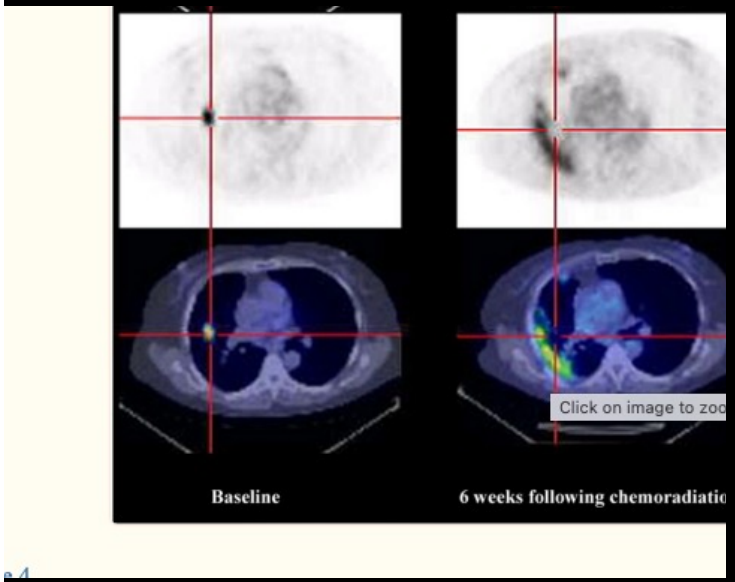


PET SCAN APPLICATIONS; HOSPITAL MANAGEMENT POV

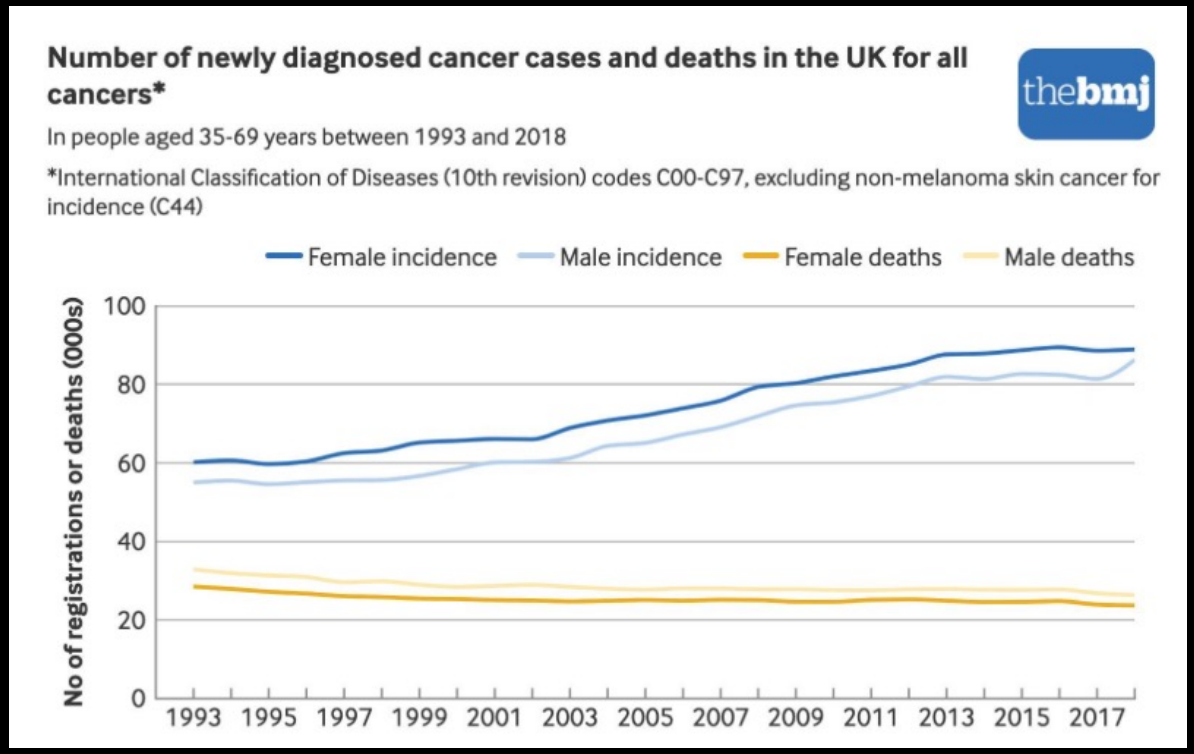
Hans Wijaya

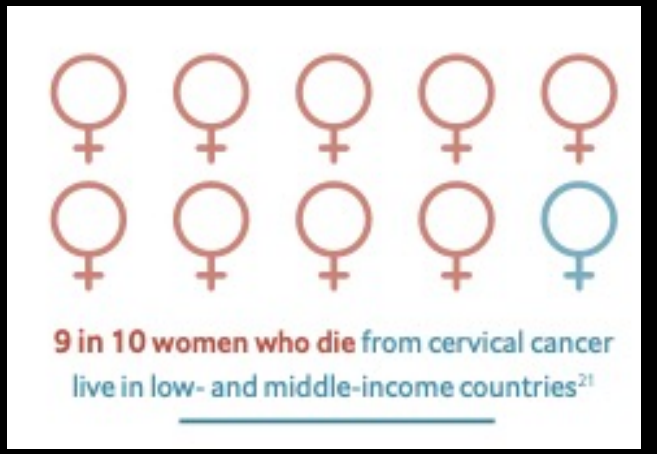
