Addressing Societal Challenges Through Advancing the Medical, Industrial and Research Applications of Nuclear and Radiation Technology

20 – 21 March 2018

Charlemagne, Brussels

SESSION 2 - Health: Novel nuclear medicine to advance patient care

Introductory remarks

Kristoff Muylle

EANM President

Nuclear medicine innovations in the past decade

Instrumentation	Targeted therapy	Molecular imaging
• PET/CT • SPECT/CT • PET/MR	• Introduction of α-emitter (^{223}Ra, boneM+) • PRRT (Neuroendocrine tumours) • RIT (lymphoma)	• Wide range of clinical applications for ^{18}FDG • Imaging of intra- & extracellular targets • Molecular characterisation
• Significant increase of impact of nuclear medicine on patient management	• Renewed interest in radionuclide therapy	• Patient tailored image guided therapy

^{177}Lu-Dotatate Significantly Improves Progression-Free Survival in Patients with Midgut Neuroendocrine Tumours: Results of the Phase III NETTER-1 Trial

Jonathan Strosberg[1], Edward Wolin[2], Beth Chasen[3], Matthew Kulke[4], David Bushnell[5], Martyn Caplin[6], Richard P. Baum[7], Erik Mittra[8], Timothy Hobday[9], Andrew Hendifar[10], Kjell Oberg[11], Maribel Lopera Sierra[12], Philippe Ruszniewski[13], Dik Kwekkeboom[14]
on behalf of the NETTER-1 study group

[1] Moffitt Cancer Center, Tampa, FL 33612, USA;[2] Markey Cancer Center, University of Kentucky, Lexington, KY 40536-0093, USA;[3] University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA;[4] Dana-Farber Cancer Institute, Boston, MA 02215, USA;[5] University of Iowa, Iowa City, IA 52242, USA;[6] Royal Free Hospital, London, United Kingdom;[7] Zentralklinik, Bad Berka, Germany;[8] Stanford University Medical Center, Stanford, CA 94305, USA;[9] Mayo Clinic College of Medicine, Rochester, MN 55905, USA;[10] Cedars Sinai Medical Center, Los Angeles, CA 90048, USA;[11] University Hospital, Uppsala University, Uppsala, Sweden;[12] Advanced Accelerator Applications, New York, NY 10118, USA;[13] Hopital Beaujon, Clichy, France;[14] Erasmus Medical Center, Rotterdam, Netherlands

