High Levels of Patient Satisfaction During Rapidly Initiated Therapy With Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) for Treatment of HIV-1 Infection Through 24 Weeks of the DIAMOND Study

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INTRODUCTION

- Patients newly diagnosed with human immunodeficiency virus (HIV)–1 infection may be hesitant to rapidly begin antiretroviral therapy (ART) due to concerns such as the need for lifelong therapy, side effects, and dosing requirements, as well as psychological considerations associated with diagnosis[1]
- Rapid initiation models of care for individuals newly diagnosed with HIV-1 infection have demonstrated reduced time to virologic suppression, improved retention in care, and decreased morbidity and mortality[2-4]
  - Guidelines from the World Health Organization and International Antiviral Society–USA (IAS-USA) now recommend rapid initiation of treatment for newly diagnosed HIV-1–infected patients in most cases[1,5]
- The low proportions of HIV-1–infected individuals in the US who were in receipt of care (63%) or were virologically suppressed (51%) in 2015 suggests the importance of understanding patients' preferences in HIV care for their outcomes[6]
- Patient-reported outcome (PRO) data in rapid initiation scenarios are not currently available
- The HIV Treatment Satisfaction Questionnaire-status version (HIVTSQs) is a 10-item PRO instrument that measures patient satisfaction with ART[7]
  - In previously reported studies of ART initiation in treatment-naïve patients, median HIVTSQs scores of 57 to 58 after 48 weeks[8] and 53 to 55 after 96 weeks[9] have been observed
- Darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) 800/150/200/10 mg is an oral, once-daily, single-tablet regimen (STR) approved to treat ART-naïve and ART-experienced, suppressed patients with HIV-1 infection in Europe, the US, and Canada
  - The efficacy and safety of D/C/F/TAF have been demonstrated in the phase 3 AMBER and EMERALD studies, with high proportions of patients (>91%) achieving HIV-1 RNA <50 copies/mL and low rates (<2%) of adverse events (AEs) leading to study discontinuation at Week 48; PRO data were not reported[10,11]
- D/C/F/TAF is an ideal, abacavir-sparing regimen for rapid initiation models of care based on the high barrier to resistance of darunavir and potential to improve adherence with an STR[12,13]

OBJECTIVES

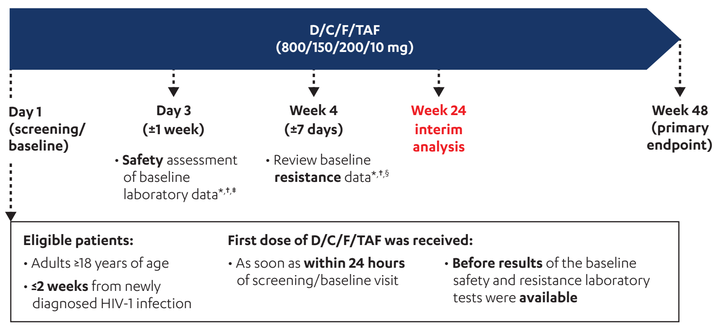
- To assess treatment satisfaction at 4 and 24 weeks after rapid initiation of D/C/F/TAF in newly diagnosed, HIV-1–infected, treatment-naïve patients
- To assess the efficacy and safety of D/C/F/TAF in a rapid initiation model of care

METHODS

Study Design

- DIAMOND (ClinicalTrials.gov: NCT03227861) is an ongoing, phase 3, single-arm, open-label, prospective, multicenter study evaluating D/C/F/TAF in a rapid initiation model of care over 48 weeks of treatment (**Figure 1**)[14]
- Key inclusion criteria:
  - Adults ≥18 years of age, with HIV-1 infection diagnosed within 2 weeks of the screening/baseline visit
  - ART-naïve, except for use of emtricitabine/tenofovir disoproxil fumarate for pre-exposure prophylaxis
- Key exclusion criteria included certain known active infections or another acquired immunodeficiency syndrome (AIDS)–defining condition that in the investigator's judgement would increase morbidity/mortality risk, and certain clinically relevant hepatic and renal conditions
- Eligible patients were enrolled and started on D/C/F/TAF immediately, without screening/baseline laboratory information
- Investigators reviewed screening/baseline laboratory findings as the results became available; patients who did not meet predefined safety or resistance stopping rules continued treatment (see **Figure 1** footnotes)