Cyclotek Pharmaceutical Indonesia

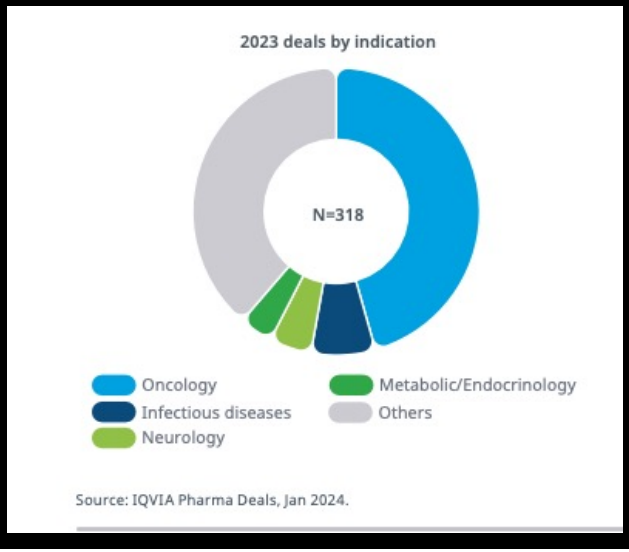
POINTS

- Changing Landscape
- Innovations in Precision Medicine
- Indonesia Challenge
- Strategizing the Hospitals

