Patient-Reported Outcomes After Switching to a 2-Drug Regimen of Dolutegravir + Rilpivirine: Results From the SWORD-1 and SWORD-2 Studies

BPD1/2

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Introduction

- Most antiretroviral (ARV) regimens consist of ≥3 drugs (including pharmacokinetic [PK] boosting agents) from 2 distinct classes in order to achieve and maintain durable virologic suppression
- Two-drug regimens may provide better treatment options for patients with virologic suppression who want to simplify their therapy or lessen the risk of long-term toxicities associated with a 3- or 4-drug regimen
- Two identically designed phase III studies, SWORD-1 and SWORD-2, demonstrated noninferior efficacy and similar tolerability of switching virologically suppressed adults infected with HIV-1 from their current 3- or 4-drug antiretroviral regimen (CAR) to dolutegravir (DTG) + rilpivirine (RPV)[1]
- This analysis describes the pooled SWORD-1 and SWORD-2 results of patient-reported outcome measures at Week 48, including assessments of treatment satisfaction, change in treatment symptom score, health-related quality of life, willingness to switch regimens, and adherence to treatment

Methods

- SWORD-1 (NCT02429791) and SWORD-2 (NCT02422797) are phase III, randomized (1:1), multicenter, open-label, parallel-group, noninferiority studies evaluating the efficacy and safety of a once daily 2-drug regimen (DTG 50 mg + RPV 25 mg) compared with continuation of CAR in virologically suppressed adults infected with HIV-1
- Eligible participants (age ≥18 years) were virologically suppressed while on their first or second ART regimen (viral load <50 copies/mL) for ≥6 months
  - Regimens consisted of 2 nucleoside reverse transcriptase inhibitors (NRTIs) plus a third agent (non-nucleoside reverse transcriptase inhibitor, integrase strand transfer inhibitor, or protease inhibitor [PI])

Health Outcomes Assessments

- Patient-reported outcomes were assessed at baseline and at Weeks 4, 24, and 48, except for the willingness-to-switch question, which was assessed at baseline alone
- The HIV Treatment Satisfaction Questionnaire, status version (HIVTSQs), is a 10-item, self-reported instrument that measures overall satisfaction with treatment and by specific domains[2]
  - Each of the 10 items can receive a score ranging from 0 (less improvement) to 6 (greater improvement), resulting in the total score (range, 0-60)
  - 5 items (satisfaction, well controlled, side effects, recommend, and continue) determine the score on the general satisfaction/clinical subscale, whereas the other 5 items (demands, convenience, flexibility, understanding, and lifestyle) determine the score on the lifestyle/ease subscale
- The Symptom Distress Module is a 20-item, self-reported measure that addresses the presence of and perceived distress linked to symptoms associated with HIV infection or its treatment[3]
  - Symptom count score (range, 0-20) assesses the presence of 20 predefined symptoms
  - The symptom bother score assesses the level of bother (range, 0-4) for each symptom, with a total score for all symptoms ranging from 0 (no symptoms present) to 80 (all symptoms present at worst level)
- The European Quality of Life 5-Dimensional 5-Level instrument is a standardized questionnaire that provides a profile of patient function and global health state rating[4]
  - The tool assesses 5 dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression
  - 5 levels exist for each dimension, ranging from "no problems" to "extreme problems"
  - The health state is defined by combining the levels of answers from each of the 5 dimensions translated to a utility score (range, −0.594-1)[5]
- Patient-reported adherence to their CAR over the past several weeks was reported using a visual analog scale (VAS), with response options ranging from 0 (no HIV medication) to 100 (every dose of HIV medication)
- A single-item, willingness-to-switch question with 7 response options was administered at baseline to assess reason(s) for study participation and participants' willingness to switch therapies

Results

Participant Demographics

- The patient population in both arms was well balanced and represents a diverse and broad population (women, age ≥50 years, and nonwhite participants; Table 1)
  - Those who switched to DTG + RPV had been on their ART regimen for a median of 51 months prior to Day 1
  - 87% of participants enrolled in the study were new to DTG and RPV

Table 1. Baseline Demographics

Characteristic	DTG + RPV (n=513)	CAR (n=511)
Age, mean (range), y	43 (21-79)	43 (22-76)
≥50 y, n (%)	147 (29)	142 (28)
Female, n (%)	120 (23)	108 (21)
Nonwhite race, n (%)	92 (18)	111 (22)
Baseline third-agent class, n (%)		
PI	133 (26)	136 (27)
NNRTI	275 (54)	278 (54)
INI	105 (20)	97 (19)
Baseline ART, n (%)		
TDF	374 (73)	359 (70)
RPV	33 (6)	39 (8)
DTG	33 (6)	33 (6)
Duration of ART prior to Day 1, median, months	50.8	52.6

ART, antiretroviral therapy; CAR, current ART; DTG, dolutegravir; INI, integrase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RPV, rilpivirine; TDF, tenofovir disoproxil fumarate.

