AbstractID: 13189 Title: Assessment of normal tissue response to therapy using FLT PET

Purpose: In treatment of disease, dosing of drugs is often limited by normal tissue toxicities. The feasibility of [^{18}F]-fluoro-3'-deoxy-3'-L-fluorothymidine (FLT) PET to assess changes in normal tissue physiology over the course of therapy was investigated.

Methods: Sixteen cancer patients representing a variety of disease pathologies received sunitinib, a multi-targeted receptor tyrosine kinase inhibitor with anti-angiogenic and anti-proliferative effects. Doses of 50mg/kg/day were administered in two schemes: Cohort A (n = 8) used a 4/2 (four weeks on/two weeks off) schedule; Cohort B (n = 6) used a 2/1 schedule. FLT-PET images were acquired at baseline, peak drug exposure, and the end of the first planned treatment break. Regions of interest in liver, spleen, and marrow were segmented, and the mean standardized uptake value (SUV_{mean}) was compared across the three scans. Two patients with liver metastases were excluded from analysis.

Results: At peak exposure, both cohorts exhibited similar trends; SUV_{mean} was elevated relative to baseline in liver (30% ± 9%) and spleen (15% ± 10%), and reduced in marrow (-10% ± 7%). During treatment break, SUV_{mean} in all tissues approached pre-treatment levels for Cohort A, decreased in liver (13% ± 6%) and spleen (10% ± 9%) and increased in marrow (5% ± 2%). For Cohort B, SUV_{mean} approached pre-treatment levels in spleen (3% ± 10%), but remained near peak exposure levels in liver (29% ± 14%) and marrow (-10% ± 9%). This suggests a one-week break may not allow sufficient time for normal tissue recovery. Large standard errors reflect a high degree of inter-patient variability.

Conclusions: Significant changes in FLT uptake during sunitinib treatment were observed in liver, marrow, and spleen. A high degree of inter-patient variability was noted. FLT-PET may provide a unique tool to monitor physiological changes prior to the development of dose-limiting toxicities.

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