Advances in targeted alpha therapy of cancer

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There is remarkable interest worldwide on the use of targeted alpha therapy on several cancers such as brain tumors, bladder cancer, neuroendocrine tumors, leukemia, and prostate cancer [1]. This rapidly increasing use of alpha-emitting radionuclides is based on the advantages over other forms of radiation due to the shorter path length and high linear energy transfer (LET) of alpha radiation that also leads to the strongly reduced dependency of a damaging effect on oxygenation [1, 2].

The high-LET radiation's biological efficacy causes complex multiple clusters and double-strand DNA breaks, reactive oxygen species (ROS), and the abscopal effect via the immune system [1, 3]. This process makes the α-particles highly potent and specific with potential to overcome radio-resistance, while the limited range can reduce the radiation effects on the healthy tissue.

Whereas the cytotoxic effect on the target lesions is appreciated, the recoil effect and the exact impact of off-target and daughter redistribution on a clinical effect might depend on the pharmacokinetic details of the carrier, its individual variation, and the extent of internalization upon cell binding [4,5,6], effects that should be well understood going forward.

The potency and the potential recoil effects make the half-life, the stable binding to a chelating system, the particle energy, the possible decay chain properties, and the kinetics of the daughters, as well as the costs and availability very essential in the choice of alpha-particle–emitting radionuclides. The currently available alpha-particle–emitting radionuclides that are suitable, include thorium-227, actinium-225, radium-223/-224, bismuth-212/-213, lead-212, astatine-211, and terbium-149 [1, 7, 8].

The ongoing studies that capture the potential of TAT therapeutic options for patients who are resistant to conventional therapies, especially/such as the commercially available radium-223 dichloride (^{223}Ra), ^{225}Ac-PSMA for prostate cancer, ^{225}Ac-labeled somatostatin analogs for Neuroendocrine tumors (NETs), and ^{212}Pb-labeled somatostatin analogs for NET, pose enormous opportunities [9,10,11,12,13,14].

Yet there are still gaps due to limited clinical experience with α-particles to date with unknown maximum tolerable doses in humans, including the chronic effects of these radiations. Hence dosimetry optimization, radiobiology and synthetic lethality tracers, combination therapies, and patient/tumor selection will play fundamental roles going forward with α-particle emitters [9, 15].

Therefore, this collection aims to comprehensively present current preclinical and clinical studies, including the development of radiotracers, interesting results from new tracers, new

methods for data analysis, and new approaches regarding alpha-emitting therapies. We invite researchers to submit original research articles, case series, or reviews for this collection issue.

Ethical approval

Not applicable to this Editorial.

Consent to participate

Not applicable.

Conflict of interest

Mike Sathekge is associate editor of the EJNMMI. Alfred Morgenstern is member of the editorial board of the EJNMMI. The authors declare no other conflict of interest.

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