Health Outcomes

Willingness to Switch

- The most frequently selected reasons (occurring ≥25%) at baseline for participants being willing to switch from their existing regimen were interest in new HIV therapies, physician recommendation, and concern about the long-term side effects of their current regimen (Table 2)

Table 2. Reasons Given by Participants for Willingness to Switch From Current Treatment Regimen

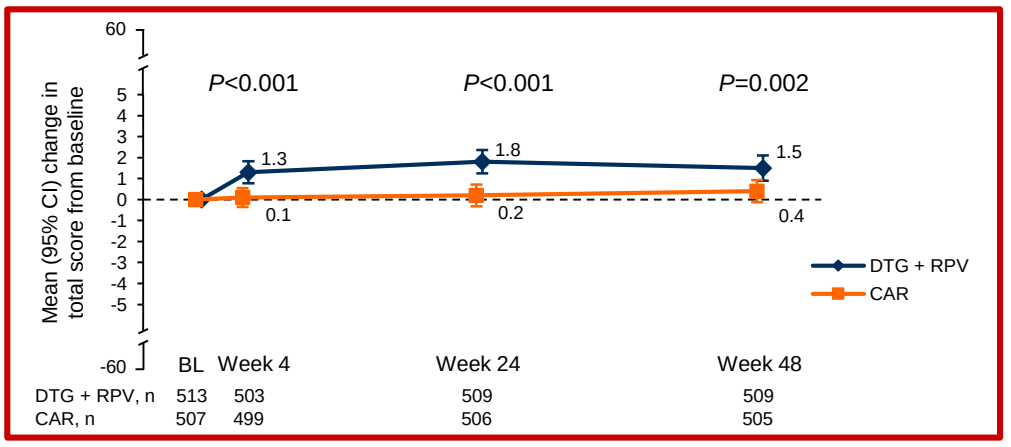
Reason, n (%)[a]	DTG + RPV (n=513)	CAR (n=511)	Total (N=1024)
I am not tolerating my current regimen well because of side effects	20 (4)	15 (3)	35 (3)
I am concerned about the long-term side effects of my current anti-HIV regimen	134 (26)	140 (27)	274 (27)
I am having trouble with adherence or taking my current regimen on a regular basis	13 (3)	7 (1)	20 (2)
I am interested in research of new therapies in HIV	295 (58)	312 (61)	607 (59)
My physician asked me to participate	245 (48)	246 (48)	491 (48)
Cost of current HIV drug or to receive free study drug	33 (6)	30 (6)	63 (6)
Some other reason	33 (6)	40 (8)	73 (7)

CAR, current ART; DTG, dolutegravir; RPV, rilpivirine. [a]Participants could select ≥1 reason.

HIVTSQs

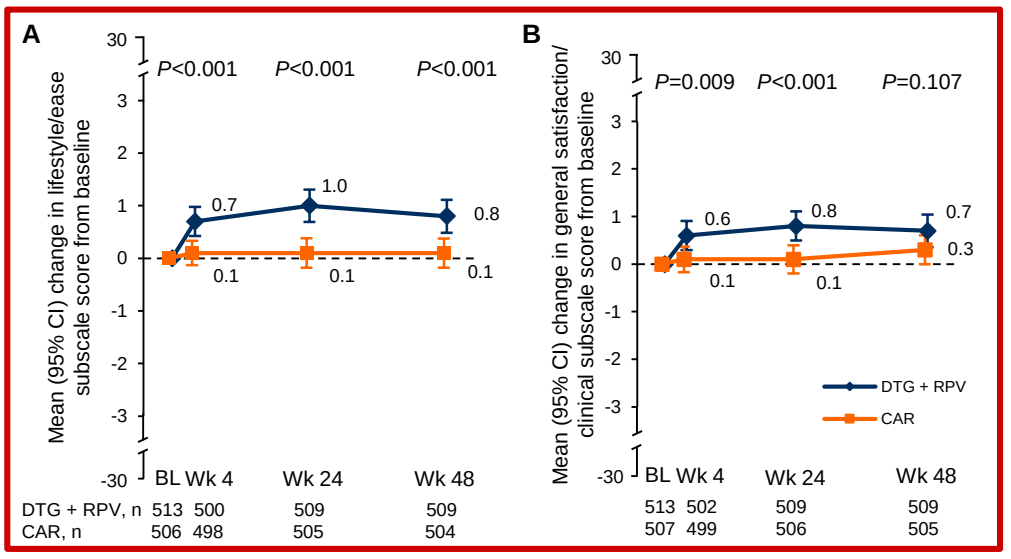
- Small but statistically significant improvements from baseline in the HIVTSQs total score (Figure 1) and subscores for the lifestyle/ease (Figure 2A) and general satisfaction/clinical (Figure 2B) subscales were seen in the DTG + RPV group compared with the CAR group at each assessed time point, except for the general satisfaction/clinical subscale during Week 48