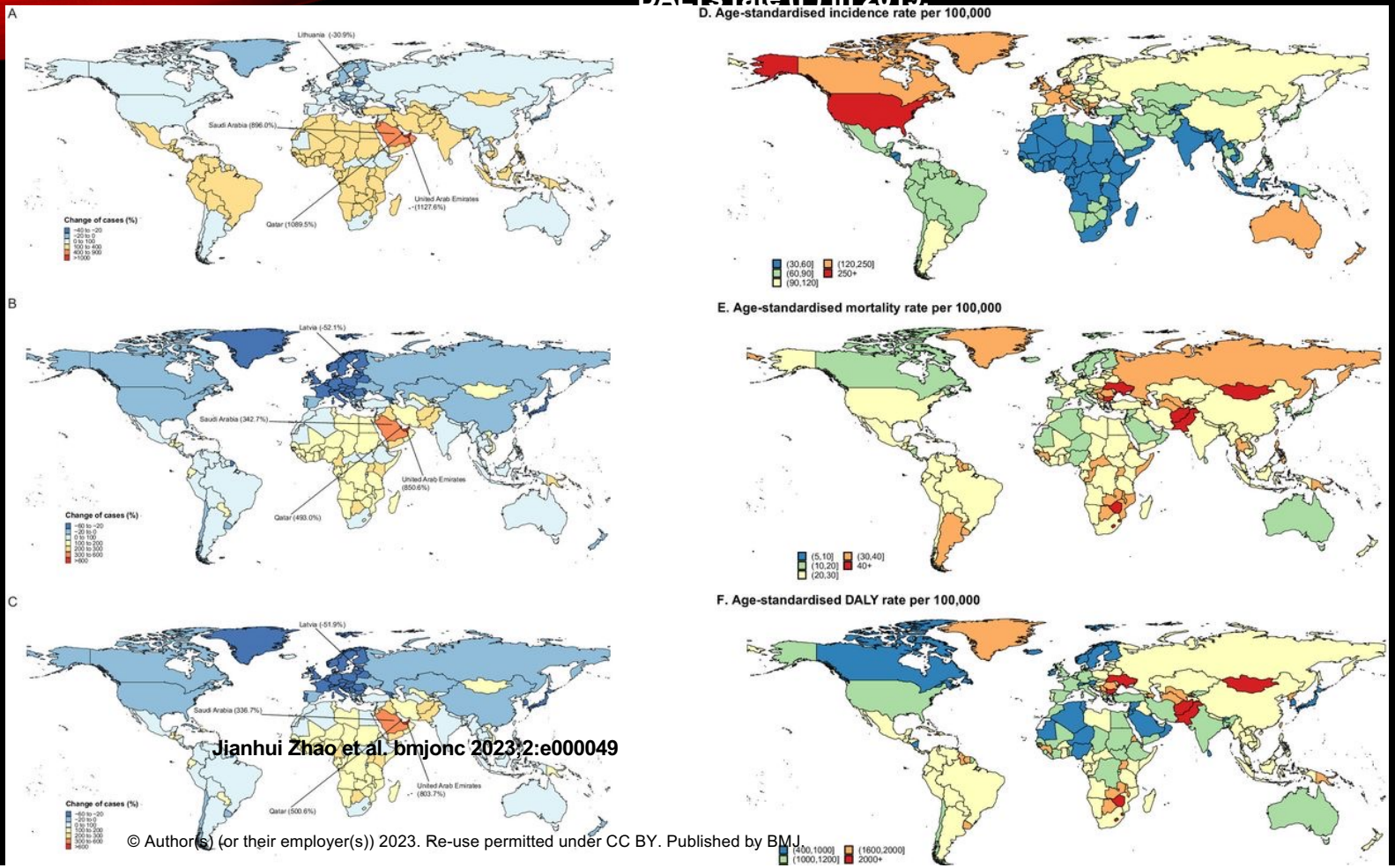
UNDERSTANDING LANDSCAPES







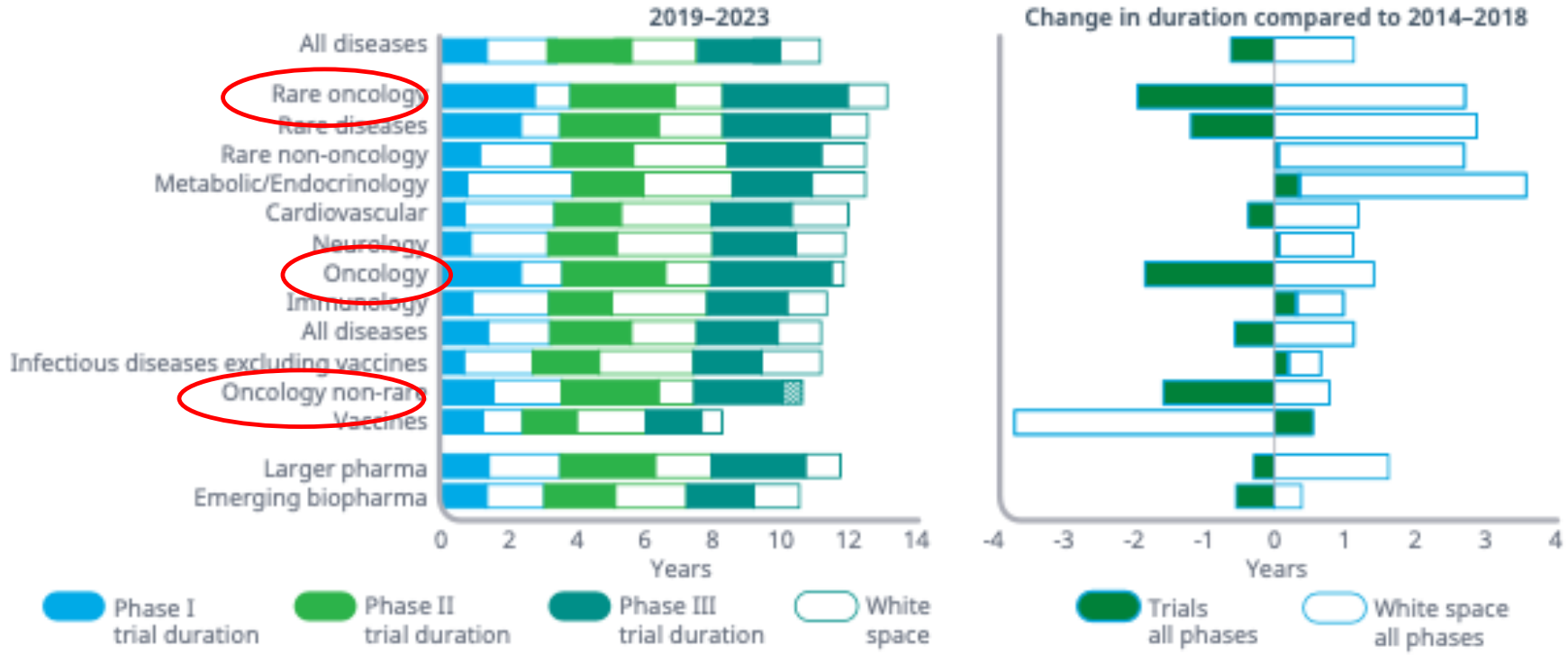
Among 204 countries and territories, the relative change of incident (A), death (B) and DALYs (C) cases of early-onset cancers from 1990 to 2019, and ASIR (D), ASDR (E), age-standardised DALYs rate (F) in 2019.



