Efficacy of Dolutegravir/Abacavir/Lamivudine (DTG/ABC/3TC) Fixed Dose Combination (FDC) Compared With Ritonavir-Boosted Atazanavir (ATV/r) Plus Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC) in Treatment-Naive Women With HIV-1 Infection (ARIA Study): Subgroup Analyses

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Introduction

- The fixed-dose combination (FDC) of dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) offers a complete antiretroviral therapy (ART) regimen for treatment of HIV-1 infection with good tolerability and a high barrier to resistance
- To gain additional data for women, we conducted the ARIA (**A**nti**R**etroviral treatment **I**n **A**RT-naive women) study, an international, randomized, open-label study to evaluate the safety and efficacy of DTG/ABC/3TC versus ritonavir-boosted atazanavir (ATV/r) plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC)

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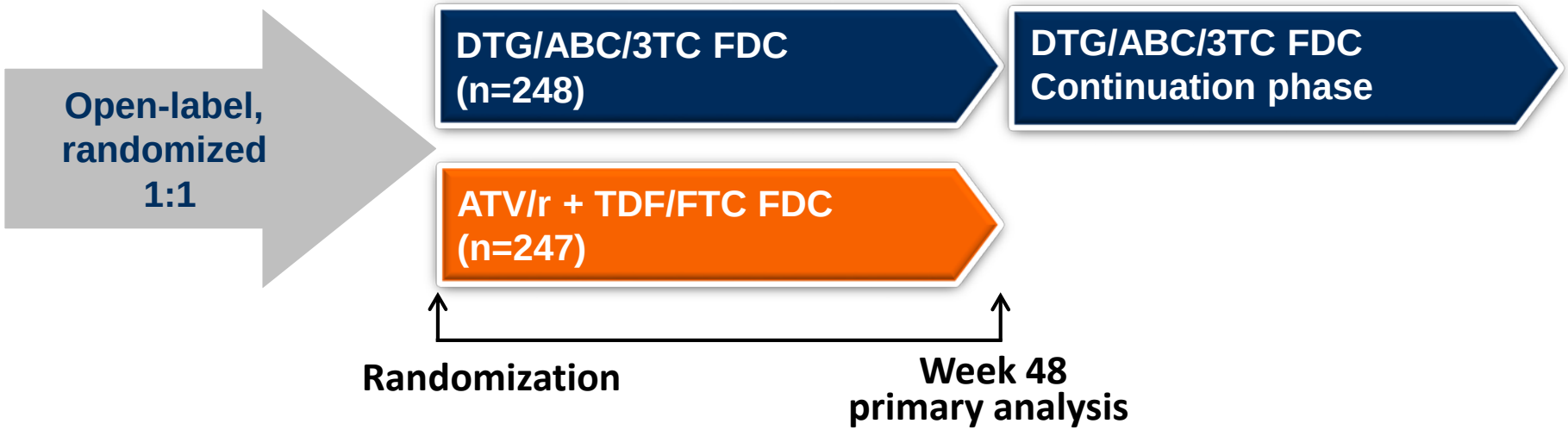
ARIA Study: Efficacy and Safety of DTG/ABC/3TC vs ATV/r + TDF/FTC in Women

Open-label randomized non-inferiority phase 3b study



Key eligibility criteria: women ≥18 years of age, ART-naive, *HLA-B*5701* negative, HIV-1 RNA >500 c/mL, hepatitis B negative
Stratification: by HIV-1 RNA (≤ or >100,000 c/mL) and CD4+ count (≤ or >350 cells/mm^3)
Primary endpoint: proportion with HIV-1 RNA <50 c/mL at Week 48 using the FDA Snapshot algorithm (−12% non-inferiority margin)

ART, antiretroviral therapy; FDA, US Food and Drug Administration; FDC, fixed-dose combination; HLA, human leukocyte antigen.

