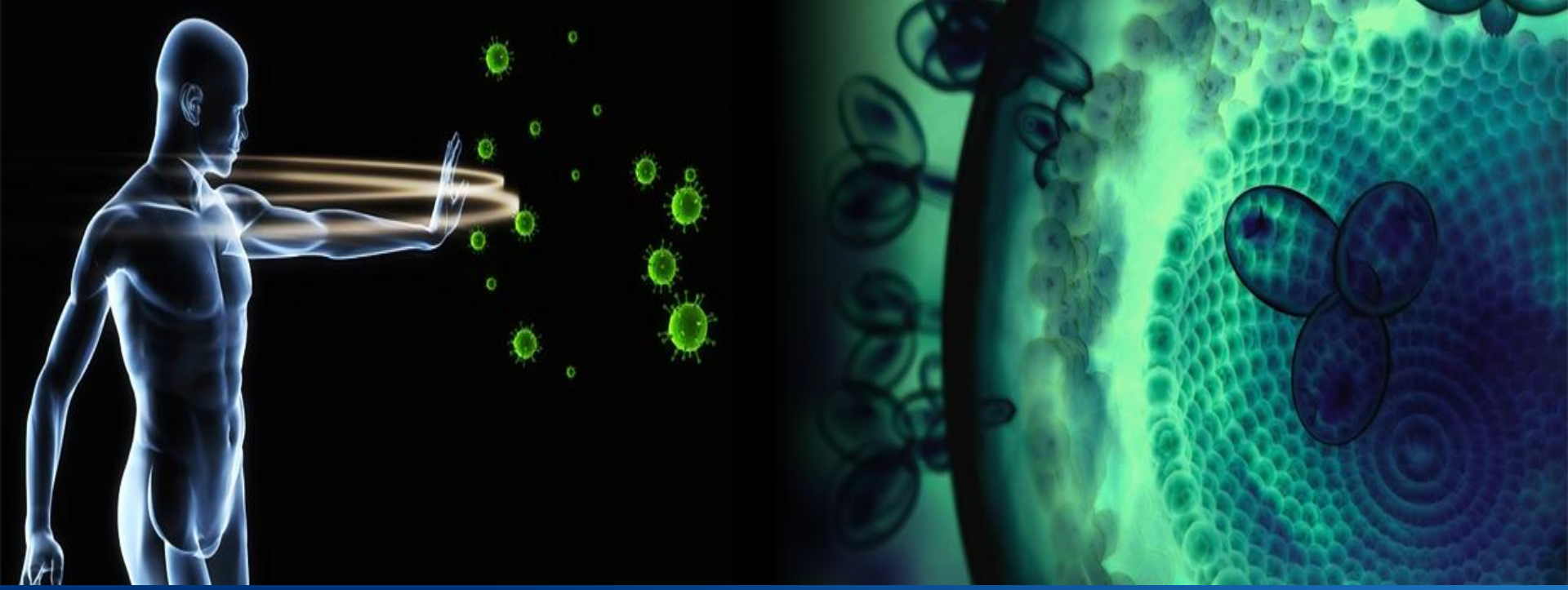

Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) in a Rapid Initiation Model of Care for HIV-1 Infection: Week 24 Interim Analysis of the DIAMOND Study

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Disclosures

Keith Dunn
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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.

1. DHHS Panel on Antiretroviral Guidelines. 2018.
2. Bacon O, et al. Poster at: CROI 2018.
3. Koenig SP, et al. *PLoS Med*. 2017;14(7):e1002357.
4. Rosen S, et al. *PLoS Med*. 2016;13(5):e1002015.
5. WHO Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy. July 2017.
6. Saag MS, et al. *JAMA*. 2018;320(4):379-396.
Huhn GD, et al. HIV DART 2018. Paper number 6.

