HIGH RATES OF VIROLOGIC SUPPRESSION WITH DTG/3TC IN NEWLY DIAGNOSED ADULTS WITH HIV-1 INFECTION AND BASELINE VIRAL LOAD ≥500,000 C/ML: 48-WEEK SUBGROUP ANALYSIS OF THE STAT STUDY

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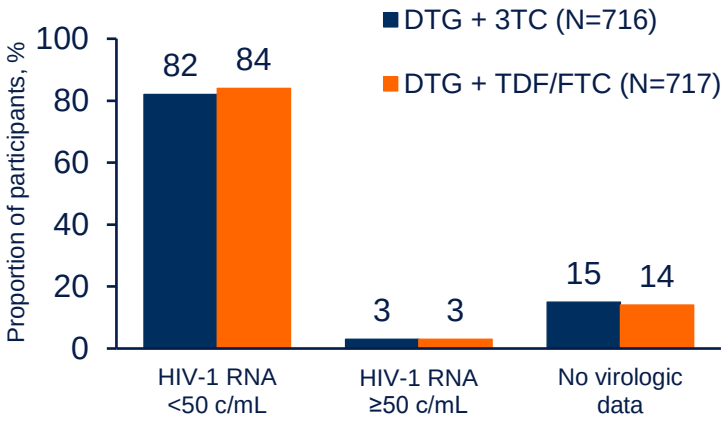
Disclosures

- Charlotte-Paige Rolle has received grants from ViiV Healthcare, Gilead, and Janssen and has served on advisory boards/speakers bureaus for ViiV Healthcare, Gilead, and Theratechnologies
- Tulika Singh has received grants from Gilead, ViiV Healthcare, GlaxoSmithKline (GSK), and Anchor and has served on advisory boards/speakers bureaus for ViiV Healthcare and Gilead
- Moti Ramgopal has received grants and served on advisory boards/speakers bureaus for Gilead, ViiV Healthcare, Janssen, and Merck
- Dushyantha T. Jayaweera has received grants from Gilead and Janssen
- Peter A. Leone, Jessica E. Matthews, Mark R. Underwood, Brian R. Wynne, Deanna Merrill, Christopher Nguyen, Jean van Wyk, and Andrew R. Zolopa are employees of ViiV Healthcare and shareholders in GSK; Mark R. Underwood has a patent WO2011/094150 pending
- Michael Cupo and Konstantinos Angelis are employees of and shareholders in GSK
- Mezgebe Berhe, Roberto Ortiz, and Anson Wurapa have nothing to disclose

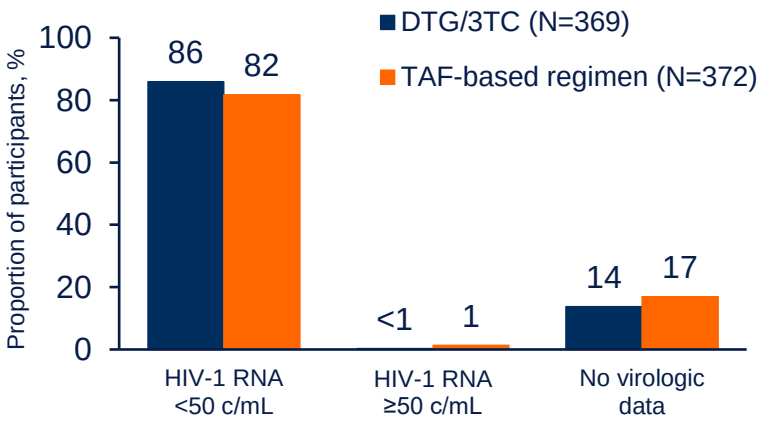
DTG/3TC Has Demonstrated Non-Inferior Efficacy Versus Other ART Regimens in Treatment-Naive and Treatment-Experienced PLWH

- Rapid treatment of HIV-1 infection has been associated with improved linkage to and retention in care and reduced time to virologic suppression in PLWH[1,2]
- DTG/3TC has demonstrated non-inferior efficacy, a good safety profile, and a high barrier to resistance in treatment-naive PLWH in the GEMINI studies (vs DTG + TDF/FTC)[3-5] and treatment-experienced, virologically suppressed PLWH in the TANGO (vs continuing 3- or 4-drug TAF-based regimens)[6-8] and SALSA studies (vs continuing any current 3- or 4-drug ART regimen)[9]

