44LB. PHASE III SWORD 1&2: SWITCH TO DTG+RPV MAINTAINS VIROLOGIC SUPPRESSION THROUGH 48 WKS

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Background:
The requirement for life-long antiretroviral therapy (ART) of HIV infection has highlighted interest in 2-drug regimens (2DR) to minimize cumulative drug exposure. Dolutegravir's (DTG) potency, safety and resistance barrier make it an optimal core agent for 2DR. Rilpivirine's (RPV) safety, tolerability and efficacy in switch regimens make it an ideal potential partner.

Methods:
Two identical open-label, multicenter, global, phase III, non-inferiority studies evaluated the efficacy and safety of switching from a 3 or 4-drug current antiretroviral regimen (CAR) to DTG+RPV once daily in HIV-1-infected adults, with HIV-1 RNA<50c/mL (VL<50c/mL) for at least 12 months and no history of virologic failure. Participants (pts) were randomized 1:1 (stratified by baseline 3rd agent class; age</≥50) to switch immediately to DTG+RPV or continue CAR through Wk48. The primary endpoint was the proportion of pts with plasma VL<50c/mL at Wk48 using the Snapshot algorithm for the ITT exposed (ITTe) population. Non-inferiority of DTG+RPV was assessed using a 8% margin for pooled SWORD-1 and SWORD-2 data and -10% margin for individual studies for the adjusted difference in proportion of pts with VL<50c/mL at Wk48.

Results:
1024 pts were randomized and exposed (DTG+RPV 513; CAR 511), across both studies. Switching to DTG+RPV was non-inferior to continuing CAR at Wk48 for VL<50c/mL in pooled analysis of both the ITTe population [95% vs. 95%; difference: -0.4% (95% CI: -3.1%, 2.3%)] and the per-protocol population [96% vs. 96%; difference: 0.7% (95% CI: -3.3%, 1.8%)]. Efficacy results for SWORD-1 (VL<50c/mL in ITTe [95% vs. 96%; difference: -0.6% (95% CI: -4.3%, 3.0%)]) and SWORD-2 (VL<50c/mL in ITTe [94% vs. 95%; difference: -0.2% (95% CI: -4.2%, 3.8%)]) were comparable. Low rates of snapshot virologic failures (VFs) at Wk48 were observed for both studies (Table 1). One pt on DTG+RPV with protocol defined VF had an NNRTI RAM (K101K/E); no pts had any INI RAMs. More adverse events (AEs) were reported and led to discontinuation in the DTG+RPV arm; no unexpected AEs were identified for either drug.

Conclusion:
A switch to a novel, once daily 2DR of DTG+RPV demonstrated high efficacy and was non-inferior to the continuation of CAR in virologically suppressed HIV-1-infected adults. The safety profiles of both DTG and RPV were consistent with the respective labels. A DTG+RPV 2DR offers the potential for reduction in cumulative ART exposure, without an increased risk of virologic failure.