875. Indirect Treatment Comparison of 48-Week Efficacy and Safety of Cabotegravir + Rilpivirine Long-Acting Every 2 Months to Bictegravir/ Emtricitabine/Tenofovir Alafenamide in Suppressed HIV-1 Infected Participants

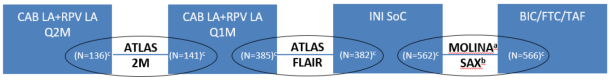
Sonya J. Snedecor, PhD[1]; Melanie Schroeder, MSc[2]; Nicolas Van de Velde, PhD[2]; [1]OPEN Health, Bethesda, MD; [2]ViiV Healthcare, Brentford, UK

Session: P-51. HIV: Treatment

Background. Switching to cabotegravir long-acting + rilpivirine long-acting (CAB LA + RPV LA) administered every month (Q1M) has demonstrated non-inferiority in viral suppression versus a range of standard of care (SoC) antiretroviral regimens, including tenofovir alafenamide based regimens, in two pivotal phase 3 clinical trials (ATLAS [NCT02951052] and FLAIR [NCT02938520]). Furthermore, CAB LA + RPV LA every 2 months (Q2M) has demonstrated non-inferiority in maintaining viral suppression compared with CAB LA + RPV LA Q1M in a phase 3b study (ATLAS-2M [NCT03299049]). As bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) was not widely used at study initiation, the regimen was not present in the SoC arms of ATLAS and FLAIR. The objective was to compare efficacy and safety of CAB LA + RPV LA Q2M to BIC/FTC/TAF using indirect treatment comparison.

Methods. Two switch studies appropriate for facilitating indirect comparison to BIC/FTC/TAF were identified via systematic literature review (Molina et al. 2018 [NCT02603120] and Sax et al. 2020 [NCT03110380]). Indirect comparison using a generalisation of Bucher's methodology to calculate relative risk, odds ratio, and risk differences in efficacy (Week 48 HIV RNA < 50 c/mL and ≥50 c/mL per FDA Snapshot approach and CD4+ cell change from baseline) and safety (discontinuation due to adverse events [AEs] and overall and serious AEs excluding injection site reactions [ISRs]) was conducted. Results for CAB LA + RPV LA Q2M in ATLAS-2M participants with prior integrase inhibitor (INI) exposure, but without prior CAB exposure, were indirectly compared to those with prior INI use in ATLAS and FLAIR via the common CAB LA + RPV LA Q1M comparator and were then indirectly compared to BIC/FTC/TAF via the INI comparator (Figure 1).

Figure 1: Indirect treatment comparison of CAB LA + RPV LA Q2M versus BIC/FTC/TAF



[a]Molina et al. 2018 [NCT02603120]; [b]Sax et al. 2020 [NCT03110380]; [c]participants switching from integrase inhibitor (INI), but without prior CAB exposure.

Results. No statistically significant differences in virologic failure, virologic suppression, CD4+ cell change, discontinuations due to AEs, and non-ISR serious/non-serious AEs were found between CAB LA + RPV LA Q2M and BIC/FTC/TAF (Table 1).

Table 1: Efficacy and safety of CAB LA + RPV LA Q2M compared with BIC/FTC/TAF

	Comparative effect measure (95% CI) CAB LA + RPV LA Q2M vs BIC/FTC/TAF[b] at 48 weeks		
	Relative Risk	Odds Ratio	Risk difference, %
Virologic failure (HIV RNA ≥50 copies)	1.04 (0.09, 12.25)	1.04 (0.08, 12.70)	-0.01 (-3.84, 3.83)
Virologic suppression (HIV RNA <50 copies)	1.04 (0.95, 1.13)	1.52 (0.48, 4.77)	3.41 (-4.56, 11.37)
CD4+ cell change from baseline[a]			20.00 (-43.98, 83.99)
Discontinuation due to AEs	1.48 (0.23, 9.45)	1.48 (0.22, 9.93)	0.1 (-5.2, 5.4)
AEs (excluding ISRs)	1.06 (0.93, 1.21)	1.23 (0.54, 2.84)	4.54 (-6.34, 15.42)
Serious AEs (excluding ISRs)	4.13 (0.94, 18.06)	4.39 (0.94, 20.40)	5.84 (-0.77, 12.45)

[a] Mean difference, cells/µl; AE, adverse event; CI, confidence interval; ISR, injection site reaction

Conclusion. Indirect treatment comparison indicated efficacy and safety of CAB LA + RPV LA Q2M is not different from BIC/FTC/TAF. These regimens will be further compared in a randomized head-to-head non-inferiority trial (SOLAR, NCT04542070).