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

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

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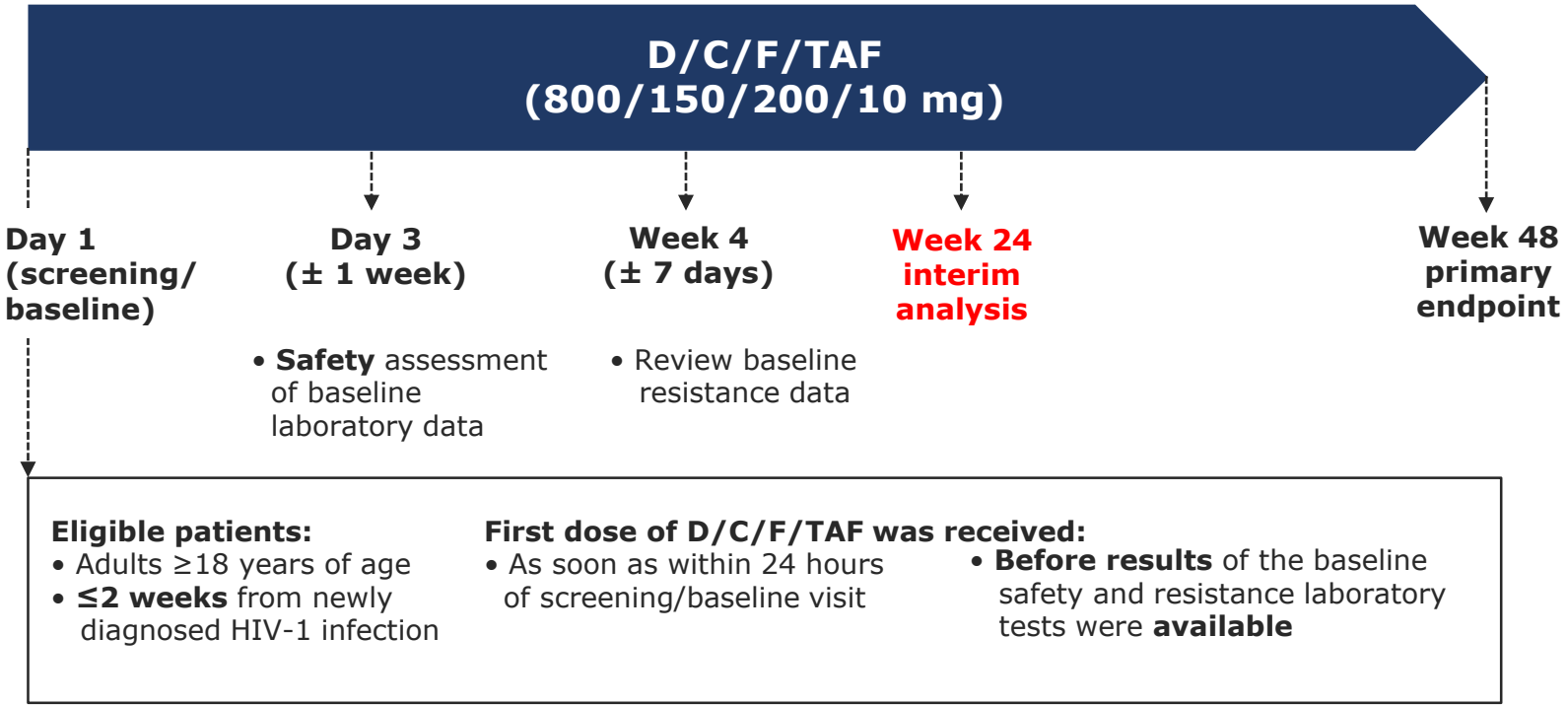
DIAMOND: Study Design

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



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

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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[1]

FDA, Food and Drug Administration; PDVF, protocol-defined virologic failure; AE, adverse event; PRO, patient-reported outcome; HIVTSQs, HIV Treatment Satisfaction Questionnaire-status version.

1. Woodcock A, Bradley C. *Value Health*. 2006;9(5):320-333.
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Patient Population

Demographic characteristics	D/C/F/TAF N = 109
Age, median (range), years	28 (19-66)
Women, n (%)	14 (13)
Race, n (%)	
White	64 (59)
Black/African American	35 (32)
Other	10 (9)
Hispanic or Latino, n (%)	48 (44)
Clinical characteristics	
HIV-1 RNA, median (range), log_{10} copies/mL*	4.6 (1.3-8.2)
HIV-1 RNA, ≥100,000 copies/mL, n (%)*	25 (23)
CD4+ cell count, median (range), cells/μL*	369 (7-1,082)
CD4+ cell count, <200 cells/μL, n (%)*	23 (21)
Time from diagnosis to screening/baseline, median (range), days	5 (0-14)
Enrolled within 48 hours of diagnosis, n (%)	32 (29)

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

Genotypic susceptibility, n (%)	D/C/F/TAF n = 102
Darunavir	102 (100)
Emtricitabine	100 (98)
Tenofovir	102 (100)
All PIs	97 (95)
All NRTIs	98 (96)
All NNRTIs	80 (78)
All INIs	97 (95)

- 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.