Progression-Free Survival

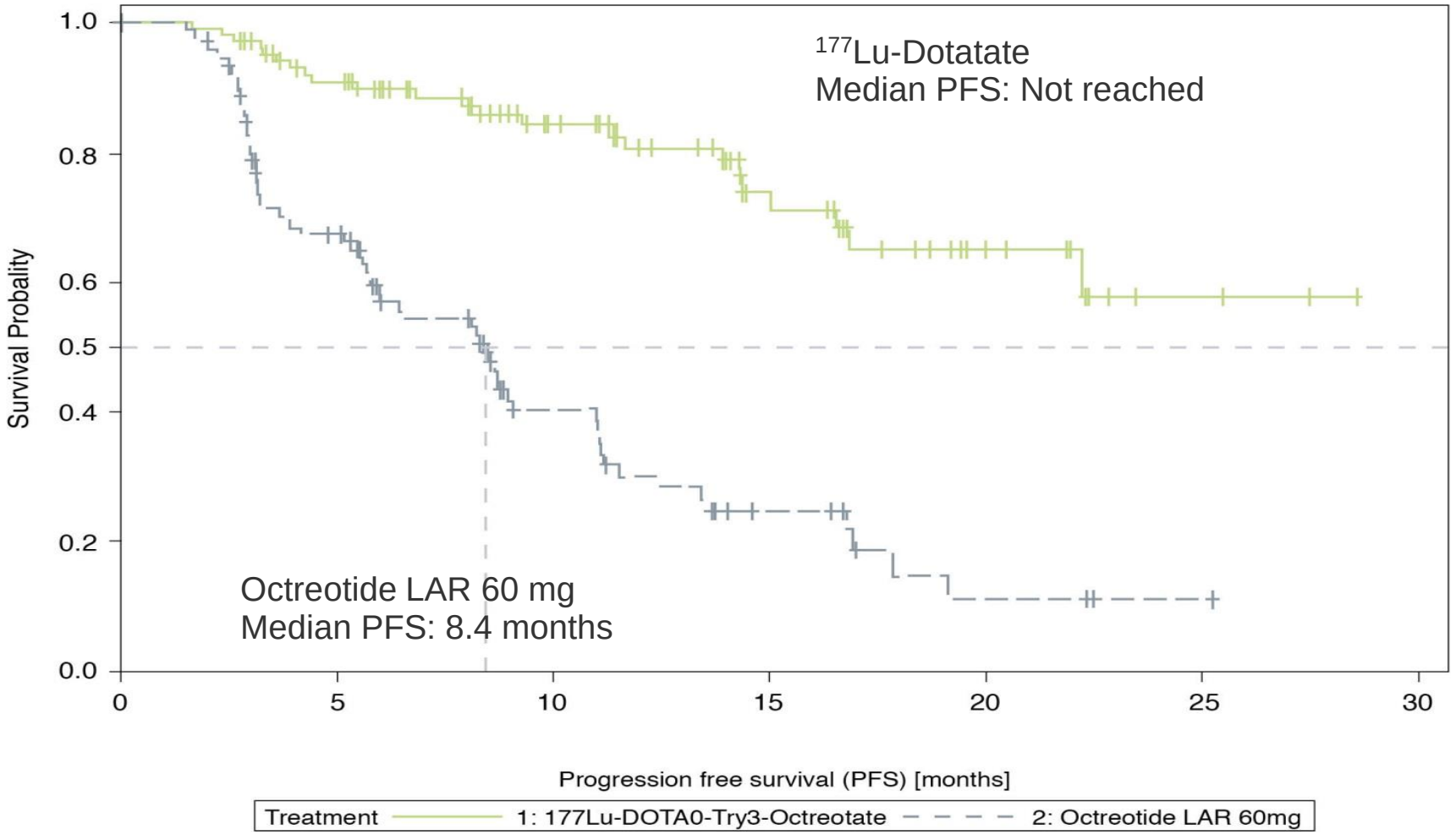
N = 229 (ITT)
Number of events: 90

- ^{177}Lu-Dotatate: 23
- Oct 60 mg LAR: 67

Hazard ratio : **0.21** [0.129 – 0.338] **p < 0.0001**

79% reduction in the risk of disease progression/death

Estimated Median PFS in the ^{177}Lu-Dotatate arm
≈ 40 months



All progressions centrally confirmed and independently reviewed for eligibility (SAP)

Nuclear medicine innovations in the next decade

Instrumentation

- Total Body PET
- Dedicated SPECT-cameras

- Higher sensitivity
- Reduction of dose to the patient
- Faster imaging
- Dynamic scanning

Targeted therapy

- Introduction of new α-emitters: ^{225}Ac, 211At,…
- New indications (prostate cancer,…)
- Combined treatments (immunotherapy,…)

