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 at 12:00 | 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 | 1.94 | 1.79 |
| | 2nd dosing at 10:00 | 04 Feb 2021, 12:00 | 11.4 | 2.0 | 15.1 | 1.00 | 0.92 |
| | | 04 Feb 2021, 13:55 | 13.3 | 3.9 | 19.3 | 1.60 | 1.48 |
| | | 04 Feb 2021, 16:10 | 15.6 | 6.2 | 15.0 | 1.47 | 1.36 |

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 at 12:00 (2g/0.5g) | 04 Feb 2021, 14:05 | 14.2 | 2.1 | 634 | 119 | 110 |
| | | 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 doing at 0:24 | 04 Feb 2021, 10:10 | 9.8 | 0.2 | 56.6 | 5.14 | 4.75 |
| | 2nd dosing at 10:00 | 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 ~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.

***Disclosures.*** **Robert A. Bonomo, MD, entasis** (Research Grant or Support)**Merck** (Grant/Research Support)**NIH** (Grant/Research Support)**VA Merit Award** (Grant/Research Support)**VenatoRx** (Grant/Research Support)

### 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 ≥ 7.5%, a clinically relevant threshold, the proportion of individuals with risk ≥ 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).

| Table 1: Characteristics of NHS Participants | |
|---|---|
| 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 | |

Table 2: Comparison of CVD Risk Calculators

| Characteristics | ASCVD | FRC | DAD | P-values ASCVD vs.FRC | P-values ASCVD vs. DAD | P-values 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.

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