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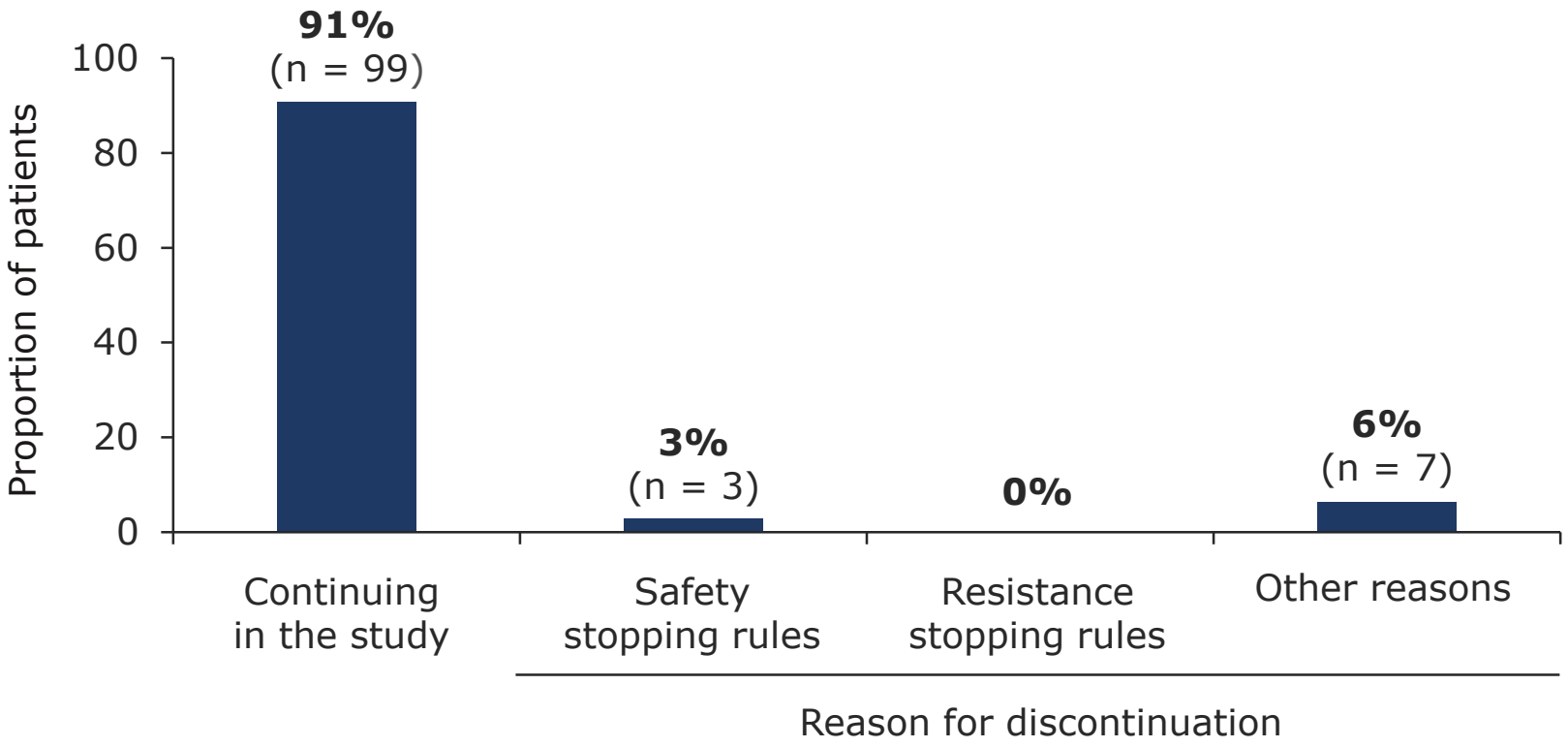
Patient Disposition Through Week 24



- 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.

