Session Title
Alpha Emitters in Therapy

Chairperson
Luca Camoni (Brescia, Italy)

Programme
11:00 - 11:24 Viviana Frantellizzi (Rome, Italy): Radionuclide Therapy with Radium-223 of Metastatic Castration-Resistant Prostate Cancer
11:24 - 11:48 Maarten Ooms (Brussels, Belgium): An Overview of Targeted Alpha Therapy with Actinium-225 and Bismuth-213

Educational Objectives
1. Identify the underlying physical characteristics that separates alpha emitting therapy from other nuclear medicine therapies
2. Understand the different biochemical forms in which alpha emitters can be used for radionuclide therapy
3. Recognize the potential applications of the nuclear medicine imaging for alpha emitting therapy planning
4. Comprehend the radiation protection and safety measures that are associated with handling alpha emitters
5. Identify the opportunities and challenges for alpha therapy in the future

Summary
In the early 1920’s a mixture of $^{226}\text{Ra}$ was sold under the commercial name Radithor. Radithor was advertised as a radioactive mineral water that contained a secret mixture of radium and mesothorium, that was claimed to cure impotence, among other ills. Later on a systematic study was done to show that levels of radiation due to drinking Radithor far exceeded levels that scientists would normally classify as lethal today. This was the dark intial experience with alpha-emission therapy.

About 100 years later, in 2013, $^{223}\text{Ra}$ radium chloride (Xofio; formerly alpharadin) became the first and only alpha-emitting radiopharmaceutical to receive FDA and EMEA approval for clinical use, with an intended purpose to treat metastases associated with metastatic bone disease from castration resistant prostate cancer (mCRPC). Alpha particles are monoenergetic, high-energy helium nuclei with a high linear energy transfer (LET) and decreased particle range. This unique characteristic of high energy deposition in closely packed region has reinserted alpha emitters in the radionuclide therapy scene.

The evidence-based success treating bone metastasis with $^{223}\text{Ra}$ radium chloride, motivated further investigation for labelling available compounds (e.g. PSMA) with alpha emitters, which was particularly successful in the form of $^{225}\text{Ac}$-labeled PSMA (alone or in combination with beta minus emitting radionuclides). The use of alpha-emitters is also related to the pharmacodynamic performance of the isotope-carrier (e.g. antibody) complex, where the proper choice of isotope radiodecay half-life is
essential. Short-range alpha-immunotherapy tracers have been demonstrated feasible for human use in leukemia treatment with a $^{213}$Bi-IgG construct and $^{225}$Ac conjugated to lintuzumab. More recently nano-bodies have been used as vehicles for targeted alpha therapy in breast and ovarian metastatic desies.

Radiation protection precautions for handling and administration of radionuclides must be taken in accordance with national regulations. Given the high biological effectiveness of incorporated $^{223}$Ra, special incorporation measurements may be taken to monitor involved members of the staff and all costumary radiation exposure optimisation must be taken into account.

This session will be divided in an initial talk focusing in the extensive experience with $^{223}$Ra-CI (Xofigo) treatment and new perpspectives related. The second talk will have a focus on targeted alpha therapy and alpha immunotherapy.

**Key Words**
Alpha emitters, radionuclide therapy, radiation safety