Disclosures. **Sonya J. Snedecor, PhD**, **ViiV Healthcare** (Other Financial or Material Support, Author's employer, OPEN Health received funding to execute this study) **Melanie Schroeder, MSc**, **ViiV Healthcare** (Employee) **Nicolas Van de Velde, PhD**, **ViiV Healthcare** (Employee)

876. Renal Function, Lipid Profile, and Cardiovascular Events After Switching to Abacavir Containing Regimen in Antiretroviral-Therapy-Experienced People Living with HIV in Northern Thailand

Pitchaporn Phudphong, MD[1]; Quanhathai Kaewpoowat, MD[2]; Vuddhidej Ophascharoensuk, MD[3]; Saowaluck Yasri, Master of Science (Applied Statistic)[2]; [1]Department of Internal medicine, Faculty of medicine, Chiang Mai university, Thailand, muang, Chiang Mai, Thailand; [2]Faculty of Medicine, Chiang Mai University, Thailand, Iowa City, Iowa; [3]Department of internal medicine, faculty of medicine, Chiang Mai university, Thailand, Muang, Chiang Mai, Thailand

Session: P-51. HIV: Treatment

Background. Abacavir (ABC) is commonly used as part of antiretroviral therapy (ART) regimen for people living with HIV (PLWH) with renal dysfunction in resource limiting countries. While the renal function changes and association with cardiovascular (CV) events have been well described in developed countries, these information is limited in Asian population. Herein, this study aims to describe the changes in renal function, lipid profile and CV events after ABC switching in ART-experienced PLWH in Northern Thailand.

Methods. This retrospective chart-review study was conducted among adults ART-experienced PLWH (≥18 years old) who received ABC-containing regimen during January 2016 to December 2018 at Maharaj Nakorn Chiang Mai Hospital. Demographic data, HIV-related treatments, creatinine, lipid profile and CV events were collected. Patients were categorized into early switching group and late switching group (CrCl≥50 ml/min and CrCl< 50 ml/min before switching to ABC). The change of CrCl, urinalysis profiles, lipid profiles, CD4, viral load, and cardiovascular events at 12 months after ABC initiation were assessed.

Results. Total of 115 participants were enrolled with mean age of 55.2±10.7 years and 63.5% were male. Of those, 87.8% of patients had received Tenofovir disoproxil fumarate (TDF) prior to ABC. Mean of CrCl at baseline was 47.6±16.8 ml/min and at 12th month was 49.56±19.42 ml/min with mean difference of 3.7 ml/min (95%CI 1.6-5.8, P< 0.001). The improvement of CrCl at 12 months in early switching group was statistically significant compared to late switching. Other two associated factors with improved CrCl after switching to ABC were duration of TDF exposure during CrCl< 60 ml/min (OR 9.26, P 0.004) and history of protease inhibitors (PIs) exposure (OR 0.06, P 0.03). No significant changed in lipid profile, CD4 and virological outcome overtime. There were only 2 CV events observed (9.3:1000 person-year, 95%CI 2.3-37.1).