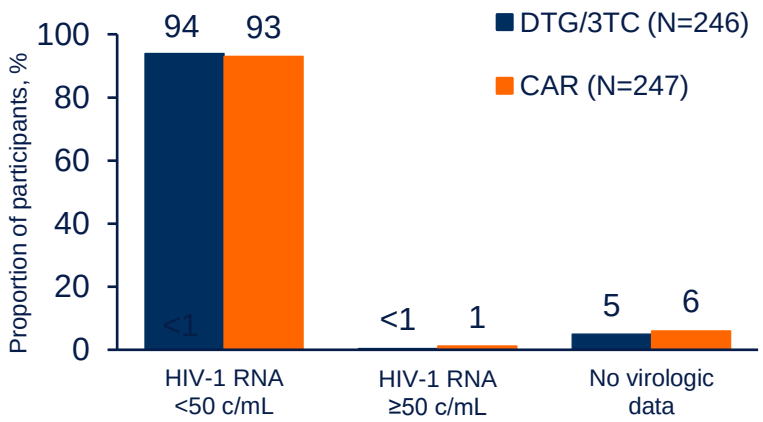
GEMINI-1 and GEMINI-2, Week 144
Virologic Outcomes (Snapshot)[5]



TANGO, Week 144
Virologic Outcomes (Snapshot)[8]



SALSA, Week 48
Virologic Outcomes (Snapshot)[9]



[a]For participants with baseline HIV-1 RNA >500,000 c/mL: DTG + 3TC, 10/13 (77%); DTG + TDF/FTC, 12/15 (80%).[10]

1. CDC. Understanding the HIV Care Continuum. 2019. **2.** DHHS. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf. Accessed August 12, 2021. **3.** Cahn et al. *Lancet*. 2019;393:143-155. **4.** Cahn et al. *J Acquir Immune Defic Syndr*. 2020;83:310-318. **5.** Cahn et al. HIV Glasgow 2020; Virtual. Poster P018. **6.** van Wyk et al. *Clin Infect Dis*. 2020;71:1920-1929. **7.** van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441. **8.** van Wyk et al. IAS 2021; Virtual. Poster PEB164. **9.** Llibre et al. IAS 2021; Virtual. Slides OALB0303. **10.** Orkin et al. CROI 2021; Virtual. Science spotlight 1991.

There Are Specific Considerations for Using DTG/3TC in a Test-and-Treat Setting

Transmitted drug resistance

- Transmitted INSTI resistance is rare, with studies from several countries reporting prevalence ranging from 0.2% to 3%[1-3]
- 3TC-associated transmitted resistance mutations at positions M184 and K65 have been estimated to occur in 1% and <1% of the global population, respectively[4]
- In the real-world REDOLA study of DTG/3TC in ART-naive adults (N=135), 72% initiated treatment before the availability of baseline drug resistance testing results. Prevalence of transmitted M184V was low, with only 2 participants requiring ART modifications; both achieved HIV-1 RNA <50 c/mL by Week 4[5]