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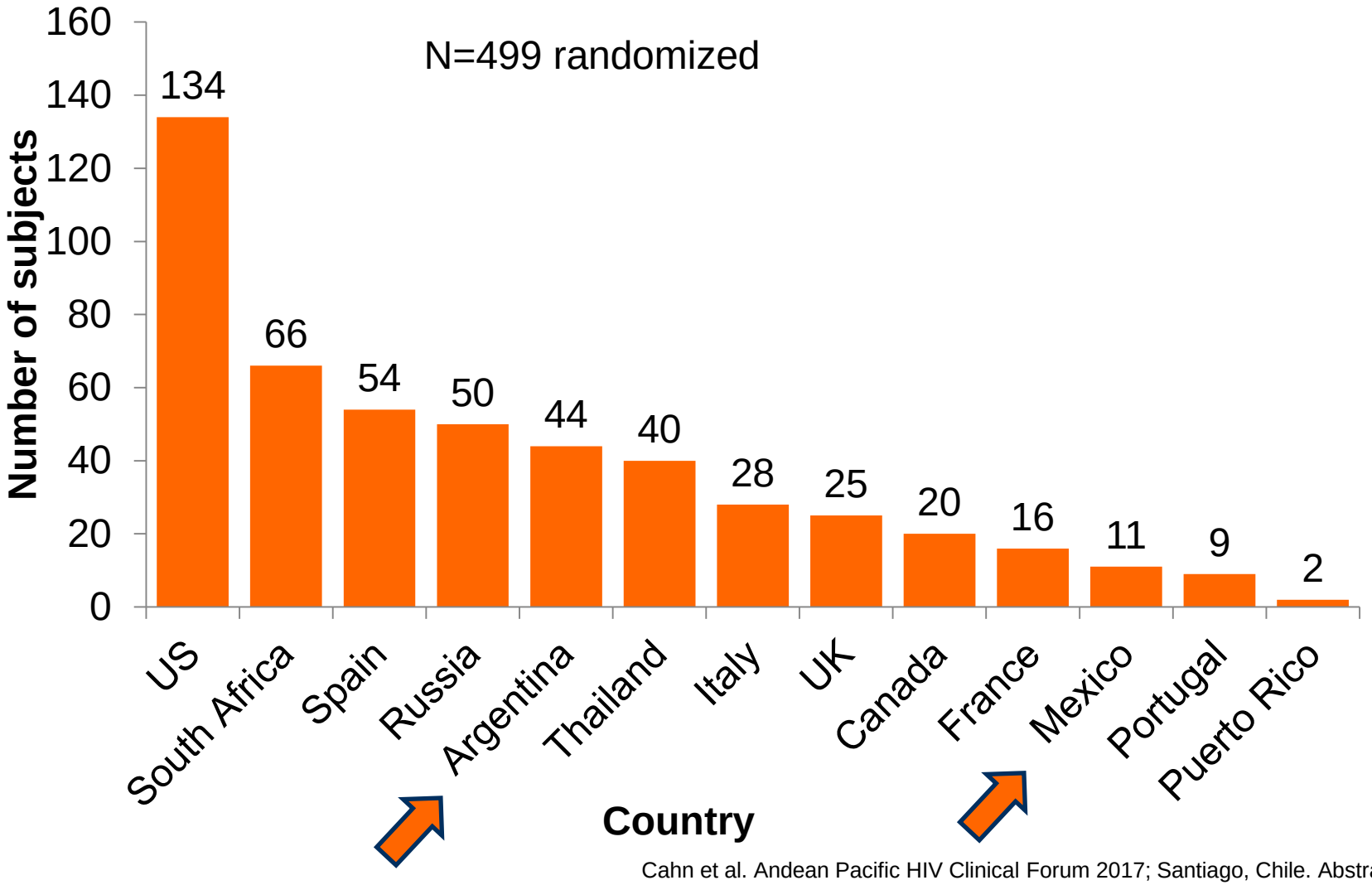
Global Enrollment



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Demographics and Baseline Characteristics

	DTG/ABC/3TC (n=248)	ATV/r +TDF/FTC (n=247)
Age, median (range), years	**37.5 (19-79)**	**37.0 (20-65)**
Race, n (%)		
African heritage	**102 (41)**	**108 (44)**
White	**115 (46)**	**107 (43)**
HIV-1 RNA, median, log c/mL	**4.41**	**4.43**
CD4+ cell count, median, cells/mm^3	**340**	**350**

