inside blood

3 SEPTEMBER 2009 | VOLUME 114, NUMBER 10

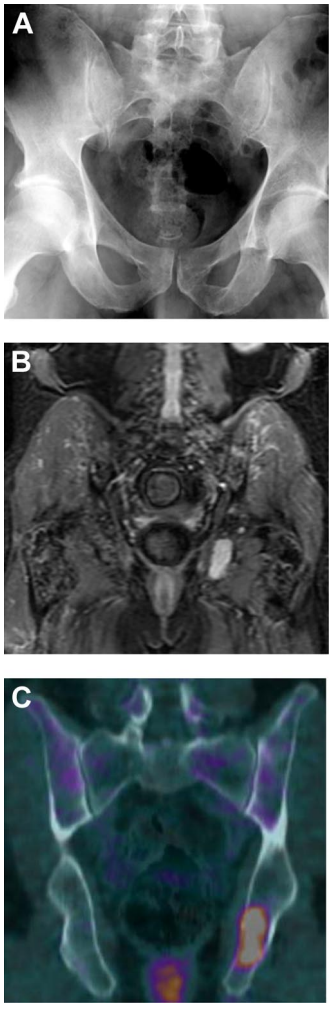
CLINICAL TRIALS

Comment on Bartel et al, page 2068

A new pet for myeloma

Meletios-Athanassios Dimopoulos, Lia A. Moulopoulos, and Evangelos Terpos

UNIVERSITY OF ATHENS



PET/CT is superior over conventional radiography. In the figure created by Bartel and colleagues, the conventional radiography of the pelvis (A) showed no osteolysis, while there were several foci on STIR-weighted MRI images with the largest in the left ischium (B), and 2 foci on FDG-PET/CT imaging (C) with the largest again in the left ischium with a max SUV of 4.1. See the complete figure in the article beginning on page 2068.

In this issue of *Blood*, Bartel and colleagues report the independent predictive value of the PET/CT and of the FDG suppression before transplantation in newly diagnosed myeloma patients who were treated using the TT3 regimen.[1]

Positron emission tomography (PET) is a tomographic nuclear imaging procedure that uses positrons as radiolabels and positron-electron annihilation reaction gamma rays to locate the radiolabels. A low dose of a radiopharmaceutical labeled with a positron emitter, such as F18-fluorodeoxyglucose (FDG), is injected into the patient, who is scanned by a tomographic system. The advent of fusion scanning combining both PET and computed tomography (CT) addresses the issue of limited spatial resolution, which was a major limitation of PET.[2] The sensitivity of FDG-PET/CT in detecting myelomatous involvement is approximately 85% and its specificity is 90% to 95%.[3] PET/CT is also more sensitive than other imaging modalities for localizing extramedullary disease, and it reveals additional lesions in almost 30% of the patients who had been diagnosed with solitary plasmacytoma by magnetic resonance imaging (MRI).[4]

The first assessment of FDG-PET/CT in myeloma showed that this examination identified patients with high-risk myeloma, could be used to monitor nonsecretory myeloma, and could detect residual disease in patients with immunofixation negative complete response (CR).[5] Larger studies of PET/CT in myeloma confirmed these data. Thus, PET/CT was included as an option for the diagnosis and monitoring of myeloma patients according to the National Comprehensive Cancer Network (NCCN) guidelines. The National Oncologic PET Registry, a large prospective program, enrolled 22 975 cancer patients, including more than 1300 patients with myeloma, and revealed that 36.5% of the time, treating physicians changed the intended management on the basis of PET/CT results.[6] But is this justified for myeloma patients? The study by Bartel et al gives us important information for the use of FDG-PET/CT in myeloma patients treated with both novel agents and high-dose therapy. In 239 patients who underwent total therapy 3 (TT3), the authors performed standard skeletal survey, MRI, and FDG-PET/CT at baseline and then at specified points in their multiphased treatment. The presence of more than 3 focal lesions (FLs) in the PET/CT (PET-FL) independently predicted for inferior overall survival (OS) and event-free survival (EFS). Furthermore, complete FDG suppression in PET-FL before transplantation conferred superior OS and EFS. As in other studies, the presence of FLs in MRI and of lytic lesions in plain radiography (MBS-osteolytic lesions [OLs]) also predicted for shorter survival in the univariate analysis. However, the logistic regression analysis showed that although PET-FL was independently positively linked to both MRI-FLs and MBS-OL, only PET-FL retained its independent predictive value for survival, identifying a subset of patients with otherwise low-risk myeloma who had inferior survival. In addition, CR based on PET/CT criteria (absence of PET-FL and extramedullary disease) occurred more rapidly than the clinical CR or near CR and especially than the MRI-CR status among patients presenting with MRI-FL. Do these data indicate that PET/CT is superior to MRI in patients with myeloma? All reported studies to date have confirmed the superiority of PET/CT over conventional radiography (see figure).[3] However, these studies have also revealed that if PET/CT was

the sole imaging procedure, it would have missed additional small lytic skeletal lesions and diffuse spine involvement, which is readily detected by MRI.[3,7] Another disadvantage of PET/CT is the false positive results especially in areas of inflammation or infection, deposits of brown fat, postsurgical changes, vertebroplasty changes, and occasionally other benign or malignant processes.[8] In a prospective comparison among FDG-PET/CT, MRI, and conventional radiography, PET-CT was superior to plain radiographs, but, in 30% of patients, PET-CT scans of the spine and pelvis failed to show abnormal findings in areas in which MRI revealed an abnormal pattern of bone marrow involvement, more frequently of diffuse type. In contrast, in 35% of patients, PET-CT enabled the detection of myelomatous lesions in areas that were outside the field of MRI. By combining MRI of the spine-pelvis and PET-CT, the ability to detect sites of active multiple myeloma (MM), both medullary and extramedullary, was as high as 92%.

