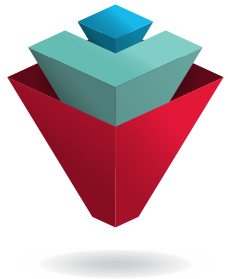
BIKTARVY®
EFFICACY, RESISTANCE, AND SAFETY DATA IN TREATMENT-NAÏVE ADULTS

▶ 144-Week Update: Studies 1489 and 1490



BIKTARVY®
bictegravir 50mg/emtricitabine 200mg/
tenofovir alafenamide 25mg tablets

Indication

BIKTARVY is indicated as a complete regimen for the treatment of HIV-1 infection:

- In adult and pediatric patients weighing ≥25 kg who have no antiretroviral (ARV) treatment history or
- To replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA <50 copies per mL) on a stable ARV regimen with no history of treatment failure and no known resistance to any component of BIKTARVY.

Important Safety Information

BOXED WARNING: POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HIV-1 and HBV and have discontinued products containing emtricitabine (FTC) and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of BIKTARVY. Closely monitor hepatic function with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue BIKTARVY. If appropriate, anti-hepatitis B therapy may be warranted.

Please click to see full Prescribing Information, including BOXED WARNINGS, for BIKTARVY and DESCOVY®.

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INTRODUCTION

BIKTARVY®: A Triple-Therapy STR

Bictegravir, a novel unboosted INSTI, combined with DESCOVY®, a dual-NRTI backbone[1,2]

144 weeks

DEMONSTRATED EFFICACY AT WEEK 144

- Demonstrated efficacy and safety profile in treatment-naïve adults through week 144[1,3-7]

#1

#1 PRESCRIBED REGIMEN FOR HIV-1 TREATMENT

- Source: Ipsos Healthcare US HIV Therapy Monitor & Scope Study, May-July 2019

RECOMMENDED BY DHHS AND IAS-USA

- DHHS: as an initial regimen for most people with HIV-1[8]
- IAS-USA: as an initial regimen for adults with HIV-1, including for rapid initiation[9]

BACKED BY ROBUST CLINICAL TRIAL EXPERIENCE

- Extensive clinical trials with over 1500 people, including various age groups and ethnicities[1,10]

INSTI = integrase strand transfer inhibitor; DHHS = US Department of Health and Human Services; IAS–USA = International Antiviral Society–USA; NRTI = nucleoside reverse transcriptase inhibitor; STR = single-tablet regimen.

Important Safety Information (cont'd)

Contraindications

Coadministration: Do not use BIKTARVY with dofetilide or rifampin.

Warnings and precautions

Drug interactions: See Contraindications and Drug Interactions sections. Consider the potential for drug interactions prior to and during BIKTARVY therapy and monitor for adverse reactions.

Immune reconstitution syndrome, including the occurrence of autoimmune disorders with variable time to onset, has been reported.

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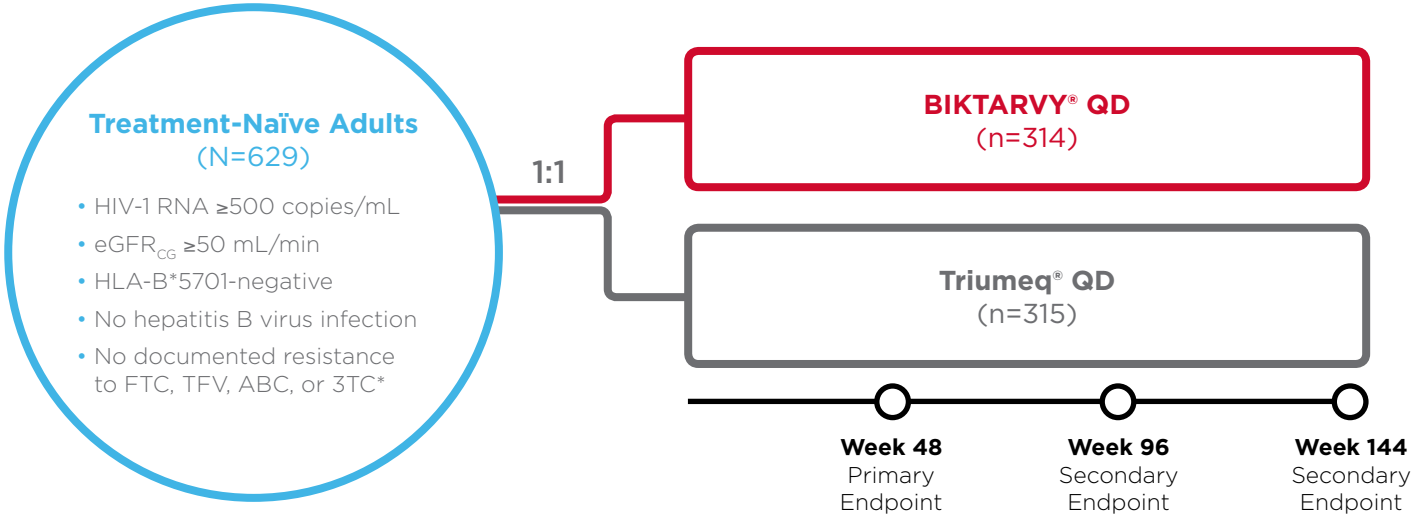
TREATMENT-NAÏVE STUDIES