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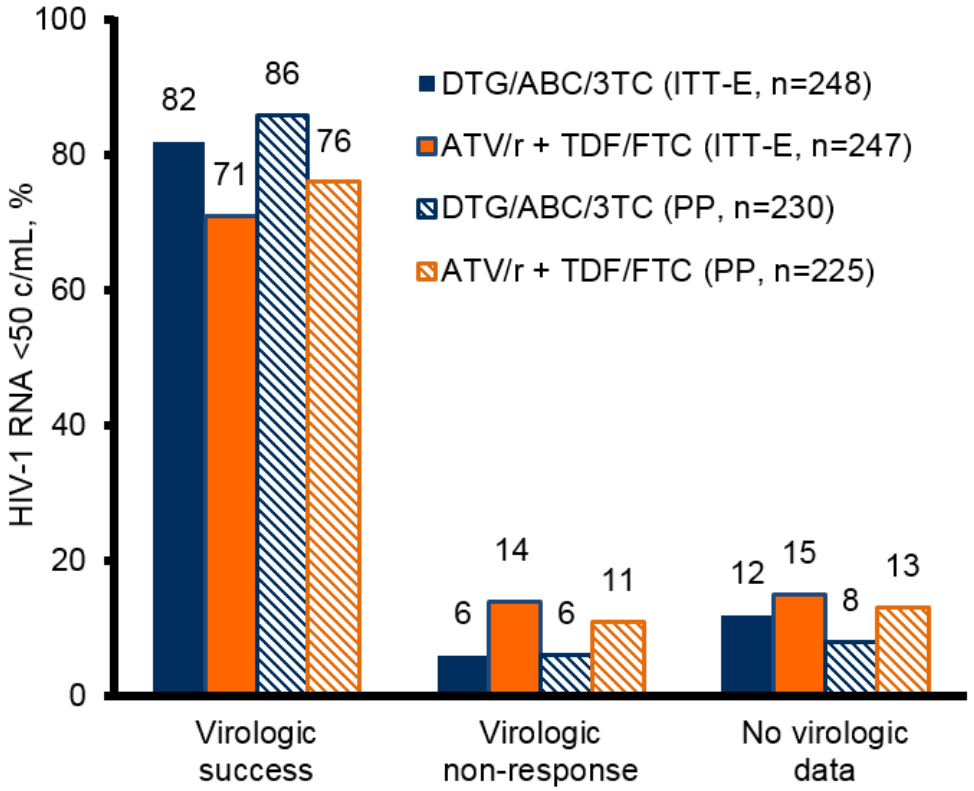
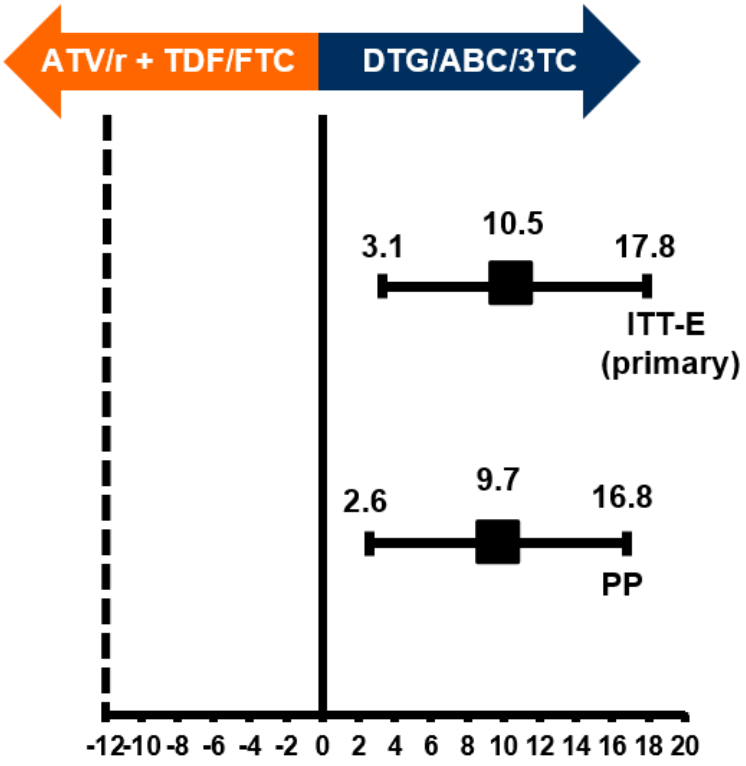
Snapshot Outcomes at Week 48: ITT-E and PP Populations

Virologic outcomes



Treatment differences (95% CI)



CI, confidence interval; ITT-E, intent-to-treat exposed; PP, per protocol.

