Rapid Initiation of Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) in Patients With Human Immunodeficiency Virus (HIV)–1 Infection: Age, Race/Ethnicity, and Gender Subgroup Analyses From the DIAMOND Study

David Anderson,[1,*] Robert Bolan,[2] Edwin DeJesus,[3] Jose Guillermo Castro,[4] Richard Bruce Simonson,[1] Patricia Cosler,[1] Sareh Seyedkazemi,[1] Donghan Luo,[5] Keith Dunn[1]

*Presenting author.

[1]Janssen Scientific Affairs, LLC, Titusville, NJ, USA; [2]Los Angeles LGBT Center, Los Angeles, CA, USA; [3]Orlando Immunology Center, Orlando, FL, USA; [4]University of Miami, Miami, FL, USA; [5]Janssen Research & Development, LLC, Titusville, NJ, USA.

INTRODUCTION

- Studies involving rapid initiation of antiretroviral therapy (ART) in newly diagnosed, HIV-1–infected patients have demonstrated improved retention in care, decreased morbidity and mortality, and reduced time to virologic suppression[1-6]
- Guidelines from the World Health Organization and the International Antiviral Society–USA recommend that most patients rapidly initiate ART, including an option for same-day initiation, while guidelines from the United States (US) Department of Health and Human Services consider this an investigational approach[7-9]
- Darunavir (DRV) is recommended as an initial ART across international guidelines for patients with unavailable or pending resistance testing results, in part due to the high barrier to resistance of DRV[9,10]
- In the US in 2017, HIV diagnosis rates were highest among adults aged 25 to 29 years versus other age groups and those who are black/African American or Hispanic/Latino versus other race/ethnicity groups, while the most common route of transmission was men-who-have-sex-with-men (MSM)[11]
- DIAMOND is the first phase 3, prospective study evaluating the efficacy and safety of a single-tablet regimen (D/C/F/TAF 800/150/200/10 mg) in a rapid initiation scenario; data from the primary analysis have been reported (see link to the complete poster in the reference list)[12]

OBJECTIVE

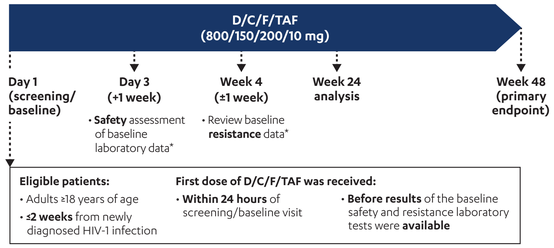
- To evaluate DIAMOND efficacy and safety results at Week 48 by age, race/ethnicity, gender, and HIV acquisition factor

METHODS

Study Design

- DIAMOND (ClinicalTrials.gov Identifier: NCT03227861) was a phase 3, prospective, open-label, single-arm, multicenter, 48-week study evaluating D/C/F/TAF rapid initiation (**Figure 1**)

Figure 1. DIAMOND study design.



*Evaluation could be performed sooner based on the availability of results.

- Key inclusion criteria:
  - Adults ≥18 years of age who were ART naïve and newly diagnosed with HIV-1 infection within 2 weeks of the screening/baseline visit (pre-exposure prophylaxis with emtricitabine/tenofovir disoproxil fumarate was allowed)
- Key exclusion criteria:
  - Certain known active infections or another acquired immunodeficiency syndrome (AIDS)–defining condition that in the investigator's judgment would increase morbidity/mortality risk
  - Certain clinically relevant hepatic and renal conditions
- Eligible patients were enrolled and started on D/C/F/TAF within 24 hours of the screening/baseline visit (prior to the availability of laboratory results)
- Investigators reviewed screening/baseline laboratory findings as results became available; patients not meeting predefined safety or resistance stopping rules continued treatment

Analyses

- Primary endpoint: proportion of patients at Week 48 with virologic response, defined as HIV-1 RNA <50 copies/mL (US Food and Drug Administration [FDA] snapshot analysis)
- Efficacy was also assessed using the observed algorithm (excluding patients with missing values) by the proportion of patients with HIV-1 RNA <50 and <200 copies/mL at Week 48
- Safety was assessed by adverse events (AEs) and discontinuations due to protocol-defined safety stopping rules

Statistical Analysis

- Analyses were performed on all patients who received ≥1 dose of study drug (intent-to-treat [ITT])
- Observed values were used in descriptive statistics; missing values were not imputed
- Results were evaluated in subgroups based on age (18-25/26-50/>50 years), race (white/black or African American/other), ethnicity (Hispanic/non-Hispanic), gender (women/men), and HIV acquisition factor (MSM/non-MSM)

