DTG Versus LPV/r in Second Line (DAWNING): Outcomes by WHO-Recommended NRTI Backbone

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Study Participants

- Patients were randomized (1:1) to 52 weeks of open-label treatment with DTG or LPV/r combined with 2 investigator-selected NRTIs
- 58 investigational centers in Argentina, Brazil, Chile, China, Colombia, Kenya, Mexico, Peru, Romania, the Russian Federation, South Africa, Thailand, and Ukraine randomized ≥1 study participant
- Of the 968 patients screened for the study, 627 (DTG group, n=312; LPV/r group, n=315) were randomly assigned to receive study medication, and 624 received ≥1 dose (DTG group, n=312; LPV/r group, n=312)
  - Most common reason for screen failure was HIV-1 RNA <400 c/mL in 134 patients (14%)
  - Only 78 (8%) were screen failures due to not having 1 fully active NRTI available

DTG, dolutegravir; LPV/r, lopinavir/ritonavir; NRTI, nucleoside reverse transcriptase inhibitor.

Aboud et al. APACC 2018; Wan Chai, Hong Kong. Poster 34.

Prior ART and Background NRTIs Received at Day 1

- Similar proportions of participants received either AZT + 3TC or TDF + (FTC or 3TC) as part of the second-line regimen within and across groups

	DTG (n=312)	LPV/r (n=312)
First-line agent, n (%)		
Efavirenz	242 (78)	242 (78)
TDF	181 (58)	186 (60)
AZT	89 (29)	89 (29)
Second-line NRTI, n (%)		
AZT + 3TC	131 (42)	121 (39)
TDF + (FTC or 3TC)	128 (41)	134 (43)
TDF + AZT	36 (12)	40 (13)
ABC + 3TC	7 (2)	7 (2)
Other[a]	10 (3)	10 (3)

ABC, abacavir; ART, antiretroviral therapy; AZT, zidovudine; DTG, dolutegravir; FTC, emtricitabine; LPV/r,lopinavir/ritonavir; NRTI, nucleoside reverse transcriptase inhibitor; 3TC, lamivudine; TDF, tenofovir disoproxil fumarate.
[a]Includes AZT + ABC, AZT + TDF + 3TC, and TDF + ABC.

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Virological Outcomes

- At Week 24, DTG + 2 NRTIs was superior to LPV/r + 2 NRTIs, with 82% (257/312) and 69% (215/312) of participants, respectively, achieving HIV-1 RNA <50 c/mL (adjusted difference, 13.8%; 95% CI, 7.3-20.3; *P*<0.001)[1]
  - Difference was mainly driven by lower rates of snapshot virologic nonresponse in the DTG group
- 56% (347/624) of participants received second-line NRTIs in accordance with the WHO algorithm, and their snapshot response rates in each arm were higher than those who did not

