NEW FINDINGS

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

Every-2-month CABENUVA was non-inferior to daily, oral therapy with BIKTARVY and preferred by 90% of trial survey respondents*[1]

SOLAR is part of the continuing clinical development program for CABENUVA, the only complete long-acting treatment 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

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

In this phase IIIb, randomized, open-label, noninferiority study, virologically suppressed adults with HIV-1 receiving Biktarvy* were randomized 2:1 to every-2-month CABENUVA or Biktarvy for the duration of the 12-month maintenance period[1,2†]

SOLAR explored virologic suppression, safety, and tolerability, as well as patient treatment experiences[1,2]

Efficacy and safety endpoints at Month 12/11‡ included:

- Proportion of patients with HIV-1 RNA ≥50 copies/mL (primary endpoint)
- Proportion with plasma HIV-1 RNA <50 copies/mL
- Incidence of CVF§
- Adverse events

Patient treatment experience outcomes included:

- Treatment preference
- Reasons for preference

*Patients were suppressed for ≥6 months, suppression defined as HIV-1 RNA <50 copies/mL and received Biktarvy for ≥6 months prior to screening.[1]
†Cabotegravir initiation and continuation injections, 600 mg; rilpivirine initiation and continuation injections, 900 mg.[1]
‡Month 12 (OLI and Biktarvy) and Month 11 (SWI).[1]
§CVF defined as 2 consecutive measurements of HIV-1 RNA ≥200 copies/mL.[1]
CVF=confirmed virologic failure.

Solar Study Design

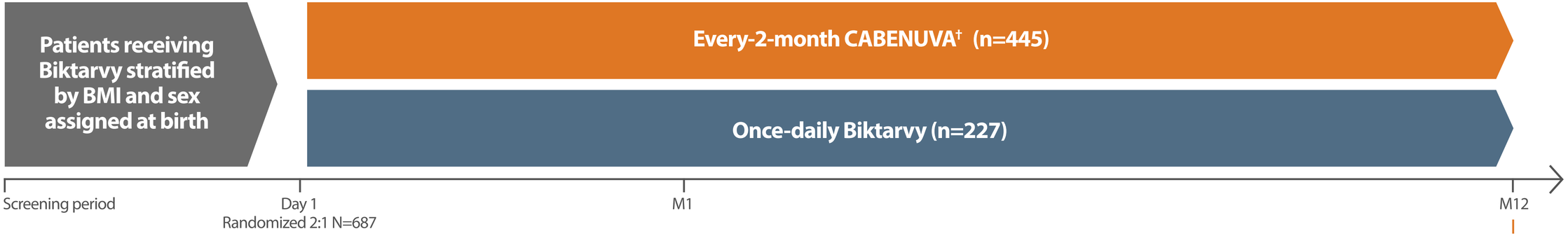
WARNINGS AND PRECAUTIONS

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

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 with HIV-1[1]



SOLAR selected 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

SOLAR selected exclusion criteria[2]

- History of virology failure
- Known or suspected presence of resistance mutations to the individual components of Biktarvy, cabotegravir, and rilpivirine
- HBV infection at screening
- Moderate to severe hepatic impairment
- Women who were pregnant or breastfeeding or planned to become pregnant or breastfeed

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

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

The SOLAR primary endpoint was met:

Every-2-month CABENUVA was virologically* noninferior to Biktarvy at Month 12* (1.1% vs 0.4% [CI -0.6 to 2.0]). Noninferiority margin = 4%.1

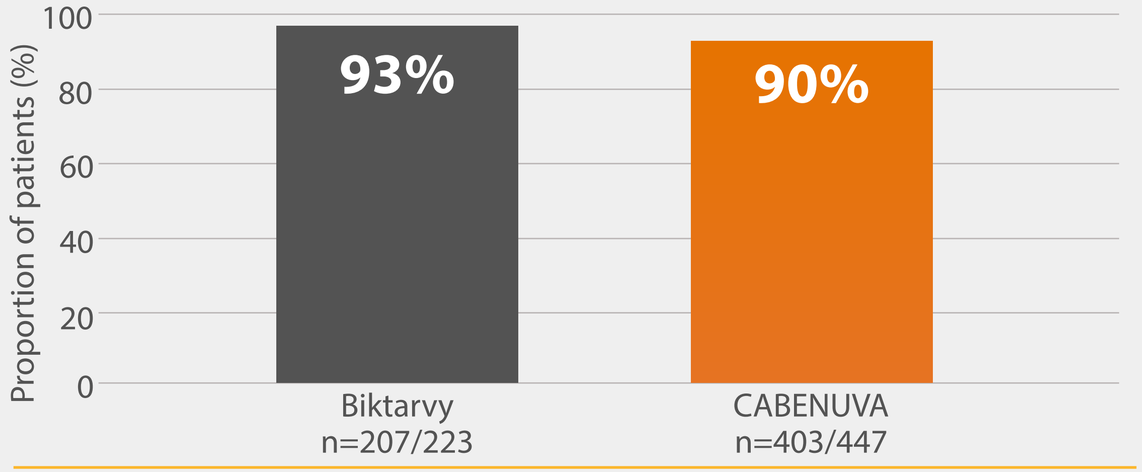
Virology Noninferiorityat month 12* (4% non inferiority margin)