RESULTS

Patient Population and Disposition

- Overall, 109 patients were enrolled in DIAMOND; the median (range) age was 28 (19-66) years, 32% were black/African American, 44% were Hispanic, 87% were men, 75% had an HIV acquisition risk factor of MSM, 25% had HIV-1 RNA ≥100,000 copies/mL, and 21% had a CD4+ cell count <200 cells/μL
  - Baseline demographics by age, race/ethnicity, gender, and HIV acquisition factor subgroups are summarized in **Table 1**
- A total of 97 (89%) patients completed the study and 12 (11%) prematurely discontinued; 3 (3%) patients discontinued due to protocol-defined safety stopping rules, 1 (<1%) patient discontinued due to AEs, 4 (4%) patients were lost to follow-up, 1 (<1%) patient had a protocol violation, 1 (<1%) patient withdrew consent, and 2 (2%) patients discontinued for other reasons not related to efficacy or safety

Efficacy

- Virologic response rates (HIV-1 RNA <50 copies/mL) by ITT-FDA snapshot and the observed algorithm were high and similar in the overall population as well as across age, race/ethnicity, and HIV acquisition factor subgroups (**Figure 2**)
  - The lower virologic response rate in women (ITT-FDA snapshot) should be interpreted with caution due to the small sample size. Among the 5 women who did not achieve HIV-1 RNA <50 copies/mL at Week 48, 1 had HIV-1 RNA ≥50 copies/mL (77 copies/mL) at Week 48, 1 had HIV-1 RNA ≥50 copies/mL at early discontinuation (due to protocol-defined safety stopping rules), and 3 did not have data in the window
  - No patients discontinued the study due to lack of efficacy or met protocol-defined virologic failure criteria
- All patients in the observed analysis (96/96) achieved HIV-1 RNA <200 copies/mL at Week 48

Safety

- Most AEs were grade 1 or 2, and no serious or grade 4 AEs were related to D/C/F/TAF across subgroups (**Table 2**)
  - Patients who were >50 years of age, black/African American, women, and non-MSM had numerically lower rates of related AEs versus other subgroups
- No patients discontinued due to immune reconstitution inflammatory syndrome or central nervous system, gastrointestinal, metabolic, bone, or renal AEs considered related to study drug
- The most common (≥2%) AEs related to study drug in the overall population were diarrhea (12%), nausea (12%), rash (5%), vomiting (4%), and fatigue (3%)
- One patient (28-year-old, Hispanic female) discontinued due to AEs, which were considered study drug–related (allergic dermatitis [grade 3], pyrexia [grade 2], and lip swelling [grade 2]); all resolved after discontinuation of study treatment

Table 1. Baseline Demographic Characteristics by Subgroups*

	Age			Race/ethnicity					Gender		HIV acquisition factor	
Parameter	18-25 y	26-50 y	>50 y	White	Black/ African American	Other	Hispanic	Non-Hispanic	Women	Men	MSM	Non-MSM
n	38	58	13	65	35	9	48	61	14	95	82	27
Age, median (range), y	22 (19-25)	33 (26-49)	60 (52-66)	30 (19-66)	28 (19-65)	27 (20-53)	27 (19-62)	30 (19-66)	33 (25-63)	27 (19-66)	27 (19-66)	33 (19-65)
18-25 y, n (%)				21 (32)	13 (37)	4 (44)	19 (40)	19 (31)	2 (14)	36 (38)	30 (37)	8 (30)
26-50 y, n (%)				36 (55)	18 (51)	4 (44)	25 (52)	33 (54)	11 (79)	47 (49)	43 (52)	15 (56)
>50 y, n (%)				8 (12)	4 (11)	1 (11)	4 (8)	9 (15)	1 (7)	12 (13)	9 (11)	4 (15)
Race, n (%)												
White	21 (55)	36 (62)	8 (62)				45 (94)	20 (33)	6 (43)	59 (62)	52 (63)	13 (48)
Black/African American	13 (34)	18 (31)	4 (31)				0	35 (57)	7 (50)	28 (29)	22 (27)	13 (48)
Other	4 (11)	4 (7)	1 (8)				3 (6)	6 (10)	1 (7)	8 (8)	8 (10)	1 (4)
Gender, n (%)												
Women	2 (5)	11 (19)	1 (8)	6 (9)	7 (20)	1 (11)	4 (8)	10 (16)			0	14 (52)
Men	36 (95)	47 (81)	12 (92)	59 (91)	28 (80)	8 (89)	44 (92)	51 (84)			82 (100)	13 (48)
HIV acquisition factor, n (%)												
MSM	30 (79)	43 (74)	9 (69)	52 (80)	22 (63)	8 (89)	40 (83)	42 (69)	0	82 (86)		
Non-MSM	8 (21)	15 (26)	4 (31)	13 (20)	13 (37)	1 (11)	8 (17)	19 (31)	14 (100)	13 (14)		