Jianhui Zhao et al. bmjonc 2023;2:e000049

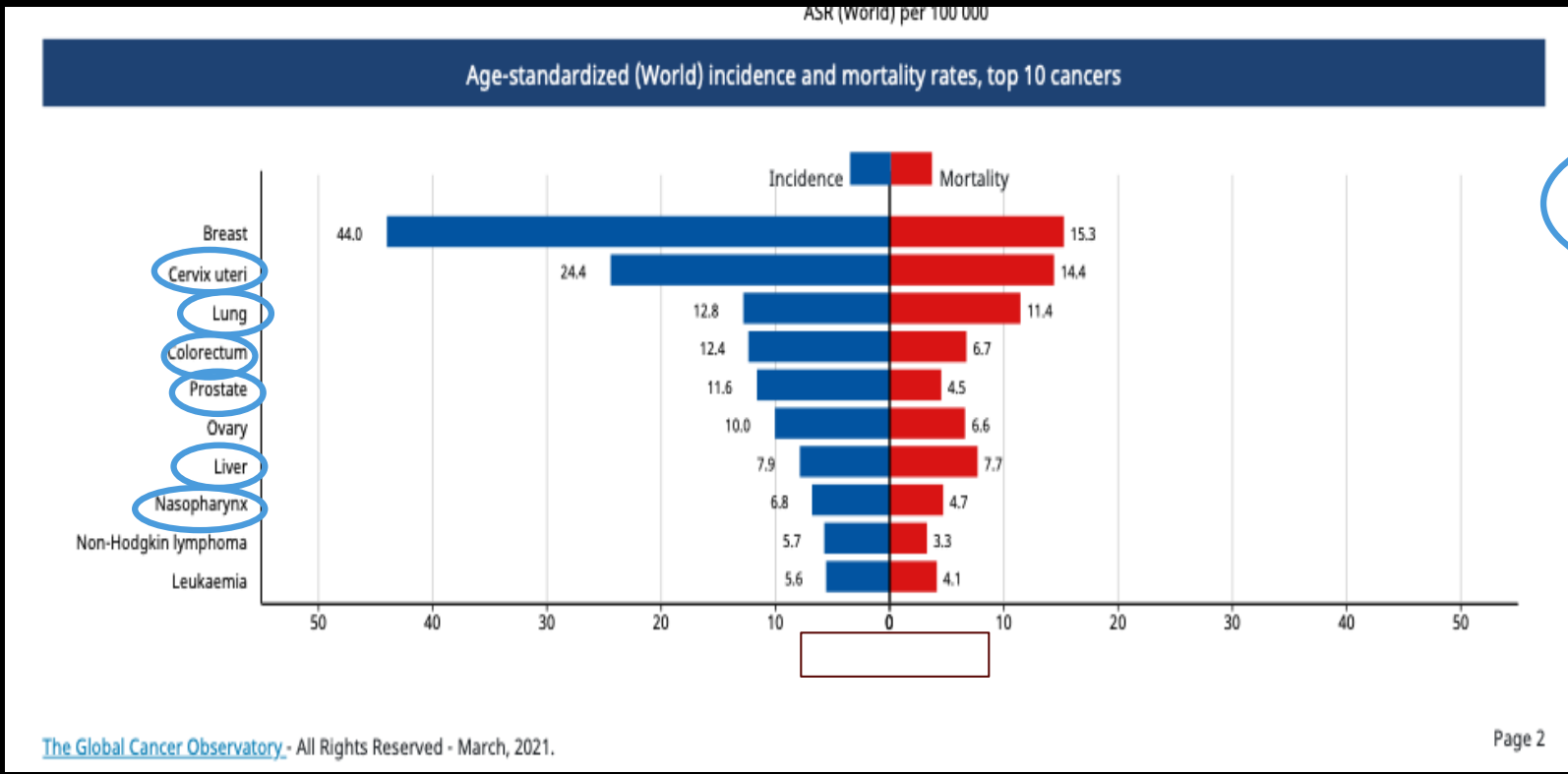
BMJ Oncology

Exhibit 46: Comparison of trial duration to phase-change duration (years) in key disease areas, 2014–2023



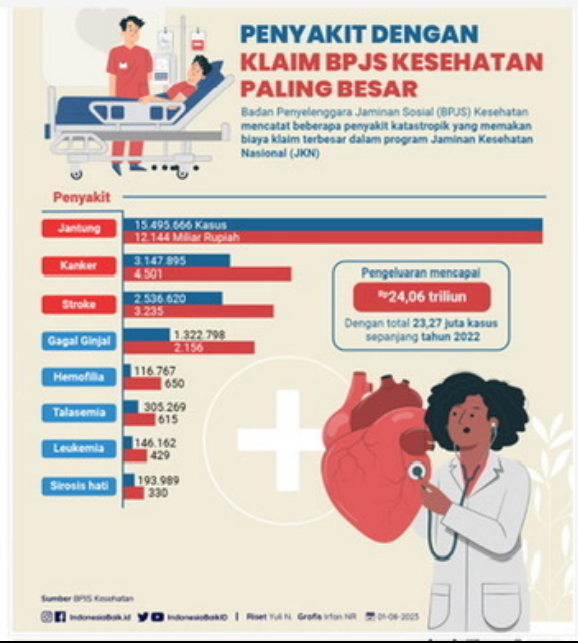
Source: IQVIA Pipeline Intelligence, Dec 2023; Citeline Trialtrove, IQVIA Institute, Jan 2024.