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Virology Outcomes

- Resistance analysis was performed on subjects meeting confirmed virologic withdrawal (CVW), defined as confirmed HIV-1 RNA ≥400 c/mL on or after Week 24
- 6 subjects in the DTG/ABC/3TC group and 4 subjects in the ATV/r + TDF/FTC group met CVW criteria
  - No subjects in the DTG/ABC/3TC group had treatment-emergent primary integrase strand transfer inhibitor (INSTI) or ABC/3TC resistance
  - 1 subject in the ATV/r + TDF/FTC group had treatment-emergent nucleoside reverse transcriptase inhibitor (NRTI) mutation M184V

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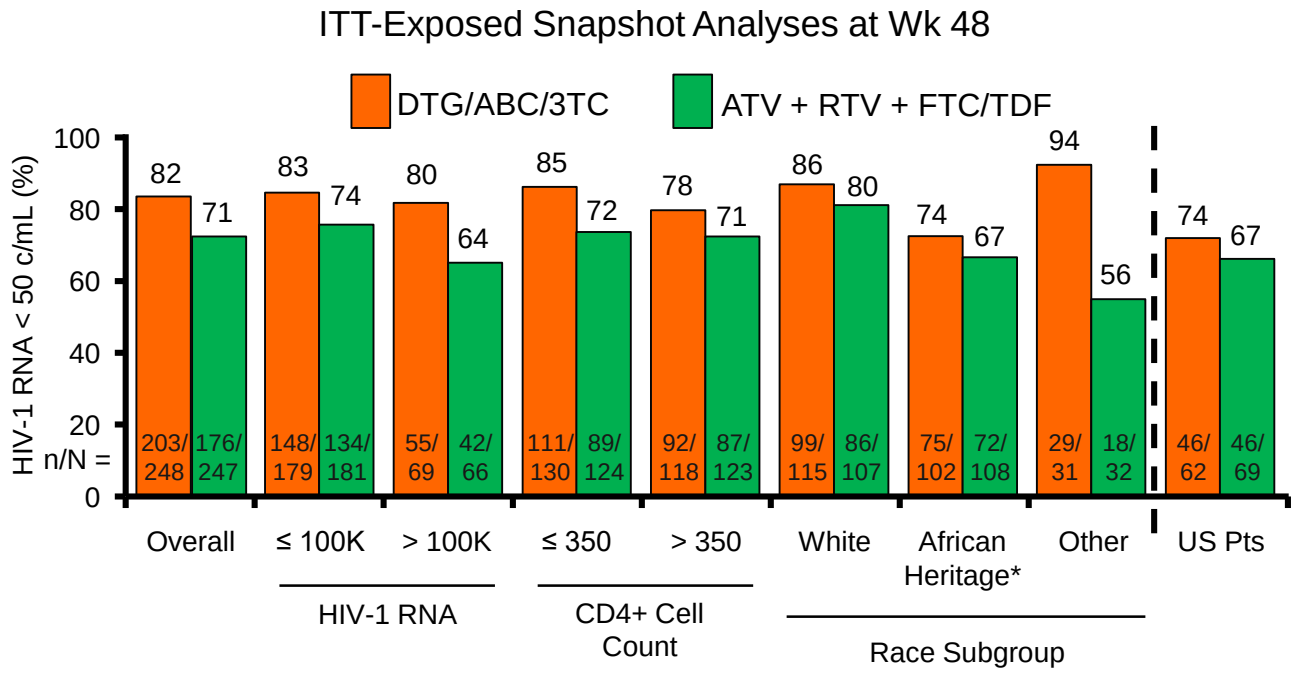
ARIA Subgroup Analyses: Virologic Outcomes at Wk 48



*African heritage includes African American.

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Hagins D, et al. IDWeek 2016. Abstract 949.

Snapshot Response Rates at Week 48: ITT-E Population

	Subgroup (n)	DTG/ABC/3TC N=248, n (%)	ATV/r + TDF/FTC N=247 n (%)
Age, years	<36	86/111 (77)	71/109 (65)
	36 to <50	84/101 (83)	79/103 (77)
	≥50	**33/36 (92)**	**26/35 (74)**
Baseline CD4+ cell count (cells/mm^3)	≤350	111/130 (85)	89/124 (72)
	>350	92/118 (78)	87/123 (71)
	<200	**52/64 (81)**	**34/49 (69)**
	≥200	151/184 (82)	142/198 (72)
Baseline HIV-1 RNA (c/mL)	≤100,000	148/179 (83)	134/181 (74)
	>100,000	**55/69 (80)**	**42/66 (64)**
HIV-1 subtype	B	76/95 (80)	77/111 (69)
	Non B	117/140 (84)	96/131 (73)
Geographic region	United States and Canada	56/73 (77)	56/80 (70)
	Western Europe	54/65 (83)	47/66 (71)
	Other	93/110 (85)	73/101 (72)

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Snapshot Outcomes at Week 48: Latin America