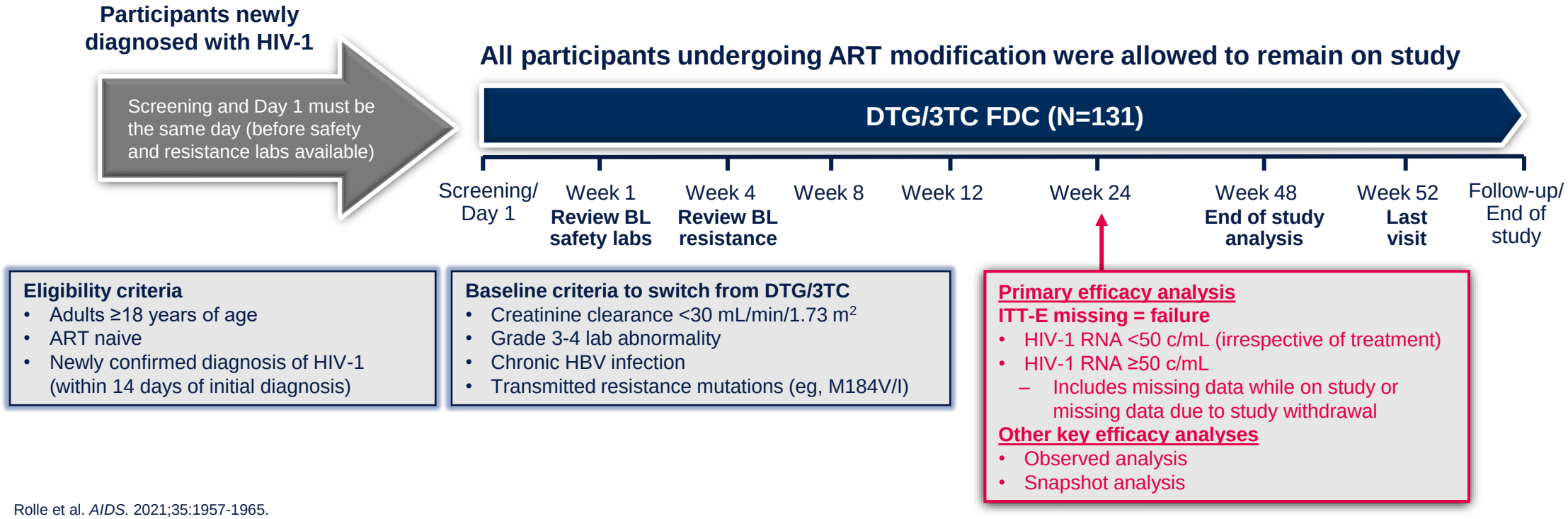
Hepatitis B virus

- Although 3TC has activity against HBV, it is not recommended for use as monotherapy in individuals with HBV because of the risk of resistance development
  - Resistance rates of 15% to 32% after 1 year of treatment have been reported in individuals with HBV treated with 3TC monotherapy, with mutations rarely detected before 36 weeks[6]

1. Rosetti et al. *HIV Med.* 2018;19:619-628. **2.** Chan et al. *Heliyon.* 2019;5:e02411. **3.** Lepik et al. *AIDS.* 2017;31:1425-1434. **4.** Vannappagari et al. *Antivir Ther.* 2019;24:393-404. **5.** Cabello et al. IAS 2021; Virtual. Poster PEB183. **6.** Lai et al. *Clin Infect Dis*. 2003;36:687-696.

STAT Is a Phase IIIb, Multicenter, Open-label, Single-Arm, Pilot Study Evaluating DTG/3TC as a Rapid Test-and-Treat Intervention

- In the primary analysis of STAT (ClinicalTrials.gov, NCT03945981) at Week 24, 78% (102/131) of all participants and 92% (102/111) of those with data available irrespective of ART achieved HIV-1 RNA <50 c/mL
- Here we show results from the key secondary efficacy analyses through Week 48 of the STAT study, including among participants with high baseline viral load (≥500,000 c/mL)



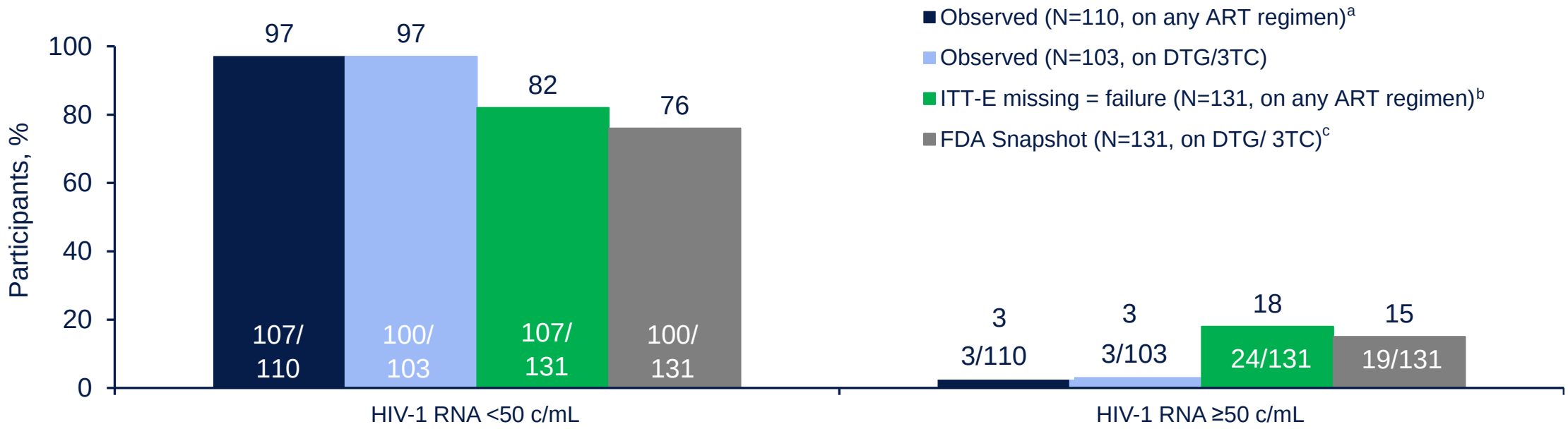
Rolle et al. *AIDS.* 2021;35:1957-1965.

