Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) in a Rapid Initiation Model of Care for HIV-1 Infection: Week 24 Interim Analysis of the DIAMOND Study

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Disclosures

Keith Dunn

Full-time employee of Janssen and stockholder in J&J
Introduction

- Since 2012, US DHHS guidelines have recommended initiation of ART in newly diagnosed HIV-1 patients regardless of CD4+ cell count\(^1\)
  - Reduces risk of transmission and AIDS- and non-AIDS-related events
- Rapid initiation models of care have demonstrated reduced time to virologic suppression, improved retention in care, and decreased morbidity and mortality\(^2-4\)
  - Recommended in guidelines from WHO and IAS-USA\(^5,6\)
- D/C/F/TAF is an ideal regimen for rapid initiation based on the high barrier to resistance of darunavir and potential to improve adherence with an STR
  - Approved in the US, Europe, and Canada


DHHS, Department of Health and Human Services; ART, antiretroviral therapy; AIDS, acquired immunodeficiency syndrome; WHO, World Health Organization; IAS-USA, International Antiviral Society–USA; D/C/F/TAF, darunavir/cobicistat/ Emtricitabine/Tenofovir alafenamide; STR, single-tablet regimen.
DIAMOND Week 24: Objectives

- Assess the efficacy and safety of D/C/F/TAF in a rapid initiation model of care in newly diagnosed, HIV-1–infected, treatment-naïve patients
- Assess baseline viral resistance in the study population
- Assess HIV Treatment Satisfaction Questionnaire-status version (HIVTSQs) results at Weeks 4 and 24
DIAMOND: Study Design

- Ongoing, phase 3, open-label, prospective, multicenter study

Eligible patients:
- Adults ≥18 years of age
- ≤2 weeks from newly diagnosed HIV-1 infection

First dose of D/C/F/TAF was received:
- As soon as within 24 hours of screening/baseline visit

Before results of the baseline safety and resistance laboratory tests were available

D/C/F/TAF, darunavir/cobicistat/emtricitabine/tenofovir alafenamide.

Methods

- Primary endpoint: proportion of patients with virologic response at Week 48 (HIV-1 RNA <50 copies/mL; FDA snapshot)
  - Efficacy also assessed using observed algorithm
- Screening/baseline resistance testing was performed using the GenoSure Prime® assay
- PDVF was defined as virologic nonresponse or virologic rebound
- Safety evaluations: AEs, discontinuations due to protocol-defined safety stopping rules, laboratory abnormalities
- PROs for treatment satisfaction evaluated via HIVTSQs at Weeks 4 and 24
  - Validated, 10-item questionnaire with a 6-point ordinal scale

# Patient Population

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>D/C/F/TAF N = 109</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), years</td>
<td>28 (19-66)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>14 (13)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>64 (59)</td>
</tr>
<tr>
<td>Black/African American</td>
<td>35 (32)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (9)</td>
</tr>
<tr>
<td>Hispanic or Latino, n (%)</td>
<td>48 (44)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1 RNA, median (range), log$_{10}$ copies/mL*</td>
<td>4.6 (1.3-8.2)</td>
</tr>
<tr>
<td>HIV-1 RNA, ≥100,000 copies/mL, n (%)*</td>
<td>25 (23)</td>
</tr>
<tr>
<td>CD4+ cell count, median (range), cells/µL*</td>
<td>369 (7-1,082)</td>
</tr>
<tr>
<td>CD4+ cell count, &lt;200 cells/µL, n (%)*</td>
<td>23 (21)</td>
</tr>
<tr>
<td>Time from diagnosis to screening/baseline, median (range), days</td>
<td>5 (0-14)</td>
</tr>
<tr>
<td>Enrolled within 48 hours of diagnosis, n (%)</td>
<td>32 (29)</td>
</tr>
</tbody>
</table>

*n = 108 (1 patient had missing values due to a shipping error of the screening/baseline samples).

D/C/F/TAF, darunavir/cobicistat/emtricitabine/tenofovir alafenamide.

# Baseline Genotypic Susceptibility

<table>
<thead>
<tr>
<th>Genotypic susceptibility, n (%)</th>
<th>D/C/F/TAF n = 102</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darunavir</td>
<td>102 (100)</td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>100 (98)</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>102 (100)</td>
</tr>
<tr>
<td>All PIs</td>
<td>97 (95)</td>
</tr>
<tr>
<td>All NRTIs</td>
<td>98 (96)</td>
</tr>
<tr>
<td>All NNRTIs</td>
<td>80 (78)</td>
</tr>
<tr>
<td>All INIs</td>
<td>97 (95)</td>
</tr>
</tbody>
</table>

- Among patients with baseline genotype data available, none had a darunavir RAM

D/C/F/TAF, darunavir/cobicistat/emtricitabine/tenofovir alafenamide; PI, protease inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; INI, integrase inhibitor; RAM, resistance-associated mutation.

