SWORD-1&-2: MAINTENANCE OR IMPROVEMENT IN RENAL FUNCTION IN PLWH THROUGH 148 WEEKS AFTER SWITCH TO THE DOLUTEGRAVIR + RILPIVIRINE 2-DRUG REGIMEN

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Introduction

- As individuals with HIV live longer, reducing exposure to antiretroviral therapy (ART) is a potential strategy to limit ART-related comorbidity[1]
- The SWORD studies demonstrated non-inferiority post-switch to dolutegravir (DTG) + rilpivirine (RPV) vs 3- or 4- drug current ART (CAR) continuation at Week 48 and maintained viral suppression to Week 148[2,3]
- The NRTI tenofovir disoproxil fumarate (TDF) and certain PIs (lopinavir, atazanavir) are associated with renal toxicity[4]
- DTG + RPV as an NRTI- and PI-sparing 2DR may be a suitable therapy for renally impaired patients
- Here we report pooled SWORD study data for renal parameters through Week 148

Methods

- SWORD-1&-2 are identically designed, multicenter, open-label, parallel-group, non-inferiority, phase III studies; participants with Baseline HIV-1 RNA <50 c/mL taking INSTI, NNRTI, or PI + 2 NRTIs were randomized 1:1 to switch to DTG + RPV (Early-Switch group, ES) or to continue CAR; those who continued CAR and were suppressed switched to DTG + RPV at Week 52 (Late-Switch group, LS)[2]
- Renal function post-switch to DTG + RPV was evaluated using eGFR estimated by serum cystatin C (eGFR(cystC); CKD-EPI equation), retinol-binding protein (RBP) to creatinine ratio, and β2-microglobulin (β2M) to creatinine ratio by receipt of TDF pre-switch
- Changes in eGFR(cystC) for participants with mild renal impairment (ie, eGFR(cystC) = 60-90 mL/min/1.73 m^2) were also assessed

Results

- After switch to DTG + RPV, minimal change was observed in eGFR(cystC), irrespective of pre-switch TDF exposure (Table 1)
- For participants with mild renal impairment pre-switch (53 in the ES group, 31 in the LS group), eGFR(cystC) remained stable or slightly increased post-switch to DTG + RPV (median change from Baseline and LS Baseline was +13.1 and 0.0 for the ES and LS groups, respectively, at Week 148), with few participants decreasing below 60 mL/min/1.73 m^2 at any time (Table 2)
- In the ES group, 3 of 4 participants who had eGFR(cystC) <60 mL/min/1.73 m^2 at Baseline improved their eGFR(cystC) to >60 mL/min/1.73 m^2 at Week 148. One 65-year-old male remained <60 but >30 mL/min/1.73 m^2 through Week 148
- In the LS group, 3 participants (one each 75-year-old male, 76-year-old female, and 55-year-old female) experienced eGFR(cystC) <60 mL/min/1.73 m^2 on CAR before switch and remained <60 but >30 mL/min/1.73 m^2 through Week 148
- No participant in the ES or LS group had a minimum post-Baseline/LS Baseline CKD-EPI <30 mL/min/1.73 m^2 during study through Week 148
- RBP and β2M to creatinine ratios had numerically greater improvements in participants taking TDF before switch compared with those not taking TDF in the pooled SWORD-1&-2 population (Table 3)

Table 1. Change in eGFR(cystC) After Switch to DTG + RPV for the Pooled SWORD-1&-2 Population Estimated by Serum Cystatin C Using CKD-EPI Equation by Pre-switch TDF

	Early-Switch DTG + RPV group		Late-Switch DTG + RPV group	
Visit	n	Median (IQR) mL/min/1.73 m^2	n	Median (IQR) mL/min/1.73 m^2
TDF exposure pre-switch				
Baseline[a]	369	115.4 (101.3, 124.6)	—	NA
Week 48	348	0 (−6.93, 9.42)	—	NA
LS Baseline[b]	—	NA	335	116.8 (108.0, 124.6)
Week 100	330	0 (−10.2, 0)	316	−6.8 (−12.1, 0)
Week 148	307	0 (−8.92, 8.22)	304	0 (−8.45, 0)
No TDF exposure pre-switch				
Baseline[a]	142	119.7 (109.5, 127.7)	—	NA
Week 48	135	0 (−9.15, 0)	—	NA
LS Baseline[b]	—	NA	142	118.0 (107.6, 125.2)
Week 100	130	−7.2 (−15.5, 0)	132	−7.3 (−12.8, 0)
Week 148	125	0 (−9.92, 0)	129	0 (−12.40, 0)

CKD-EPI, chronic kidney disease−epidemiology collaboration; eGFR(cystC), estimated glomerular filtration rate by cystatin C; IQR, interquartile range; NA, not applicable. [a]Baseline for the Early-Switch DTG + RPV group is the value at Day 1. [b]Late-Switch Baseline (LS Baseline) for the Late-Switch DTG + RPV group is the latest pre-switch value (usually from the Week 48 visit).