- New treatment options

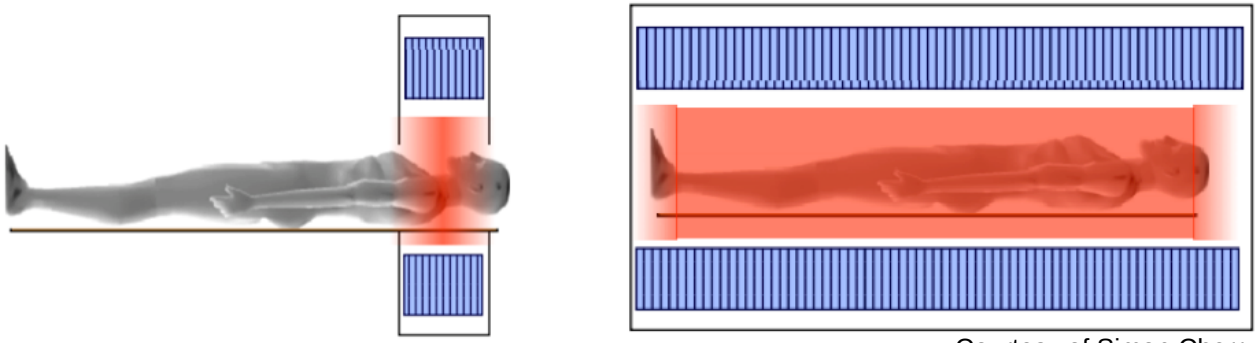
Molecular imaging

- Early response assessment with ^{18}FDG
- Introduction of molecular imaging in clinical trials /routine

- Better patient selection
- Avoiding toxicity and reduction of costs

Total Body PET Concept

From current 15-25 cm to 1-2 m long PET



Courtesy of Simon Cherry

Point peak Sensitivity: 4-6%	X 3-5 →	Point peak Sensitivity: 12-24 %
Body imaging sensitivity (NECR): 7-21 cps/kBq	X 30-50 →	Body imaging sensitivity (NECR): 200-500 cps/kBq
Acquisition time for total body 20 min	20-40 x faster →	Acquisition time for total body 0.5 min

Options

Quality

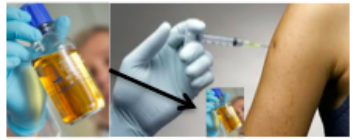
NEW

Improved images (reduce Poisson noise)

Dynamic imaging (multiple images after each other)

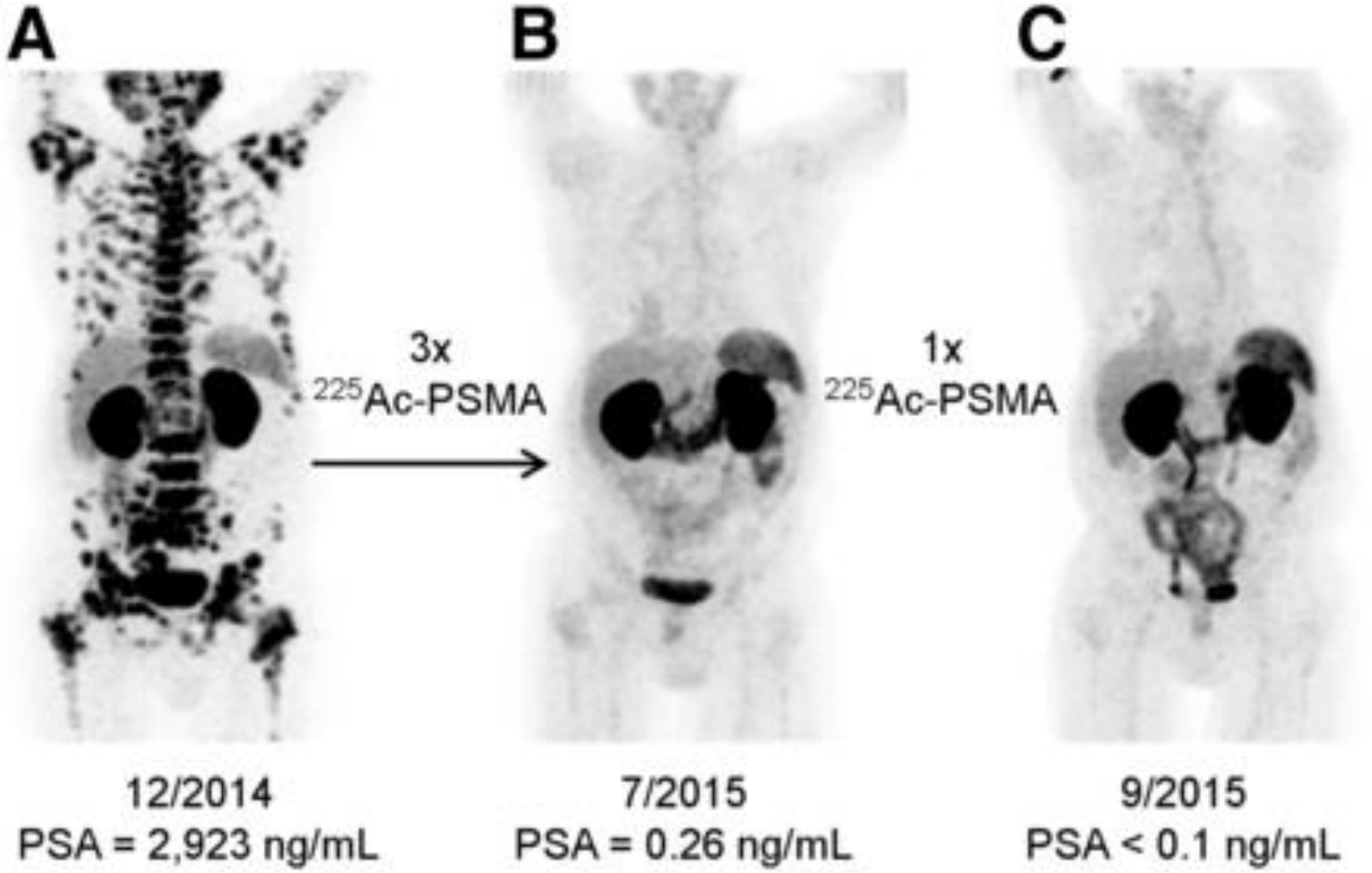
Reduce dose to patients and cost of tracer production