Table 1 Baseline Characteristic of 115 Study Patients

Characteristics	N=115 (%)
Baseline demographic data (at the time of switching to ABC)	
Age (years, mean ± SD)	55.2 ± 10.7
Male	73 (64)
Weight (kg, mean ± SD)	59.8 ± 12.2
Height (cm, mean ± SD)	162.7 ± 8.4
Body mass index (kg/m^2, mean ± SD)	22.5 ± 3.7
Co-morbidities	
Hypertension	66 (57)
Diabetes mellitus	34 (30)
Dyslipidemia	64 (56)
Hepatitis B infection	7 (6)
Hepatitis C infection	4 (3)
Chronic kidney disease	54 (46.9)
HIV History	
Previous AIDS-defining illness	58 (50)
CD4 at the time of HIV diagnosis (cell/mm^3, median (IQR))	202.5 (112-411)
CD4 before switching to ABC (cell/mm^3, median (IQR))	501 (367-670)
History of drug resistant HIV, number	6 (5)
Kidney function (CrCl)	
Baseline CrCl at the time of HIV diagnosis (mL/min, mean ± SD)	62.8 ± 22.8
CrCl before switching to ABC (ml/min, mean ± SD)	47.6 ± 16.8
Switching reasons from others NRTIs to ABC	
Renal impairment	95 (83)
Fanconi syndrome	15 (13)
Others	5 (4)
NRTIs before switching to ABC	
Tenofovir disoproxil fumarate	101 (88)
Stavudine	74 (64)
Zidovudine	61 (53)
TDF exposure (days, median, IQR)	
Duration of TDF exposure (days, median (IQR))	1981, 1187.5-2782.0
Duration of TDF usage while CrCl < 60 ml/min (n=97) (days, median (IQR))	287, 98-713
Exposure to other ART associated with renal dysfunction (lifetime)	
Lopinavir/ritonavir (LPV/r)	21 (18)
Indinavir/ritonavir (IDV/r)	2 (2)
Darunavir/ritonavir	2 (2)
History of exposure to nephrotoxic drugs within 6 months prior to ABC initiation	8 (7)
Cardiovascular Risk	
Thai CV risk score (median, IQR)	4.4, 2.8-8.3
History of smoking	3 (3)
Statin use	64 (56)

ABC; Abacavir, NRTIs; Nucleoside reverse transcriptase inhibitors, ART; Anti-retroviral therapy

Table 2 Univariable and Multivariable Factors associated with Renal Function Improvement (CrCl ≥60 ml/min) at 12 months after ABC Initiation

Factors	Univariate analysis			Multivariate analysis		
	Odd ratio	95% CI	P-value	Odd ratio	95% CI	P-value
Age <60 years	6.9	(1.92, 27.74)	0.003	4.26	(0.45, 39.62)	0.202
Male	1.2	(0.5, 2.8)	0.734	0.39	(0.07, 2.08)	0.271
BMI ≥23 kg/m^2	2.2	(0.9, 5.2)	0.073	1.13	(0.19, 6.64)	0.89
Previous AIDS-defining illness						
Pneumocystis pneumonia	1.9	(0.6, 5.8)	0.283			
Tuberculosis	0.8	(0.3, 2.5)	0.716			
Talaromycosis	1.5	(0.4, 5.6)	0.533			
Cyptococcosis	2.7	(0.5, 14.2)	0.240			
Herpes infections	2.64	(0.35, 19.67)	0.343			
Co-morbidities						
Hypertension	0.4	(0.2, 1)	0.044	0.69	(0.15, 3.12)	0.631
Diabetes mellitus	0.3	(0.1, 1)	0.049	0.16	(0.02, 1.21)	0.077
Dyslipidemia	0.6	(0.3, 1.4)	0.244			
Hepatitis B infection	0.6	(0.3, 1.4)	0.244			
Duration of TDF exposure <6 years	1.7	(0.68, 4.24)	0.255	1.03	(0.22, 4.68)	0.968
Duration of TDF usage after detected CrCl <60 ml/min for <6 months	7.42	(2.56, 21.55)	<0.001	9.26	(2.07, 41.37)	0.004
Exposure to nephrotoxic agents within 6 months before ABC initiation	0.3	(0, 2.9)	0.323	0.56	(0.03, 8.86)	0.686
Exposure to NRTIs before ABC initiation						
Lamivudine (3TC)	0.4	(0, 6.4)	0.507			
Emtricitabine (FTC)	0.7	(0.2, 2.5)	0.634			
Tenofovir (TDF)	1.4	(0.3, 5.3)	0.656			
Stavudine (d4T)	0.6	(0.2, 1.4)	0.203			
Zidovudine (AZT, ADV)	1.1	(0.5, 2.7)	0.757			
Didanosine (ddI)	0.8	(0.1, 8.4)	0.881			
Exposure to NNRTIs before ABC initiation						
Efavarenz (EFV)	2.8	(1.1, 7.3)	0.035	1.89	(0.28, 12.55)	0.507
Nevirapine (NVP)	0.7	(0.3, 1.7)	0.411			
Rilpivirine (RPV)	1.5	(0.5, 4.9)	0.511			
Exposure to PIs before ABC initiation				0.06	(0.01, 0.76)	0.03
Lopinavir/ritonavir (LPV/r)	0.1	(0, 0.9)	0.044			
Indinavir/ritonavir (IDV/r)	2.6	(0.2, 42.7)	0.507			
Baseline CrCl ≥50 ml/min before ABC initiation	11.5	(3.9, 33.9)	<0.001	4.48	(0.7, 28.56)	0.112

