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SWORD-1&-2: Switch From TDF-Containing Regimen to DTG + RPV Maintains Bone Mineral Density and Decreases Bone Turnover Markers Over 148 Weeks

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Introduction

- Bone disease is becoming an increasingly important comorbidity in the aging HIV population
- Loss of bone mineral density (BMD) has been attributed to traditional risk factors for osteoporosis, HIV infection, and ART, particularly TDF[1-3]
- Use of 2-drug regimens (2DRs) is one strategy to decrease drug exposure and potentially reduce some of the toxicities associated with ART
- DTG/RPV is an approved 2DR in patients who are virologically suppressed with their current ART regimen (CAR), based on non-inferior efficacy demonstrated in the Week 48 primary analysis of the SWORD-1 and SWORD-2 trials[4]
  - Viral load suppression was maintained through 148 weeks on the DTG + RPV regimen[5]
- A sub-study of SWORD-1 and SWORD-2 (study 202094) demonstrated a statistically significant increase in total hip and lumbar spine BMD (P=0.014 and P=0.039, respectively) and a statistically significant decrease in bone turnover markers (P≤0.001 to ≤0.029 across markers) in participants receiving DTG + RPV compared with CAR at the Week 48 primary analysis[6]
- Here, we report results on bone health from the Week 148 analysis

Methods

- Participants were HIV-1–infected adults with HIV-1 RNA <50 c/mL (≥6 months) who received ART containing TDF for ≥6 months before randomization to DTG + RPV (Early-Switch [ES] group) or CAR in the SWORD-1 or SWORD-2 parent studies
  - CAR participants who maintained HIV-1 RNA <50 c/mL at Week 48 switched to DTG + RPV at Week 52 (Late-Switch [LS] group) and continued DTG + RPV until Week 148
  - The latest assessment of CAR participants before switch at Week 52 served as the Late-Switch (LS) baseline
- Total hip and lumbar spine BMD were measured by DXA scans acquired using GE Lunar or Hologic scanners calibrated longitudinally and centrally across sites
  - DXA scans were read centrally by the imaging vendor who was blinded to each participant's treatment allocation in the SWORD parent studies. BMD was expressed as areal density (g/cm^2), T-scores, and Z-scores
- Secondary endpoints included percentage change from baseline/LS baseline through Week 148 in total hip and lumbar spine BMD
- Exploratory endpoints included change from baseline in the levels of bone turnover markers

Results

- Approximately half of the participants in the study 202094 population were female, and ~30% in each group were aged ≥50 years; 25% in each group reported smoking (Table 1)

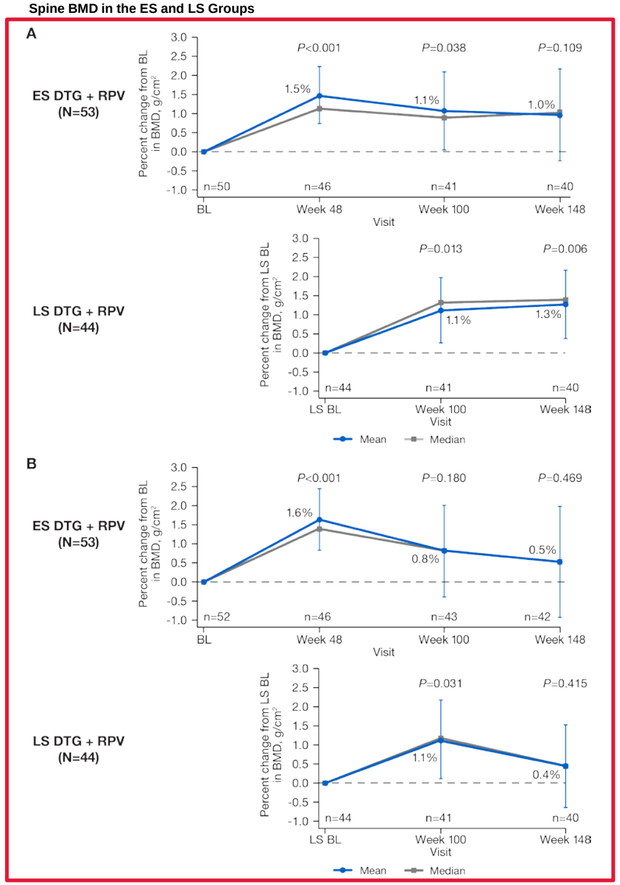
Table 1. Demographics and Baseline Characteristics