Faster imaging more patients on same day



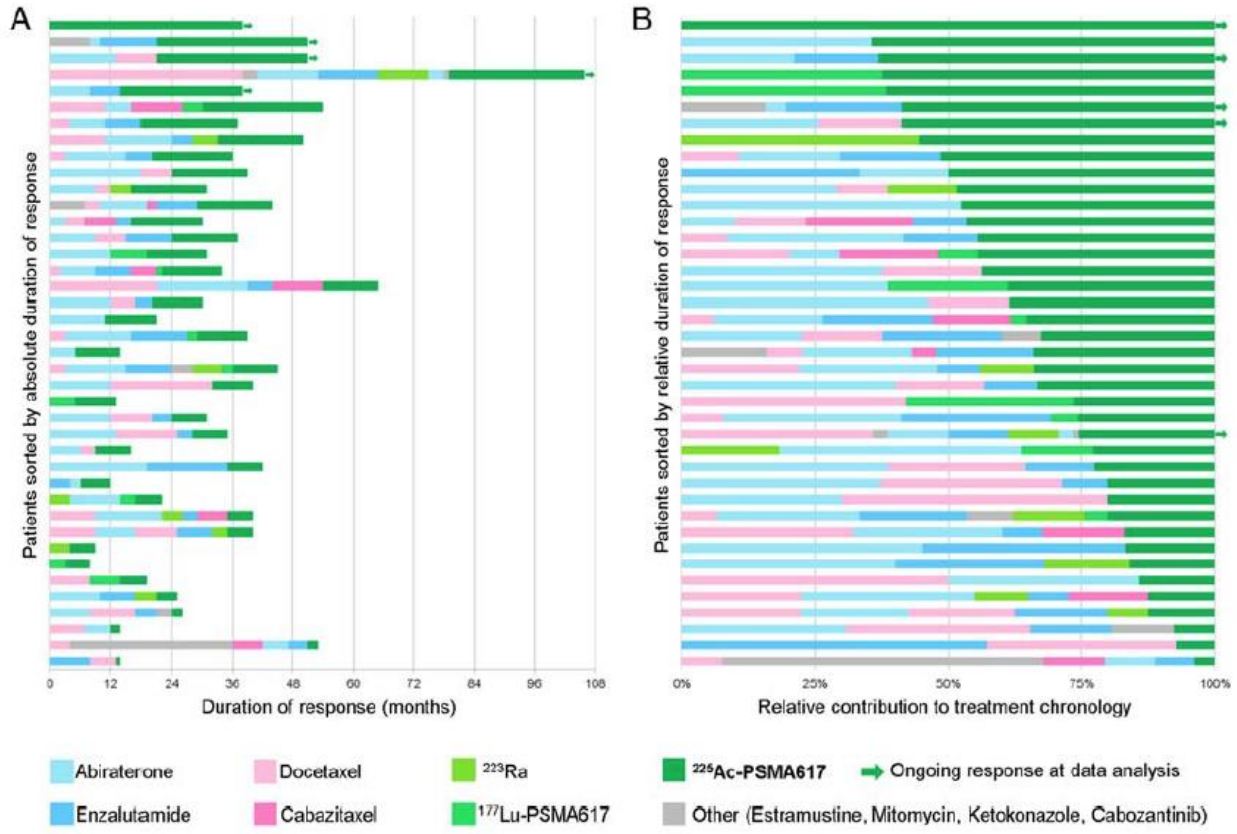
THERA(G)NOSTIC: ^{68}Ga-PSMA + ^{225}Ac-PSMA