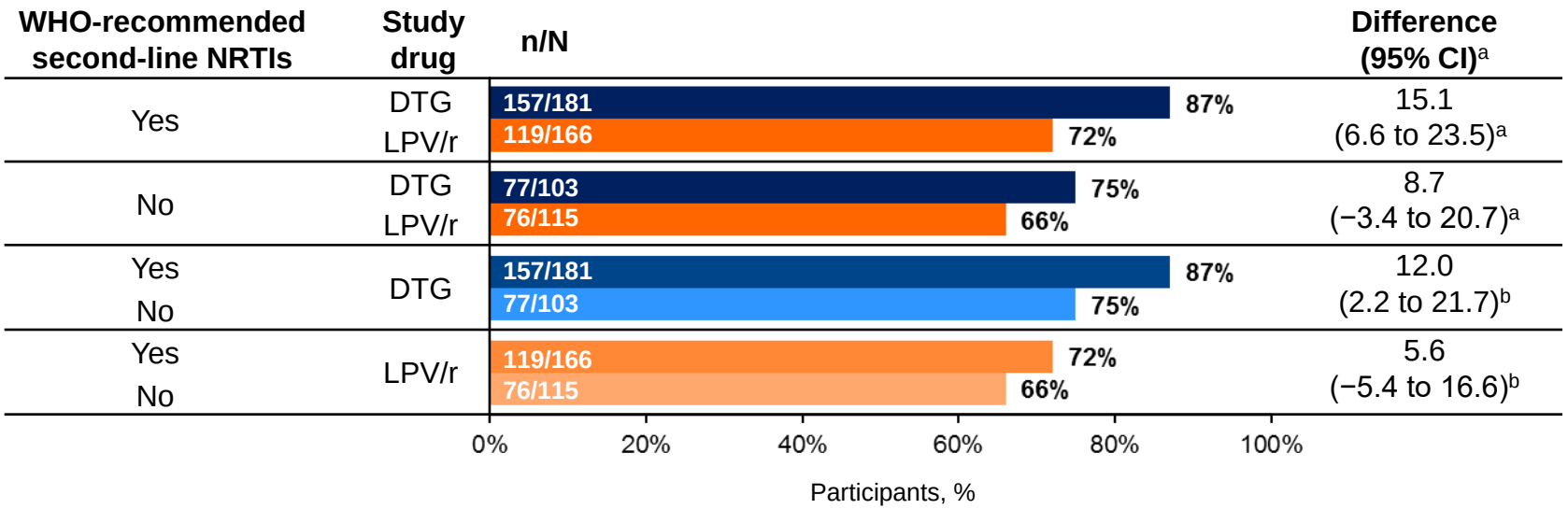
CI, confidence interval; DTG, dolutegravir; LPV/r, lopinavir/ritonavir; NRTI, nucleoside reverse transcriptase inhibitor; WHO, World Health Organization.

1. Aboud et al. IAS 2017; Paris, France. Abstract TUAB0105LB.

Aboud et al. APACC 2018; Wan Chai, Hong Kong. Poster 34.

Proportion of Participants With Plasma HIV-1 RNA <50 c/mL at Week 24 by Second-Line Background Regimen: Snapshot Analysis

- Regardless of WHO-recommended NRTI use, response rates were higher with DTG- vs LPV/r-based regimens



CI, confidence interval; DTG, dolutegravir; LPV/r, lopinavir/ritonavir; NRTI, nucleoside reverse transcriptase inhibitor; WHO, World Health Organization.