Characteristic, n (%)[a]	ES DTG + RPV (N = 53)	LS DTG + RPV (N = 44)
Age at baseline, median (range), y	43.0 (21-62)	46.5 (22-76)
≥50 y	15 (28)	15 (34)
Female	27 (51)	23 (52)
White race	44 (83)	36 (82)
BMI at baseline, mean (SD) [range], kg/m^2	25.2 (3.9) [18.7-33.3]	25.9 (5.0) [18.9-38.7]
Baseline third-agent class		
NNRTI	32 (60)	30 (68)
INSTI	9 (17)	4 (9)
PI	12 (23)	10 (23)
History of smoking at baseline		
Never/Not current smoker	40 (75)	33 (75)
<1 pack year[b]	10 (19)	7 (16)
≥1 pack year[b]	3 (6)	4 (9)
Osteopenia by total hip T-score[c]	14/50 (28)	11/44 (25)
Osteopenia by lumbar spine T-score[c]	20/52 (38)	13/44 (30)

[a]Unless otherwise noted. [b]A pack year is defined as 20 cigarettes (a pack) smoked every day for a year. [c]Osteopenia is defined as a T-score between −1 and −2.5.

- Statistically significant increases from baseline/LS baseline were observed in total hip BMD in the ES and LS groups through 100 weeks post-switch to DTG + RPV, with an increase that was not statistically significant at Week 148 in the ES group (Figure 1A)
- Lumbar spine BMD increased statistically significantly from baseline/LS baseline at 48 weeks post-switch and remained increased, though the increase was not statistically significant, post–48 weeks of DTG + RPV treatment in either group (Figure 1B)

Figure 1. Percentage Change From Baseline/LS Baseline in (A) Total Hip and (B) Lumbar Spine BMD in the ES and LS Groups



ES, Early Switch; LS, Late Switch; LS BL, LS baseline. Vertical bars represent 95% CI. P values from 1-sample 2-sided t test for percentage change from BL/LS BL.

- The majority of participants remained in their baseline or LS baseline T-score category or improved to the next category for both total hip (Table 2) and lumbar spine (Table 3) through Week 148

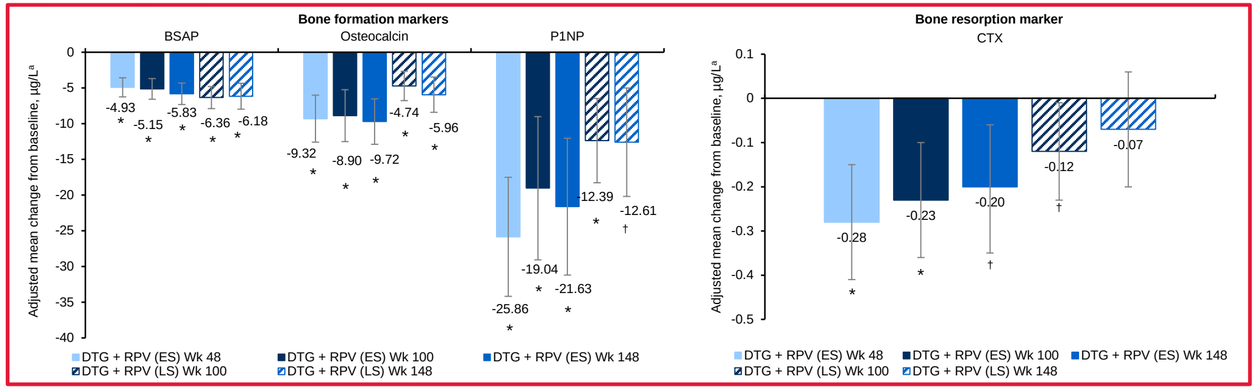
Table 2. Change From Baseline/LS Baseline in T-score Category for Total Hip Through Week 148