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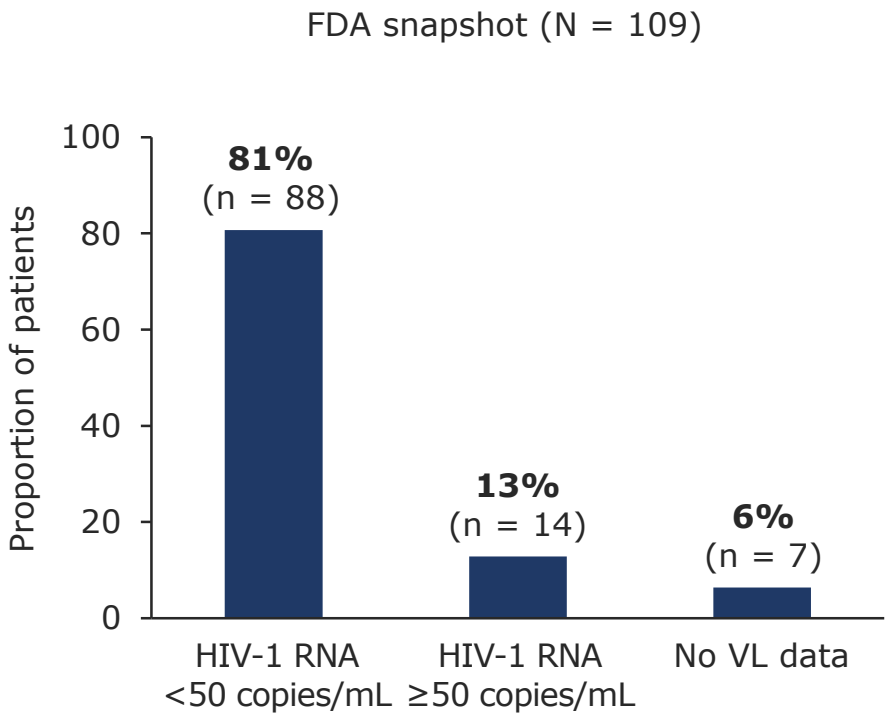
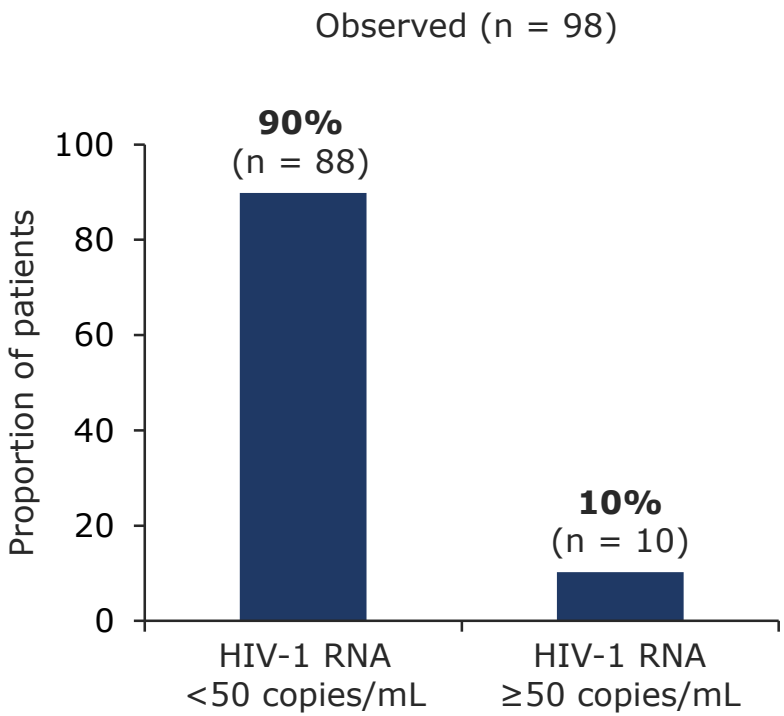
Virologic Efficacy at Week 24





- 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.

