

SARCOMA FOUNDATION OF AMERICA
FINAL REPORT

Project Title: Predicting treatment response of soft tissue sarcomas to neoadjuvant therapy by imaging proliferation with a FLT-PET/CT scan: a pilot study

Project Number: SFA08-15

1. Date project was initiated: 10/08
2. Period covered by this report: From 10/08 To 7/09
3. Publications, Abstracts, and Presentations: As the trial is not complete, no publications, abstracts or presentations have been performed. We anticipate completion of the study within the next 2 months and a manuscript is in the process of being written. We expect submission of the manuscript by 10/09.
4. Provide a brief list of keywords: (limit to 20 words) 18F-fluorodeoxythymidine-positron-emission-tomography(FLT-PET), Soft tissue sarcoma,
5. Summarize the progress during the period of this report and its impact on your plans for the remainder of the project. Include a summary of the progress toward the achievement of the originally stated aims and list the significant results:

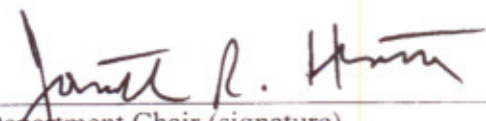
Please see abstract at the end of this document for a complete summary. This abstract represents the progress to date. In addition to the accrual stated in the abstract, three additional patients have been consented for the study and will undergo their initial baseline FLT-PET/CT scan within the next 2 weeks.

6. In layperson's terms, summarize the progress during the period of this report. Explain any medical significance or implications of your results to date:

Please see abstract at the end of this document.


Principal Investigator (signature)

7/29/09
Date


Department Chair (signature)
Vice Chair, Surgery

7/29/09
Date

SUMMARY

BACKGROUND: Although metabolic imaging with F18-fluorodeoxyglucose positron emission tomography (FDG-PET) is more sensitive than standard size-based criteria (RECIST) at monitoring pathologic response to therapy in high-grade soft tissue sarcomas (STS), its limited specificity potentially restricts its utility as a functional biomarker. We hypothesized that imaging proliferation with 18F-fluorodeoxythymidine-positron-emission-tomography (FLT-PET) may provide a more accurate assessment of response in patients with high-grade STS.

EXPERIMENTAL DESIGN: Patients with resectable biopsy-proven high-grade soft-tissue sarcomas (STS) underwent a FLT-PET/CT scan before and after neoadjuvant treatment. Relative changes in tumor FLT uptake and size from the baseline to the follow-up scan were calculated and correlated to histopathologic response. Histopathologic response was defined as $\geq 95\%$ tumor necrosis.

RESULTS: From October 2008 to July 2009, 24 patients with STS (12 males, 12 females; mean age, 57 ± 20 years) were prospectively enrolled in this study. Five patients were excluded after they underwent baseline FLT-PET/CT imaging and did not undergo a follow up FLT-PET/CT scan (2 tumors exhibited low FLT avidity, one patient with metastatic disease showed unresectable disease following neoadjuvant treatment, one FLT-PET/CT scan detected a second malignancy (hepatocellular carcinoma), and one patient refused to undergo a follow up FLT-PET/CT scan). Of the remaining 19 patients 17 completed the study up to date. FLT uptake at baseline averaged 8.98 ± 5.18 (median, 8.83; range, 2.60-21.57) and decreased significantly to 4.41 ± 4.10 (median, 3.75; range, 1.11-18.70) at follow-up ($p=0.001$). Tumor size did not significantly change with treatment. Baseline size averaged 6.95 ± 3.40 (median, 6.28; range, 1.20-15.04) and follow-up size averaged 6.41 ± 3.27 (median, 6.03; range, 1.73-14.49) ($p=0.14$). In histopathologic responders ($n=2$; 12%), reduction in tumor FLT uptake was significantly greater than in non-responders ($n=15$; 88%) ($p=0.02$), whereas no significant differences were found for tumor size ($P = 0.69$). However, 7 of 15 non-responders also showed remarkable decreases in FLT uptake by $>50\%$.

REMAINDER OF THE STUDY: Accrual will be completed by September 2009. Once complete the accuracy of FLT-PET/CT at assessing histopathologic response will be compared by receiver operating characteristic curve analysis to our FDG-PET/CT results from previous studies. To further investigate the correlation between pathology and imaging findings we will correlate the FLT tumor uptake with quantitative IHC analysis of the proliferation markers such as Ki-67.

LAYPERSON SUMMARY

We hypothesized that imaging cell proliferation with a new imaging modality [18F-fluorodeoxythymidine-positron-emission-tomography (FLT-PET)] would potentially provide a more accurate modality to monitor response in patients with high-grade soft tissue sarcomas. From October 2008 to July 2009 17 patients have completed the study and preliminary analysis reveals that changes in cellular proliferation, as measured by FLT-uptake, is more accurate than the current standard of changes in size at identifying pathologic response to therapy. Accrual will be completed by September 2009 and a complete analysis of the accuracy of FLT-PET at predicting response to therapy in patients with soft tissue sarcoma will be performed at that time.