ARV Therapies and Therapeutic Strategies

INDEPENDENT REPORTING ON IAS 2017

# COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS

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## SUPERIOR EFFICACY OF DOLUTEGRAVIR (DTG) PLUS 2 NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIS) COMPARED WITH LOPINAVIR/RITONAVIR (LPV/RTV) PLUS 2 NRTIS IN SECOND-LINE TREATMENT: INTERIM DATA FROM THE DAWNING STUDY

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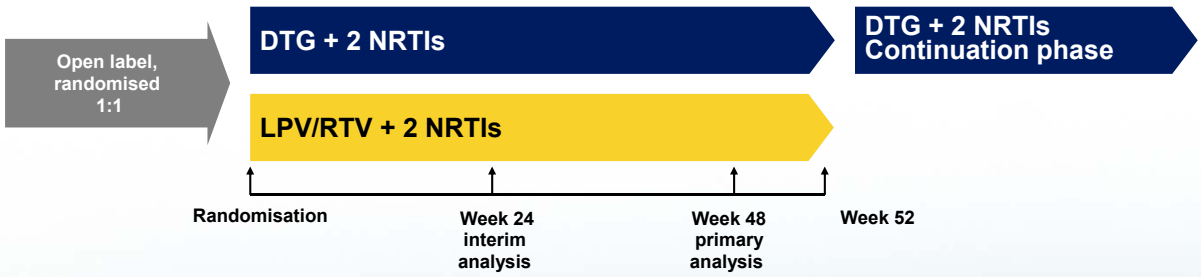
Abstract TUAB0105LB

## DAWNING: STUDY DESIGN

**Open-Label Randomised Noninferiority Phase IIIb Study**




- Key eligibility criteria: on first-line 2 NRTIs + NNRTI regimen for ≥6 months, failing virologically (HIV-1 RNA ≥400 c/mL on 2 occasions); no primary viral resistance to PIs or INSTIs
- Stratification: by HIV-1 RNA (≤ or >100,000 copies/mL), number of fully active NRTIs in the investigator-selected study background regimen (2 or <2)
- Primary endpoint: proportion with HIV-1 RNA <50 c/mL at Week 48 using the FDA snapshot algorithm (12% noninferiority margin)

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# DAWNING STUDY: BASELINE CHARACTERISTICS

| | DTG + 2 NRTIs (n=312) | LPV/RTV + 2 NRTIs (n=312) |
|---|---|---|
| **Age, median (range), years** | 37.0 (19-64) | 37.0 (18-72) |
| **Female, n (%)** | 116 (37) | 103 (33) |
| **CDC category, n (%)** | | |
| C: AIDS | 106 (34) | 95 (30) |
| **HIV-1 RNA, mean, log c/mL** | 4.21 | 4.22 |
| >100,000 c/mL, n (%) | 70 (22) | 63 (20) |
| **CD4+ cell count, cells/mm$^3$** | | |
| <200, n (%) | 166 (53) | 151 (48) |
| **Duration of first antiretroviral regimen, mean, months** | 37 | 35 |
| **Prior therapy agent, n (%)** | | |
| EFV | 242 (78) | 242 (78) |
| TDF | 181 (58) | 186 (60) |
| AZT | 89 (29) | 89 (29) |
| **NRTI background regimen, n (%)** | | |
| AZT + 3TC | 131 (42) | 121 (39) |
| TDF + 3TC or FTC | 128 (41) | 134 (43) |
| TDF + AZT | 36 (12) | 40 (13) |
| ABC + 3TC | 7 (2) | 7 (2) |
| Other | 10 (3) | 10 (3) |

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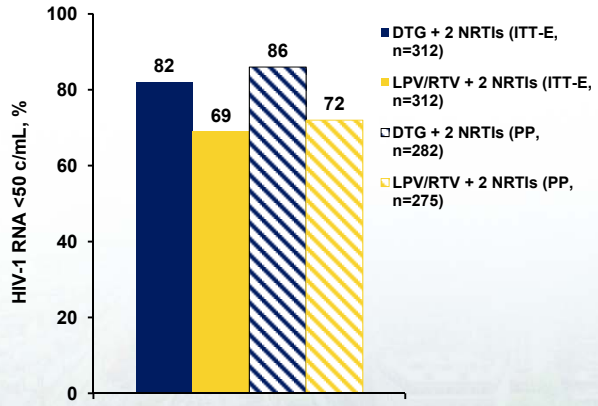
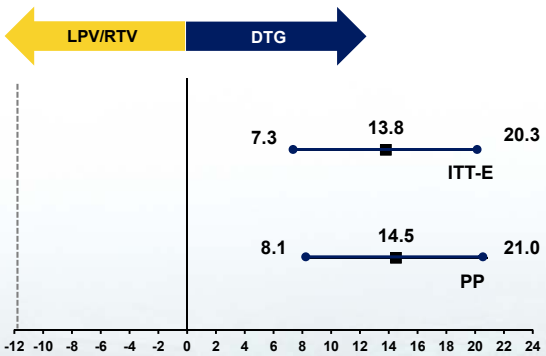
# DAWNING STUDY: EFFICACY AT WEEK 24