Study 1489: Trial Design

Phase 3, randomized, double-blind, active-controlled study in treatment-naïve adults[1,3,6,7,11,12]



Primary Endpoint

Proportion of participants who achieved HIV-1 RNA <50 copies/mL at Week 48 as defined by the FDA snapshot algorithm[3]

Secondary Endpoints

Efficacy, safety, and tolerability were assessed through Weeks 96 and 144[6,7,12]

Triumeq (abacavir/dolutegravir/lamivudine).
*Resistance testing for the viral integrase gene was not done at screening.[11]
ABC = abacavir; eGFR$_{CG}$ = estimated glomerular filtration rate (Cockcroft-Gault equation); FTC = emtricitabine; HLA = human leukocyte antigen; QD = once daily; TFV = tenofovir; 3TC = lamivudine.

Important Safety Information (cont'd)

Warnings and precautions (cont'd)

New onset or worsening renal impairment: Cases of acute renal failure and Fanconi syndrome have been reported with the use of tenofovir prodrugs. In clinical trials of BIKTARVY, there have been no cases of Fanconi syndrome or proximal renal tubulopathy (PRT). Do not initiate BIKTARVY in patients with estimated creatinine clearance (CrCl) <30 mL/min. Patients with impaired renal function and/or taking nephrotoxic agents (including NSAIDs) are at increased risk of renal-related adverse reactions. Discontinue BIKTARVY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.

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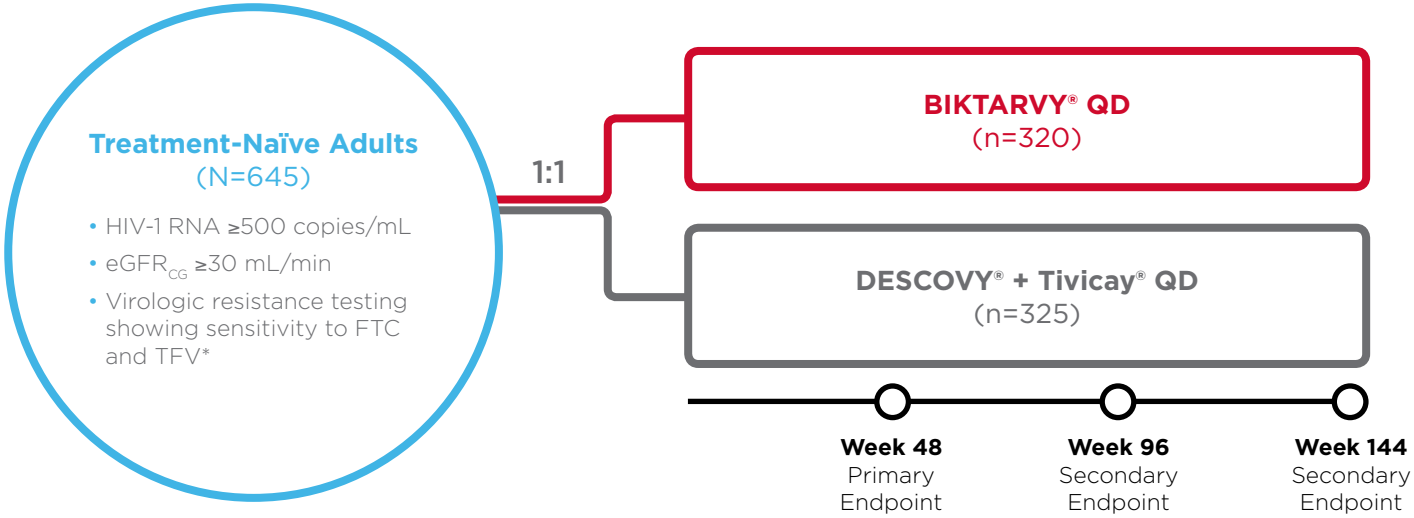
TREATMENT-NAÏVE STUDIES