	DTG/ABC/3TC N=248, n/N (%)	ATV/r + TDF/FTC N=247,n/N (%)	Treatment differences (95% CI)
Argentina	22/24 (92)	16/20 (80)	11.7% (−9.1, 32.4)
Mexico	6/6 (100)	3/5 (60)	40.0% (−2.9, 82.9)

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Summary of Adverse Events at Week 48: Regional Subgroup (Safety Population)

Region	DTG/ABC/3TC N=248, n (%)	ATV/r + TDF/FTC N=247, n (%)
United States and Canada, n (%)	**n=73**	**n=80**
Any adverse event	64 (88)	69 (86)
Nausea	15 (21)	24 (30)
Diarrhea	13 (18)	13 (16)
Nasopharyngitis	8 (11)	4 (5)
Fatigue	7 (10)	11 (14)
Cough	6 (8)	12 (15)
Headache	6 (8)	15 (19)
Upper respiratory tract infection	6 (8)	8 (10)
Vomiting	6 (8)	9 (11)
Back pain	5 (7)	10 (13)
Western Europe, n (%)	**n=65**	**n=66**
Any adverse event	54 (83)	58 (88)
Nausea	13 (20)	12 (18)
Headache	10 (15)	6 (9)
Diarrhea	7 (11)	11 (17)
Dyspepsia	2 (3)	10 (15)
Jaundice	0	7 (11)
Other, n (%)	**n=110**	**n=101**
Any adverse event	77 (70)	70 (69)
Nausea	18 (16)	13 (13)
Headache	12 (11)	11 (11)
Upper respiratory tract infection	11 (10)	11 (11)

Events reported by ≥10% of subjects in either treatment group. Additional adverse events identified post hoc for 2 ATV/r + TDF/FTC subjects at 1 site are not included in this table. The adverse events were not considered to affect overall safety findings.

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ARIA Subgroup Analyses: Most Frequent AEs by Race Through Wk 48

AE by Racial Subgroup, n/N (%)	DTG/ABC/3TC (n = 248)	ATV + RTV + FTC/TDF (n = 247)
Black/African Heritage		
▪ Any	85/102 (83)	89/108 (82)
▪ Headache	25/102 (25)	22/108 (20)
▪ Nausea	11/102 (11)	14/108 (13)
▪ Diarrhea	10/102 (10)	9/108 (8)
▪ Cough	5/102 (5)	16/108 (15)
▪ Back pain	4/102 (4)	12/109 (11)
White		
▪ Any	88/115 (77)	91/107 (85)
▪ Headache	16/115 (14)	15/107 (14)
▪ Nausea	16/115 (14)	24/107 (22)
▪ Diarrhea	12/115 (10)	20/107 (19)
▪ Dyspepsia	6/115 (5)	14/107 (13)
▪ Rash	4/115 (3)	12/107 (11)
▪ Abdominal pain	2/115 (2)	14/107 (13)
▪ Ocular icterus	0	15/107 (14)
▪ Jaundice	0	12/107 (11)

Johnson M, et al. HIV Glasgow 2016. Abstract P035.
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Snapshot Outcomes at Week 48: ITT-E

	DTG/ABC/3TC N=248 n (%)	ATV/r + TDF/FTC N=247 n (%)
Virologic response	203 (82)	176 (71)
Virologic non-response	16 (6)	35 (14)
Data in window not below threshold	4 (2)	16 (6)
Discontinued for lack of efficacy	4 (2)	2 (<1)
Discontinued for other reason while not below threshold	8 (3)	17(7)
No virologic data	29 (12)	36 (15)
Discontinued study due to AE or death	9 (4)	18 (7)
Discontinued study for other reasons	15 (6)	14 (6)
Missing data during window but on study	5 (2)	4 (2)

Differences in response rates driven by Snapshot virologic non-response and lower rates of both discontinuations due to AEs in the DTG/ABC/3TC group.

AE, adverse, event; ITT-E, intent-to-treat exposed.

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Conclusions

- In treatment-naive women, DTG/ABC/3TC was superior to ATV/r + TDF/FTC at 48 weeks
  - Treatment difference 10.5% (95% CI, 3.1% to 17.8%; *P*=0.005)
- Difference driven by a lower rate of virologic non-response (Snapshot) and fewer discontinuations due to AEs in DTG/ABC/3TC group
- DTG/ABC/3TC had a favorable safety profile
- There were no treatment-emergent primary INSTI or ABC/3TC resistance mutations in the DTG/ABC/3TC group
- Subgroup analyses performed on the basis of baseline characteristics and geographic region were consistent with overall results

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