SUPPLEMENTAL DIGITAL CONTENT

METHODS

Subjects and study design

In the ZDV arm, six healthy volunteers received a 20 µCi (approximately 100 µg) dose of ^{14}C-ZDV alone in 30 mL water, followed one month later by an oral dose of 300 mg unlabeled ZDV (Retrovir®) elixir spiked with 20 µCi (100µg) of ^{14}C-labeled ZDV (Moravek Biochemicals, Inc., Brea, CA). In the TDF arm, six healthy volunteers received a 20 µCi (approximately 100 µg) dose of ^{14}C-TDF alone in 30 mL water, followed one month later by 20 microcuries of ^{14}C-TDF in combination with a single oral dose of 300mg of TDF in 30 mL water. Subjects were fasted overnight except for water and remained fasting until after the 2 hour blood collection the next day. The 300 mg of ZDV was in solution (commercially available suspension, prepared by the Johns Hopkins Hospital Investigational Drug Service). The ^{14}C-labeled ZDV was mixed into the oral solution immediately before administration. The unlabeled 300 mg dose of TDF was administered as an oral solution (crushed tablet mixed with 30 mL of distilled water). The ^{14}C-labeled TDF was mixed into the oral solution immediately before administration. The initial oral solution was followed by 120 mL of distilled water.

AMS analysis

AMS analyses were conducted at the MIT BEAMS Lab using procedures described elsewhere in detail [34]. Sample aliquots (1.50 µL) were applied directly to a CuO matrix, and introduced into a laser-induced combustion interface for

subsequent AMS analysis. Each run contained two quantitation standards ([^{14}C-methyl] bovine serum albumin, 3 dpm/mL), followed by two blanks (1 mg/mL human serum albumin), 10 samples and another two standards. Quantitation was performed by integrating peaks produced in the continuous trace of ^{14}C detector count rate versus time generated during operation of the combustion interface, which produces and delivers the CO_2 of combustion to the AMS ion source, and taking the product of the sample/standard peak area ratio multiplied by the standard concentration as the concentration of the sample. The purpose of the blank was to test for “memory” in the ion source cathode, which occurs to a variable extent; detection of ^{14}C when analyzing a blank is not an indication that the blank contains detectable ^{14}C. Cathodes exhibiting “memory” as determined by a response to a blank indicates that subsequent test samples will analyze high by a comparable amount. Thus, whenever the albumin blank produced a peak capable of being integrated, the area of this peak was subtracted from the area of the following sample peaks.