Efficacy and Safety of Switching to Dolutegravir Plus Rilpivirine in Virologically Suppressed Older PLWH: Pooled Week 148 Results From SWORD-1 and SWORD-2

Manyu Prakash,[1] Richard Grove,[2] Brian Wynne,[3] Jean van Wyk,[1] Bryn Jones,[1] Andrew Clark[1]

[1]ViiV Healthcare, Brentford, UK; [2]GSK, Brentford, UK; [3]ViiV Healthcare, Durham, NC, USA

Key Takeaways

- **Through 148 weeks after early or late switch to the 2-drug regimen dolutegravir + rilpivirine (DTG + RPV) in the SWORD-1 and SWORD-2 studies, DTG + RPV maintained high rates of virologic suppression and high CD4+ cell counts in all individuals irrespective of age (<50, ≥50 to <65, and ≥65 years)**
- **In older adults living with HIV (OALWH) aged ≥50 years, switching to DTG + RPV demonstrated a good safety profile, consistent with that observed in younger participants, despite an increased frequency of comorbidities**

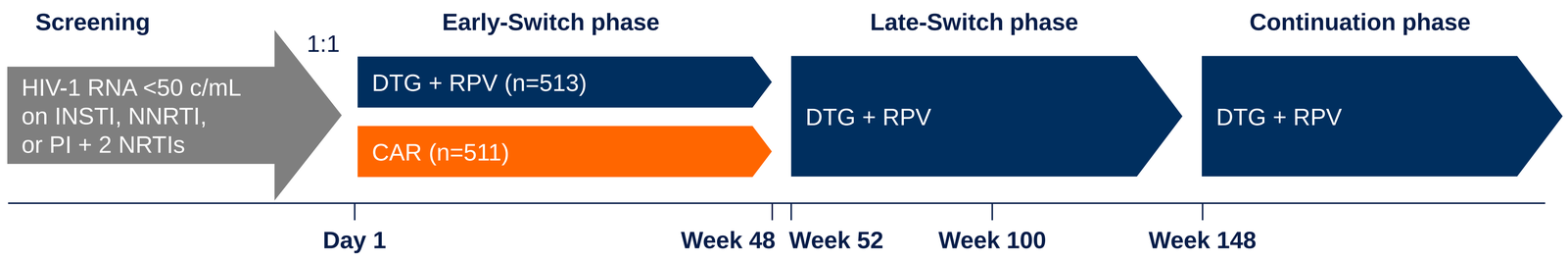
Introduction

- As older adults aged ≥50 years are among the fastest growing populations living with HIV and represent a diverse group with unique and complex needs,[1] more data evaluating the efficacy of antiretroviral therapy regimens are needed in this population
  - Comorbidities occur more frequently among OALWH aged ≥50 years and increase with age[2,3]
  - Managing age-related comorbidities and polypharmacy, including potential toxicity when taking multiple antiretrovirals, while maintaining virologic suppression is an important consideration for OALWH[4]
- Among adult participants in the SWORD-1 and -2 studies, switching to the 2-drug regimen DTG + RPV was non-inferior in maintaining virologic suppression vs continuing current 3- or 4-drug antiretroviral regimens at Week 48; results were sustained through Week 148[5]
- In this post hoc analysis, we present pooled efficacy and safety results from the SWORD-1 and SWORD-2 studies analyzed by age (<50, ≥50 to <65, and ≥65 years)

Methods

- In the open-label, phase 3 SWORD studies, virologically suppressed adults were randomized to switch to once-daily DTG + RPV on Day 1 (Early-Switch [ES] group) or to continue their current antiretroviral regimen and switch to DTG + RPV at Week 52 (Late-Switch [LS] group; Figure 1)
- Proportions of participants with HIV-1 RNA <50 c/mL (Snapshot, ITT-E) and safety were analyzed through Week 148

Figure 1. Study Design



Results

Baseline Characteristics

- Among all participants who switched to DTG + RPV (N=990 [ES, n=513 and LS, n=477]), 72% were aged <50 years, 25% were aged ≥50 to <65 years, and 3% were aged ≥65 years (Table 1)
  - The study population was primarily composed of non-Hispanic/Latinx, White, male individuals
- Proportions of participants with concomitant medication use were high (>90%) across age groups
- Proportions with comorbidities increased with age in the ES group (<50 years, 48%; ≥50 to <65 years, 74%; ≥65 years, 89%)

Table 1. Demographics and Baseline Characteristics: Pooled SWORD-1 and SWORD-2 ITT-E Population