Patient-A
LHRH (urupeptyl, leuprorelin)
zoledronate
Docetaxel (50 cycles)
Carmustin/Epirubicin in hyperthermia
Arbiraterone
Enzalutamide
Ra-223 (6 cycles)
Arbiraterone re-exposition
Estramustine



J Nucl Med December 1, 2016 vol. 57 no. 12 1941-1944

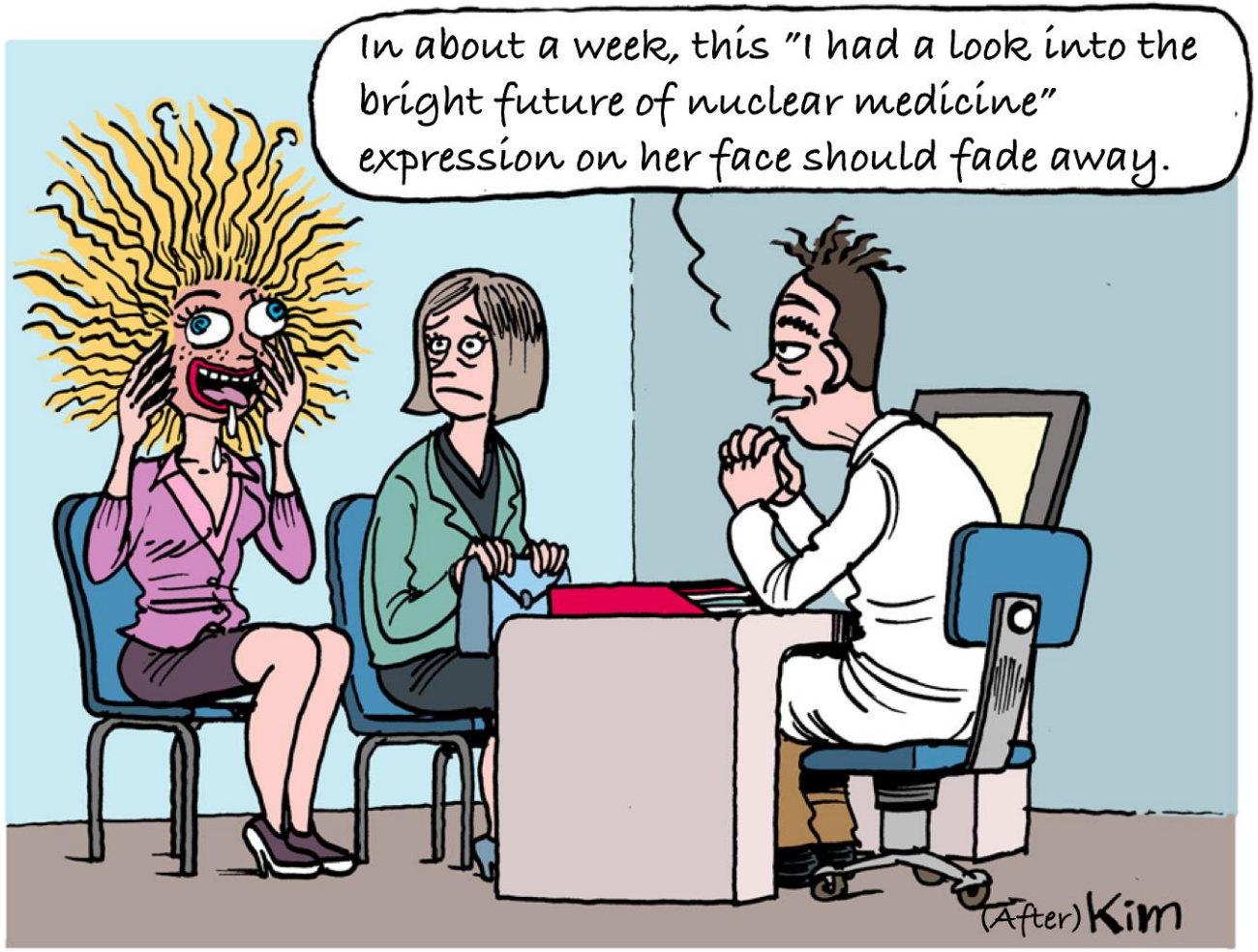
Radionuclide therapy with ^{225}Ac-PSMA in CRPC



