Scientific program

Cancerfondens planeringsgrupp för Onkologisk radionuklidterapi

The planning group for Oncological radionuclide therapy

– supported by The Swedish Cancer Society

Digital meeting 08th – 10th June 2021

Cancerfonden

Stockholms universitet

Karolinska Institutet

GÖTEBORGS UNIVERSITET

Cancerfondens planeringsgrupp för Onkologisk radionuklidterapi
The planning group for Oncological radionuclide therapy
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SCIENTIFIC PROGRAM FOR THE ONLINE MEETING ON ZOOM 8th - 10th JUNE 2021

Organized by Thuy Tran, Lovisa Lundholm, Kristina Viktorsson, Eva Forssell-Aronsson and Charlotte Andersson

Register for the meeting at radionuklidterapi.se
Zoom link to test your presentation 7th - 10th June
https://stockholmuniversity.zoom.us/j/62750422769

Tue 08th June 2021	13.30 – 17.00 Zoom link: https://stockholmuniversity.zoom.us/j/62820645913
13.30	**ZOOM OPENING – CHECK-IN**
14.00 – 14.10	**WELCOME TO THE MEETING** **Thuy Tran – Karolinska Institutet** **Eva Forssell-Aronsson – University of Gothenburg**
14.10 – 14.45	**Early phase clinical studies of radiopharmaceuticals – what is needed?** ***Qualified Person (QP), MSc Pharm Carsten Steiger,*** ***Karolinska University Hospital***
14.45 – 14.50	**Biobreak**
SESSION 1	**Moderator: Michael Ljungberg - Lund University**
14.50 **ABS 1**	Iodine avidity in papillary thyroid cancer is associated with thyroglobulin expression, tissue proliferation and histological variant ***Joachim Nilsson – Karolinska University Hospital and Karolinska Institutet***
15.05 **ABS 2**	A comparison and improvements of small VOI method for kidney absorbed dose measures in patients undergoing ^{177}Lu-DOTATATE ***Jehangir Khan – University of Gothenburg***
15.20 **ABS 3**	Changes in tumour dosimetric quantities over treatment cycles in [^{177}Lu]Lu-DOTATATE therapy ***Johan Gustafsson – Lund University***
15.35 **ABS 4**	A Phase II trial of ^{177}Lu-DOTATATE in children with primary refractory or relapsed high-risk neuroblastoma, LuDO-N ***Jakob Stenman – Karolinska University Hospital and Karolinska Institutet***
15.50 – 15.55	**Biobreak**
SESSION 2	**Moderator: Annelie Lindström - Linköping University**
15.55 **ABS 5**	Phase I evaluation of ^{99m}Tc-labelled HER2-binding DARPin G3 ***Vladimir Tolmachev – Uppsala University***
16.10 **ABS 6**	Development of novel Immuno-theranostic compounds targeting Leucine-Rich Repeat-Containing protein 15 (LRRC15), a TGFβ-driven pan-cancer biomarker. ***Mohamed Altai – Lund University***
16.25 **ABS 7**	Bone marrow dosimetry S values for terbium-161 show increased source distribution dependency compared to lutetium-177 ***Jens Hemmingsson – University of Gothenburg***
16.40 **ABS 8**	Translation of the GRPR antagonist [^{99m}Tc]Tc-maSSS-PEG2-RM26 in clinics for imaging of prostate tumors ***Ayman Abouzayed – Uppsala University***
16.55 – 17.00	**CLOSING FIRST DAY**