Parameter	ES group, DTG + RPV, Weeks 1-148 (N=513)	LS group, DTG + RPV, Weeks 52-148 (N=477)
Age, median (range), y	43 (21-79)	43 (22-76)
<50, n (%)	366 (71)	344 (72)
≥50 to <65, n (%)	129 (25)	120 (25)
≥65, n (%)	18 (4)	13 (3)
Sex, n (%)		
Female	120 (23)	96 (20)
Male	393 (77)	381 (80)
Ethnicity, n (%)		
Hispanic/Latinx	67 (13)	76 (16)
Non-Hispanic/Latinx	446 (87)	401 (84)
Race, n (%)		
American Indian or Alaska Native	14 (3)	11 (2)
Asian	38 (7)	49 (10)
Black or African American	37 (7)	43 (9)
Native Hawaiian or Oher Pacific Islander	2 (<1)	0
White	421 (82)	372 (78)
Mixed race	1 (<1)	2 (<1)
Median baseline/LS baseline CD4+ cell count, cells/mm^3	611	661
CDC category		
A: Asymptomatic, lymphadenopathy, or acute HIV	401 (78)	359 (75)
B: Symptomatic, not AIDS	55 (11)	64 (13)
C: AIDS	57 (11)	54 (11)
Baseline third agent class, n (%)		
NNRTI[a]	275 (54)	267 (56)
PI[b]	133 (26)	121 (25)
INSTI[c]	105 (20)	89 (19)

[a]The most commonly reported NNRTI at baseline was EFV (ES, n=185 [36%]; LS, n=182 [38%]). [b]The most commonly reported PI at baseline was DRV/r (ES, n=58 [11%]; LS, n=35 [7%]). [c]The most commonly reported INSTI at baseline was RAL (ES, n=43 [8%]; LS, n=41 [9%]).

Efficacy

- Through Week 148, proportions of participants with HIV-1 RNA <50 c/mL were high across all ages in both the ES and LS groups (Figure 2)
- Of note, the lower response observed in participants aged ≥65 years at Week 148 (ES, 72%; LS, 69%) was mostly driven by no virologic data and low numbers of participants (ES, n=18; LS, n=13; Table 2)

Table 2. Summary of Snapshot Analysis at Weeks 48, 100, and 148: Pooled SWORD-1 and SWORD-2 ITT-E Population

	ES group (N=513)			LS group (N=477)	
n (%)	DTG + RPV Weeks 1-48	DTG + RPV Weeks 1-100	DTG + RPV Weeks 1-148	DTG + RPV Weeks 52-100	DTG + RPV Weeks 52-148
HIV-1 RNA <50 c/mL					
<50 y	350/366 (96)	332/366 (91)	316/366 (86)	321/344 (93)	311/344 (90)
≥50 to <65 y	118/129 (91)	108/129 (84)	103/129 (80)	113/120 (94)	108/120 (90)
≥65 y	18/18 (100)	16/18 (89)	13/18 (72)	11/13 (85)	9/13 (69)
HIV-1 RNA ≥50 c/mL					
<50 y	1/366 (<1)	8/366 (2)	9/366 (2)	7/344 (2)	6/344 (2)
≥50 to <65 y	2/129 (2)	5/129 (4)	5/129 (4)	0/120 (0)	3/120 (3)
≥65 y	0/18 (0)	0/18 (0)	0/18 (0)	1/13 (8)	2/13 (15)
No virologic data					
<50 y	15/366 (4)	26/366 (7)	41/366 (11)	16/344 (5)	27/344 (8)
≥50 to <65 y	9/129 (7)	16/129 (12)	21/129 (16)	7/120 (6)	9/120 (8)
≥65 y	0/18 (0)	2/18 (11)	5/18 (28)	1/13 (8)	2/13 (15)

- Mean CD4+ cell count was high (>500 cells/mm^3) at baseline and maintained through Week 148 across all ages in both the ES and LS groups
- Frequency of resistance was low across all ages in both the ES and LS groups: of the 11 participants who met the confirmed virologic withdrawal criterion, no DTG resistance-associated mutations were observed; emergent NNRTI or RPV resistance-associated mutations were observed in 6 participants (<1%)