**Virologic Outcomes**




**Treatment Differences (95% CI)**




| n (%) | DTG + 2 NRTIs (n=312) | LPV/RTV + 2 NRTIs (n=312) |
|---|---|---|
| **Virologic nonresponse** | 37 (12) | 77 (25) |

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

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# DAWNING STUDY: EFFICACY AT WEEK 24

| n (%) | DTG + 2 NRTIs (n=312) | LPV/RTV + 2 NRTIs (n=312) |
|---|---|---|
| **Virologic response** | **257 (82)** | **215 (69)** |
| **Virologic nonresponse** | **37 (12)** | **77 (25)** |
| Data in window not below <50 c/mL | 32 (10) | 67 (21) |
| Discontinued for other reason while not <50 c/mL | 1 (<1) | 4 (1) |
| Change in ART | 4 (1) | 6 (2) |
| **No virologic data** | **18 (6)** | **20 (6)** |
| Discontinued study due to AE or death | 4 (1) | 12 (4) |
| Discontinued study for other reasons | 12 (4) | 4 (1) |
| Missing data during window but on study | 2 (<1) | 4 (1) |

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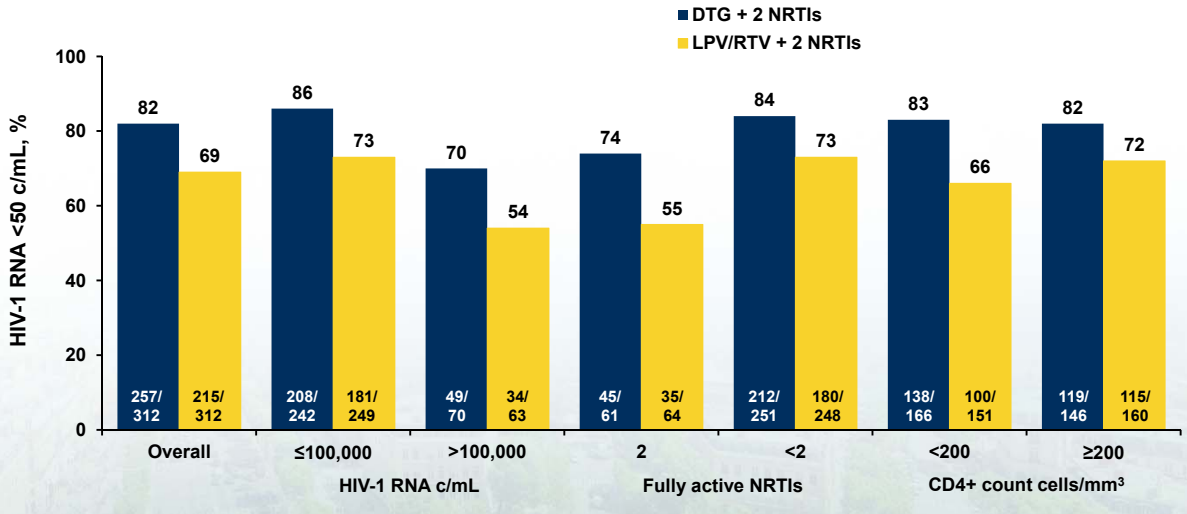
# DAWNING STUDY: OUTCOMES - SUBGROUPS AT WEEK 24




ITT-E, intent-to-treat exposed.

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# DAWNING STUDY: RESISTANCE

## Confirmed Virologic Withdrawal Criteria Any Time DTG 10 (3%), LPV/r 28 (9%)

| Resistance Analysis | DTG + 2 NRTIs (n=8) | LPV/RTV + 2 NRTIs (n=24) |
|---|---|---|
| **INSTI** | **0** | **0** |
| **NRTI** | **0** | **3** |
| K70R | 0 | 2 |
| M184V | 0 | 1 |
| K219Q | 0 | 1 |
| K219E | 0 | 1 |
| **PI** | **0** | **0** |

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# DAWNING STUDY: SAFETY

| | DTG + 2 NRTIs (n=314) | LPV/RTV + 2 NRTIs (n=310) |
|---|---|---|
| **Any adverse event, n (%)** | 204 (65) | 231 (75) |
| **Most common AEs (≥5% in either arm)** | | |
| Diarrhoea | 28 (9) | 98 (32) |
| Nausea | 11 (4) | 28 (9) |
| Vomiting | 5 (2) | 17 (5) |
| **AEs leading to withdrawal** | 7 (2) | 17 (5) |

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