Selected Baseline Demographics and Participant Characteristics

Characteristic	DTG/3TC (N=131)
Age, median (range), years	31 (18-63)
Cisgender female, n (%)	10 (8)
Transgender female, n (%)	1 (<1)
Race, n (%)	
Black/African American	61 (47)
White	65 (50)
Other	5 (4)
Time to enrollment since diagnosis, median (range), days	5 (0-15)[a]
HIV-1 RNA, median (range), c/mL, n (%)[b]	63,056 (<40 to 68,706,840)[c]
<100,000	79 (60)
100,000 to <500,000	32 (24)
500,000 to <1,000,000	9 (7)
≥1,000,000	10 (8)
CD4+ cell count, median (range), cells/mm^3	389 (<20 to 1466)[d]
<200, n (%)	37 (28)[e]
HBV co-infection, n (%)[f,g]	7 (5)
M184V resistance mutation, n (%)[f]	1 (<1)
Enrolled on day of diagnosis	34 (26)
Weight, median (range), kg	74.2 (66.0-86.7)

[a]1 participant joined the study past the 14-day window after diagnosis (15 days) due to error in entry of diagnosis date; participant remained on study. [b]1 (<1%) participant had missing plasma HIV-1 RNA results at baseline. [c]Lower limit of quantification is 40 c/mL. [d]Lower limit of quantification is 20 cells/mm^3. [e]11/37 participants had baseline viral load ≥500,000 c/mL. [f]Baseline HIV-1 resistance was identified at Week 4 and HBV co-infection was identified at Week 1 from samples taken at baseline. [g]2 participants with HBV co-infection but no evidence of ongoing HBV viral replication remained on DTG/3TC.

High Rates of Virologic Suppression Were Observed Across All Efficacy Analyses at Week 48



- ITT-E non-suppression rates were driven by non-virologic factors (ie, high withdrawal rate)
- Snapshot non-suppression rates were driven by study withdrawals and ART modifications

[a]The observed analysis included all participants with available HIV-1 RNA data, regardless of ART regimen. [b]The ITT-E missing = failure analysis included all participants in the ITT-E population, regardless of ART regimen. Of the 24 participants classified as HIV-1 RNA ≥50 c/mL, 3 had HIV-1 RNA ≥50 c/mL, 3 were on study but missing data at Week 48 (1 due to COVID-19), and 18 discontinued from study for non–treatment-related reasons (eg, withdrawn consent, lost to follow-up). [c]In the Snapshot analysis (missing data or switch considered failure), the 100 participants with HIV-1 RNA <50 c/mL were all on DTG/3TC; of the 19 participants classified as HIV-1 RNA ≥50 c/mL, 3 had HIV-1 RNA ≥50 c/mL (all under DTG/3TC), 10 modified ART, and 6 discontinued from study for non–treatment-related reasons (eg, withdrawn consent, lost to follow-up) and had HIV-1 RNA ≥50 c/mL; 12/131 had no virologic data at Week 48.

Rolle et al. IAS 2021; Virtual. Poster PEB182

Few Participants Required a Change From DTG/3TC for Baseline Resistance or HBV Co-infection

Reason for switch	Baseline plasma HIV-1 RNA, c/mL	Baseline CD4+ cell count, cells/mm^3	Visit window	Modified ART	Plasma HIV-1 RNA at Week 48, c/mL
BL HBV	108,597	60	Week 1	DTG/3TC + TAF	<40
BL HBV	129,665	98	Week 1	BIC/FTC/TAF	<40
BL HBV	37,290	101	Week 4	DTG + TAF/FTC	<40
BL HBV	256,879	<20[a]	Week 4	BIC/FTC/TAF or DTG + TDF/FTC[b]	NA[c]
Decision by participant or proxy	90,575	133	Week 4	BIC/FTC/TAF	NA[d]
BL HBV	13,170	327	Week 8	DTG/3TC + TAF	<40
BL M184V	18,752	456	Week 8	DTG/RPV	NA[e]
AE (rash)[f]	2,592,169	464	Week 12; Week 12	DRV/COBI/FTC/TAF; BIC/FTC/TAF	<40
Decision by participant or proxy	8091	308	Week 24	BIC/FTC/TAF	<40
Pregnancy	8406	1192	Week 24	RAL + TDF/FTC	327; <40
Participants who switched after Week 48 HIV-1 RNA assessment					
Lack of efficacy	123,644	41	Week 48	DTG + 3TC[g]	223; 182; 831
Non-adherence	27,294	423	Post–Week 48	Off treatment[h]	NA

