International Conference on Clinical PET-CT and Molecular Imaging (IPET 2015): PET-CT in the Era of Multimodality Imaging and Image-Guided Therapy

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BOOK OF ABSTRACTS

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Development of Rituximab Radioimmunoconjugates as PET-Radiopharmaceuticals

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Background: Positron emission tomography (PET) has a growing use in medical decision making and management of patients. To further apply the unique properties of PET, more clinically validated PET-radiopharmaceuticals are required and subsequently new and better radiochemical preparation methods are under development. With respect to radiochemistry development, most efforts have been made with the use of 11C and 18F as radionuclides. Also, labeling methods development stimulates the use of different radiometals as 68Ga, 89Zr and 64Cu for clinical use. These radionuclides have their specific characteristics with respect to half-life, positron energy (resolution), positron abundance and availability. Depending on the biological target of interest and the properties of the PET-radiopharmaceutical the proper radionuclide should be selected.
For the treatment and diagnosis of malignancies, various radiolabeled monoclonal antibodies have also been developed. Rituximab selectively binds with high affinity to the CD20 antigen (human B-lymphocyte restricted differentiation antigen, Bp35), which is expressed on B-lymphocytes and on >90 % of B cell non-Hodgkin lymphomas (NHL). These properties make the CD20 receptor a suitable target for radiotherapy/diagnostic purposes.

Methodology: After promising results (in vitro and in vivo studies) that we obtained in an investigation performed with 177Lu-rituximab immunoconjugates intended for NHL therapy, in order to obtain 68Ga anti-CD20 radioimmunoconjugates for use in PET studies, different bifunctional chelating agents-anti-CD20 conjugates (BFCA-rituximab) were assessed for preliminary chemical characterization. Rituximab, conjugated with three different BFCA, p-SCN-Bn-DOTA, p-SCN-Bn-DTPA and 1B4M-DTPA in form of freeze-dried preparation, was subjected to characterization and determination of secondary structure (which is mandatory for protein-based radiopharmaceuticals), quality parameters (purity, integrity, fragmentation and aggregation of the antibody), and average number of BFCA attached with employment of different analytical techniques such as Matrix-Assisted Laser Desorption Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF-MS), Sodium Dodecyl Sulphate-Polyacrylamide Gel Electrophoresis (SDS-PAGE), Fourier Transform Infrared (FT-IR) and Raman Spectroscopy.

Results: The results demonstrate that after lyophilisation, diluted rituximab immunoconjugates remain stable. No modification of its chemo-physical characteristics, no aggregation, and preservation of antibody secondary structure were observed. Binding of an average 6.1 (p-SCN-Bn-DOTA), 8.8 (p-SCN-Bn-DTPA) and 8.3 (1B4M-DTPA) molecules per antibody was determined.

Conclusion: The results indicate that the time frame for the practical use of rituximab immunoconjugates can be safely extended using lyophilisation, enabling, for example, safe and longer storage and supporting

the possibility of developing a "ready-to-label" rituximab immunoconjugates for imaging/therapy. Further experiments are still needed in order to demonstrate biological and pharmacological properties. 68Ga-labeled rituximab immunoconjugates may provide PET screening of the therapeutic outcomes following 177Lu therapy. Therefore, developing a kit containing this antibody, intended for 68Ga labeling, will be a part of our future investigation.