

Table 1b. Therapeutic Drug Monitoring of CAZ-AVI concentrations in CSF and Human Plasma (HP) pertaining to patient 2 and 3

Cerebrospinal fluid (CSF)							
Patient ID	Ceftazidime-avibactam (2g/0.5g) dosing time	Sample Collection Time	Time elapsed since last dose (h)	Time relative to 2nd dosing (h)	Ceftazidime (µg/ml) in CSF	Avibactam sodium (µg/ml) detected in CSF	Avibactam (µg/ml) in CSF
Patient 2	03 Feb 2021 at 23:52	04 Feb 2021, 10:00	10.1	-2.0	26.3	1.72	1.59
		04 Feb 2021, 11:50	12 *	-0.2*	29.1	1.54	1.42
		04 Feb 2021, 14:05	14.2	2.1	21.0	1.62	1.50
		04 Feb 2021, 16:15	16.1	4.3	26.7	2.44	2.25
			Time elapsed since last dose (h)	Time relative to 2nd dosing (h)			
Patient 3	04 Feb 2021, 1st dosing at 0:24	04 Feb 2021, 10:10	9.8	0.2	23.0	3.98	3.79
		04 Feb 2021, 12:00	11.4	2.0	35.1	1.90	0.92
		04 Feb 2021, 13:55	13.3	3.9	39.3	1.50	1.48
		04 Feb 2021, 16:10	15.6	6.2	35.0	1.47	1.36
			After 1st dosing time (h)	Time relative to 2nd dosing (h)			
Human plasma (HP)							
Patient ID	Ceftazidime-avibactam (2g/0.5g) dosing time	Collection Time	After 1st dosing time (h)	Time relative to 2nd dosing (h)	Ceftazidime (µg/ml) in HP	Avibactam sodium (µg/ml) detected in HP	Avibactam (µg/ml) in HP
Patient 2	03 Feb 2021 at 23:52 (2g/0.5g)	04 Feb 2021, 10:00	10.1	-2.0	112	5.52	5.10
		04 Feb 2021, 11:50	12	-0.2	91.8	4.24	3.91
		04 Feb 2021, 14:05	14.2	2.1	69.8	1.19	1.10
		04 Feb 2021, 16:15	16.1	4.3	202	17.5	16.2
			After 1st dosing time (h)	Time relative to 2nd dosing (h)			
Patient 3	04 Feb 2021, 1st dosing at 0:24	04 Feb 2021, 10:10	9.8	0.2	56.6	5.14	4.75
		04 Feb 2021, 12:00	11.4	2.0	53.8	3.45	3.19
		04 Feb 2021, 13:55	13.3	3.9	110	14.0	12.9
		04 Feb 2021, 16:10	15.6	6.2	84.8	7.22	6.67

Conclusion. Measuring CZA concentration levels in CSF was achieved in 3 patients with complicated CNS infections. Post-infusion concentrations indicated that adequate CAZ and AVI exposures were attained in the CSF. Notably, avibactam was shown to achieve concentrations ≥ 1 µg/ml in the CSF throughout the dosing interval. For avibactam and ceftazidime, the PK/PD target correlated with bacterial killing is $\sim 50\%$ fT $>$ MIC. In 2 out of 3 patients, concentrations were determined to be above the respective MICs throughout the entire dosing interval in the CSF. All patients attained clinical and microbiological cure. A novel CZA TDM method was successfully employed to establish that CZA maintains therapeutic CSF concentrations that exceed the MIC throughout the dosing interval.

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67. Agreement Among Bayesian Dosing Software for Calculating Vancomycin Area Under the Curve

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Session: O-14. Have We Peaked? Updates in PK/PD

This abstract has been withdrawn.

68. Comparison of Cardiovascular Risk Assessment Calculators in the US Military HIV Natural History Study

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Session: O-15. HIV Co-infections and Co-morbidities

Background. People living with HIV (PLHIV) have increased risk of cardiovascular disease (CVD), however CVD risk assessment can be challenging as HIV-related factors are not included in most calculators. We compared CVD risk calculators in US Military HIV Natural History Study (NHS) participants.

Methods. The NHS database was screened for participants enrolled between 2009-2019 who were ≥ 40 years of age with no previous history of CVD or statin use. Of the 399 participants meeting criteria, 385 (96.5%) had available data to assess 3 CVD risk calculators: Atherosclerotic CVD risk calculator (ASCVD), Framingham Risk Calculator (FRC), and the Data Collection on Adverse Effects of Anti-HIV Drugs Study (DAD) risk calculator. Risk calculators were applied cross-sectionally at the first available time point at or after age 40 years and calculators were compared using a Wilcoxon signed rank test. Demographic and HIV-related characteristics were analyzed as independent variables.

