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CD38-Targeted ^{89}Zr-DFO-Daratumumab PET of Myeloma: Immuno-PET Impacting Clinical Care

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Currently, the determination of disease burden in multiple myeloma is suboptimal. Myeloma cells may not secrete abnormal immunoglobulins or free light chains, limiting blood and urinary analysis (*1*). Imaging by radiography and MRI is limited, and approximately 30% of myeloma lesions are not appreciable by ^{18}F-FDG PET (*2*). Bone marrow biopsies are also limited by the limited sites that can be sampled (*3*). Thus, better methods of detecting, localizing, and quantitating myeloma cells are needed.

Here, we report on a 76-y-old man with multiple myeloma who experienced new biochemical progression after stem cell transplantation. A masked bone marrow biopsy showed no evidence of myeloma cells. ^{18}F-FDG PET/CT was ordered to measure tumor burden and determine whether systemic therapy was appropriate; however, no lesions were visualized by ^{18}F-FDG PET (Fig. 1).

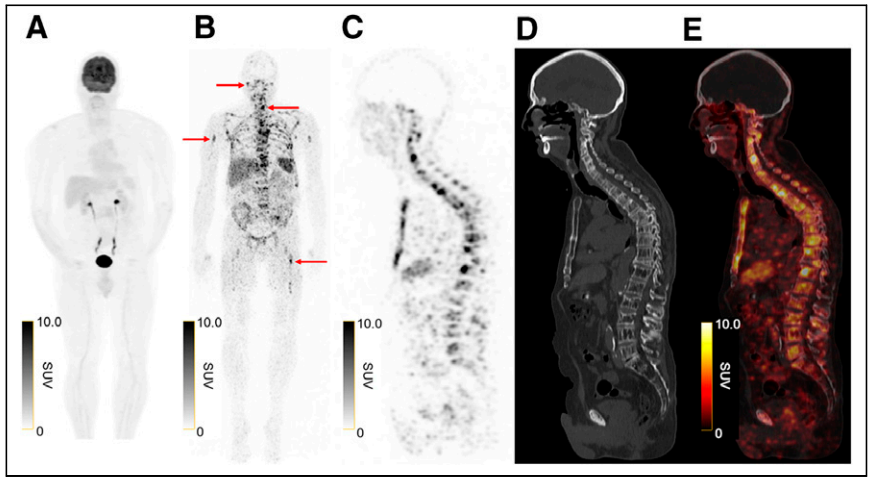

FIGURE 1. (A) ^{18}F-FDG maximum-intensity projection of 76-y-old patient with biochemically relapsed/refractory multiple myeloma is without abnormal foci of disease. (B) In contrast, ^{89}Zr-DFO-daratumumab maximum-intensity projection, 7 d after tracer administration, demonstrates more than 100 abnormal foci in head, neck, chest, abdomen, pelvis, and extremities (arrows). (C–E) Sagittal ^{89}Zr-DFO-daratumumab PET (C), CT (D), and ^{89}Zr-DFO-daratumumab PET/CT (E) demonstrate abnormal foci corresponding to osseous structures, representing non–^{18}F-FDG–avid osseous myeloma lesions.

He was accrued into a phase II trial (NCT04814615) of CD38-targeted immuno-PET with ^{89}Zr-deferoxamine (DFO)-daratumumab. CD38 is a transmembrane glycoprotein that is expressed on virtually all myeloma cells, as well as at lower levels on normal lymphoid and myeloid cells (*4*). ^{89}Zr-DFO-daratumumab comprises the CD38-targeting antibody daratumumab, chelated through DFO to the positron-emitting radiometal ^{89}Zr, whose half-life of 78.4 h allows for imaging up to at least 9 d after administration (*5*). As antibodies such as daratumumab may take 6–7 d to optimally biodistribute onto tumor, the long half-life of ^{89}Zr allows optimal timing of imaging. ^{89}Zr-DFO-daratumumab was able to demonstrate widespread foci of disease, with subsequent image-guided biopsy providing proof of myeloma. The identification, localization, and quantification of disease led to initiation of systemic therapy with daratumumab, lenalidomide, and dexamethasone. This case suggests that ^{89}Zr-DFO-daratumumab immuno-PET has the potential to have an important clinical impact on patients diagnosed with multiple myeloma.

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DISCLOSURE

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