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### 2541. Steady-state PK of Fixed Dose Dolutegravir+Rilpivirine in Hemodialysis

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**Background.** Fixed dose combination (FDC) dolutegravir (DTG) plus rilpivirine (RPV) is an approved antiretroviral treatment regimen for people with HIV. The steady-state PK of FDC DTG+RPV in those requiring hemodialysis (HD) has not been previously studied.

**Methods.** We performed a single-center, prospective evaluation of the steady-state PK of FDC DTG (50mg)+RPV(25mg) in HIV-negative adults either requiring HD (n=4; 2 men, 2 women) or with normal renal function, defined as CrCl  $\geq$  75mL/min (n=2; 1 man, 1 woman). All participants received DTG+RPV daily for 10-14 days with food before undergoing an intensive 24-hour PK evaluation (performed between dialysis days for those requiring HD). Plasma drug and metabolite concentrations were measured using a validated LC/MS/MS assay method (QTRAP 6500+LC-MS/MS system) with turboelectrospray source operating in both positive (confirmation) and negative (quantification) modes. We did not evaluate dialysis extraction of DTG+RPV. Descriptive PK parameters were calculated.

**Results.** No participant experienced serious or grade 3-4 adverse events; there were no study discontinuations. The 4 HD and 2 normal renal function participants were of similar ages (range, 50-60 vs 53-58 years) and BMI (range, 18.5-28.2 vs 20.3-24.0 kg/m<sup>2</sup>). The Table shows the PK parameters assessed in the study population for circulating plasma DTG, DTG-glucuronide (DTG's primary metabolite), and RPV.

Table. Mean (SD) PK parameters of FDC DTG+RPV in HIV-negative volunteers requiring HD (n=4) and with normal renal function (n=2).

Compound	Study group	Half-life, h	T <sub>max</sub> , h	C <sub>max</sub> , ng/mL	AUC <sub>0-24</sub> , h*ng/mL	C <sub>min</sub> , ng/mL	C <sub>tau</sub> , ng/mL	C <sub>ls</sub> , mL/h
DTG	HD	8.3 (1.8)	2.5 (1.0)	6346 (2592)	78,095 (28,979)	1033 (252)	1259 (447)	742 (377)
	Normal renal function	13.2 (6.4)	5.5 (3.5)	6007 (3829)	67,058 (21,253)	918 (432)	1385 (228)	785 (249)
	Ratio	0.6	0.4	1.1	1.2	1.1	0.9	0.9
DTG-glucuronide	HD	18.2 (9.3)	5.0 (2.4)	2864 (333)	46,891 (12,856)	755 (357)	1234 (689)	
	Normal renal function	10.3 (4.1)	2.5 (0.7)	604 (293)	7528 (1831)	85 (25)	155 (51)	
	Ratio	1.8	2.0	4.7	6.2	8.8	7.9	
RPV	HD	45.7 (40.1)	2.6 (2.9)	109 (50)	1701 (663)	49 (18)	50 (16)	17,672 (10,377)
	Normal renal function	23.9 (10.6)	6.0 (2.8)	98 (60)	1304 (653)	22 (0.3)	38 (23)	21,922 (10,983)
	Ratio	1.9	0.4	1.1	1.3	2.2	1.3	0.8

**Conclusion.** In this study, HD did not lead to clinically appreciable differential exposures to DTG and RPV; the markedly increased exposure to DTG-glucuronide (which is considered inert) in HD suggests increased UGT1A1 activation. All participants maintained exposures throughout the dosing interval greater than the reported IC<sub>90</sub> efficacy values for DTG (64ng/mL) and RPV (12ng/mL). These data suggest no dosing modifications are needed for the FDC DTG+RPV regimen in HD.

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