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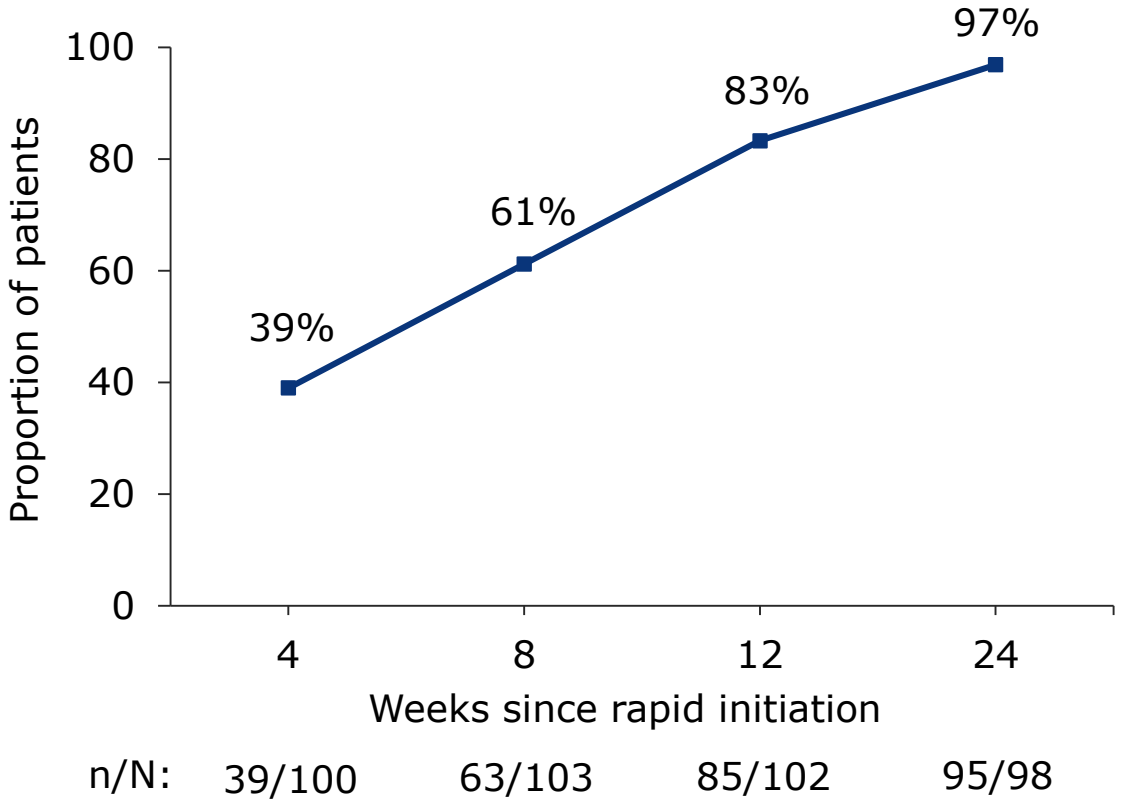
Virologic Efficacy Over Time (HIV-1 RNA <200 copies/mL; Observed Algorithm)



- 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[1]

1. Prevention Access Campaign. Available at: www.preventionaccess.org. Accessed November 20, 2018.

U = U, undetectable = untransmittable.

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Safety Through Week 24

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 ADRs (≥2% of patients), n (%)	**Any grade**	**≥ Grade 2**
Nausea	13 (12)	2 (2)
Diarrhea	10 (9)	1 (1)
Rash	5 (5)	4 (4)
Vomiting	4 (4)	0
Headache	3 (3)	0

- 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.