	ES DTG + RPV (N = 53)			LS DTG + RPV (N = 44)	
Shift from BL/LS BL, n (%)	Week 48 (n=46)	Week 100 (n=41)	Week 148 (n=40)	Week 100 (n=41)	Week 148 (n=40)
Improvement					
Osteopenia to normal	3 (7)	2 (5)	**2 (5)**	5 (12)	**3 (8)**
No change					
Normal	32 (70)	27 (66)	**26 (65)**	29 (71)	**28 (70)**
Osteopenia	11 (24)	11 (27)	**11 (28)**	6 (15)	**8 (20)**
Deterioration					
From normal to osteopenia	0	1 (2)	**1 (3)**	1 (2)	**1 (3)**

BL, baseline; ES, Early Switch; LS, Late Switch; n, number of participants with T-score total hip data at BL/LS BL and week of interest. Normal: T-score > −1. Osteopenia: −2.5 < T-score ≤ −1.

- Through Week 148, bone turnover markers decreased statistically significantly (P<0.001 to P=0.042 across markers) from baseline/LS baseline except for type I collagen C-telopeptide at Week 148 in the LS group (P=0.279; Figure 2)

Figure 2. Summary of Changes From Baseline/LS Baseline to Week 148 in Bone Turnover Markers in the ES and LS Groups



BSAP, bone-specific alkaline phosphatase; CTX, type I collagen C-telopeptide; ES, Early Switch; LS, Late Switch; P1NP, procollagen 1 N-terminal propeptide. [a]Last pre-switch data (usually Week 48) used for LS baseline. *P<0.001 vs baseline/LS baseline. †P<0.05 vs baseline/LS baseline. P values from 1-sample 2-sided t test for percentage change from BL/LS BL.

- One or more characteristics reported in the literature as associated with decreased BMD (eg, menopause/perimenopause, current smoker/recent cessation of smoking, and being overweight/obese) were observed in 38/50 (76%) ES group participants and in 34/44 (77%) LS group participants during the study through Week 148 (data not shown)
  - However, no consistent pattern in relation to BMD changes was observed
- Furthermore, approximately 30% of participants were aged ≥50 years

Table 3. Change From Baseline/LS Baseline in T-score Category for Lumbar Spine Through Week 148

	ES DTG + RPV (N = 53)			LS DTG + RPV (N = 44)	
Shift from BL/LS BL, n (%)	Week 48 (n=46)	Week 100 (n=43)	Week 148 (n=42)	Week 100 (n=41)	Week 148 (n=40)
Improvement					
From osteopenia to normal	3 (7)	4 (9)	**1 (2)**	1 (2)	**2 (5)**
From osteoporosis to osteopenia	1 (2)	1 (2)	**1 (2)**	1 (2)	**0**
From severe osteoporosis to osteoporosis	2 (4)	1 (2)	**2 (5)**	0	**0**
No change					
Normal	26 (57)	23 (53)	**23 (55)**	26 (63)	**26 (65)**
Osteopenia	14 (30)	12 (28)	**14 (33)**	12 (29)	**9 (23)**
Severe osteoporosis	0	1 (2)	**0**	1 (2)	**1 (3)**
Deterioration					
From osteopenia to osteoporosis	0	1 (2)	**1 (2)**	0	**2 (5)**

BL, baseline; ES, Early Switch; LS, Late Switch; n, number of participants with T-score lumbar spine data at BL/LS BL and week of interest. Normal: T-score > −1. Osteopenia: −2.5 < T-score ≤ −1. Osteoporosis: −3.5 < T-score ≤ −2.5. Severe osteoporosis: T-score ≤ −3.5.

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Conclusions

- Switch to the 2DR DTG + RPV was associated with a sustained improvement in BMD with maintenance above baseline/LS baseline through Week 148, along with reductions in markers of bone turnover
- Despite ageing over the 3-year study and presence of 1 or more characteristics that decrease BMD in 77% of participants, mean values illustrate favorable effects on skeletal health parameters (BMD, bone biomarkers) through Week 148
- Data indicate that a switch to DTG + RPV in virologically suppressed patients is a robust option for preserving bone health while continuing suppressive HIV-1 treatment