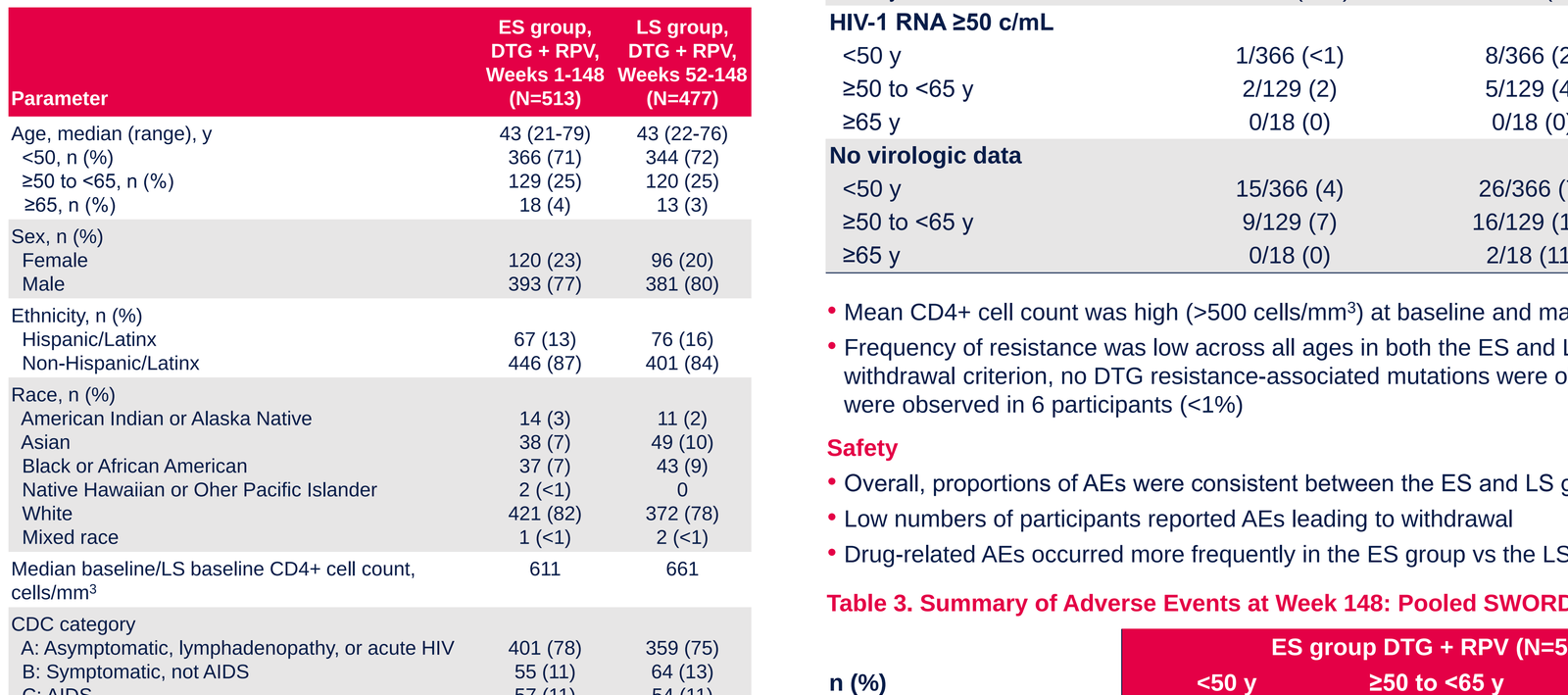
Safety

- Overall, proportions of AEs were consistent between the ES and LS groups; all participants aged ≥65 years reported AEs (Table 3)
- Low numbers of participants reported AEs leading to withdrawal
- Drug-related AEs occurred more frequently in the ES group vs the LS group

Table 3. Summary of Adverse Events at Week 148: Pooled SWORD-1 and SWORD-2 Safety Population

	ES group DTG + RPV (N=513)			LS group DTG + RPV (N=477)		
n (%)	<50 y	≥50 to <65 y	≥65 y	<50 y	≥50 to <65 y	≥65 y
Any AE	335/366 (92)	119/129 (92)	18/18 (100)	295/344 (86)	111/120 (93)	13/13 (100)
AEs leading to withdrawal	30/366 (8)	10/129 (8)	2/18 (11)	11/344 (3)	6/120 (5)	2/13 (15)
Drug-related AEs	70/366 (19)	26/129 (20)	6/18 (33)	43/344 (13)	19/120 (16)	1/13 (8)
Serious AEs	50/366 (14)	16/129 (12)	6/18 (33)	27/344 (8)	12/120 (10)	5/13 (38)
Grade 3 or 4 AEs	48/366 (13)	17/129 (13)	5/18 (28)	25/344 (7)	11/120 (9)	4/13 (31)

Figure 2. Percentage of Participants With HIV-1 RNA <50 c/mL at Week 148 by Age and Treatment Group: Pooled SWORD-1 and SWORD-2 ITT-E Population



Conclusions

- Through 148 weeks in the SWORD-1 and SWORD-2 studies, switching to the 2-drug regimen DTG + RPV maintained high rates of virologic suppression as well as high CD4+ cell counts and demonstrated a good safety profile in all individuals irrespective of age
- Consistent with other studies,[2,3] frequency of comorbidities increased with age
- Given the unique considerations of treating the growing population of OALWH, including managing age-related comorbidities and polypharmacy, it is important to continue to include this population in clinical trials

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Presenting author: Manyu Prakash; manyu.x.prakash@viivhealthcare.com