Study 1490: Trial Design

Phase 3, randomized, double-blind, active-controlled study in treatment-naïve adults[1,4,5,7,13]



Primary Endpoint

Proportion of participants who achieved HIV-1 RNA <50 copies/mL at Week 48 as defined by the FDA snapshot algorithm[4]

Secondary Endpoints

Efficacy, safety, and tolerability were assessed through Weeks 96 and 144[5,7,13]

DESCOVY (emtricitabine/tenofovir alafenamide); Tivicay (dolutegravir).
*Resistance testing for the viral integrase gene was not done at screening.[4]
eGFR$_{CG}$ = estimated glomerular filtration rate (Cockcroft-Gault equation); FTC = emtricitabine; QD = once daily; TFV = tenofovir.

Important Safety Information (cont'd)

Warnings and precautions (cont'd)

New onset or worsening renal impairment (cont'd): *Renal monitoring:* Prior to or when initiating BIKTARVY and during therapy, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients as clinically appropriate. In patients with chronic kidney disease, assess serum phosphorus.

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TREATMENT-NAÏVE STUDIES

Selected Baseline Characteristics

Demographics and baseline characteristics were similar between study groups[3-6,14]

	STUDY 1489[3,6]		STUDY 1490[4,5,14]	
	BIKTARVY® (n=314)	**Triumeq®** (n=315)	**BIKTARVY** (n=320)	**DESCOVY® + Tivicay®** (n=325)
Median age, years (range)	**31** (18-71)	**32** (18-68)	**33** (18-71)	**34** (18-77)
Sex				
Male, %	**91**	**90**	**88**	**89**
Female, %	**9**	**10**	**12**	**11**
Race/Ethnicity				
White, %	**57**	**57**	**57**	**60**
Black, %	**36**	**36**	**30**	**31**
Hispanic or Latino, %	**23**	**21**	**26**	**25**
Asian, %	**2**	**3**	**2**	**3**

Important Safety Information (cont'd)

Warnings and precautions (cont'd)

Lactic acidosis and severe hepatomegaly with steatosis: Fatal cases have been reported with the use of nucleoside analogs, including FTC and TDF. Discontinue BIKTARVY if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity develop, including hepatomegaly and steatosis in the absence of marked transaminase elevations

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TREATMENT-NAÏVE STUDIES

Selected Baseline Characteristics (cont'd)

Demographics and baseline characteristics were similar between study groups[3-6]

	STUDY 1489[3,6]		STUDY 1490[4,5]	
	BIKTARVY® (n=314)	**Triumeq®** (n=315)	**BIKTARVY** (n=320)	**DESCOVY® + Tivicay®** (n=325)
Median HIV-1 RNA, log_{10} copies/mL (IQR)	**4.42** (4.03-4.87)	**4.51** (4.04-4.87)	**4.43** (3.95-4.90)	**4.45** (4.03-4.84)
HIV-RNA >100,000 copies/mL, %	**17**	**16**	**21**	**17**
Median CD4 cell count, cells/µL (IQR)	**443** (299-590)	**450** (324-608)	**440** (289-591)	**441** (297-597)
CD4 cell count <200 cells/µL, %	**11**	**10**	**14**	**10**
Median $eGFR_{CG}$, mL/min (IQR)	**125.9** (107.7-146.3)	**123.0** (107.0-144.3)	**120.4** (100.8-141.8)	**120.6** (102.8-145.1)

$eGFR_{CG}$ = estimated glomerular filtration rate (Cockcroft-Gault equation); IQR = interquartile range.

Important Safety Information (cont'd)

Adverse reactions

Most common adverse reactions (incidence ≥5%; all grades) in clinical studies through week 144 were diarrhea (6%), nausea (6%), and headache (5%).

