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Use of Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in kidney transplant recipients living with HIV-1 receiving calcineurin & mTOR inhibitors: a pilot switch study (IMEA 064 KINETIK)

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Background: Management of antiretroviral therapy (ART) in kidney transplant recipients living with HIV (HIV-KTR) has historically been problematic because of nephrotoxicity of some antiretrovirals and drug–drug interactions between immunosuppressants and ART.

Methods: Prospective study to assess the safety and the efficacy of B/FTC/TAF in virologically suppressed (< 50 copies/ml) HIV-KTR with sensitive virus (genotypic susceptibility score [GSS] ≥ 2). Changes in pharmacokinetics of calcineurin & mTOR inhibitors, estimated and measured glomerular filtration rate (eGFR and mGFR), bone mineral density (BMD), serum bone alkaline phosphatase, immunovirological responses, clinical outcomes and HIV treatment satisfaction (questionnaire) were recorded through 48 weeks.

Results: 5 HIV-KTR were enrolled and were receiving 3TC/ABC+RAL (n=4) or RPV+DTG (n=1) before switching to B/FTC/TAF: 2 women, median (IQR) age 58 (48-66) years and BMI 25.0 kg/m^2 (20.6-26.1), 2 with AIDS. At baseline (BL): in median, CD4 count was 312/mm^3 (296-499), time since HIV diagnosis 13.9 years (11.4-29.0), duration on last ART 5.7 years (5.1-8.9), duration of viral suppression 8.5 years (6.6-15.2), time since kidney transplantation 5.9 years (3.3-7.0). In addition to corticosteroids, immunosupressant regimen included calcineurin inhibitors (ciclosporine n=1, mycophenolate mofetil n=3, tacrolimus n=1) and mTOR inhibitors (everolimus n=2). Two subjects had resistance-associated mutations to NRTI or INSTI prior to switch (M184V for 1, N155H for 1). Variations of studied parameters from BL to W48 for the 5 subjects (data from 4 subjects from W30) are presented in Table below.

Time from switch to B/FTC/TAF	D0	W2	W4	W12	W24	W36	W48	*Δ (D0-W48)*
mGFR (iohexol clearance) ml/min/1.73m2 Median (IQR)	46.7 (45.4-52.3)						50,8 (43-55)	*+3,95 (-2,5-6,10)*
***Creatinine-based eGFR (CKD-EPI 2009)* ml/min/1.73m2** Median (IQR)	48 (35-49)	41 (34-42)	43 (32-43)	36 (35-41)	39 (35-49)	40.5 (35-49.5)	40 (33-51)	*-1.5 .0 (-5.0 – 3.0)*
Bone mineral density g/cm^2 Median (IQR)								
Lumbar spine	0,82 (0,754-1,012)						0,79 (0,682-0,976)	*-0,036 (-0,072 - -0,035)*
⇒ ***T-score*** Median (IQR)	-1 (-3,-0.7)						-2,15 (-3.5,-0.5)	-0,3 (-0.45,-0,3)
Hip	0,72 (0,71 - 1,03)						0,70 (0,60 - 1,06)	*-0,01 (-0,03 - 0,01)*
⇒ ***T-score*** Median (IQR)	-0,5 (-2.1,0.2)						-1 (-2.45,0.25)	*-0.1 (-0.15, 0)*
Serum bone alkaline phosphatase μg/L Median (IQR)	19.21 (7.7,30)						14.5 (8.55-24.10)	-2.12 (-2.49, -1.75)
HIV RNA viral load cpml Median (IQR)	20 (20,30)	20 (20,20)	20 (20,20)	20 (20,30)	20 (20,30)	20 (20,25)	25 (20,38)	
CD4 count cells/μL Median (IQR)	312 (296-499)				315 (286-452)		435 (342-562)	*+38.5 (-36.5 – 144.0)*
CD4/CD8 ratio Median (IQR)	1.01 (0.84-1.27)				1.24 (1-1.37)		1.21 (0.61-1.78)	*+0.09 (0.04 – 0.23)*
HIV Treatment Satisfactory Questionnaire* Median (IQR)	18.5 (9.5,27.5)			27 (25.5, 30.5)	33.5 (24,33)	19,5 (15.5, 36)	32 (24, 33)	+ 19.5 (-7, 27)

* A scale ranging from -36 (least satisfied) to +36 (most satisfied); according to the revised HIV Treatment Satisfaction Questionnaire status (*Woodcock & Bradley. Value Health 2006 9:320-33*)

No adjusting dose of single tablet regimen was needed through 48 weeks. Median eGFR decreased from 48 (35-49) at BL to 40 ml/min/1.73m^2 (33-51) at W48 but median mGFR measured (iohexol clearance) was 46.7 (45.4-52.3) at BL and 50.8 ml/min/1.73m2 (43.0 – 55.0) at W48.

Median change in BMD from BL to W48 was -0.036 g/cm^2 (-0.07 to -0.03) at lumbar spine and -0.01 g/cm^2 (-0.03 to 0.01) at the hip.

All patients remained virologically suppressed during the study period. Median change in CD4 count was +38 mm3 (-36 to 144) at 48 weeks.

There was one grade 1 treatment-related adverse event (nightmare). One patient died after intracranial hemorrhage (Week 30) and another developed an autoimmune encephalitis (Week 42), both not related to the treatment.

Conclusions: Switching to B/FTC/TAF in HIV-KTR maintains immuno-virological control through 48 weeks without requiring dose adjustments of calcineurin or mTOR inhibitors. The regimen is well-tolerated, particularly with stable renal function, and results in high satisfaction with the single-tablet regimen.

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