**Table 2: Laboratory values (mean ± SD) of the 20 patients at each time point and corresponding one-way Anova *P* values across all time points.**

| | Pre-FLT | Immediate <5 h | 5 – 24 Hours | 1 – 7 days | > 1 week | *P* |
|---|---|---|---|---|---|---|
| **Sodium (mEq/L ± SD)** | 139.4 ± 1.5 | 138.2 ± 2.1 | 138.3 ± 2.0 | 137.5 ± 1.8 | 138.1 ± 2.3 | 0.064 |
| **Potassium (mEq/L ± SD)** | 4.2 ± 0.5 | 4.2 ± 0.4 | 4.1 ± 0.4 | 4.2 ± 0.3 | 4.2 ± 0.4 | 0.968 |
| **Chloride (mEq/L ± SD)** | 102.3 ± 3.3 | 104.2 ± 3.7 | 104 ± 3.8 | 102.3 ± 2.4 | 101.2 ± 3.1 | 0.055 |
| **Glucose (mg/dL ± SD)** | 95.1 ± 14.8 | 96.6 ± 20.7 | 98.5 ± 23.1 | 105.4 ± 17.7 | 109.5 ± 14.6 | 0.175 |
| **Creatinine (mg/dL ± SD)** | 0.885 ± 0.198 | 0.882 ± 0.207 | 0.881 ± 0.180 | 0.910 ± 0.190 | 0.844 ± 0.217 | 0.949 |
| **BUN (mg/dL ± SD)** | 15.8 ± 5.0 | 15.1 ± 5.6 | 15.2 ± 6.3 | 14.3 ± 5.2 | 15.3 ± 5.7 | 0.959 |
| **SGOT (U/L ± SD)** | 20.8 ± 5.0 | 22.0 ± 5.1 | 22.0 ± 5.3 | 22.2 ± 11.4 | 21.8 ± 6.7 | 0.973 |
| **SGPT (U/L ± SD)** | 18.7 ± 6.7 | 18.5 ± 6.6 | 19.1 ± 6.5 | 17.6 ± 5.3 | 17.2 ± 6.5 | 0.978 |
| **Albumin (g/dL ± SD)** | 3.9 ± 0.5 | 3.5 ± 0.4 | 3.44 ± 0.3 | 3.1 ± 0.6 | 3.2 ± 0.8 | 0.003 |
| **Alk Phos (U/L ± SD)** | 73.8 ± 19.4 | 61.1 ± 14.7 | 58.3 ± 17.0 | 59.5 ± 22.7 | | 0.081 |
| **Bilirubin (mg/dL ± SD)** | 0.647 ± 0.181 | 0.573 ± 0.246 | 0.581 ± 0.263 | 0.621 ± 0.286 | 0.752 ± 0.418 | 0.714 |
| **RBC (x10$^6$/μL ± SD)** | 4.5 ± 0.4 | 4.3 ± 0.5 | 4.2 ± 0.5 | 3.8 ± 0.3 | 3.7 ± 0.4 | <0.0001 |
| **Hematocrit (% ± SD)** | 40.9 ± 3.1 | 39.1 ± 4.4 | 38.4 ± 4.0 | 35.2 ± 3.4 | 35.0 ± 3.4 | <0.0001 |
| **WBC (x10$^3$/μL ± SD)** | 7.6 ± 2.1 | 7.7 ± 3.4 | 7.9 ± 3.3 | 9.5 ± 2.8 | 9.0 ± 3.2 | 0.262 |
| **Platelets (x10$^3$/μL ± SD)** | 278.1 ± 96.8 | 259.1 ± 103.1 | 255.9 ± 103.0 | 230.1 ± 76.7 | 233.5 ± 69.5 | 0.674 |

asymptomatic HIV-positive patients treated with FLT over a period of 16 weeks. These patients received a de-escalating oral dose of FLT starting from 0.125 mg/Kg ($AUC_{12}$ ~ 417 ng*h/mL) every 12 hours to reach a target area under the curve of 300 ng*h/mL for a 12 hour dosing interval [17]. Serious grade III hematologic toxicity (anemia and leukopenia) was observed with concentrations greater than 300 ng*h/mL. Grade II+ anemia was observed within 4 weeks with a concentration of 300 ng*h/mL. Subsequently, a randomized, double-blind phase I/II trial was designed to characterize FLT pharmacokinetics, antiviral activity, and toxicity. Forty-eight patients were randomized into 3 groups with different target areas of FLT concentration (50 ng*h/mL, 100 ng*h/mL, or 200 ng*h/mL) for up to 16 weeks of treatment. Grade II+ anemia developed at doses greater than 100 ng*h/mL, granulocytopenia at doses greater than 200 ng*h/mL, and mild peripheral neuropathy within 40 days at any dose. The bone marrow toxicity was reversible when the drug was discontinued. This type of toxicity was not seen with reduced FLT doses. However, this phase I/II trial was suspended because two patients died from acute hepatic failure after 12 weeks of therapy, one in Flexner's study at $AUC_{12}$ of 200 ng*h/mL, the other from a European trial using a 10 mg/day regimen. Therefore, the FLT toxicology data reported for human therapeutic use shows the lowest toxicity regimen tested to be 50 ng*h/mL for a 12 hour dosing interval which led to only mild peripheral neuropathy within a mean of 40 days of therapy [17]. Therefore, in addition to discussing our toxicology data for a single radiotracer dose of $^{18}$F-FLT, we will compare this dose level to the multiple larger doses used in this lowest toxicity clinical regimen.

We evaluated the toxicity of $^{18}$F-FLT in a series of 20 patients who underwent $^{18}$F-FLT PET imaging. We took two different approaches to this evaluation: first, a direct laboratory measure of electrolytes, hepatic, metabolic, and renal function of these patients; second, a comparison of the maximal amount of FLT compound injected for a $^{18}$F-FLT PET study to the therapeutic dose shown to be the least toxic in clinical trials. To this end, $AUC_{12}$ values for our study patients were calculated from both imaging-derived TACs and actual blood samples.

No change was found in the renal function (BUN and creatinine levels) of the 20 patients studied or in the following hepatic function measures: AST, ALT, alkaline phosphatase, and total bilirubin. As described in the results section, decreases in the patients' average hematocrit, RBC and hemoglobin levels were observed. One of the challenges of this study is that it was designed as a companion analysis to a primary imaging study performed in potentially resectable NSCLC. As a result, seventeen of 20 (85%) patients studied underwent surgical staging (mediastinoscopy and/or video assisted thoracoscopy) with 14/20 also undergoing a tumor resection procedure, at the same time as the mediastinoscopy, under general anaesthesia after $^{18}$F-FLT PET. Thirteen of the 14 (93%) had resection within 1 week of the $^{18}$F-FLT PET study, 7 of these were the day after the $^{18}$F-FLT PET study. Because surgery involves blood loss and metabolic stress, hematological values were consequently affected and a long-term relationship between the $^{18}$F-FLT PET study and hematological values is difficult to establish. Nonetheless, when we only consider pre-surgical lab values and all lab values for patients who did not undergo any surgical procedure, analysis of the data reveals a single small early drop in hemoglobin, hematocrit and RBC. This suggests that the additional drop observed in these parameters at later time points for the whole population is due to surgical blood loss. The initial decrease in hemoglobin, hema-