Figure 1. DIAMOND study design.



eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ULN, upper limit of normal.
*Evaluations could be performed sooner based on the availability of results.
†Interim analyses were performed once all patients had been assessed for safety at Day 3 and resistance at Week 4, and were updated when all patients continuing treatment reached Week 24.
‡Safety stopping criteria were as follows (retesting of abnormal screening/baseline safety laboratory values allowed once): eGFR (MDRD formula) <50 mL/min; AST or ALT ≥2.5 times the ULN; serum lipase ≥1.5 times the ULN; positive pregnancy test for women of childbearing potential; laboratory results that the investigator believed should result in discontinuation of study medication; and active hepatitis C infection that in the opinion of the investigator required immediate treatment or was expected to require treatment during the study with agents not compatible with D/C/F/TAF.
§Resistance was based on predicted genotypic sensitivity (patients who did not show full sensitivity to all drugs were to be discontinued [with the exception of M184I/V]).

Analyses

- The primary endpoint is the proportion of patients with virologic response at Week 48, defined by HIV-1 RNA <50 copies/mL (US Food and Drug Administration [FDA] snapshot); for this interim analysis, virologic response (same definition) at Week 24 was evaluated
  - The observed algorithm was also used to assess efficacy at Week 24, as determined by the proportion of patients with HIV-1 RNA <50 copies/mL
- Screening/baseline resistance testing was performed using the GenoSure Prime® assay
- Safety was assessed by discontinuations due to protocol-defined safety stopping rules, AEs, and laboratory abnormalities
- PROs for treatment satisfaction were evaluated using the HIVTSQs at Weeks 4 and 24, as well as the time of early study treatment discontinuation
  - The HIVTSQs is a validated, 10-item questionnaire using a 6-point ordinal scale (Version 2006), with 6 as high favorability and 0 as low favorability (**Figure 2**)[7]
  - Responses to questions 1-3 and 9-10 are summed to produce the general satisfaction/clinical subscale score (range: 0-30) and responses to questions 4-8 are summed to produce the lifestyle/ease subscale score (range: 0-30)
  - Responses to all questions are summed to produce the total treatment satisfaction score (range: 0-60)

Figure 2. HIVTSQs questions.*,[7]

- Question 1: How satisfied are you with your current treatment?
- Question 2: How well controlled do you feel your HIV has been recently?
- Question 3: How satisfied are you with any side effects of your present treatment?
- **Question 4: How satisfied are you with the demands made by your current treatment?**
- **Question 5: How convenient have you been finding your treatment to be recently?**
- **Question 6: How flexible have you been finding your treatment to be recently?**
- **Question 7: How satisfied are you with your understanding of your HIV?**
- **Question 8: How satisfied are you with the extent to which the treatment fits in with your lifestyle?**
- Question 9: Would you recommend your present treatment to someone else with HIV?
- Question 10: How satisfied would you be to continue with your present form of treatment?

*Unbolded font denotes questions that comprise the general satisfaction/clinical subscale. Bolded font denotes questions that comprise the lifestyle/ease subscale.

Statistical Analyses

- Analyses were performed on all patients who received ≥1 dose of study drug (intent-to-treat [ITT] population)
- Observed values were used in descriptive statistics; missing values were not imputed
- Descriptive statistics for absolute values and changes in HIVTSQs scores were calculated for each question, for each subscale and overall score at each time point, where applicable; in case of a missing item score, the overall score of a patient was calculated as follows:
  1. Sum the existing item scores
  2. Divide the sum by the number of existing item scores
  3. Multiply by 10

RESULTS

Patient Population and Disposition

- A total of 109 patients were enrolled in the study; 29% were enrolled within 48 hours of diagnosis and the median (range) time from HIV-1 diagnosis to screening/baseline was 5 (0-14) days (**Table 1**)
- Among patients with available genotype data at screening/baseline (n = 102), none had a darunavir resistance-associated mutation