Table 2. Change in eGFR(cystC) After Switch to DTG + RPV for the Pooled SWORD-1&-2 Population Estimated by Serum Cystatin C Using CKD-EPI Equation in Participants With Mild Renal Impairment Pre-switch

	Early-Switch DTG + RPV group		Late-Switch DTG + RPV group	
Visit	n	Median (IQR) mL/min/1.73 m^2	n	Median (IQR) mL/min/1.73 m^2
Baseline[a]	53	82.6 (74.4, 85.9)	—	NA
Week 48	46	12.1 (0.0, 22.2)	—	NA
LS Baseline[b]	—	NA	31	81.6 (75.1, 86.1)
Week 100	45	0 (0.0, 11.4)	28	0 (−9.6, 9.7)
Week 148	41	13.1 (0.0, 22.2)	27	0 (−11.2, 14.8)

CKD-EPI, chronic kidney disease−epidemiology collaboration; eGFR(cystC), estimated glomerular filtration rate by cystatin C; IQR, interquartile range; NA, not applicable. [a]Baseline for the Early-Switch DTG + RPV group is the value at Day 1. [b]Late-Switch Baseline (LS Baseline) for the Late-Switch DTG + RPV group is the latest pre-switch value (usually from the Week 48 visit).

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Table 3. Percent Change in Retinol-Binding Protein to Creatinine Ratio and β2-Microglobulin to Creatinine Ratio Post-switch to DTG + RPV Through Week 148 by Pre-switch TDF Exposure

	Early-Switch DTG + RPV group		Late-Switch DTG + RPV group	
Visit	n	Median (IQR)	n	Median (IQR)
Retinol-binding protein to creatinine ratio (urine), µg/mmol				
TDF exposure pre-switch				
Baseline[a]	352	9.02 (6.11, 14.96)	—	NA
Week 48	326	−43.4% (−65.1%, −12.6%)	—	NA
LS Baseline[b]	—	NA	335	7.33 (4.37, 13.29)
Week 100	312	−59.5% (−83.0%, −34.3%)	313	−50.2% (−78.8%, −8.6%)
Week 148	285	−28.8% (−56.3%, 8.76%)	294	−22.3% (−52.8%, 25.8%)
No TDF exposure pre-switch				
Baseline[a]	134	6.27 (4.41, 8.74)	—	NA
Week 48	125	−23.7% (−50.4%, 15.7%)	—	NA
LS Baseline[b]	—	NA	138	6.11 (3.94, 9.32)
Week 100	123	−37.4% (−70.8%, −2.1%)	127	−34.5% (−61.6%, 28.9%)
Week 148	114	−2.27% (−33.8%, 32.4%)	125	0.4% (−31.0%, 53.3%)
β2-microglobulin to creatinine ratio (urine), mg/mmol				
TDF exposure pre-switch				
Baseline[a]	222	0.02 (0.01, 0.04)	—	NA
Week 48	112	−30.7% (−55.5%, 6.0%)	—	NA
LS Baseline[b]	—	NA	255	0.02 (0.01, 0.05)
Week 100	108	−38.4% (−62.4%, −3.4%)	139	−38.5% (−69.9%, 1.45%)
Week 148	102	−34.8% (−68.9%, 14.2%)	118	−41.5% (−68.9%, 11.9%)
No TDF exposure pre-switch				
Baseline[a]	94	0.01 (0.01, 0.02)	—	NA
Week 48	48	7.11% (−15.9%, 60.9%)	—	NA
LS Baseline[b]	—	NA	111	0.01 (0.01, 0.02)
Week 100	40	3.6% (−29.0%, 44.3%)	60	12.3% (−27.3%, 56.4%)
Week 148	38	28.9% (−23.2%, 68.9%)	58	1.6% (−19.6%, 51.4%)

IQR, interquartile range; NA, not applicable. [a]Baseline for the Early-Switch DTG + RPV group is the value at Day 1. [b]Late-Switch Baseline (LS Baseline) for the Late-Switch DTG + RPV group is the latest pre-switch value (usually from the Week 48 visit).

Conclusions

- Irrespective of receipt of TDF pre-switch to DTG + RPV, renal function was maintained for SWORD study participants through 148 weeks post-switch, with greater improvement in renal tubular function for those switching off TDF
- The switch to DTG + RPV in suppressed participants, including those with mild renal impairment, did not adversely affect renal function while maintaining suppressive HIV-1 treatment
  - eGFR(cystC) in the few participants with moderate renal impairment remained stable or increased after switch