WED 09th June 2021	12.30 – 17.00 Zoom link: https://stockholmuniversity.zoom.us/j/62820645913
12.30	**ZOOM LINK OPENING – CHECK-IN**
SESSION 3	**RAPID FIRE**
	Moderator: Marika Nestor – Uppsala University
13.00	Fusion of breast cancer cells and macrophages is a spontaneous biological process
ABS 9	that can be influenced by ionizing radiation
	Annelie Lindström – Linköping University
13.10	Mechanistic insights from high resolution DNA damage analysis to understand
ABS 10	mixed high and low LET radiation exposure and its therapeutic potential
	Lovisa Lundholm – Stockholm University
13.20	Evaluation of the antioxidant α1-microglobulin (A1M) as a kidney radioprotector in
ABS 11	mouse models
	Amanda Kristiansson – Lund University
13.30	Early response in expression of radiation related proteins in mouse kidney after
ABS 12	injection of ^{177}Lu-octreotate with or without recombinant α1-microglobulin
	Charlotte Andersson – University of Gothenburg
13.40 – 13.50	**Short break**
SESSION 4	**RAPID FIRE**
	Moderator: Stig Palm – University of Gothenburg
13.50	Radionuclide Therapy Using ^{177}Lu-labeled ABD-fused ADAPT6 Scaffold Protein
ABS 13	***Javad Garousi – KTH***
14.00	In vitro characterizations of ^{177}Lu-anti-CEA antibody and HSP90 inhibition for
ABS 14	potentiated radioimmunotherapy of gastrointestinal cancer
	Tabassom Mohajer Shojai – Uppsala University
14.10	A conjugation strategy to modulate antigen binding as well as FcRn interaction lead
ABS 15	to improved tumor targeting and radioimmunotherapy efficacy with an antibody
	targeting Prostate Specific Antigen
	Joanna Strand – Lund University
14.20	Evaluation of molecular design of HER2-targeting affibody-drug conjugates for drug
ABS 16	delivery to ovarian cancer
	Tianqi Xu – Uppsala University
14.30 – 14.40	**Short break**
SESSION 5	**INVITED SPEAKERS**
	Moderator: Lovisa Lundholm – Stockholm University
14.40 – 15.20	**An in-depth analysis of the anti-tumor immune response induced by radiation & CTLA-4 therapy**
	Invited speaker: Dr. Nils Rudqvist, MD Anderson, Texas, USA
15.20 – 16.00	**Alpha therapy in breast cancer**
	Invited speaker: Dr. Sarah M Cheal, MSKCC, New York, USA
16.00 – 16.10	**Short break**
SESSION 6	**RAPID FIRE**
	Moderator: Anzhelika Vorobyeva – Uppsala University
16.10	Intratumoral distribution of ^{177}Lu-PSMA-617 over time and in comparison with
ABS 17	^{18}F-PSMA-1007
	Anders Örbom – Lund University
16.20	HER3 PET-imaging using a ^{68}Ga-labeled affibody molecule provides favorable image
ABS 18	contrast compared with ^{89}Zr-labeled antibody and F(ab´)$_2$-fragment based tracers
	Sara Rinne – Uppsala University
16.30	Characterization of a new panel of ^{89}Zr-labeled anti-RON monoclonal antibodies as a
ABS 19	targeting agent for molecular imaging and cancer therapeutics
	Diana Spiegelberg – Uppsala University
16.40	New doctoral project on improving dosimetry for targeted alpha therapies
ABS 20	***Erik Leidermark – University of Gothenburg***
16.50 – 17.00	**CLOSING SECOND DAY**