[a]Lower limit of quantification is 20 cells/mm^3. [b]Participant modified ART by subsequently joining a double-blind clinical trial and was switched to either BIC/FTC/TAF or DTG + TDF/FTC. [c]Week 36 HIV-1 RNA was 57 c/mL. [d]Participant withdrew consent after switch from DTG/3TC. [e]Participant had HIV-1 RNA <40 c/mL on Day 47, switched to DTG/RPV on Day 49 due to M184V (despite viral load <40 c/mL), and had last HIV-1 RNA 54 c/mL on Day 57; participant withdrew consent (due to relocation) on Day 106 (Week 12). [f]Participant switched ART twice. [g]Participant switched to BIC/FTC/TAF post–Week 48 HIV-1 RNA assessment (after the 831 c/mL assessment); HIV-1 RNA was 51 c/mL at last follow-up visit. [h]Participant stopped DTG/3TC on Day 314 (before Week 48 assessment) due to non-adherence and re-started DTG/3TC ~4 months later; last HIV-1 RNA was 104 c/mL at last follow-up visit.

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Among Participants With CVF or Baseline HBV Co-infection, No Evidence of Treatment-Emergent Resistance Was Observed

	Participants meeting CVF criteria at Week 48	Number of HIV resistance-associated mutations detected
Total population	2	0
Participants with baseline HIV-1 RNA ≥500,000 c/mL	1	0

- Both participants meeting CVF criteria remained on DTG/3TC in study (1 participant suppressed to HIV-1 RNA <50 c/mL and 1 participant had HIV-1 RNA 70 c/mL at Week 48)
  - The participant with high baseline viral load (13,987,640 c/mL) was not suppressed at Week 24; HIV-1 RNA was 220 c/mL at Week 36 (CVF criteria met) and 63 c/mL at Week 48 followed by a retest at 48 c/mL

	Participants with baseline HBV co-infection	Number of HBV resistance-associated mutations detected
Total population	7	0
Participants with successful resistance tests	3	0

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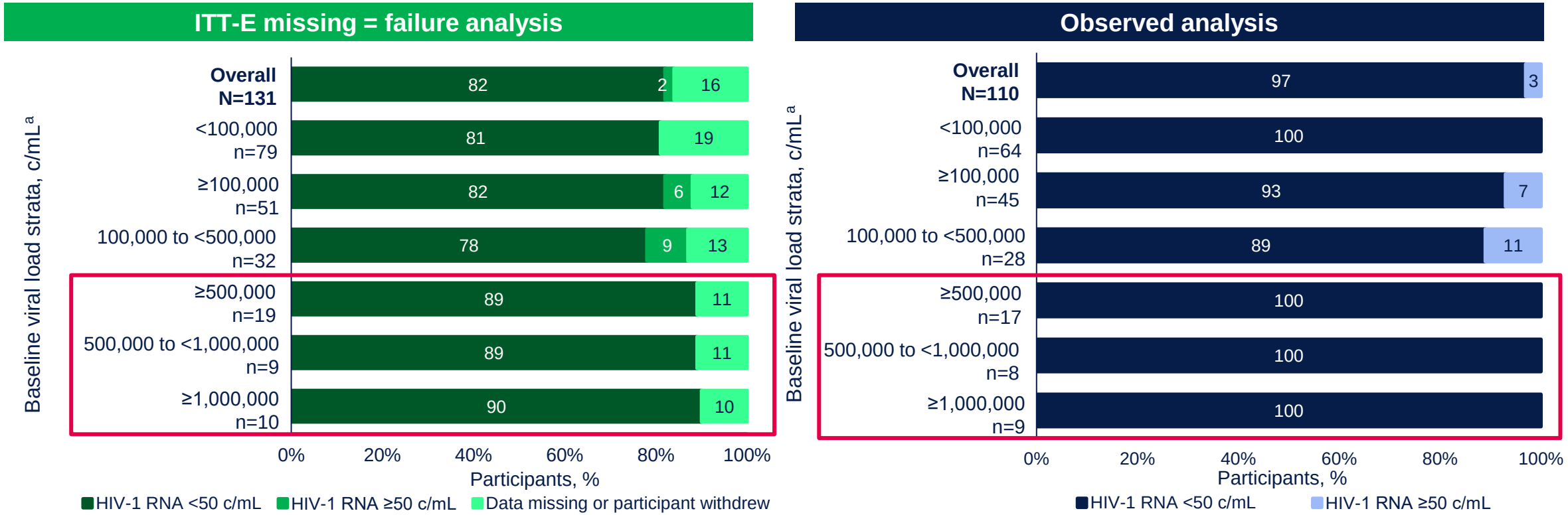
At Week 48, Virologic Suppression Rates Were High in Participants With Baseline Viral Load ≥500,000 c/mL



