PET Imaging of Multiple Myeloma : Comparison of 89Zr- and 64Cu-labeled anti-CD138 Conjugates to 64CuCl2 and 18F-FDG in a Preclinical Syngeneic Model

Clément Bailly, Sébastien Gouard, Benjamin Chalopin, Thomas Carlier, Catherine Sai-Maurel, Patricia Remaud-Le Saec, Mickaël Bourgeois, Nicolas Chouin, Raphaël Tripier, Ferid Haddad, et al.

OP-040

PET Imaging of Multiple Myeloma: Comparison of ^{89}Zr- and ^{64}Cu-labeled anti-CD138 Conjugates to $^{64}CuCl_2$ and ^{18}F-FDG in a Preclinical Syngeneic Model

C. Bailly[1], S. Gouard[2], B. Chalopin[2], T. Carlier[1], C. Maurel[2], P. Remaud-Le Saëc[2], M. Bourgeois[1], N. Chouin[2], R. Tripier[3], F. Haddad[4], A. Faivre-Chauvet[1], F. Kraeber-Bodere[1], C. Bodet-Milin[1], M. Cherel[2]; [1]University Hospital, Nantes, FRANCE, [2]Nantes-Angers Cancer Research Center CRCINA, University of Nantes, Nantes, FRANCE, [3]CNRS-UMR6521, University of Bretagne Occidentale, Brest, FRANCE, [4]Groupement d'intérêt public ARRONAX, St Herblain, FRANCE.

Purpose: Although recent data from the literature suggest that PET imaging with [18]-Fluorodeoxyglucose (^{18}F-FDG) is a promising technique in multiple myeloma (MM), the development of other radiopharmaceuticals seems relevant. CD138 is currently used as a standard marker in many laboratories for the identification and purification of myeloma cells, and could be used in phenotype tumor imaging. In this study, we evaluated 2 conjugates of an anti-CD138 murine antibody (9E7.4) and compared them to metabolic tracers ($^{64}CuCl_2$and ^{18}F-FDG) for PET imaging in a MM syngeneic mouse model. **Subjects and Methods:** 9E7.4 was conjugated to TE2A-benzyl isothiocyanate (TE2A) and desferrioxamine (DFO) chelators for copper-64 (64Cu) and zirconium-89 (89Zr) labeling. ^{64}Cu-TE2A-9E7.4 and 89Zr-DFO-9E7.4 antibodies and $^{64}CuCl_2$ were evaluated via PET imaging and biodistribution studies in C57BL / KaLwRij mice bearing either 5T33-MM subcutaneous tumors or bone lesions. These results were compared to ^{18}F-FDG-PET imaging. Autoradiography and histology of representative tumors were secondly conducted. **Results:** In biodistribution and PET studies, ^{64}Cu-TE2A-9E7.4 and89Zr-DFO-9E7.4displayed comparable good tumor uptake of subcutaneous tumors. On the opposite, only low-level concentrations of $^{64}CuCl_2$ were accumulated in MM lesions. PET/CT imaging of the disseminated model with ^{64}Cu-TE2A-9E7.4 and 89Zr-DFO-9E7.4 showed high uptake of the probes at the site

of intra-medullary lesions, greater than that demonstrated with ^{18}F-FDG-PET and correlating with the bioluminescence imaging of the tumor. Histopathologic analysis of the immuno-PET-positive lesions also confirmed the presence of plasma cell infiltrates within the bone marrow. Comparison of both 9E7.4 conjugates revealed higher non specific bone uptakes of ^{89}Zr-DFO-9E7.4 than 64Cu-TE2A-9E7.4 (3.1±1.15 vs 1.48±0.29 respectively at 24h PI; p=0.0061; non-parametric test) while the opposite was observed for tumor-to-blood ratio (1.42±0.24 vs 4.08±1.09 respectively at 24h PI; p=0.0391; non-parametric test). Such observations were consistent with the known in vivo gradual transchelation of 89Zr over time which could reduce the efficacy of a 89Zr-labeled immuno-PET probe as an effective tool for bone lesions imaging. **Conclusion:** ^{64}Cu- and ^{89}Zr-labeled anti-CD138 antibody can detect subcutaneous MM tumors and bone marrow lesions with high sensitivity, outperforming ^{18}F-FDG-PET and $^{64}CuCl_2$ in this preclinical model. 64Cu- anti-CD138 antibody had the most optimal tumor-to-nontarget tissue ratios for translation into humans as a specific and promising new imaging radiopharmaceutical agent in MM.