions conferring resistance

- Patient 1: Emergent RPV RAM (M230L) and an INSTI RAM (Q148R) at Month 6
- Patient 2: Emergent RPV RAM (K101E) and an INSTI RAM (G118R) at Month 11
- An additional patient on CABENUVA in the ITT-E population met CVF at Month 3 with treatment-emergent RPV RAMs E138E/K and Y181Y/C

Patients who met CVF resuppressed on alternative, highly suppressive antiretroviral therapies

Key differences in ATLAS-2M†: all patients had previously received an NNRTI-, PI-, or INSTI-based regimen. Through Week 152, there were 12 (2%) CVFs in the every-2-month arm and 2 (<1%) in the once-monthly arm.[4]

*CVF was defined as 2 consecutive RNA levels ≥200 copies/mL.
†ATLAS-2M was a large, phase IIIb, open-label, noninferiority study comparing every-2-month CABENUVA to once-monthly CABENUVA. Primary endpoint: HIV-1 RNA ≥50 copies/mL 2.7% vs 1% (treatment difference 1.7% [95% CI: 0.1, 3.3]) for every-2-month vs once-monthly CABENUVA, respectively, at Week 152.
CVF=confirmed virologic failure; INSTI RAM=integrase strand transfer inhibitor resistance–associated mutations; NNRTI=non-nucleoside reverse transcriptase inhibitors; PI=protease inhibitors; RPV RAM=rilpivirine resistance–associated mutations.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Depressive Disorders:

- Depressive disorders (including depressed mood, depression, major depression, mood altered, mood swings, dysphoria, negative thoughts, suicidal ideation or attempt) have been reported with CABENUVA or the individual products
- Promptly evaluate patients with depressive symptoms

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SOLAR: Drug-related adverse reactions reported in patients through Month 12 analysis[1,2]

Drug-related AEs* Occurring in ≥1% of Patients in Either Group[2]	Every-2-month CABENUVA (N=454)	Daily BIKTARVY (n=227)
ISRs	70%	N/A
Pyrexia†	4%	0%
Fatigue‡	3%	0%
Diarrhea	2%	0%
Headache	2%	0%
Musculoskeletal pain§	2%	0%
Sleep disorders‖	1%	0%
Nausea	1%	0%
Dizziness	1%	0%
Discontinuation rate due to drug-related AEs[1]	4%	<1%

Injection-Site Reactions ≥5% of Patients[2]	Every-2-month CABENUVA (N=454)
Total ISRs	70%
Pain	62%
Nodule	9%
Swelling	9%
Discomfort	9%
Induration	7%

- Most drug-related AEs were Grade 1 or 2 in CABENUVA patients; all were Grade 1 or 2 in BIKTARVY patients[2]
- Most ISRs were mild to moderate and decreased over time
  - –Self-reported ISRs could potentially underestimate the true rate of ISRs over time. ISRs may still be present but not reported during the course of the study
- The median duration (IQR) of ISRs was 3 days (2, 5)[1]
- 2% of CABENUVA patients (event level) discontinued treatment due to injection-related reasons, and 2% discontinued due to non-ISR drug-related AEs[1]

*Adverse reactions defined as "treatment-related" as assessed by the investigator. Only maximum-graded report per adverse reaction contributes to table. †Pyrexia: includes pyrexia, feeling hot, chills, influenza-like illness, body temperature increased. ‡Fatigue: includes fatigue, malaise, asthenia. §Musculoskeletal pain: includes musculoskeletal pain, musculoskeletal discomfort, back pain, myalgia, pain in extremity. ‖Sleep disorders: includes insomnia, poor quality sleep, somnolence.
AE=adverse event; IQR=interquartile range; ISR=injection-site reaction; N/A=not applicable.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions:

- The concomitant use of CABENUVA and other drugs may result in known or potentially significant drug interactions (see Contraindications and Drug Interactions)
- Rilpivirine doses 3 and 12 times higher than the recommended oral dosage can prolong the QTc interval
- CABENUVA should be used with caution in combination with drugs with a known risk of Torsade de Pointes

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Every-2-month CABENUVA was preferred by 9 out of 10 survey respondents vs daily oral therapy with BIKTARVY[1,2]

At Month 12 analysis or study withdrawal (secondary endpoint), all SOLAR participants in the mITT-E population (N=447) were asked to respond to a question about which regimen they preferred. 22 participants did not respond. Of the 425 survey respondents:[1,2]

90% reported a preference for CABENUVA

- Patients were asked to compare their experience using CABENUVA versus BIKTARVY, to select the treatment they preferred, and then select from a list of provided statements to support their preference[2]
- 5% (n=21/425) preferred daily oral therapy and 5% (n=22/425) had no preference[1,2]

These results are descriptive in nature and should not be used to infer clinical significance.