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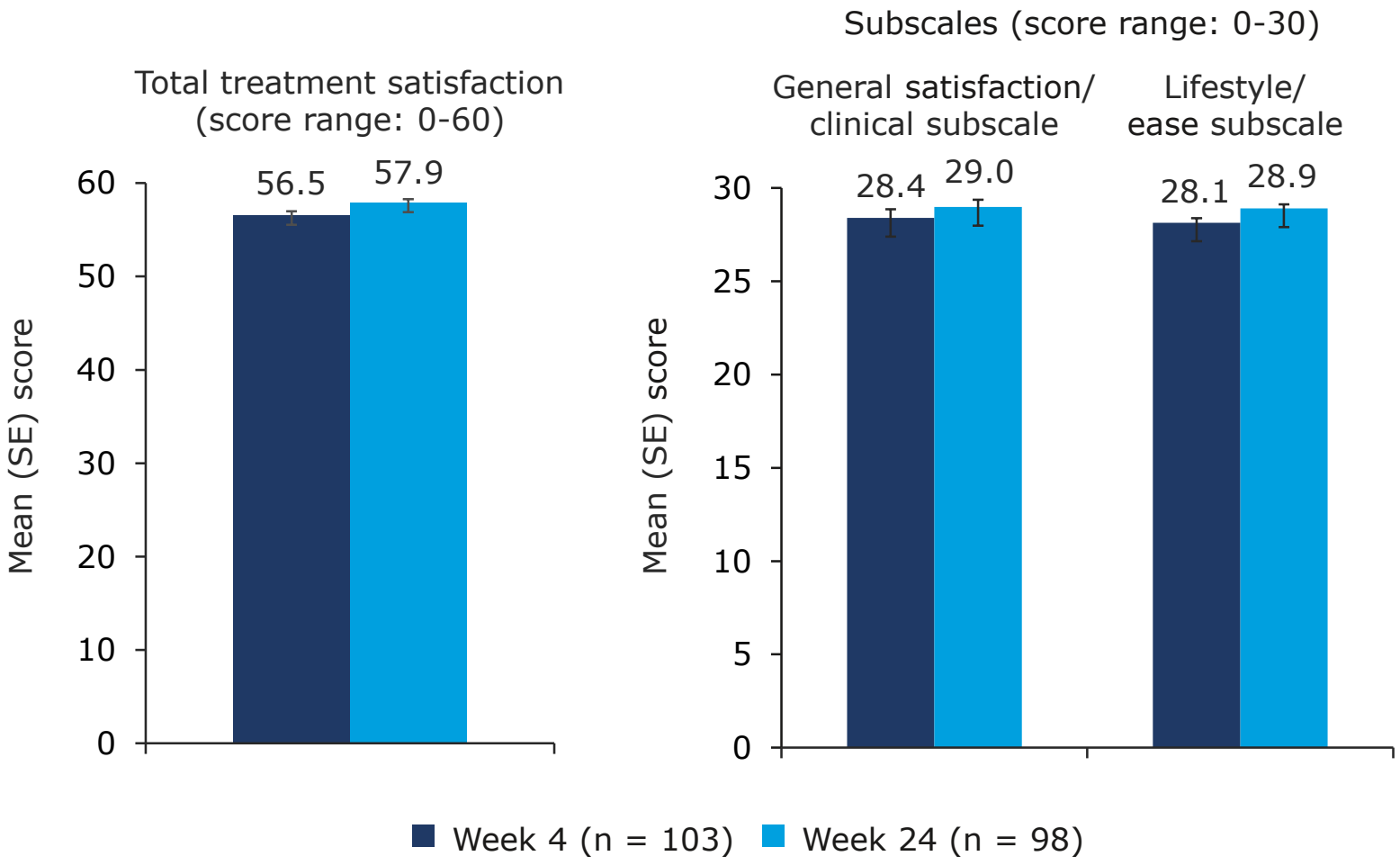
PRO: HIVTSQs Score



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

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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

STR, single-tablet regimen; PDVF, protocol-defined virologic failure; AE, adverse event; HIVTSQs, HIV Treatment Satisfaction Questionnaire-status version; D/C/F/TAF, darunavir/cobicistat/emtricitabine/tenofovir alafenamide; PRO, patient-reported outcome.

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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]

1. Saag MS, et al. *JAMA*. 2018;320(4):379-396.
2. Prevention Access Campaign. Available at: www.preventionaccess.org. Accessed November 20, 2018.
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D/C/F/TAF, darunavir/cobicistat/emtricitabine/tenofovir alafenamide; IAS-USA, International Antiviral Society–USA.

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- 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