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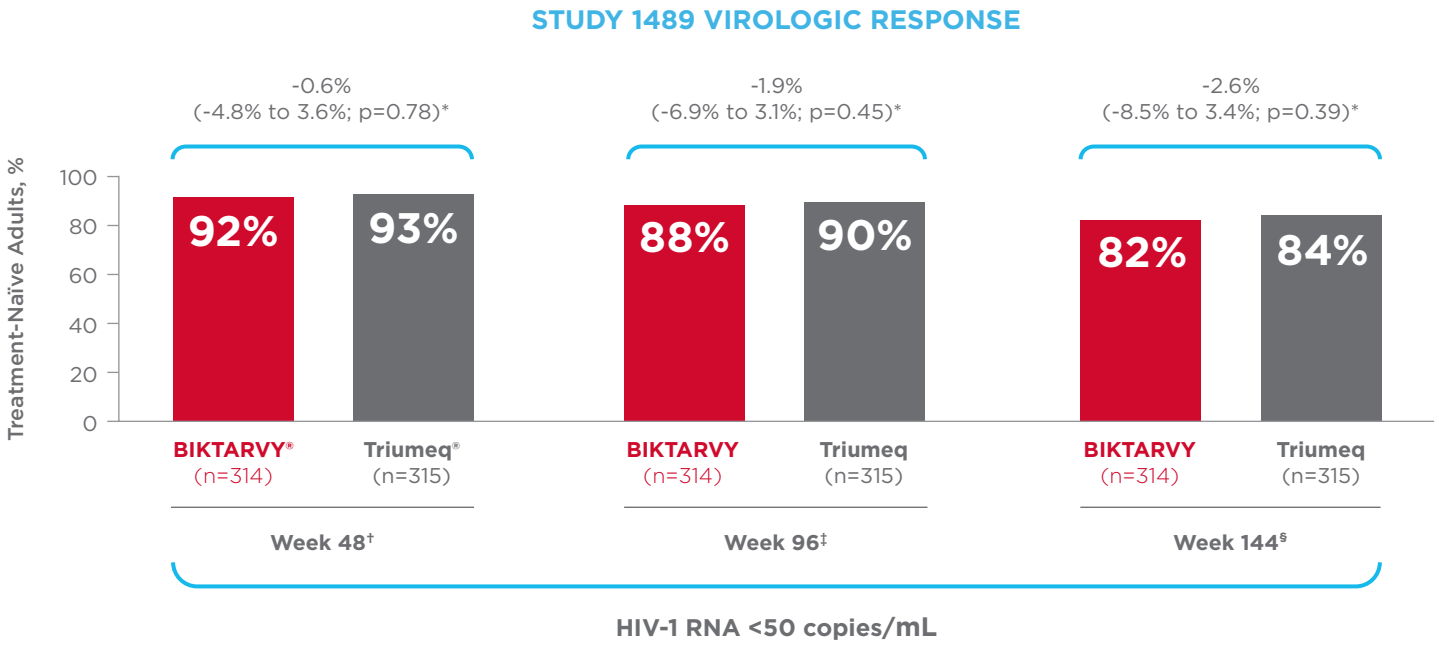
TREATMENT-NAÏVE STUDIES

Durable Power: Long-Term Efficacy in Treatment-Naïve Adults at Week 144

Study 1489: Results noninferior to comparators[1,3,6,7]



▶ **Treatment outcomes were similar across subgroups, regardless of age, sex, race, baseline viral load, and baseline CD4 cell count[7]**

*95% confidence interval.
†Week 48 window was between Day 295 and Day 378 (inclusive).
‡Week 96 window was between Day 631 and Day 714 (inclusive).
§Week 144 window was between Day 967 and Day 1050 (inclusive).

Important Safety Information (cont'd)

Drug interactions

Prescribing information: Consult the full prescribing information for BIKTARVY for more information on Contraindications, Warnings, and potentially significant drug interactions, including clinical comments.