CI; Confident interval, BMI; Body mass index, HSV; Herpes infection, TDF; Tenofovir disoproxil fumarate, ABC; Abacavir, NRTIs: Nucleoside reverse transcriptase inhibitors, NNRTIs: Non-nucleoside reverse transcriptase inhibitors

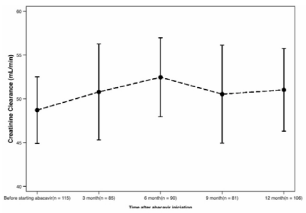


Figure 1 CrCl (Mean ± SD)

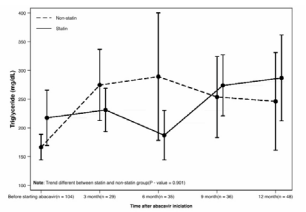


Figure 2 Triglyceride (Mean ± SD)

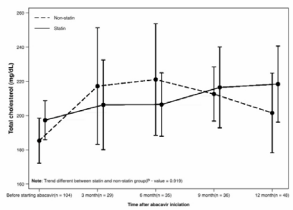


Figure 3 Total cholesterol (Mean ± SD)

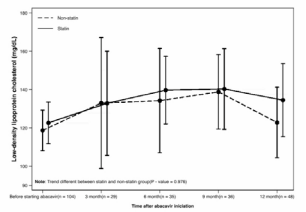


Figure 4 LDL (Mean ± SD)

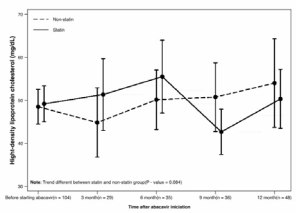


Figure 5 HDL (Mean ± SD)

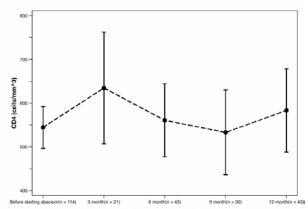


Figure 6 CD4 (Median, IQR)

Figure. (1) Creatinine clearance (ml/min) during follow up period. (2) Triglyceride (mg/dl) during follow-up period. (3) Total cholesterol (mg/dl) during follow up period. (4) LDL (mg/dl) during follow up period. (5) HDL (mg/dl) during follow up period. (6) CD4 (cells/mm^3) during follow up period

Conclusion. ABC used in Thai ART-experienced PLWH appeared to be effective with low CV event in the first year. Despite the statistically significant in the change of CrCl after ABC switching, the change was subtle and need further evaluation.

Disclosures. **All Authors**: No reported disclosures

877. North American Phase 3/3b Experience with Long-Acting Cabotegravir and Rilpivirine: Efficacy, Safety, and Virologic Outcomes

Babafemi O. Taiwo, MBBS[1]; Darrell Tan, MD PhD[2]; Parul Patel, PharmD[3]; Paula Teichner, PharmD[3]; Joseph Polli, PhD, FAAPS[3]; Louise Garside, PhD[4]; Ronald D'Amico, DO, MSc[3]; Christine L. Talarico, M.S.[3]; Rodica Van Solingen-Ristea, MD[5]; Bryan Baugh, MD[5]; William Spreen, PharmD[3]; Michael Aboud, MBChB, MRCP[3]; Matthew Bosse, DO[3]; [1]Northwestern University, Chicago, IL; [2]Division of Infectious Diseases, Department of Medicine, St. Michael's Hospital, Toronto, Ontario, Canada; [3]ViiV Healthcare, Research Triangle Park, NC; [4]GlaxoSmithKline, London, England, United Kingdom; [5]Janssen Research & Development, LLC, Beerse, Antwerpen, Belgium

Session: P-51. HIV: Treatment

Background. Cabotegravir (CAB) plus rilpivirine (RPV) is the first complete long-acting (LA) regimen recommended by treatment guidelines for the maintenance of HIV-1 virologic suppression. CAB+RPV LA dosed every 4 weeks (Q4W) or every 8 weeks (Q8W) demonstrated noninferior efficacy in multinational Phase 3/3b trials. This *post hoc* descriptive analysis summarizes efficacy, virologic outcomes, safety, and treatment preference for US and Canadian (CAN) participants through Week (W) 48.

