Radiolabeling of DOTA-conjugated Lintuzumab with $^{225}$Ac: Comparison of $^{229}$Th-produced and High-Energy Proton Accelerator-produced $^{225}$Ac

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INTRODUCTION

Lintuzumab is a monoclonal antibody (mAb) against CD33, an antigen widely expressed on myeloid stem cells and leukemic blast cells in patients with Acute Myeloid Leukemia (AML). Lintuzumab is undergoing preclinical and clinical development for the treatment of leukemia and other hematological malignancies. Actinium-225 (225Ac) is an alpha emitting radionuclide with a half-life of 10.6 hours, which can deliver supraphysiological doses of radiation to AML cells in a highly selective manner.

Challenges Associated with Accelerator Derived 225Ac: Unavoidable 227Ac Content

During production of 225Ac from 229Th using an energy proton accelerator, the presence of 227Ac and other minor impurities is unavoidable. At 1% activity, molar ratio of 227Ac to 225Ac is 8.01.

Even though molar ratio of 227Ac is higher than 225Ac in accelerator generated material, labeling efficiency is similar and no free 225Ac was detected after labeling.

Critical quality attributes such as Radiochemical Purity and Immunoreactivity were similar between both 225Ac.

225Ac-labeled anti-CD33 lintuzumab showed comparable effectiveness in an in vitro cellular cytotoxicity study irrespective of 225Ac source.

These studies demonstrate the feasibility of using accelerator generated 225Ac for targeted alpha therapy.

SUMMARY

1. 225Ac-labeled anti-CD33 lintuzumab showed comparable effectiveness in an in vitro cellular cytotoxicity study irrespective of 225Ac source.

References:

Characteristics of the 229Th Cow Generated 225Ac and the Accelerator Generated 225Ac

Radiochemical purity analysis of labeled 225Ac-lintuzumab from the two 225Ac sources.