THERANOSTICS INSIGHTS

^{225}Ac-Lintuzumab

Radioisotope

Ac-225 Actinium-225
actinide metal
T½ : 9.9 days

Production

^{229}Th/ ^{225}Ac generators.
Other methods under development

Radiation

alpha particle (α)

Use

In clinical studies, in combination with different molecules for relapsed or refractory acute myeloid leukaemia (AML).

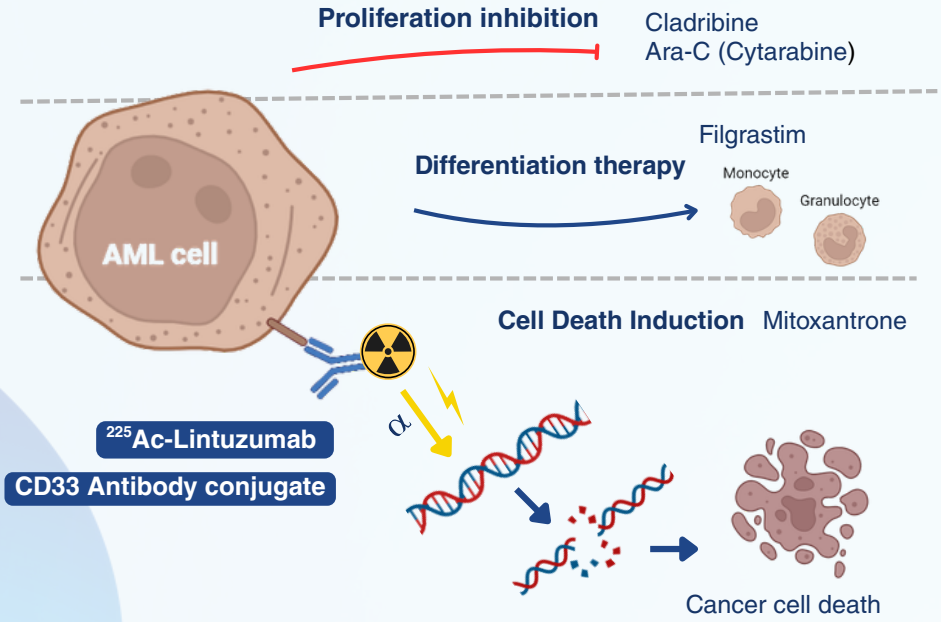
Target/Mechanism

^{225}Ac-Lintuzumab is a conjugated monoclonal antibody binding the CD33 receptors, expressed predominantly in AML cells. Thanks to the selective target, AML cells receive at a close range the high-energy α particles, undergoing double-strand DNA breakage and cancer cell death.

Insight

The NCT03441048 phase 1 study assessed the safety and efficacy of adding ^{225}Ac-Lintuzumab to the CLAG-M chemotherapy regimen in relapsed or refractory AML.

Study design:
The protocol used a 3 + 3 dose-escalation design for ^{225}Ac-Lintuzumab, and fixed dose for CLAG-M. ^{225}Ac-Lintuzumab was administered as a single dose, after CLAG-M, on day 8 of therapy. 26 patients were enrolled in total.



Results: The combination regimen was well tolerated with, expected and manageable, myelotoxicity grade 3/4 adverse events. The composite complete remission (CRc) rates (CR/CRi) were 56.6% overall, 50% in patients with mutated TP53, and 38.5% in prior venetoclax-treated patients.

Measurable residual disease (MRD)-negativity was achieved in 8 of 12 responders. Estimated 2-year OS was 23.1%, and estimated 1-year PFS was 30.8%.