Biktarvy n=223	CABENUVA n=447	Confidence Interval
0.4%	1.1%	0.6 to 2.0

CVF breakdown

*Plasma HIV-1 RNA ≥50 copies/mL.
CI=confidence interval.

SOLAR plasma HIV-1 RNA <50 copies/mL at Month 12/11[1,2]*
(secondary endpoint; 4% noninferiority margin)



- In total, 57 patients (9%) withdrew from the study (every-2-month CABENUVA, n=43; Biktarvy, n=14)[1]

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

CVF and resistance mutations at Month 12[1,2]

As a prespecified secondary endpoint, patients who met the protocol-defined CVF criteria (n=2/447) were tested for emergent INSTI (cabotegravir) or NNRTI (rilpivirine) substitutions conferring resistance at Month 12

Resistance-associated mutations in patients who met protocol-defined CVF[1,2]*	Biktarvy n=223	CABENUVA n=447
Patients with CVF, n (%)	0 (0)	2 (0.4)
INSTI resistance-associated mutations	0	Q148R and G118R
NNRTI resistance-associated mutations	0	M230L and K101E

*One subject excluded from the mITT analysis met CVF at Month 3 with treatment-emergent RPV resistance-associated mutations E138E/K and Y181Y/C. The INSTI assay failed.
INSTI=integrase strand transfer inhibitor; RPV=rilpivirine.

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

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

90% of survey respondents in the SOLAR study reported a preference for CABENUVA at Month 12 (secondary endpoint; n=425)*

- In the survey, patients were asked: "For about a year, you received CABENUVA every 2 months. Compare your experience using the LA injectable vs the daily oral medication. Which do you prefer?"
- 5% (n=21/425) preferred daily, oral and 5% (n=22/425) had no preference; At Month 12 or study withdrawal, 22/43 participants withdrew from the study and did not complete the final survey, leaving 425 respondents

*At Month 12, patients responded to a questionnaire assessing their preference for HIV treatment.1
LA=long-acting.

Top 5 Reasons Survey Respondents Chose For Preferring CABENUVA

1. I don't have to worry as much about remembering to take HIV medication every day (85%)
2. It is more convenient for me to receive injections every 2 months (83%)
3. I don't have to carry my HIV medication with me (74%)
4. I don't have to think about my HIV status every day (61%)
5. I don't have to worry about others seeing or finding my HIV pills (59%)

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

Every-2-month CABENUVA was generally well tolerated[1,2]

- Any AE leading to withdrawal: <1% for Biktarvy, 6% for CABENUVA

ISR breakdown

	CABENUVA n=454	Biktarvy n=227
Any drug-related event	72%	<1%
Total ISRs	69%	0%
Pyrexia	3%	0%
Fatigue	2%	0%
Diarrhea	2%	0%
Headache	2%	0%
Chills	1%	0%
Nausea	1%	0%
Dizziness	1%	0%

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

Every-2-month CABENUVA was generally well tolerated[1,2]

- Most ISRs (98%) were characterized as mild to moderate (Grade 1 or 2) and decreased over time
- Only 2% of patients discontinued treatment due to ISRs

	CABENUVA n=454
Total ISRs	69%
Injection site pain	60%
Injection site discomfort	8%
Injection site nodule	8%
Injection site swelling	8%
Injection site induration	7%
Injection site erythema	4%
Injection site pruritis	3%
Injection site bruising	3%
Injection site warmth	2%
Discontinuations due to ISRs	2%

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

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Every-2-month CABENUVA was as effective as daily oral Biktarvy

Every-2-month CABENUVA was preferred by 90% of trial survey respondents*[1]

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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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