Other reasons for discontinuation were: lost to follow-up (n = 3), withdrawal of consent (n = 2), protocol violation (n = 1), and AE (n = 1 [allergic dermatitis]).

AE, adverse event.
Virologic Efficacy at Week 24

- No patients had PDVF and no patients discontinued the study due to lack of efficacy

FDA, US Food and Drug Administration; VL, viral load; PDVF, protocol-defined virologic failure.

Virologic Efficacy Over Time (HIV-1 RNA <200 copies/mL; Observed Algorithm)

- A high proportion of patients achieved HIV-1 RNA <200 copies/mL early in the study
- The U = U Prevention Access Campaign states that individuals with a viral load <200 copies/mL cannot transmit HIV

U = U, undetectable = untransmittable.


## Safety Through Week 24

<table>
<thead>
<tr>
<th>Parameter, n (%)</th>
<th>D/C/F/TAF N = 109</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
</tr>
<tr>
<td>≥1 AE</td>
<td>80 (73)</td>
</tr>
<tr>
<td>≥1 serious AE</td>
<td>7 (6)</td>
</tr>
<tr>
<td>≥1 grade 1 AE</td>
<td>40 (37)</td>
</tr>
<tr>
<td>≥1 grade 2 AE</td>
<td>31 (28)</td>
</tr>
<tr>
<td>≥1 grade 3 AE</td>
<td>9 (8)</td>
</tr>
<tr>
<td>≥1 grade 4 AE</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Most common ADRs (≥2% of patients), n (%)</th>
<th>Any grade</th>
<th>≥ Grade 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>13 (12)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10 (9)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Rash</td>
<td>5 (5)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4 (4)</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (3)</td>
<td>0</td>
</tr>
</tbody>
</table>

- The majority of AEs were grade 1 or 2, and there were no grade 4 AEs or deaths

D/C/F/TAF, darunavir/cobicistat/emtricitabine/tenofovir alafenamide; AE, adverse event; ADR, adverse drug reaction.

**PRO: HIVTSQs Score**

Total treatment satisfaction (score range: 0-60)

- **Week 4 (n = 103)**: Mean (SE) score = 56.5 (SE = 57.9)
- **Week 24 (n = 98)**: Mean (SE) score = 57.9 (SE = 56.5)

Subscales (score range: 0-30)

- General satisfaction/clinical subscale
  - Week 4: Mean (SE) score = 28.4 (SE = 29.0)
  - Week 24: Mean (SE) score = 28.9 (SE = 28.1)
- Lifestyle/ease subscale
  - Week 4: Mean (SE) score = 28.1 (SE = 28.9)
  - Week 24: Mean (SE) score = 28.9 (SE = 28.1)

**PRO, patient-reported outcome; HIVTSQs, HIV Treatment Satisfaction Questionnaire-status version; SE, standard error.**

Summary

- In the first known phase 3 trial of an STR in a rapid initiation model of care, a high proportion of patients achieved HIV-1 RNA <50 copies/mL
  - Nearly two-thirds of patients achieved HIV-1 RNA <200 copies/mL by Week 8

- No patients had PDVF or discontinued due to lack of efficacy
  - Only 1 (<1%) patient discontinued due to AEs

- High HIVTSQs satisfaction scores were reported 4 and 24 weeks after rapid initiation of D/C/F/TAF
  - This is the first known PRO data in a rapid initiation setting
Conclusion

- These findings from DIAMOND, together with the demonstrated efficacy, high barrier to resistance, safety profile, and convenience of D/C/F/TAF, support its placement in IAS-USA guidelines as a recommended treatment option in a rapid initiation model of care\(^1\)

- Treatment with D/C/F/TAF can achieve rapid virologic suppression at thresholds known to help prevent HIV-1 transmission to uninfected individuals\(^2\)

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D/C/F/TAF, darunavir/cobicistat/emtricitabine/tenofovir alafenamide; IAS-USA, International Antiviral Society–USA.
Acknowledgments and Disclosures

- This study was funded by Janssen Scientific Affairs, LLC
- Medical writing support was provided by Courtney St. Amour, PhD, and Dan Jackson, PhD, of MedErgy, and was funded by Janssen Scientific Affairs, LLC
- These data, in part, have been presented previously: (1) Huhn GD, et al. Poster presented at: the 22nd International AIDS Conference; July 23-27, 2018; Amsterdam, The Netherlands. Poster WEPEC200; and (2) Benson C, et al. Poster presented at: HIV Drug Therapy Glasgow 2018; October 28-31, 2018; Glasgow, UK. Poster P049