After autologous stem cell transplantation, 15 of 23 patients had negative PET-CT scans (including 13 with very good partial response or near CR), while only 8 had normal MRI.[9]

The results of the study by Bartel et al are important as they reveal PET/CT as a technique that could lead to individualized therapeutic decisions especially in patients who have residual disease detected only by this procedure. Furthermore, PET/CT is the procedure of choice when extramedullary involvement is suspected (ie, in patients with rising serum LDH). However, further studies are needed before the recommendation of using PET/CT as the standard tool in both diagnosis and follow-up of MM patients.

Conflict-of-interest disclosure: The authors declare no competing financial interests. ■

REFERENCES

1. Bartel TB, Haessler J, Brown TLY, et al. F18-fluorodeoxyglucose positron emission tomography in the context of other imaging techniques and prognostic factors in multiple myeloma. *Blood*. 2009;114(10):2068-2076.

2. Bredella MA, Steinbach L, Caputo G, Segall G, Hawkins R. Value of FDG PET in the assessment of patients with multiple myeloma. *AJR Am J Roentgenol*. 2005;184(4):1199-1204.

3. Dimopoulos MA, Terpos E, Comenzo RL, et al. International Myeloma Working Group (IMWG) consensus statement and guidelines regarding the current role of imaging techniques in the diagnosis and monitoring of multiple myeloma. *Leukemia*. 2009;in press. PubMed doi:10.1038/leu.2009.89.

4. Mulligan ME, Badros AZ. PET/CT and MR imaging in myeloma. *Skeletal Radiol*. 2007;36(1):5-16.

5. Durie BG, Waxman AD, D'Agnolo A, Williams CM. Whole-body F-FDG PET identifies high-risk myeloma. *J Nucl Med*. 2002;43(11):1457-1463.

6. Hillner BE, Siegel BA, Shields AF, et al. Relationship between cancer type and impact of PET and PET/CT on intended management: findings of the National Oncologic PET Registry. *J Nucl Med*. 2008;49(12):1928-1935.

7. Fonti R, Salvatore B, Quarantelli M, et al. 18F-FDG PET/CT, 99mTc-MIBI, and MRI in evaluation of patients with multiple myeloma. *J Nucl Med*. 2008;49(2):195-200.

8. Gorospe L, Raman S, Echeveste J, Avril N, Herrero Y, Hernandez S. Whole-body PET/CT: spectrum of physiological variants, artifacts and interpretative pitfalls in cancer patients. *Nucl Med Commun*. 2005;26(8):671-687.

9. Zamagni E, Nanni C, Patriarca F, et al. A prospective comparison of 18F-fluorodeoxyglucose positron emission tomography-computed tomography, magnetic resonance imaging and whole-body planar radiographs in the assessment of bone disease in newly diagnosed multiple myeloma. *Haematologica*. 2007;92(1):50-55.

● ● ● CLINICAL TRIALS

Comment on Claviez et al, page 2060

Allotransplantation in pediatric HL

James Nachman UNIVERSITY OF CHICAGO

In this issue of *Blood*, Claviez and colleagues report on the outcomes of 91 patients younger than 18 years of age who underwent an allogeneic bone marrow transplantation for HL between 1987 and 2005. The outcomes were reported to the European Group for Blood and Marrow Transplantation.[1]

Fifty-one patients received a reduced intensity transplantation (primarily a fludarabine-based regimen) while 40 patients received a myeloablative conditioning regimen. The probability of progression-free survival at 2 and 5 years was 40% plus or minus 6% and 30% plus or minus 6%, respectively. Overall survival at 2 and 5 years was 54% plus or minus 6% and 41% plus or minus 6%, respectively. Although the relapse rate for patients receiving myeloablative conditioning was similar to that for patients receiving a reduced-intensity conditioning for the first 9 months after transplantation, subsequent relapses were more frequent in the group receiving reduced-intensity conditioning.

Before one examines the overall and subgroup analyses presented by the authors, the potential problems associated with the analysis of "registry" data need to be considered. Because the clinical history for an individual patient is not presented, it is not clear why a particular treatment was given to an individual patient. In this registry dataset, approximately 55% of patients received an allogeneic transplantation as their first transplantation. Currently, no guidelines for treating relapsed Hodgkin lymphoma (HL) recommend allogeneic transplantation as the initial transplantation.[2] It would be interesting to know why investigators chose allogeneic transplantation over the more standard autologous transplantation. It would have been helpful if the authors had presented separate outcome data for patients who received an initial allogeneic transplantation and those who received an allogeneic transplantation after a failed autologous transplantation. The fact that more than half of the patients reported had nonstandard treatment limits the usefulness of this data.

In this paper, the authors compare the results of patients receiving myeloablative to reduced-intensity conditioning. The authors conclude that reduced-intensity conditioning is associated with similar nonrelapse mortality and a higher relapse rate. But, before considering whether differences in outcome among subgroups are relevant, one must ensure comparability of the analyzed groups.

Salvage chemotherapy followed by autologous stem cell transplantation is the standard of care for pediatric HL patients who present with advanced-stage disease and fail front-line therapy. Patients who received reduced-intensity conditioning were more likely to have received 4 or more salvage regimens ($P = .001$) and were more likely to have undergone an