THU 10th June 2021	12.30 -17.00 Zoom link: https://stockholmuniversity.zoom.us/j/62820645913
12.30	**ZOOM LINK OPENING – CHECK-IN**
SESSION 6	**RAPID FIRE**
	Moderator: Bo Stenerlöw – Uppsala University
13.00	Cellular and gene expression changes in VH10 and AHH-1 cells after chronic and
ABS 21	acute exposure to low doses of low, high and mixed LET ionizing radiation
	Milagrosa Lopez Riego – Stockholm University
13.10	High-yield synthesis of clinically relevant DOTA-based tracers using cyclotron-
ABS 22	produced gallium-68
	Emma Jussing – Karolinska Institutet
13.20	Combined treatment of mice bearing HER2-expressing xenografts by trastuzumab
ABS 23	and Affibody-mediated PNA-based pretargeting improves their survival
	Maryam Oroujeni – Uppsala University
13.30	DOTA-conjugation and ^{177}Lu-DOTA-radiolabeling optimizations of IgG4 antibodies
ABS 24	***Preeti Jha – Uppsala University***
13.40	Impact of DOTA position on biodistribution of ^{177}Lu-labelled ABD-fused Affibody
ABS 25	molecules
	Yongsheng Liu – Uppsala University
13.50 – 13.55	**Biobreak**
SESSION 7	**RAPID FIRE**
	Moderator: Kristina Viktorsson – Karolinska Institutet
13.55	Selection of optimal radiolabel position and composition in DARPin Ec1 for high-
ABS 26	contrast imaging of EpCAM Expression in Prostate cancer
	Anzhelika Vorobyeva – Uppsala University
14.05	Development of ^{211}At and ^{125}I Radiopharmaceuticals for Pretargeted
ABS 27	Radioimmunotherapy of Disseminated Cancer
	Chiara Temperanza - University of Gothenburg
14.15	Monte Carlo simulated cell dosimetry for γ-H2AX foci distribution prediction in
ABS 28	alpha particle irradiated cells
	Emma Mellhammar – Lund University
14.25	Cyclotron production of ^{66}Ga for radiolabelling of nanoparticles for simultaneous
ABS 29	detection using PET/MR
	Emmy Dalqvist – Karolinska Institutet
14.25-14.35	**Short break**
SESSION 8	**INVITED SPEAKERS**
	Moderator: Thuy Tran – Karolinska Institutet
14.35 – 15.05	**PET/MR in the clinics: Possibilities and challenges**
	Invited speaker: Prof. Håkan Ahlström,Uppsala University
15.05 – 16.05	**Workshop: "What have we learnt & future directions" – Breakout session**
	Moderators:
	Kristina Viktorsson – Karolinska Institutet
	Eva Forssell-Aronsson – University of Gothenburg
16.05 – 16.50	**Immunotherapy and PET imaging**
	Invited speaker: Prof. Elisabeth de Vries, University Medical Center Groningen, The Netherlands
16.50– 17.00	**CLOSING OF THE MEETING**
	Eva Forssell-Aronsson – University of Gothenburg

ZOOM-meeting guidelines: Please, mute yourself at all points when you are not presenting or given the word by the moderator to ask questions. Moderators, please mute your microphones during the presentations. If you have questions to the speakers, write them in the chat and we will give you the word to ask yourself or ask it for you as time permits. For the breakout sessions, we will put you in different ZOOM rooms automatically and take you back to a joint wrap-up. Thank you!

INVITED SPEAKERS' ABSTRACTS

Early phase clinical studies of radiopharmaceuticals – what is needed?

Carsten Steiger, Qualified Person (QP), MSc Pharm, Karolinska University Hospital, Sweden

The number of novel radiopharmaceuticals being developed is increasing rapidly. Understanding regulatory requirements and knowing how to practically apply Good Manufacturing Practice (GMP) regulations when setting up your production process are essential for being able to conduct first-in-human studies.

This presentation aims to give an overview of the regulatory drug development process in Europe; to clarify regulatory requirements for conducting early phase clinical trials in Sweden and to give practical guidance on how to setup GMP production of a novel radiopharmaceutical.

An in-depth analysis of the anti-tumor immune response induced by radiation and CTLA-4 therapy

Nils-Petter Rudqvist, PhD, Assistant professor, Department of Thoracic/Head & Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Texas, USA.

Radiation therapy (RT) in combination with CTLA-4 inhibition (CTLA4i) activates anti-tumor T cells in mice and in some patients with tumors unresponsive to CTLA4i alone, but complete tumor rejection is rare. Here we performed an in-depth analysis of the T cells infiltrating mouse tumors treated with RT and/or CTLA4i to identify T cell functional subsets and actionable targets to improve the response. CTLA4i promoted the expansion of polyfunctional CD4+ and CD8+ T cells, whereas RT enhanced the quantity and clonality of CD8+ T cells. The combination therapy resulted in a marked increase in intratumoral T cells with a shift of antigen-specific CD8+ T cells from terminally differentiated cytotoxic to polyfunctional effectors. Gene signatures defining the three dominant T cell functional states within RT+CTLA4i treated tumors were associated with improved survival in breast and melanoma cancer patients. Among multiple combinations tested, only agonistic CD40 therapy enhanced significantly responses to RT+CTLA4i.