- 11/19 participants with baseline HIV-1 RNA ≥500,000 c/mL had CD4+ cell count <200 cells/mm^3; 10 achieved HIV-1 RNA <50 c/mL at Week 48 and 1 withdrew at Week 4 due to physician decision
- Median (95% CI) time to suppression for participants with baseline viral load ≥500,000 c/mL was 60 (56-169) days

ITT-E missing = failure analysis: all participants in the ITT-E population, regardless of ART regimen; observed analysis: all participants with available HIV-1 RNA data, regardless of ART regimen.
[a]1 (<1%) participant had missing plasma HIV-1 RNA results at baseline.

Most Participants With HIV-1 RNA ≥1,000,000 c/mL Achieved HIV-1 RNA <50 c/mL by Week 48

- 9/10 (90%) participants with very high baseline viral load (≥1,000,000 c/mL) achieved virologic suppression by Week 48; 8 were suppressed by Week 24
  - 1 participant switched from DTG/3TC before the Week 48 assessment because of an AE (rash)

Participant	Baseline CD4+ cell count	HIV-1 RNA (c/mL) by study visit							
		Baseline	Week 1	Week 4	Week 8	Week 12	Week 24	Week 36	Week 48
A	410	68,706,840	518,812	9781	NA	90,912	NA[a]	—	—
B	128	13,987,640	123,843	1682	297	493	191/ 157 / 302	124	63 / 48
C	613	5,794,931	98,499	96	<40	<40	<40	<40	<40
D	534	5,034,556	33,293	304	<40	<40	<40	NA	<40
E	464	2,592,169	1046	115	<40	<40[b]	<40	<40	<40
F	387	2,319,328	19,210	122	<40	52	<40	<40	<40
G	532	2,252,702	6241	136	48	42	<40	NA	<40
H	671	1,981,995	8373	245	<40	<40	<40	<40	<40
I	56	1,291,792	2618	222	147	71	<40	<40	<40
J	94	1,013,606	8646	725	242	185	<40	<40	<40

HIV-1 RNA ≥50 c/mL HIV-1 RNA <50 c/mL On modified ART

Values after / denote viral load at retesting. NA, not available.
[a]Participant confirmed many missed doses before Week 12 and withdrew consent due to incarceration. [b]Participant switched to DRV/COBI/FTC/TAF on Day 92 (Week 12) due to AE (rash); participant switched again to BIC/FTC/TAF on Day 113 (Week 12) due to a different rash.

Among Participants With HIV-1 RNA Between 500,000 and 1,000,000 c/mL, Most Achieved HIV-1 RNA <50 c/mL by Week 48

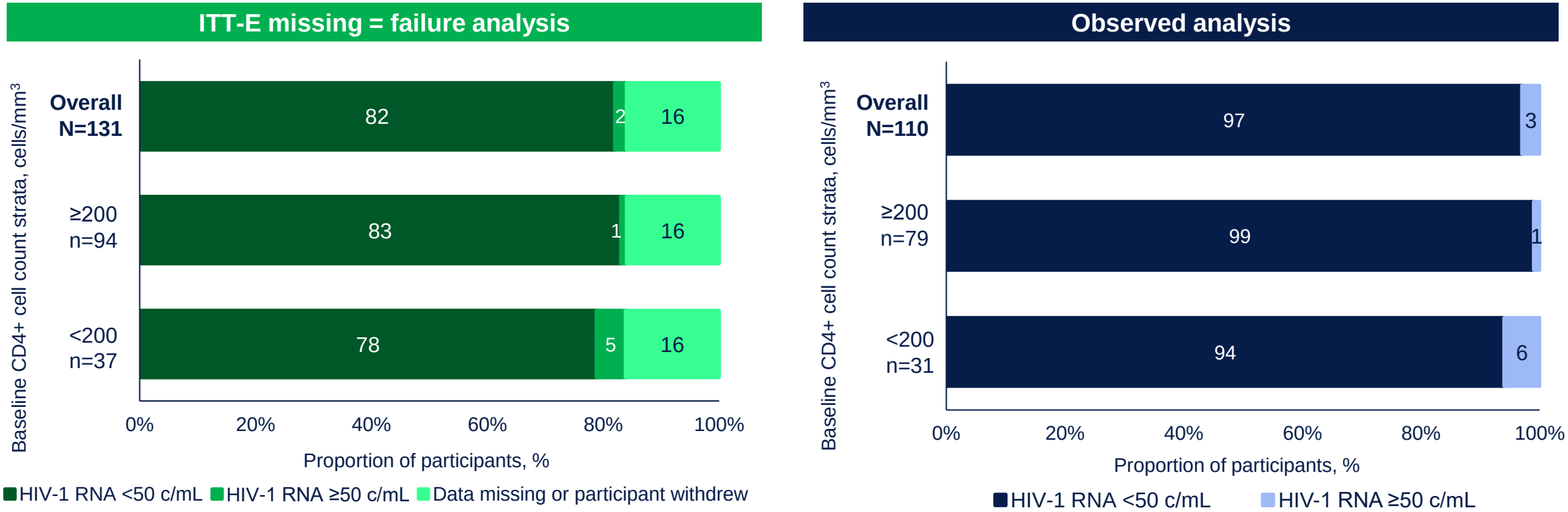
- 8/9 (89%) participants with baseline viral load between 500,000 and 1,000,000 c/mL achieved virologic suppression by Week 48; 5 were suppressed by Week 24
  - None switched from DTG/3TC

