Special Track Session 3
Oncology & Theranostics Committee
Sunday, October 5, 15:00 – 16:30

Session Title
Debate: Will Alpha Therapy be the Main Radionuclide Therapy Approach in the Future?

Moderators
Chiara Grana (Milan, Italy)
Christophe Deroose (Leuven, Belgium)

Point of view: PRO: A breakthrough that should improve response and long term outcome
Désirée Deandreis (Villejuif, France)

Point of view: CON: Complex techniques difficult to validate at the era of effective 177Lu-theranostic approaches
Clément Bailly (Nantes, France)

Educational Objectives
1. Clinical trials demonstrating the efficacy and tolerance of radiopharmaceuticals labelled with beta emitters in various tumours
2. Toxicity and limits of beta emitter and alpha radiopharmaceuticals
3. Availability of alpha emitters for clinical trials and routine
4. Arguments/ proof of concept showing that alpha emitters represent a technological breakthrough based on preclinical and clinical data

Summary
Identification of new biomarkers and access to innovative radionuclides have paved the way for «radiotheranostics». In current clinical practice, radiotheranostics have been approved for use with peptides and small molecules labeled with the beta emitter lutetium-177. This has primarily been in the «niche» of gastro-entero-pancreatic neuroendocrine tumors (GEP-NET) based on the phase III Netter-1 trial showing clinical benefit using radiolabeled somatostatin analogs 177Lu-DOTATATE in patients with tumors that express somatostatin receptors. More recently, in the broader context of advanced prostate cancer, following the phase III Vision clinical trial, demonstrating that 177Lu-PSMA-617 (Pluvicto™) prolonged imaging-based progression-free survival (rPFS) and overall survival, when added to standard care in patients with advanced PSMA-positive metastatic castration-resistant prostate cancer. This represents a major evolution in oncology, expanding the horizons of radiotheranostics to earlier stages of these diseases or other tumor subtypes with distinct specific biomarkers and radiopharmaceuticals. Indeed, recently, the Phase III PSMAfore trial assessing Pluvicto™ in metastatic castration-resistant prostate cancer in the pre-taxane setting, met its primary endpoint of rPFS. Other clinical trials are on going.

The first clinical trials using alpha emitters are underway, especially for advanced NET and prostate cancer with actinium-225, in heavily pre-treated patients, in particular relapsing or refractory after lutetium-177-based therapy. Alpha-TRT is also evaluated in other refractory solid tumors, acute myeloid leukemia and MM, with different vectors and ligands, mostly labeled with 225Ac but also in some studies with other emitters such as lead-212 or astatine-211.A recent retrospective analysis reported experience across the world using 225Ac-PSMA in 488 patients with metastatic castration-resistant prostate cancer. 225Ac-PSMA shows a substantial antitumor effect and represents a viable therapy option in patients treated with previous lines of approved agents, with xerostomia as common side-effect. Severe bone marrow and renal toxicity were less common adverse events. However, the widespread adoption of alpha emitters in clinical practice will imply prospective clinical trials with the demonstration of an impact on survival and acceptable toxicity.

Key Words
Alpha-emitters; beta-emitters; radiopharmaceuticals therapy