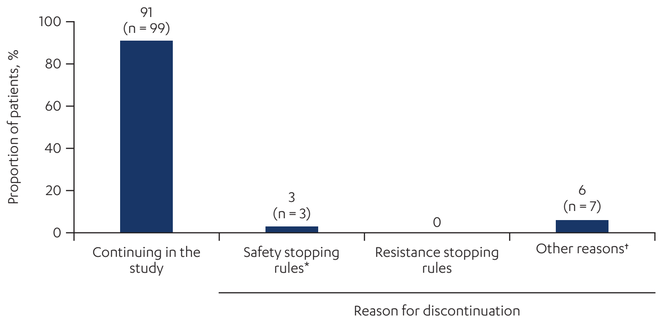
Table 1. Baseline Demographic and Clinical Characteristics

	D/C/F/TAF N = 109
Demographic characteristics	
Age, median (range), years	28 (19-66)
Women, n (%)	14 (13)
Race, n (%)	
White	64 (59)
Black/African American	35 (32)
Other	10 (9)
Clinical characteristics	
HIV-1 RNA, n	108*
Median (range), log_{10} copies/mL	4.6 (1.3-8.2)
≥100,000 copies/mL, n (%)	25 (23)
CD4+ cell count, n	108*
Median (range), cells/mm³	369 (7-1,082)
<200 cells/mm³, n (%)	23 (21)
Time from diagnosis to screening/baseline, median (range), days	5 (0-14)
Enrolled within 48 hours of diagnosis, n (%)	32 (29)

*One patient had missing values due to a shipping error of the screening/baseline samples.

- At the time of the Week 24 interim analysis, 99 (91%) patients remained on D/C/F/TAF and 10 (9%) patients had discontinued (**Figure 3**)
  - Three (3%) patients discontinued due to protocol-defined safety stopping rules
  - No patients discontinued due to resistance stopping rules
  - Seven (6%) patients discontinued for other reasons

Figure 3. Patient disposition through Week 24.

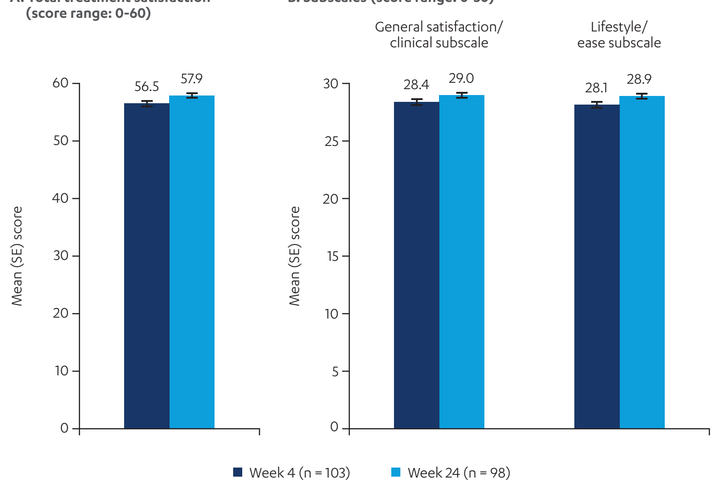


*Five patients met safety stopping rules criteria, all with confirmed elevations in AST or ALT ≥2.5 times the ULN at the screening/baseline visit. Three of these patients discontinued according to the protocol and 2 remained in the study based on clinical assessment by the investigator and agreement of the sponsor. Transaminases appeared to normalize after screening/baseline in all 5 patients, suggesting that treatment may have been beneficial for these patients.
†Other reasons were: lost to follow-up (n = 3), withdrawal of consent (n = 2), protocol violation (n = 1), and AE (n = 1 [allergic dermatitis]).

PROs

- Patients rapidly starting and continuing D/C/F/TAF demonstrated high total treatment satisfaction scores on the HIVTSQs; mean scores were 56.5 at Week 4 and 57.9 at Week 24 (maximum score: 60; **Figure 4A**)
- Four patients completed the HIVTSQs upon early study discontinuation (3 due to predefined protocol stopping rules prior to Week 2, and 1 after withdrawal of consent at Week 36); the mean HIVTSQs total score for these patients was 49.3

Figure 4. HIVTSQs scores at Weeks 4 and 24 after rapid initiation of D/C/F/TAF.