Participant	Baseline CD4+ cell count	HIV-1 RNA (c/mL) by study visit							
		Baseline	Week 1	Week 4	Week 8	Week 12	Week 24	Week 36	Week 48
K	167	899,271	3076	476	326	104	51/58	46	41
L	20	672,828	41,003	313	NA[a]	—	—	—	—
M	196	642,333	1045	43	<40	<40	<40	<40	<40
N	24	610,485	2107	112	116	98	<40	<40	<40
O	28	599,427	7981	2248	1364	419	82/164	176	132/47
P	<20	598,848	3173	339	<40	<40	<40	<40	<40
Q	301	540,063	1369	<40	73	69	<40	<40	<40
R	43	527,632	1076	112	<40	90	<40	<40	<40
S	150	520,354	16,766	403	280	216	90/106/72	NA[b]	65/40

☐ HIV-1 RNA ≥50 c/mL ■ HIV-1 RNA <50 c/mL

Values after / denote viral load at retesting. NA, not available.
[a]Participant withdrew at Week 4 due to physician decision. [b]Participant had a remote visit without labs (hence HIV-1 RNA assessment was missed) due to COVID-19.

At Week 48, Virologic Suppression Rates Were High in Participants Irrespective of Baseline CD4+ Cell Count

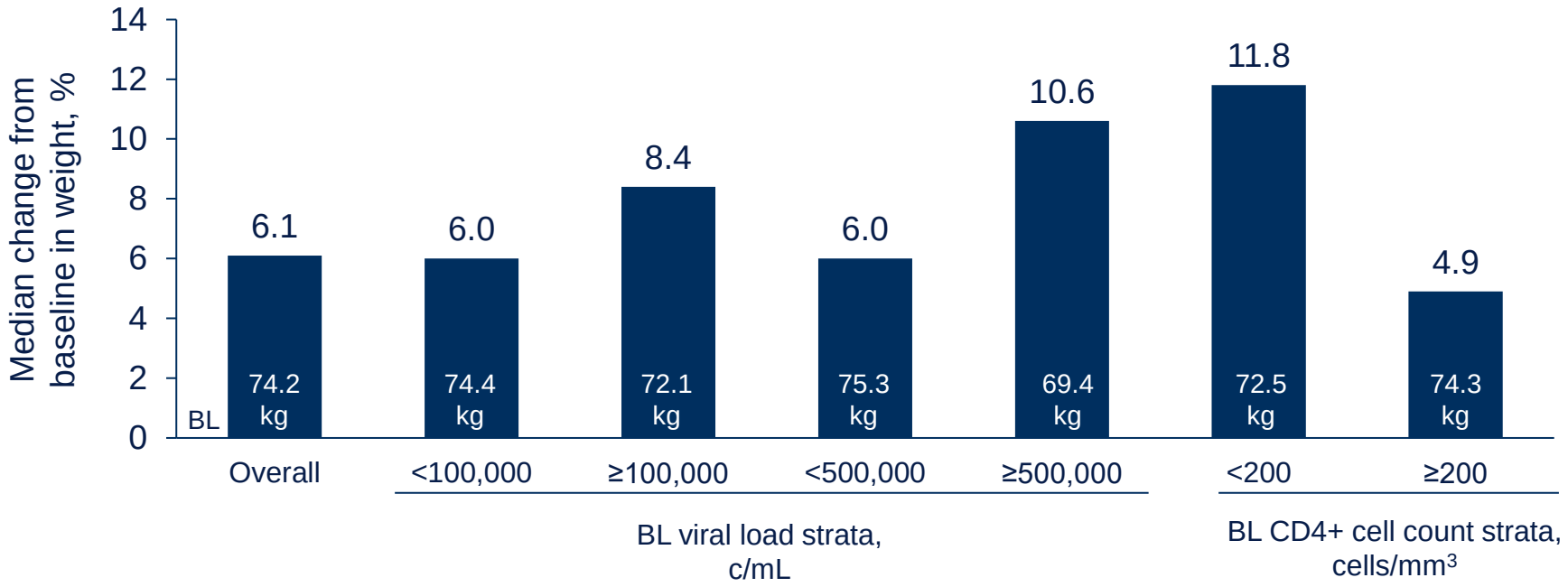


- 25/37 participants with baseline CD4+ cell count <200 cells/mm^3 had CD4+ cell count ≥200 cells/mm^3 at Week 48; 6 participants discontinued study and did not have Week 48 assessments
- Median (95% CI) time to suppression for participants with baseline CD4+ cell count <200 cells/mm^3 was 79 (57-168) days

ITT-E missing = failure analysis: all participants in the ITT-E population, regardless of ART regimen; observed analysis: all participants with available HIV-1 RNA data, regardless of ART regimen.

Weight Gain Overall and by Baseline Viral Load and CD4+ Cell Count

- On DTG/3TC, median (IQR) percent change in weight was 5.2% (1.4%-8.4%) from baseline to Week 24 and 6.1% (0.5%-11.7%) from baseline to Week 48
- Median percent change in weight from baseline to Week 48 was 6.0% in participants with baseline viral load <500,000 c/mL vs 10.6% in those with baseline viral load ≥500,000 c/mL
- Weight gain after treatment initiation may be related to improvements in viral load and CD4+ cell count



Rolle et al. IDWeek 2021™; Virtual. Slides 75.

DTG/3TC Was Well Tolerated Through Week 48, With Low Rates of Discontinuation Due to AEs