Figure 1. Treatment Satisfaction Total Score, Mean (95% CI) Change From Baseline, Assessed by HIVTSQs



BL, baseline; CAR, current antiretroviral treatment; CI, confidence interval; DTG, dolutegravir; HIVTSQs, HIV Treatment Satisfaction Questionnaire, status version; RPV, rilpivirine. *P* values of DTG + RPV vs CAR are based on a Wilcoxon rank sum test. Mean score at BL: DTG + RPV, 54.4; CAR, 53.9.

Figure 2. Treatment Satisfaction Score, Mean (95% CI) Change From Baseline, Assessed by (A) Lifestyle/Ease Subscale and (B) General Satisfaction/Clinical Subscale of HIVTSQs

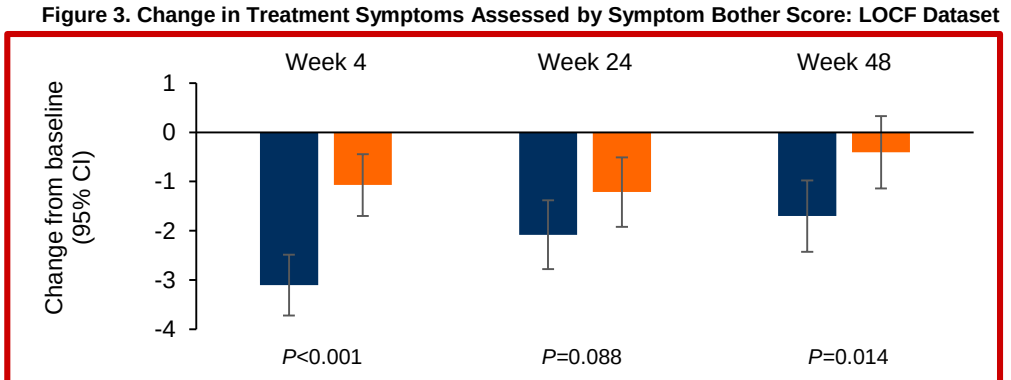


BL, baseline; CAR, current antiretroviral treatment; CI, confidence interval; DTG, dolutegravir; HIVTSQs, HIV Treatment Satisfaction Questionnaire, status version; RPV, rilpivirine; Wk, week. *P* values of DTG + RPV vs CAR are based on a Wilcoxon rank sum test. Mean score of lifestyle/ease subscale at BL: DTG + RPV, 27.5; CAR, 27.2. Mean score of general satisfaction/ clinical subscale at BL: DTG + RPV, 26.9; CAR, 26.7.

Symptom Distress Module

- Mean (SD) baseline symptom bother scores were 9.6 (10.0) and 11.0 (11.2) in the DTG + RPV and CAR treatment arms at Weeks 4 and 48, respectively
  - A statistically significant reduction in symptom bother score was apparent in the DTG + RPV group compared with the CAR group (Figure 3)

Figure 3. Change in Treatment Symptoms Assessed by Symptom Bother Score: LOCF Dataset



CAR, current antiretroviral therapy; CI, confidence interval; DTG, dolutegravir; LOCF, last observation carried forward; RPV, rilpivirine. [a]Number of participants with a value at baseline and time point after LOCF. *P* values are calculated from an ANCOVA model adjusting for age, baseline third agent, sex, race, and baseline symptom bother score.

European Quality of Life 5-Dimensional 5-Level Instrument

- No significant change in health-state utility score was seen between treatment groups at Week 48 (*P*=0.847) and remained stable from baseline

Patient-Reported Adherence

- Assessed by the VAS, self-reported treatment regimen adherence was high (>98%) and was not significantly different when comparing treatment groups from baseline and at each time point (*P*=0.913)

Conclusions

- High levels of treatment satisfaction and health status and a low level of symptom burden were reported by patients entering the study, as would be expected from patients on a stable, long-term regimen (median duration, >50 months)
- These levels were maintained or slightly improved after switching to DTG + RPV compared with CAR, despite the introduction of 2 new agents for the majority of participants
- These results suggest that DTG + RPV is a well-tolerated, alternative treatment option for virologically suppressed patients

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