Contrast CT, PET/CT assess cancer therapy for melanoma

ABSTRACT
Pamela DePiro, MD, et al, SSC09-08, Monday, Nov 28, 2011, Radiologic Society of North America, Chicago, IL

PURPOSE
Immune-modulated and anti-angiogenic cancer therapeutics may not cause tumor shrinkage by conventional radiographic response. FDG-PET/CT and CT perfusion imaging were used to evaluate response to therapy.

METHOD AND MATERIALS
FDG-PET/CT and CT perfusion imaging were performed in a phase I trial of bevacizumab plus ipilimumab in patients (pts) with unresectable stage III or IV melanoma. Helical CT, dynamic contrast enhanced (DCE) CT, and FDG-PET/CT were performed at baseline; helical CT and DCE-CT were repeated at weeks 12 and 24, and FDG-PET/CT was performed at 8 and 16 weeks after treatment. Anatomic response was evaluated on the helical CT scans using Response Criteria for Solid Tumors (RECIST) 1.1. The SUVmax was used to evaluate metabolic response on FDG-PET according to the European Organisation for Research and Treatment of Cancer guidelines (EORTC). Kinetic analysis was performed on DCE-CT images to estimate tumor blood flow, mean transit time, and volume of distribution.

RESULTS
To date, 21 pts have enrolled in the trial and had imaging obtained at baseline and at least one follow up time point. At 8 weeks, 6 pts had metabolic PR, 7 pts were SD, and 8 were PD. Of the pts that had FDG-PET/CT scans at 16 weeks, 6 pts had metabolic PR, 4 were SD, and 4 were PD. Those pts having evaluable perfusion CT studies had reductions in perfusion parameters in patients with metabolic PR, while there were increases in pts with metabolic PD.

CONCLUSION
Dynamic Contrast Enhanced CT and FDG-PET/CT provide additional information for evaluating response to anti-angiogenic and immune-modulated therapeutics in melanoma. This may be particularly important for evaluating early response to a novel class of therapeutics, particularly in lesions increasing in size due to inflammation and tumor destruction, where standard response criteria do not predict response.

CLINICAL RELEVANCE/APPLICATION
Detection of changes in FDG-avidity and tumor blood flow in melanoma patients may suggest early response or progression and will be evaluated with future clinical outcome and pathologic correlation.
SUMMARY - By Wayne Forrest, AuntMinnie.com staff writer

January 11, 2012 -- Dynamic contrast-enhanced CT and FDG-PET/CT can provide additional information to evaluate and confirm how well melanoma patients respond to immune-modulated and antiangiogenic cancer therapy, according to researchers from Dana-Farber Cancer Institute.

The group performed FDG-PET/CT and CT perfusion imaging scans in a phase I clinical trial of the use of bevacizumab plus ipilimumab to treat patients with unresectable stage III or IV melanoma. The researchers found that patients with FDG-PET/CT images showing partial metabolic response achieved longer disease-free survival than those with stable metabolic disease or progressive metabolic disease.

Bevacizumab, marketed by Genentech as Avastin, has received clearance from the U.S. Food and Drug Administration (FDA) to inhibit angiogenesis, or the development of new blood vessels that advance the progress of a tumor. Ipilimumab is marketed under the brand name Yervoy by Bristol-Myers Squibb and was cleared by the FDA in March 2011 to treat patients with advanced melanoma.

In the Dana-Farber study, helical CT, contrast-enhanced CT, and FDG-PET/CT were performed on 21 patients at baseline. Helical CT and contrast-enhanced CT scans were repeated at 12 weeks and 24 weeks, while FDG-PET/CT imaging was performed at eight and 16 weeks after treatment with the drug combination, according to Dr. Pamela DiPiro, co-author and clinical director of CT at Dana-Farber. She presented the results at the recent 2011 RSNA meeting in Chicago.

The researchers measured anatomic response on the helical CT scans using the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1. Maximum standardized uptake values were used to evaluate metabolic response on FDG-PET based on the European Organization for Research and Treatment of Cancer (EORTC) guidelines. In addition, a kinetic analysis was performed on contrast-enhanced CT images to estimate tumor blood flow, mean transit time, and volume of distribution.

At eight weeks, six patients had a metabolic partial response to treatment, seven patients had stable disease, and eight patients had progressive disease.

Of the patients who had FDG-PET/CT scans at 16 weeks, six had a metabolic partial response to therapy, four had stable disease, and four had progressive disease. Among the evaluable perfusion CT studies, the researchers detected reductions in perfusion parameters in patients with metabolic partial response to therapy, while there were increases in patients with metabolic progressive disease.

**Significant results**

The most significant finding was that FDG-PET/CT images of patients who had a metabolic partial response indicated that these individuals achieved a longer disease-free survival than those with stable or progressive metabolic disease, DiPiro said.
"While the results are preliminary and further studies are needed, these results suggest both dynamic contrast-enhanced CT and FDG-PET may be important imaging biomarkers of efficacy for these therapeutic targets in this clinical setting," DiPiro told AuntMinnie.com. "If successful, this could provide an early means of determining treatment efficacy for melanoma patients or, conversely, identify when treatments are not working and discontinuation and/or alternative therapy is warranted."

She did note that bevacizumab and ipilimumab were not evaluated separately to determine the efficacy of each drug for melanoma. In the study, patients received ipilimumab immediately followed by bevacizumab.

"There was no time to look at one [drug] or the other to see if there were any confounding effects," DiPiro said. "If future studies use a mono phase [to study the drugs independently], that could be helpful."

Still, the findings regarding FDG-PET's and contrast-enhanced CT's capabilities could help evaluate early response to novel therapeutics, particularly in lesions increasing in size due to inflammation and in tumor destruction, where standard response criteria do not predict response.