- DTG/3TC was well tolerated, with low rates of grade 2-5 drug-related AEs (2%) and serious AEs (2%)
- 1 participant with very high baseline viral load (≥1,000,000 c/mL) had an AE leading to discontinuation of DTG/3TC (rash); the event resolved

AEs, n (%)	DTG/3TC (N=131)
Any AE	100 (76)
AEs occurring in ≥7% of participants	
Headache	12 (9)
Diarrhea	10 (8)
Depression	9 (7)
Nausea	9 (7)
Drug-related AEs	10 (8)
Grade 2-5 drug-related AEs[a]	3 (2)
AEs leading to discontinuation of DTG/3TC	1 (<1)
Any SAE[b]	2 (2)
Psychiatric disorders[c]	24 (18)

[a]All AEs were grade 2. [b]2 SAEs occurred (cellulitis, streptococcal bacteremia). No fatal SAEs occurred. [c]All psychiatric AEs were grade 1 or 2. AEs were coded using MedDRA v23.1.

Rolle et al. IAS 2021; Virtual. Poster PEB182.

Conclusions

- These data provide evidence for the efficacy and feasibility of using DTG/3TC as a first-line regimen in a test-and-treat setting, including among individuals with high baseline viral load
- In participants with newly diagnosed HIV-1 who initiated DTG/3TC in a test-and-treat setting, high virologic suppression rates were observed at Week 48, including in those with baseline viral load ≥500,000 c/mL
  - 17 of the 19 participants with baseline viral load ≥500,000 c/mL suppressed to <50 c/mL by Week 48; 1 participant modified ART before 48 weeks because of an AE (rash)
  - 9 of the 10 participants with baseline viral load ≥1,000,000 c/mL suppressed to <50 c/mL by Week 48
- Only 2 participants met criteria for confirmed virologic failure (1 with baseline viral load ≥500,000 c/mL), and none had evidence of treatment-emergent resistance; both participants remained on DTG/3TC
- No participants with available genotyping developed treatment-emergent HBV resistance
- DTG/3TC was well tolerated, with only 1 AE leading to discontinuation of study drug
  - Weight gain was high in participants with high baseline viral loads and low CD4+ cell counts

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- Contact Charlotte-Paige Rolle at crolle@oicorlando.com with questions