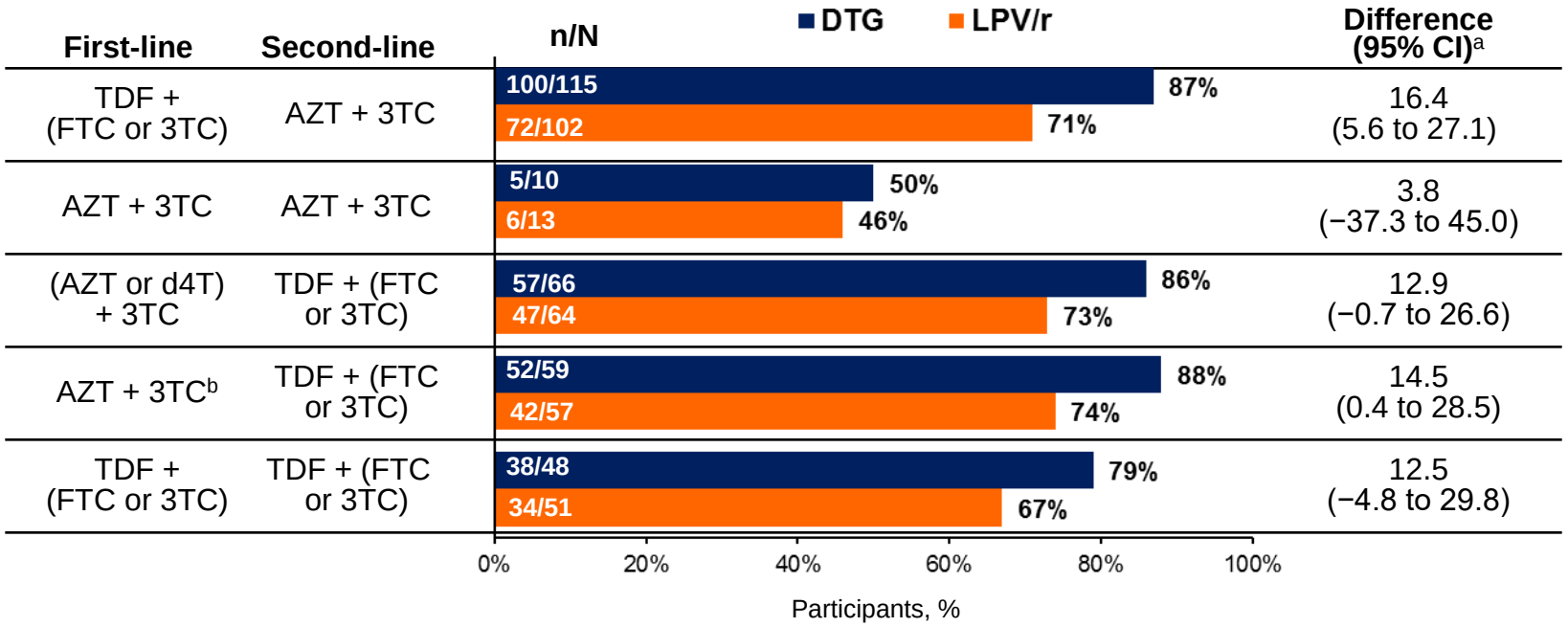
[a]Proportion on DTG – proportion on LPV/r.

[b]Proportion with WHO-recommended NRTIs – proportion without WHO-recommended NRTIs.

Aboud et al. APACC 2018; Wan Chai, Hong Kong. Poster 34.

Proportion of Participants With Plasma HIV-1 RNA <50 c/mL at Week 24 by First- and Second-Line NRTI Choice: Snapshot Analysis

- Snapshot response rates were higher with DTG- vs LPV/r-based regimens regardless of the first-line to second-line NRTI change



AZT, zidovudine; CI, confidence interval; d4T, stavudine; DTG, dolutegravir; FTC, emtricitabine; LPV/r, lopinavir/ritonavir; NRTI, nucleoside reverse transcriptase inhibitor; 3TC, lamivudine; TDF, tenofovir disoproxil fumarate.

[a]Proportion on DTG – proportion on LPV/r (unadjusted).

[b]Excludes participants who received d4T + 3TC in their first-line regimen (7 per treatment arm).

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Safety Outcomes, Discussion, and Conclusions

- The overall safety profile of DTG + 2 NRTIs was favorable compared with LPV/r + 2 NRTIs, with more drug-related AEs reported in the LPV/r group[1]
- In this 24-week interim analysis, there were no treatment-emergent primary INSTI or NRTI resistance mutations in the DTG group through the randomization phase[1]
- Subgroup analyses of virologic efficacy based on stratification of whether or not a WHO-recommended second-line NRTI background regimen was taken not only favor DTG versus LPV/r but also the regimen with WHO-recommended NRTIs within each treatment group
- One limitation of these analyses is that genotyping was used to select ≥1 fully active NRTI, and the resulting NRTI background regimen conforming to WHO guidance or not was incidental
- The DAWNING study provides important information to help guide second-line treatment decisions in resource-limited settings

AE, adverse event; DTG, dolutegravir; INSTI, integrase strand transfer inhibitor; LPV/r, lopinavir/ritonavir; NRTI, nucleoside reverse transcriptase inhibitor; WHO, World Health Organization.

1. Aboud et al. IAS 2017; Paris, France. Abstract TUAB0105LB.

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