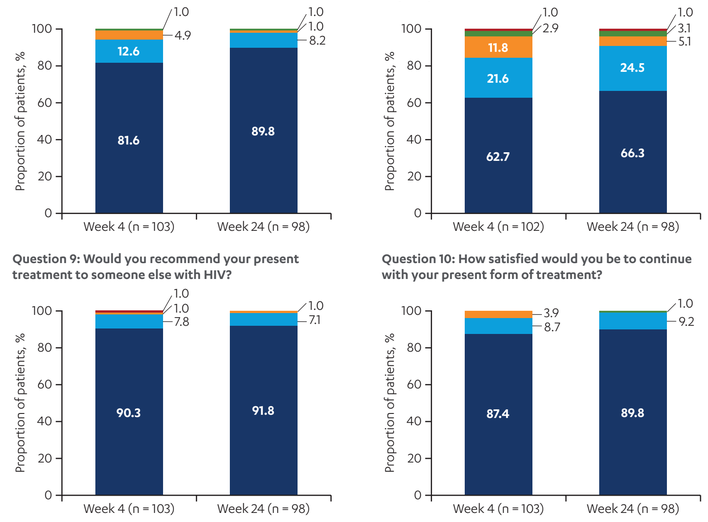


SE, standard error.

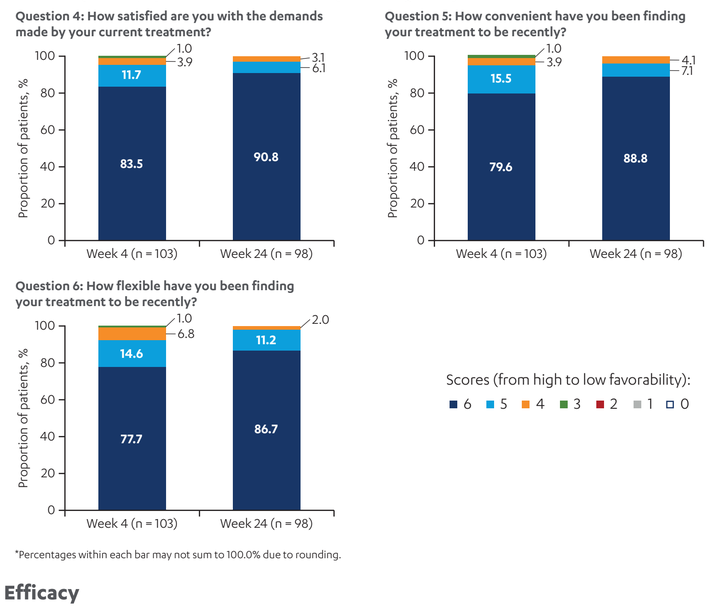
- Assessment of the general satisfaction/clinical subscale demonstrated mean scores of 28.4 at Week 4 and 29.0 at Week 24 (maximum score: 30; **Figure 4B**)
  - The distribution of scores to select individual questions (regarding current treatment, side effects, recommendation to others, and continuation) showed that the proportion of patients giving the maximum score of 6 remained generally similar or increased from Week 4 to Week 24 after rapid initiation of D/C/F/TAF (**Figure 5A**)
  - After 24 weeks of D/C/F/TAF treatment, 89.8% of patients responded that they would be "very satisfied" to continue their current treatment
- For the lifestyle/ease subscale, mean scores were 28.1 at Week 4 and 28.9 at Week 24 (maximum score: 30; **Figure 4B**)
  - For select individual questions (regarding demands, convenience, and flexibility), the distribution of scores showed that the proportion of patients giving the maximum score of 6 tended to increase from Week 4 to Week 24 (**Figure 5B**)

Figure 5. Patient responses to select HIVTSQs questions at Weeks 4 and 24.*

A. HIVTSQs general satisfaction/clinical subscale questions (score range: 6-0)



B. HIVTSQs lifestyle/ease subscale questions (score range: 6-0)

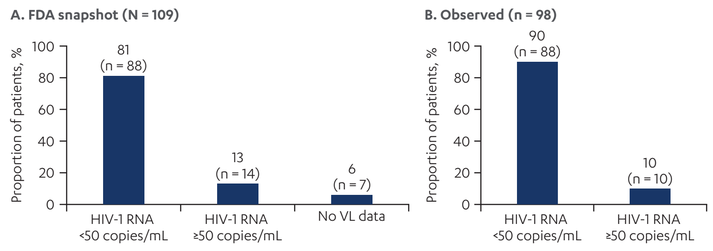


*Percentages within each bar may not sum to 100.0% due to rounding.