*Percentages may not total 100% due to rounding.

Figure 2. Virologic response (HIV-1 RNA <50 copies/mL) at Week 48, overall and by subgroups.

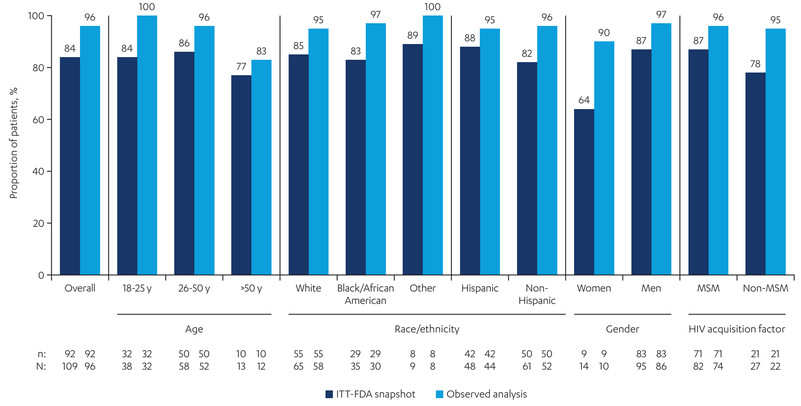


Table 2. AEs Related to Study Drug Through Week 48, Overall and by Subgroups

		Age			Race/ethnicity					Gender		HIV acquisition factor	
Related AE, n (%)	Overall	18-25 y	26-50 y	>50 y	White	Black/ African American	Other	Hispanic	Non-Hispanic	Women	Men	MSM	Non-MSM
n	109	38	58	13	65	35	9	48	61	14	95	82	27
Any	36 (33)	14 (37)	20 (34)	2 (15)	26 (40)	6 (17)	4 (44)	22 (46)	14 (23)	2 (14)	34 (36)	31 (38)	5 (19)
Serious	0	0	0	0	0	0	0	0	0	0	0	0	0
Grade 2	7 (6)	2 (5)	5 (9)	0	6 (9)	1 (3)	0	3 (6)	4 (7)	0	7 (7)	7 (9)	0
Grade 3	2 (2)	1 (3)	1 (2)	0	2 (3)	0	0	2 (4)	0	1 (7)	1 (1)	1 (1)	1 (4)
Grade 4	0	0	0	0	0	0	0	0	0	0	0	0	0

CONCLUSIONS

- **DIAMOND, the first phase 3 study of a single-tablet regimen in a rapid initiation setting, enrolled patients reflective of the population most affected by HIV-1 infection in the US**
- **A high proportion of patients who rapidly initiated treatment with D/C/F/TAF achieved HIV-1 RNA <50 copies/mL at Week 48, across a variety of baseline demographic characteristics**
  - Virologic response rates were consistent across subgroups by age, race/ethnicity, and HIV acquisition factor
  - Gender analyses were limited by the small number of women enrolled in the study
- **Treatment with D/C/F/TAF was safe and well tolerated**
  - No patients discontinued due to bone or renal AEs related to study drug
- **Findings support D/C/F/TAF as a preferred option for rapid initiation of ART for patients with a variety of baseline demographic characteristics**

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If you have any additional questions or would like to request a copy of this poster, call +1-800-JANSSEN (+1-800-526-7736) or go to www.janssenMD.com.

DISCLOSURES

This study was sponsored by Janssen Scientific Affairs, LLC. DA, RBS, SS, DL, and KD are employees of Janssen and may be stockholders in Johnson & Johnson. RB and JGC have no disclosures to report. ED has served on a speakers bureau for Gilead, and advisory boards for Gilead, Janssen, and Theratechnologies. PC was an employee of Janssen at the time of the study/analysis of the data and is a stockholder in Johnson & Johnson.

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