- Median duration of tumor-control under 225Ac-PSMA-617 last-line therapy 9.0 months in 40 patients
- 5 patients with enduring responses of > 2 years.

Courtesy of Prof. Uwe Haberkorn, UniversitätsKlinikum, Heidelberg

A look into the future of nuclear medicine



Radiopharmaceuticals =

= radioactive Drugs

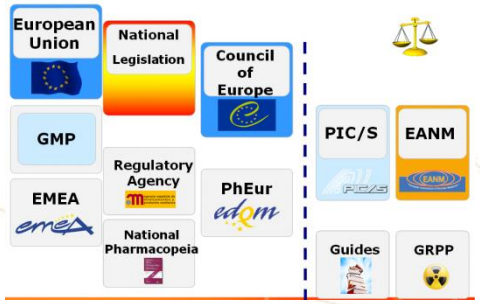
Legislation concerning radiation protection/ safety

Directive 96/29/ EURATOM → Basic safety standards

Directive 97/43/ EURATOM → Medical exposure directive

Directive 2013/59/EURATOM → Basic safety standards

„Radionuclide therapy is considered as part of radiotherapy“



Legislation concerning drugs / medicines

Directive 2001/20/EC → “Clinical Trial Directive”

Directive 2001/83/EG → Qualified Person, MA, …

Directive 2003/94/EG → GMP Annex 13 (IMP`s)

Directive 2004/27/EC → API according to GMP

Directive 2005/28/EC → GCP / Authorization for IMP

Regulation (EC) No 1394/2007 → Advanced therapy regulation

Regulation EU No 536/2014 → “Clinical Trial Regulation”

“Radiopharmaceuticals (including their precursors) are considered as pharmaceuticals”

A common legal framework for radiopharmaceuticals

Marketing Authorisation

Directive 2001/83 (Medicinal Products for human use) as amended by 2004/27:

Clinical Trial

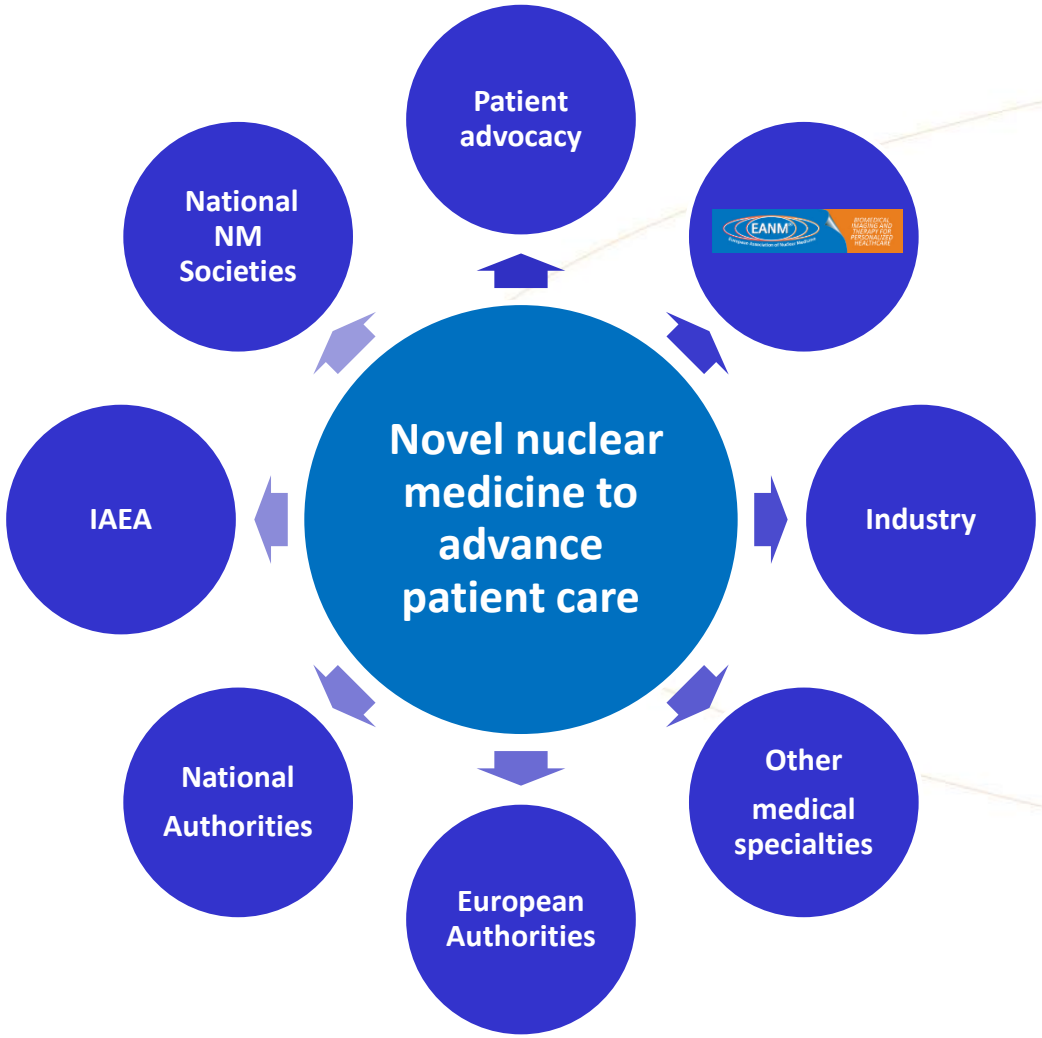
Directive 2001/20/EC
Directive 2003/94/EG
Directive 2005/28/EC

Regulation EU No 536/2014
From 2018

„Extemporaneous Preparation“ Compounding
In-house

Reality in Europe:
High Diversity

Building the future of Nuclear Medicine together



Conclusions:

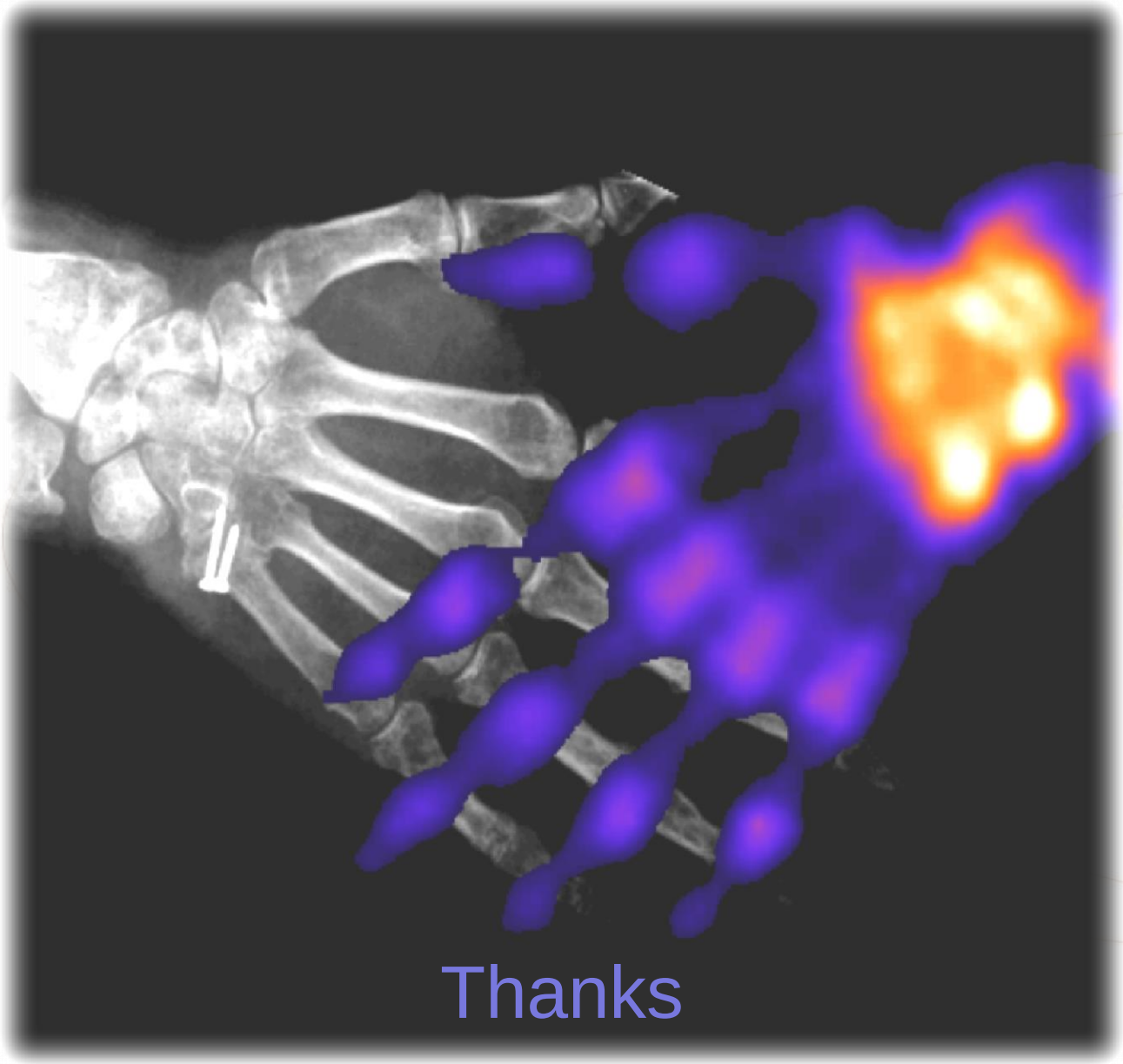
In the past decade, the technical and scientific progress within our specialty has led to a fast increasing impact on patient management.

In the next decade, this progress has the potential to make nuclear medicine one of the, if not “the” key player in the development of “personalised medicine”.

Further development of scientific research and a broad access to these new diagnostic and therapeutic applications will not only improve patients’ care, but has also the potential to reduce significantly the expenses related to specialised healthcare.

The main challenge is to facilitate and accelerate patient access to these new highly promising diagnostic and therapeutic procedures, while maintaining high quality standards.

This goal can only be achieved with a “personalised” Nuclear Medicine tailored legal framework, taking in account the particularities of radiopharmaceuticals and by collaboration and consultation of all involved stakeholders.



Thanks