Methods. This analysis focuses on data for US/CAN participants naive to CAB+RPV (n=376) from the larger pooled population of the ATLAS, FLAIR, and ATLAS-2M Phase 3/3b studies (N=1245). Endpoints included the proportion of participants with plasma HIV-1 RNA ≥ 50 and < 50 c/mL at W48 (FDA Snapshot algorithm), incidence of confirmed virologic failure (CVF; 2 consecutive HIV-1 RNA ≥ 200 c/mL), safety, and treatment preference through W48.

Results. 376 US/CAN participants received CAB+RPV LA Q4W or Q8W. Median (range) age was 39y (20–74); 14.9% were female, 66.0% were White. At W48, 93.1% (350/376) maintained virologic suppression (HIV-1 RNA < 50 c/mL), 1.9% (7/376) had HIV-1 RNA ≥ 50 c/mL, and 0.8% (3/376) met the CVF criterion, consistent with the overall global pooled population (Table 1). Two of the three participants with CVF had ≥ 2 of the three baseline factors (archived RPV resistance-associated mutations [RAMs], HIV subtype A6/A1, body mass index [BMI] ≥ 30 kg/m^2) previously associated with CVF. Among the US/CAN participants with a single baseline factor, none met CVF. Overall, archived RPV RAMs were observed in 3.2% (12/376), HIV subtype A6/A1 in 1.1% (4/376), and BMI ≥ 30 kg/m^2 in 26.3% (99/376) of participants. Safety and injection site reaction findings were similar to the overall pooled population (Table 2). Most participants (120/134, 89.6%) preferred LA over oral dosing (7/134, 5.2%).

Table 1. Snapshot outcomes following CAB+RPV LA Q4W and Q8W at Week 48 in participants naive to CAB+RPV from ATLAS, FLAIR, and ATLAS-2M (ITT-E population)

	US/CAN Q4W + Q8W (n=376)	Overall pooled Q4W + Q8W (N=1245)
HIV-1 RNA <50 c/mL, n (%)	350 (93.1)	1156 (92.9)
HIV-1 RNA ≥50 c/mL, n (%)	7 (1.9)	21 (1.7)
Data in window not below threshold	4 (1.1)	6 (0.5)
Discontinued for lack of efficacy*	3 (0.8)	13 (1.0)
Discontinued for other reason while not below threshold	0	2 (0.2)
No virologic data, n (%)	19 (5.1)	68 (5.5)
Discontinued study due to AE or death	9 (2.4)	36 (2.9)
Discontinued study for other reason	10 (2.7)	32 (2.6)
On study but missing data in window	0	0

AE, adverse event; CAB, cabotegravir; CVF, confirmed virologic failure; ITT-E, intention-to-treat exposed; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine; US/CAN, United States and Canada.

* Participants meeting the CVF criterion.

Table 2. Safety summary through Week 48 following CAB+RPV LA Q4W and Q8W or comparator ART in participants naive to CAB+RPV from ATLAS, FLAIR, and ATLAS-2M

Parameter, n (%)	US/CAN Q4W + Q8W (n=376)	US/CAN CAR (n=165)	Overall pooled Q4W + Q8W (n=1245)	Overall pooled CAR (n=591)
Any AE	351 (93)	114 (69)	1172 (94)	444 (75)
Excluding ISRs	307 (82)	114 (69)	1035 (83)	444 (75)
Any Grade ≥3 AE	37 (10)	13 (8)	119 (10)	35 (6)
Excluding ISRs	19 (5)	13 (8)	78 (6)	35 (6)
Any drug-related AE	301 (80)	5 (3)	1035 (83)	35 (6)
Excluding ISRs	82 (22)	5 (3)	335 (27)	35 (6)
Any Grade ≥3 drug-related AE	22 (6)	1 (<1)	58 (5)	1 (<1)
Excluding ISRs	2 (<1)	1 (<1)	14 (1)	1 (<1)
AE leading to withdrawal	9 (2)	4 (2)	42 (3)	9 (2)
Any SAE	9 (2)	10 (6)	51 (4)	25 (4)
Drug related	0	1 (<1)	3 (<1)	1 (<1)
Any fatal SAE	0	1 (<1)	0	1 (<1)
Drug related	0	0	0	0

AE, adverse event; ART, antiretroviral therapy; CAB, cabotegravir; CAR, current antiretroviral therapy; ISR, injection site reaction; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine; SAE, serious adverse event; US/CAN, United States and Canada.