Results. Participants were predominantly male (91.1%), mostly White (49.6%) or Black/African American (44.7%), and commonly had a history of tobacco use (38.9%).

The mean age at HIV diagnosis and at CVD risk calculation was 33 and 41.8 years, respectively (Table 1). Overall, there was significant variability between calculators with mean scores of 3.66%, 2.50% and 1.38% for ASCVD, FRC, and DAD, respectively for all pairwise comparisons ($p < 0.001$; Table 2). When assessing those with CVD risk $\geq 7.5\%$, a clinically relevant threshold, the proportion of individuals with risk $\geq 7.5\%$ varied for the ASCVD (10.4%), FRC (7.5%), and DAD ($< 0.8\%$) calculators. Associations or trends toward higher CVD risk was observed among the various calculators for race/ethnicity and both age < 30 years and CD4 ≤ 350 cells/uL at HIV diagnosis (Table 2).

Characteristic	N (%) or Mean (±SD)
Mean age at HIV diagnosis	33 (±7.97)
<30 years	238 (61.8)
≥ 30 years	147 (38.2)
Race/ethnicity	
White	191 (49.6)
Black/African American	172 (44.7)
Other	22 (5.7)
Mean CD4 count at HIV diagnosis (cells/uL)	494 (±261)
≤ 350 cells/uL	102 (25.9)
> 350 cells/uL	237 (61.6)
Missing	46 (11.9)
Mean CD4 count at nadir (cells/uL)	301 (±170)
≤ 350 cells/uL	260 (67.5)
> 350 cells/uL	125 (32.5)
Mean time from HIV diagnosis to first HAART	3.1 (±4.23)
<3.1 years	247 (65.9)
≥ 3.1 years	128 (34.1)
Age at calculator application	42 (±4.18)
Ever Smoker	150 (38.9)
Current smoker	65 (16.8)
HAART, highly active antiretroviral therapy	

Characteristics	ASCVD	FRC	DAD	P-values		
				ASCVD vs. FRC	ASCVD vs. DAD	FRC vs. DAD
All participants	3.66%	2.50%	1.38%	<0.001	<0.001	<0.001
Age at HIV diagnosis						
<30 years	3.90%	2.94%	1.47%	<0.001	<0.001	<0.001
≥ 30 years	3.29%	1.80%	1.23%	<0.001	<0.001	0.001
P-value	0.079	<0.001	0.078			
Race/ethnicity						
White	2.74%	2.81%	1.50%	0.170	<0.001	<0.001
Black/African American	4.73%	2.03%	1.18%	<0.001	<0.001	<0.001
Other	3.31%	3.55%	1.92%	0.667	<0.001	0.001
P-value	<0.001	0.010	0.029			
CD4 count at HIV diagnosis						
≤ 350 cells/uL	3.95%	2.62%	1.42%	<0.001	<0.001	<0.001
> 350 cells/uL	3.37%	2.28%	1.18%	<0.001	<0.001	<0.001
Missing	4.53%	3.41%	2.28%	0.032	<0.001	0.003
P-value	0.072	0.057	<0.001			
CD4 count at nadir						
≤ 350 cells/uL	3.69%	2.53%	1.41%	<0.001	<0.001	<0.001
> 350 cells/uL	3.60%	2.45%	1.32%	<0.001	<0.001	<0.001
P-value	0.818	0.795	0.584			
Time from HIV diagnosis to first HAART						
<3.1 years	3.47%	2.47%	1.34%	<0.001	<0.001	<0.001
≥ 3.1 years	4.11%	2.57%	1.48%	<0.001	<0.001	<0.001
P-value	0.093	0.756	0.438			

CVD, cardiovascular disease; ASCVD, Atherosclerotic CVD risk calculator; FRC, Framingham Risk Calculator; DAD, Data Collection on Adverse Effects of Anti-HIV Drugs Study (DAD) risk calculator; HAART, highly active antiretroviral therapy

Conclusion. Since significant variability among CVD risk calculators was observed in the NHS cohort, it may be challenging to apply overall CVD risk calculators in a clinically relevant manner. HIV-related factors, such as duration of HIV infection and CD4 nadir, are not accounted for in CVD calculators and may be indicators of increased CVD risk. Future studies are warranted in order to determine the optimal clinical use of CVD risk calculators for PLHIV.

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