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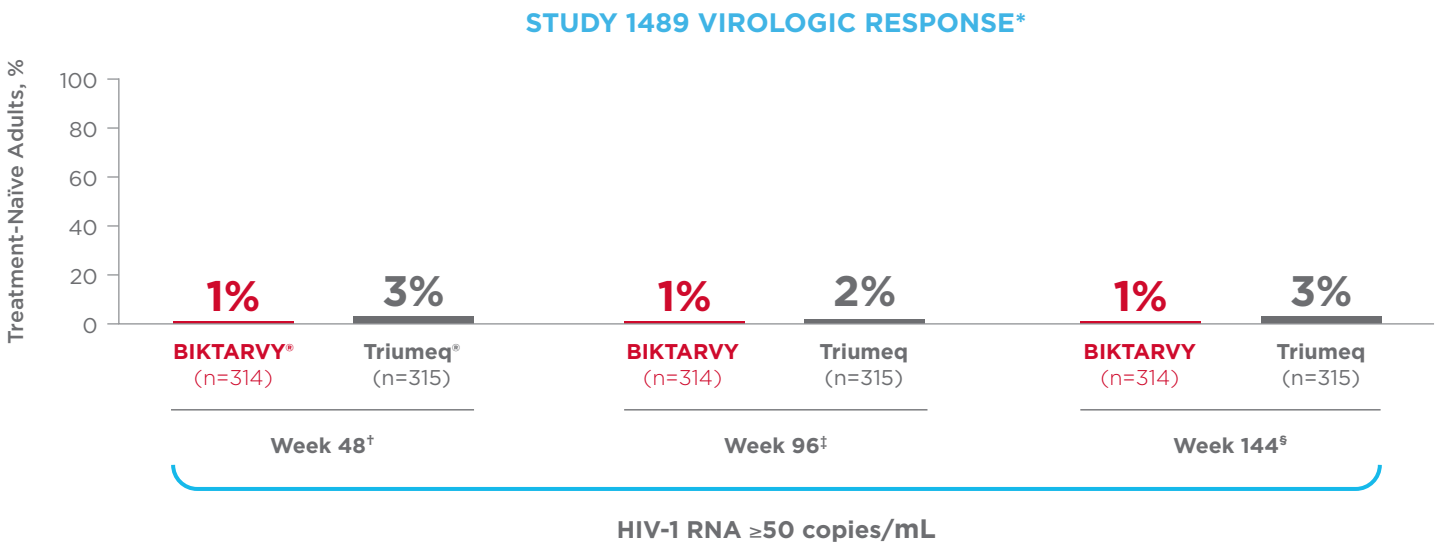
TREATMENT-NAÏVE STUDIES

Durable Power: Long-Term Efficacy in Treatment-Naïve Adults at Week 144

Study 1489: Results noninferior to comparators[1,3,6,7]



▶ **Treatment outcomes were similar across subgroups, regardless of age, sex, race, baseline viral load, and baseline CD4 cell count[7]**

*Includes subjects who had ≥50 copies/mL in the Week 48, 96, or 144 window; subjects who discontinued early due to lack or loss of efficacy; subjects who discontinued for reasons other than an adverse event, death, or lack or loss of efficacy and at the time of discontinuation had a viral value of ≥50 copies/mL.
†Week 48 window was between Day 295 and Day 378 (inclusive).
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Important Safety Information (cont'd)

Drug interactions (cont'd)

Enzymes/transporters: Drugs that induce P-gp or induce both CYP3A and UGT1A1 can substantially decrease the concentration of components of BIKTARVY. Drugs that inhibit P-gp, BCRP, or inhibit both CYP3A and UGT1A1 may significantly increase the concentrations of components of BIKTARVY. BIKTARVY can increase the concentration of drugs that are substrates of OCT2 or MATE1.

