Evaluation of osteosarcoma response to Radium-223 treatment using bone scintigraphy, NaF-PET, and FDG-PET

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BACKGROUND: We investigated the role of different imaging modalities in a phase I clinical trial of radium 223 ($^{223}RaCl_2$) in the treatment of patients (N=18) with high-risk relapsed bone-forming osteosarcoma (NCT01833520).

HYPOTHESIS: Do the different imaging modalities give additional information?

METHODS: Patients received 1–6 cycles of $^{223}RaCl_2$, and cumulative doses varied from 6.84 MBq to 57.81 MBq. Molecular imaging with technetium (Tc)- 99m phosphonate scintigraphy, 2-F-18-fluorodeoxyglucose (FDG) positron emission tomography (PET) or sodium fluoride-18 (NaF) PET was used to characterize the disease. All 18 patients had multiple lesions diagnosed with one of the imaging techniques. Bone scintigraphy and FDG-PET studies could be compared in 10 patients at two time points and in two patients before $^{223}RaCl_2$ administration. Bone scintigraphy and NaF-PET could be compared in 10 patients at two time points, in two patients at three time points and in one patient before $^{223}RaCl_2$ administration. Lesion number, lesion volume, and total lesion volume were analyzed via FDG-PET and NaF-PET studies. We also developed methods to analyze lung volume and skeletal volume to compare disease behavior using different PET tracers.

RESULTS: Of the 18 patients, 17 had bone lesions that were visible in at least one of the imaging studies. In four of the seven patients with multiple skeletal lesions (>5), FDG-PET and NaF-PET studies could be compared. In these four patients, the sclerotic bone volume and pathologic NaF and FDG volumes varied widely. The skeletal tumor locations varied in our patient population: two patients had skull lesions, seven patients had lesions in the extremities, 10 patients had pelvic bone tumors, 12 patients had lesions in the spine, and nine patients had lesions in the ribs. The FDG-PET and NaF-PET studies could be compared in all four patients who had multiple lung lesions (>5). In these patients, the lung volume, calcified lung nodules, and pathologic NaF and FDG volumes varied substantially. One patient had brain metastases at baseline, and the other developed brain metastases during the study. Most of the patients (14/18) had soft-tissue metastases, and at least some of the metastases were calcified in all 14 patients. In two patients, the soft-tissue lesions could be identified as lymph nodes. One patient had a liver metastasis. In most of the patients, the soft-tissue lesions were extensions of bone tumors. Overall response was seen in only one patient, but 4 patients experienced mixed responses, in which the bone lesion decreased in intensity, and the surrounding soft tissues increased in intensity. Lung tumors, which were rarely calcified, seldom responded to $^{223}RaCl_2$ treatment. The PET response criteria demonstrated a weak correlation with alkaline phosphatases.

Our results indicate that NaF-PET is an essential part of osteosarcoma staging and NaF PET and FDG PET are complementary to each other in osteosarcoma.