Efficacy

- At Week 24, 88 of 109 (81%) patients had achieved HIV-1 RNA <50 copies/mL (FDA snapshot; **Figure 6A**)
  - According to the observed algorithm, 88 of 98 (90%) patients had achieved HIV-1 RNA <50 copies/mL at Week 24 (**Figure 6B**)
- No patients had protocol-defined viral failure (PDVF) and no patients discontinued the study due to lack of efficacy

Figure 6. Virologic efficacy of D/C/F/TAF in a rapid initiation model of care through Week 24.



VL, viral load.

Safety

- The majority of AEs were grade 1 or 2, and there were no grade 4 AEs or deaths (**Table 2**)
  - Incidences of grade 3 AEs and serious AEs were low, and no serious AEs were related to study drug
- One patient discontinued due to AEs (allergic dermatitis [grade 3], pyrexia [grade 2], and lip swelling [grade 2]); all AEs resolved after discontinuation of study treatment
- There was 1 grade 3-4 laboratory abnormality that occurred in ≥2% of patients (increased AST in 4 [4%] patients)

Table 2. Summary of AEs

Parameter, n (%)	D/C/F/TAF N = 109	
	Overall	Related
≥1 AE	80 (73)	33 (30)
≥1 serious AE	7 (6)	0
≥1 grade 1 AE	40 (37)	25 (23)
≥1 grade 2 AE	31 (28)	6 (6)
≥1 grade 3 AE*	9 (8)	2 (2)
≥1 grade 4 AE	0	0
Most common AEs (all grades; ≥5% of patients)		
Diarrhea	23 (21)	10 (9)
Nausea	17 (16)	13 (12)
Rash†,‡	15 (14)	5 (5)
Vomiting	9 (8)	4 (4)
Headache	9 (8)	2 (2)
Pyrexia	8 (7)	1 (1)
Fatigue	6 (6)	3 (3)

*Two grade 3 AEs were considered related to study drug: allergic dermatitis (resolved after discontinuation of study treatment) and nausea (resolved with no changes to study drug dosing).
†Pooled preferred terms of dermatitis, allergic dermatitis, rash, macular rash, maculo-papular rash, papular rash, and pruritic rash.
‡All rash AEs were grade 1 or 2, except for one that was grade 3.

CONCLUSIONS

- **In the first known phase 3 study of an STR in a rapid initiation model of care, D/C/F/TAF treatment demonstrated high satisfaction scores after 4 and 24 weeks in patients newly diagnosed with HIV-1 infection**
  - **Despite this patient population having less time to adjust to their HIV-1 diagnosis and consider treatment options, D/C/F/TAF showed HIVTSQs scores consistent with other naïve studies[8,9] and nearly 90% of patients would be "very satisfied" to continue D/C/F/TAF treatment**
- **A high proportion of patients achieved HIV-1 RNA <50 copies/mL after rapid initiation of D/C/F/TAF; no patients had PDVF or discontinued the study due to baseline resistance results**
  - **At Week 24, a high proportion of patients (>90%) continued to receive treatment, and only 1 patient discontinued the study due to AEs**
- **Findings from DIAMOND, together with the demonstrated efficacy, high barrier to resistance, safety profile, and convenience of an STR, support the placement of D/C/F/TAF in IAS-USA guidelines as a recommended treatment option in a rapid initiation model of care[5]**

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DISCLOSURES

C. Benson contributed to the analysis plan and interpretation of the data. R.B. Simonson and K. Dunn contributed to the design of the study and interpretation of the data. C. Bicer contributed to statistical analysis and interpretation of the data. All authors contributed to drafting the poster and approved the final version.

C. Benson, R.B. Simonson, and K. Dunn are full-time employees of Janssen and may be Johnson & Johnson stockholders. C. Bicer is a consultant for Janssen.

These data, in part, have been presented previously: Huhn GD, et al. Poster presented at: the 22nd International AIDS Conference; 23-27 July, 2018; Amsterdam, The Netherlands. Poster WEPEC200.

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