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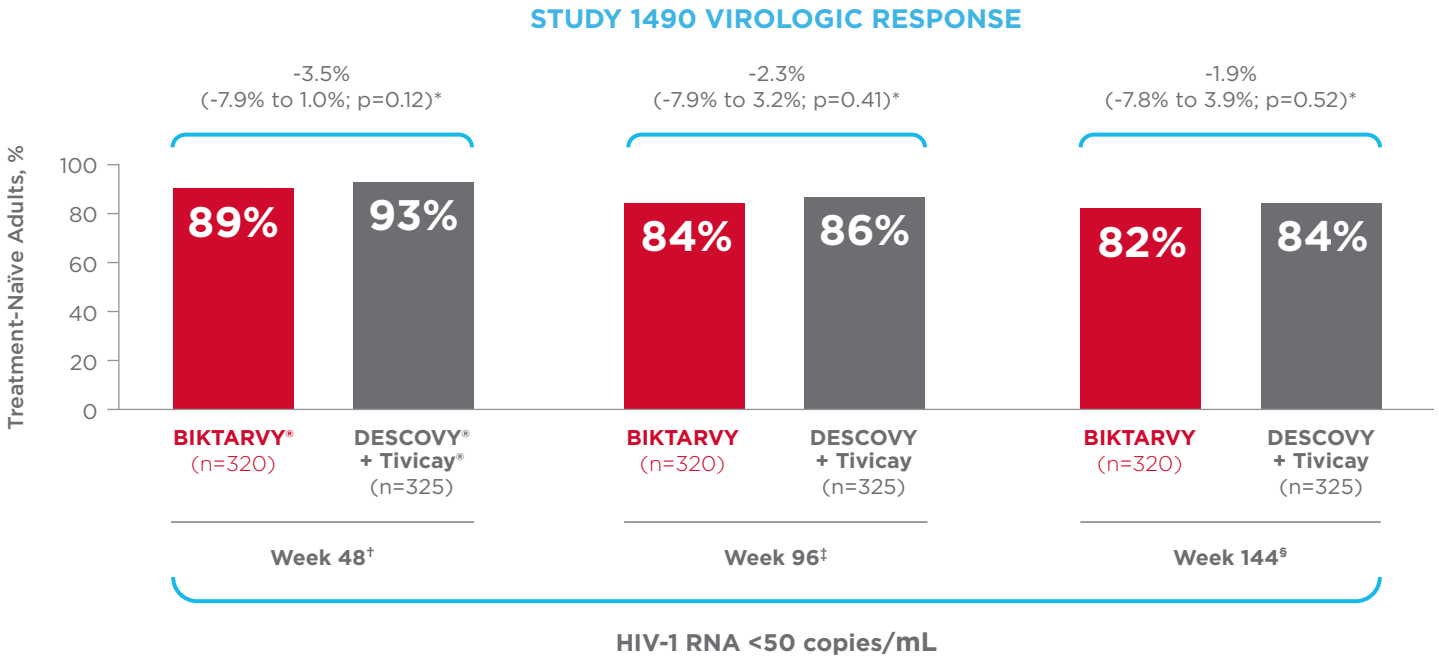
TREATMENT-NAÏVE STUDIES

Durable Power: Long-Term Efficacy in Treatment-Naïve Adults at Week 144

Study 1490: Results noninferior to comparators[1,4,5,7]



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Important Safety Information (cont'd)

Drug interactions (cont'd)

Drugs affecting renal function: Coadministration of BIKTARVY with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of FTC and tenofovir and the risk of adverse reactions.

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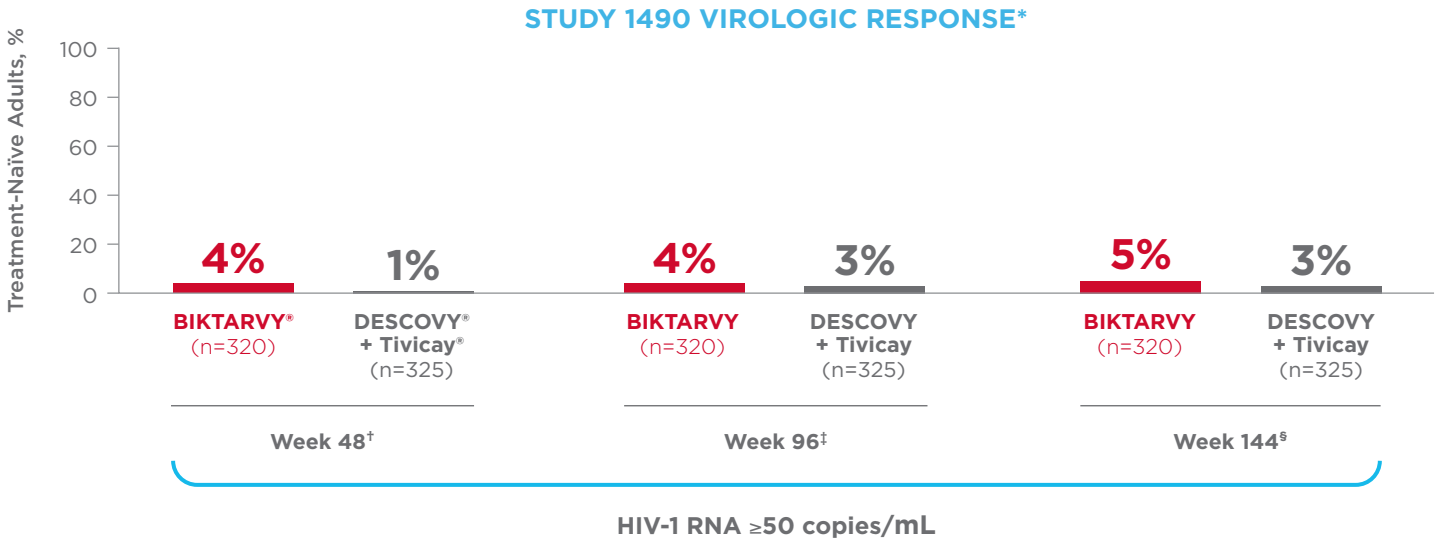
TREATMENT-NAÏVE STUDIES