*Patients who preferred CABENUVA were given a list of 11 reasons to choose from; more than one reason could be chosen.

The most commonly chosen responses were[1,2*]:

- **85%** "I do not have to worry as much about remembering to take HIV medication every day"
- **83%** "It is more convenient for me to receive injections every 2 months"
- **74%** "I do not have to carry my HIV medication with me"
- **61%** "I do not have to think about my HIV status every day"
- **59%** "I do not have to worry about others seeing or finding my HIV pills"

Respondents could choose one or more reasons for their preference.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Long-Acting Properties and Potential Associated Risks with CABENUVA:

- Residual concentrations of cabotegravir and rilpivirine may remain in the systemic circulation of patients for prolonged periods (up to 12 months or longer). Select appropriate patients who agree to the required monthly or every-2-month injection dosing schedule because non-adherence could lead to loss of virologic response and development of resistance
- To minimize the potential risk of developing viral resistance, it is essential to initiate an alternative, fully suppressive antiretroviral regimen no later than 1 month after the final injection doses of CABENUVA when dosed monthly and no later than 2 months after the final injections of CABENUVA when dosed every 2 months. If virologic failure is suspected, switch the patient to an alternative regimen as soon as possible

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ViiV Healthcare

NEW FINDINGS

SOLAR, the first head-to-head study for CABENUVA vs daily oral BIKTARVY, showed:

Challenges addressed[1,2]

47% of patients in SOLAR (N=670, mITT-E) reported experiencing at least one challenge taking daily oral therapy "always" or "often" at baseline (exploratory endpoint)

Proven efficacy[1]

Every-2-month CABENUVA was proven noninferior vs daily oral therapy with BIKTARVY

The SOLAR primary endpoint was met (HIV-1 RNA ≥50 copies/mL at Month 12 analysis):
CABENUVA 1% vs BIKTARVY <1% (adjusted difference 0.7%, 95% CI -0.7, 2.0; noninferiority=upper bound of 95% CI <4%)

Patient preferred[1]

CABENUVA was preferred by 9 out of 10 survey respondents (n=425) over daily oral therapy with BIKTARVY

- 5% of participants preferred BIKTARVY and 5% had no preference
- At Month 12 analysis or study withdrawal (secondary endpoint), participants were asked to respond to a question about which regimen they preferred

Patient preference results should not be used to infer clinical significance.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

- The most common adverse reactions in adults (incidence ≥2%, all grades) treated with CABENUVA were injection site reactions, pyrexia, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, and rash
- The safety of CABENUVA in adolescents is expected to be similar to adults

DRUG INTERACTIONS

- Refer to the applicable full Prescribing Information for important drug interactions with CABENUVA, VOCABRIA (cabotegravir), or EDURANT (rilpivirine)
- Because CABENUVA is a complete regimen, coadministration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended
- Drugs that are strong inducers of UGT1A1 or UGT1A9 are expected to decrease the plasma concentrations of cabotegravir. Drugs that induce or inhibit CYP3A may affect the plasma concentrations of rilpivirine
- CABENUVA should be used with caution in combination with drugs with a known risk of Torsade de Pointes

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IMPORTANT SAFETY INFORMATION (cont'd)

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** There are insufficient human data on the use of CABENUVA during pregnancy to adequately assess a drug-associated risk for birth defects and miscarriage. Discuss the benefit-risk of using CABENUVA during pregnancy and conception and consider that cabotegravir and rilpivirine are detected in systemic circulation for up to 12 months or longer after discontinuing injections of CABENUVA. An Antiretroviral Pregnancy Registry has been established
- **Lactation:** The CDC recommends that HIV-1–infected mothers in the United States not breastfeed their infants to avoid risking postnatal transmission of HIV-1 infection. Breastfeeding is also not recommended due to the potential for developing viral resistance in HIV-positive infants, adverse reactions in a breastfed infant, and detectable cabotegravir and rilpivirine concentrations in systemic circulation for up to 12 months or longer after discontinuing injections of CABENUVA

References:
1. Ramgopal MN, Castagna A, Cazanave C, et al. SOLAR 12-month results—randomized switch trial of CAB + RPV LA vs. oral B/FTC/TAF. Presented at: CROI 2023. **2.** Data on file, ViiV Healthcare. **3.** ClinicalTrials.gov. SOLAR Study. Available at: https://clinicaltrials.gov/ct2/show/NCT04542070. Accessed February 16, 2023. **4.** Overton ET, Richmond G, Rizzardini G, et al. Long-acting cabotegravir+rilpivirine every 2 months: ATLAS-2M week 152 results. Poster presented at: Conference on Retroviruses and Opportunistic Infections; Virtual and Denver, CO; February 12-16, 2022. Poster H-03.

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