Alpha Therapy in Breast Cancer

Sarah M. Cheal, PhD, Senior Research Scientist, Memorial Sloan Kettering Cancer Center, New York, USA

Molecularly targeted radiotherapy, especially with alpha-emitting isotopes, is highly promising for treating advanced breast cancer (BCa) patients who may present immune- or chemo-refractive disease, as well as occult and diffuse micro-metastatic tumors. Preclinical investigations of alpha(α)therapy in BCa have included directly radiolabeled antibodies (e.g., anti-HER2 antibodies labeled with 225Ac, 213Bi, or 227Th; 213Bi-hu3S193 targeting anti-Lewis Y; 227Th-BAY 86-1903targeting mesothelin; 212Pb-225.28 targeting chondroitin sulfate proteoglycan 4; 225Ac-hu11B6 targeting hK2), and with other vectors. An alternative drug delivery approach to conventional radioimmunotherapy is pre-targeted radioimmunotherapy (PRIT), which aims to achieve efficient tumor targeting of a non-radioactive bifunctional antibody followed with a rapidly clearing radioactive carrier molecule. We recently reported a theranostic beta-PRIT treatment of HER2-expressing BCa using an anti-tumor/anti-DOTA hapten bispecific approach (DOTA-PRIT) with 177Lu-DOTA hapten. For α-therapy, we recently adapted DOTA-PRIT for delivery of 225Ac and its diagnostic surrogate, 111In. Anti-HER2 DOTA-PRIT + [225Ac]PrDOTA is an active therapeutic agent in BT474 human BCa xenografts, resulting in cures with minimal toxicity. Efforts to improve the probability of CR and histologic cure are ongoing, with an emphasis on optimizing [225Ac]Pr dosing.

PET/MR in the clinics: Possibilities and challenges

Håkan Ahlström, Professor, Department of Surgical Sciences, Radiology, Uppsala University, Sweden

The PET/MR scanner combines two existing technologies and collects information from these simultaneously. In addition to superior anatomical information, this concatenated information provides the opportunity to analyze and quantify biochemical processes at both molecular, cellular and organ levels simultaneously and with exactly compliant anatomical localization. PET/MR is currently performed at a number of centres around the world as part of the clinical radiology.

This lecture focuses on questions and considerations for clinical PET/MRI. Although local factors influence how clinical PET/MRI imaging is implemented, the methods and considerations described here intend to be applied to most clinical issues. PET/MR provides more options than PET/CT, with diagnostic benefits for some clinical applications, but with extra complexity. A recurring theme is to match PET/MR to the clinical application to balance diagnostic accuracy with efficiency. Another challenge is the amount of information you get and how to present and analyse it. The computerised methods developed to take care of and analyse all available information will provide new knowledge that would otherwise not be possible to obtain. This knowledge is needed to be able to choose from the currently increasing arsenal of drugs, and other treatment, which is adapted to each individual and not as before to each disease group. The results will hopefully provide increased knowledge about diagnosis, prevention, prognosis, treatment and how to evaluate treatment outcomes.

Immunotherapy and PET imaging

Elisabeth de Vries, Professor, Department of Medical Oncology, Radiology, University Medical Center Groningen, Grongen, The Netherlands.

Immune checkpoint inhibitors have substantially changed the field of oncology over the past few years. They offer an alternative treatment strategy by exploiting the patients' immune system, resulting in a T cell-mediated anti-tumor response. These therapies are effective in multiple different tumor types. Unfortunately, a substantial group of patients does not respond to immune checkpoint inhibitors. Molecular imaging, using single-photon emission computed tomography (SPECT) and positron emission tomography (PET), can provide non-invasive whole-body visualization of the tumor and immune cell characteristics and might support the patient selection or response evaluations for immune checkpoint inhibitor therapies. We studied especially with PET the role of imaging of immune checkpoints and immune cells.