Durable Power: Long-Term Efficacy in Treatment-Naïve Adults at Week 144

Study 1490: Results noninferior to comparators[1,4,5,7]



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§Week 144 window was between Day 967 and Day 1050 (inclusive).

Important Safety Information (cont'd)

Dosage and administration

Dosage: Patients weighing ≥25 kg: 1 tablet taken once daily with or without food.
Renal impairment: Not recommended in patients with CrCl <30 mL/min.
Hepatic impairment: Not recommended in patients with severe hepatic impairment.
Prior to or when initiating: Test patients for HBV infection.
Prior to or when initiating, and during treatment: As clinically appropriate, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, assess serum phosphorus.

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TREATMENT-NAÏVE STUDIES

No Treatment-Emergent Resistance Associated With BIKTARVY®

Results from Studies 1489 and 1490 through Week 144[7]

0 CASES
OF RESISTANCE
WITH BIKTARVY

- **Among 634 treatment-naïve adults, 8 treatment failure subjects were tested and no amino acid substitutions emerged that were associated with BIKTARVY resistance**

Important Safety Information (cont'd)

Pregnancy and lactation

Pregnancy: There is insufficient human data on the use of BIKTARVY during pregnancy. Dolutegravir, another integrase inhibitor, has been associated with neural tube defects. Discuss the benefit-risk of using BIKTARVY during pregnancy and conception. An Antiretroviral Pregnancy Registry (APR) has been established. Available data from the APR for FTC shows no difference in the rates of birth defects compared with a US reference population.

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TREATMENT-NAÏVE STUDIES

Adverse Reactions

Demonstrated long-term safety and tolerability profile in treatment-naïve adults through Week 144[7]

Adverse Reactions (ARs) (All Grades) Reported in ≥2% of Adults Who Received BIKTARVY*	STUDY 1489		STUDY 1490	
	BIKTARVY® (n=314)	Triumeq® (n=315)	BIKTARVY (n=320)	DESCOVY® + Tivicay® (n=325)
Nausea, %	6	18	3	5
Diarrhea, %	6	4	3	3
Headache, %	5	5	4	3
Fatigue, %	3	3	2	2
Abnormal dreams, %	3	3	0	0
Dizziness, %	2	3	2	1
Insomnia, %	2	3	2	<1
Abdominal distension, %	2	2	1	2

▶ **The majority (84%) of AEs associated with BIKTARVY through Week 144 were Grade 1**

*Frequencies of adverse reactions are based on all adverse events attributed to trial drugs by the investigator. No adverse reactions of Grade 2 or higher occurred in >1% of subjects treated with BIKTARVY.

Important Safety Information (cont'd)

Pregnancy and lactation (cont'd)

Lactation: Women infected with HIV-1 should be instructed not to breastfeed, due to the potential for HIV-1 transmission.

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TREATMENT-NAÏVE STUDIES

Discontinuations Due to Adverse Events

Overall, 1% of treatment-naïve adults discontinued BIKTARVY® due to AEs through Week 144[7]

	BIKTARVY (n=314)	Triumeq® (n=315)
Study 1489[1,7]	0.0%	1.6%

	BIKTARVY (n=320)	DESCOVY® + Tivicay® (n=325)
Study 1490[1,7]	1.9%	1.8%

- **No adults discontinued BIKTARVY due to renal-, hepatic-, or bone-related adverse events[7]**
- Prior to or when initiating BIKTARVY and during therapy, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients as clinically appropriate. In patients with chronic kidney disease, assess serum phosphorus[1]

AEs = adverse events.

Important Safety Information (cont'd)

Adverse reactions

Most common adverse reactions (incidence ≥5%; all grades) in clinical studies through week 144 were diarrhea (6%), nausea (6%), and headache (5%).

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References

1. BIKTARVY [package insert]. Foster City, CA: Gilead Sciences, Inc.; 2019.
2. DESCOVY [package insert]. Foster City, CA: Gilead Sciences, Inc.; 2019.
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