The purpose of this study was to evaluate the role of F18-FDG-PET (FDG-PET) imaging in comparison with standard anatomical imaging using CT in monitoring response to STI571 in patients with advanced gastrointestinal stromal tumor (GIST). CT and attenuation-corrected 2-D whole-body F18-FDG-PET were performed in 25 patients at baseline. All patients had subsequent FDG-PET scans and CT scans (1 to 7 studies/patient) between 24 hours and 9 months following initiation of daily oral therapy. Interpreters were blinded to the results of the other imaging modality. F18-FDG-PET uptake was assessed using standard uptake values (SUVs) and tumor-to-background ratios. Bi-dimensional measurements were used for CT. Sites of disease defined by CT at baseline were noted with areas of abnormality on FDG-PET. FDG-PET showed additional sites of disease, metabolic activity within tumor sites, and response to therapy as early as 24 hours following initiation of therapy. Lack of metabolic response on FDG-PET was noted in 5 (20%) patients; one of these patients exhibited primary resistance to STI571 with tumor progression by CT and conventional clinical criteria, while the others demonstrated either stable or progressive disease by morphologic criteria. The mechanisms behind FDG-PET changes are under study, and the roles and correlative evaluation of FDG-PET and CT will need to be further studied prospectively to assess the respective predictive value of each test. These findings suggest that the functional information provided by FDG-PET may play an important role in the evaluation of therapies such as STI571, which target specific cell-signaling mechanisms. (Sponsored by Novartis Oncology)

Materials and Methods

Twenty-five patients were selected sequentially from a phase 2 clinical trial at the Dana-Farber Cancer Institute, Boston, MA in this multicenter study of STI571 in patients with advanced GIST. Baseline F18-FDG-PET imaging, CT, and routine laboratory testing were performed. The patient population consisted of 14 men, mean age 52 years (range 28-72 y), and 11 women, mean age 51 years (range 30-71 y). All had unresectable metastatic disease. Most of the patients were randomly started on 400 mg (n = 10) or 600 mg (n = 15) of STI571 taken started on 400 mg (n = 10) or 600 mg (n = 15) of STI571 taken daily. Interpreters were blinded to the results of the other imaging modality. F18-FDG-PET uptake was assessed using standard uptake values (SUVs) and tumor-to-background ratios. Bi-dimensional measurements were used for CT. Sites of disease defined by CT at baseline were noted with areas of abnormality on FDG-PET. FDG-PET showed additional sites of disease, metabolic activity within tumor sites, and response to therapy as early as 24 hours following initiation of therapy. Lack of metabolic response on FDG-PET was noted in 5 (20%) patients; one of these patients exhibited primary resistance to STI571 with tumor progression by CT and conventional clinical criteria, while the others demonstrated either stable or progressive disease by morphologic criteria. The mechanisms behind FDG-PET changes are under study, and the roles and correlative evaluation of FDG-PET and CT will need to be further studied prospectively to assess the respective predictive value of each test. These findings suggest that the functional information provided by FDG-PET may play an important role in the evaluation of therapies such as STI571, which target specific cell-signaling mechanisms. (Sponsored by Novartis Oncology)

Standard uptake values (SUVs) and Tumor-to-background ratios (TBRs)

SUVs (Strauss and Conti 1991) and TBRs were calculated for the lesion with the most intense uptake at baseline and subsequently calculated for the same lesion on follow-up scans.

Baseline SUVs were calculated using the following methodology: first, the image plane containing the maximum pixel intensity for the selected lesion was identified. Then a region of interest (ROI) was drawn on the lesion, with the boundary set to 70% of the lesion maximum. Finally, the SUV within the ROI was calculated using the following formula:

$$SUV = \frac{\text{mean pixel value (Bq/cc, decay corrected to start of scan)}}{\text{normal tissue pixel value}}$$

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Follow-up studies

The maximum response seen was a decrease of approximately 90% in both SUV and TBR at 8 months. All patients but one who showed complete response by PET criteria also showed decrease in tumor volume as estimated by CT one month following initiation of therapy. The overall decrease in tumor size based on bi-dimensional CT measurements ranged from 39% to 91% (Figure 5). The findings demonstrated concordant results by FDG-PET and CT. Six patients remained stable or progressed on STI571 therapy based on CT criteria (Figure 5). The study findings are summarized in Table 2.

Conclusions

1. Most GIST tumors demonstrate high glycolytic activity at baseline prior to STI571 therapy.
2. Sites of disease defined by F18-FDG-PET at baseline correlated with areas of abnormally seen on CT. F18-FDG-PET provided additional information regarding extent of disease.
3. Response to STI571 therapy could be demonstrated by FDG-PET as early as 24 hours following initiation of therapy.
4. Patients with stable or progressive disease, concordant findings between F18-FDG-PET and bi-dimensional CT were seen in all but one case. The roles and correlative evaluation of FDG-PET and CT will need to be further studied prospectively to assess the respective predictive value of each test.
5. These findings suggest that the functional information provided by FDG-PET may play an important role in the early evaluation of therapies that target specific cell-signaling mechanisms, such as STI571. (Sponsored by Novartis Oncology)

References