Incidence and Mortality



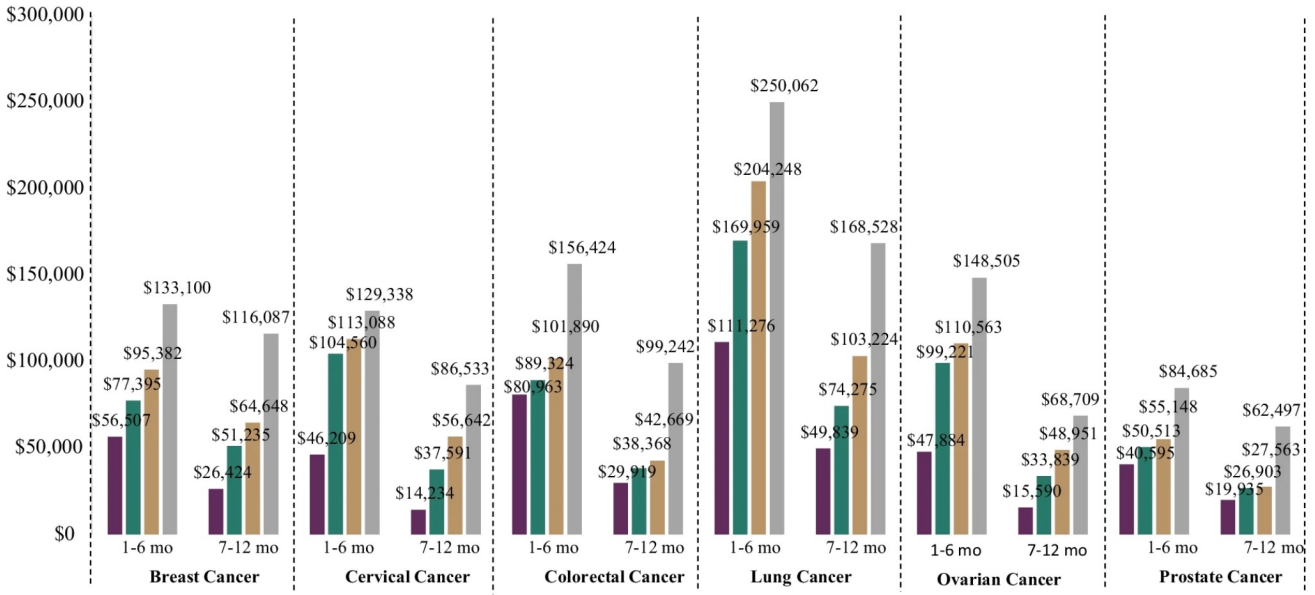
Late Stage Diagnosis

Facts 2022		
Breast Ca 5 yrs Survival Rate	51.07 %	91%
Average Initial Stage Diagnose of Breast Cancer	2-3	1-2



Opportunity Loss Up to 45%

From: Increased healthcare costs by later stage cancer diagnosis



PRECISION MEDICINE

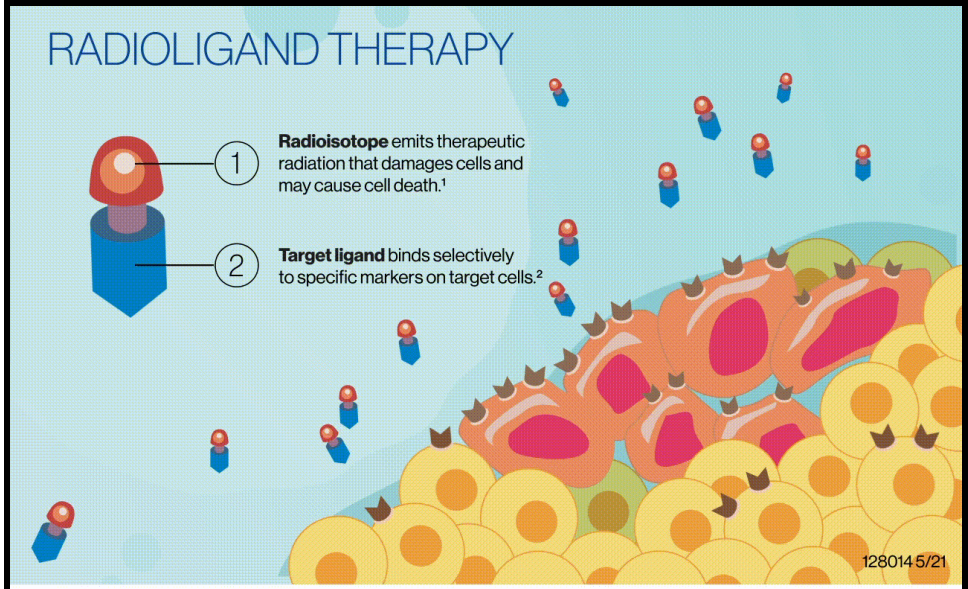
Diagnostic:

Morphological → Cell → Atomic
PET/CT/MR Scan

Familial → Genomic
Next Genome Sequencing

Therapy:

Targeted Chemotherapy
ImmunoTherapy
Targeted Radiotherapy
Radioligand Therapy



References: 1. Jadvar H. Targeted radionuclide therapy: an evolution toward precision cancer treatment. *AJR Am J Roentgenol.* 2017;209(2):277-288. **2.** Jurcic JG, Wong JYC, Knox SJ, et al. Targeted radionuclide therapy. In: Tepper JE, Foote RE, Michalski JM, eds. *Gunderson & Tepper's Clinical Radiation Oncology*. 5th ed. Elsevier, Inc; 2021;71(3):209-249.

Radioligand therapy

Radioligand therapy is an innovative approach to treating certain types of cancer. It delivers radiation to specifically targeted cancer cells, with a minimal effect on healthy cells.

Radioligand therapy has shown clinical benefit in treating certain tumor types and is being studied extensively in others

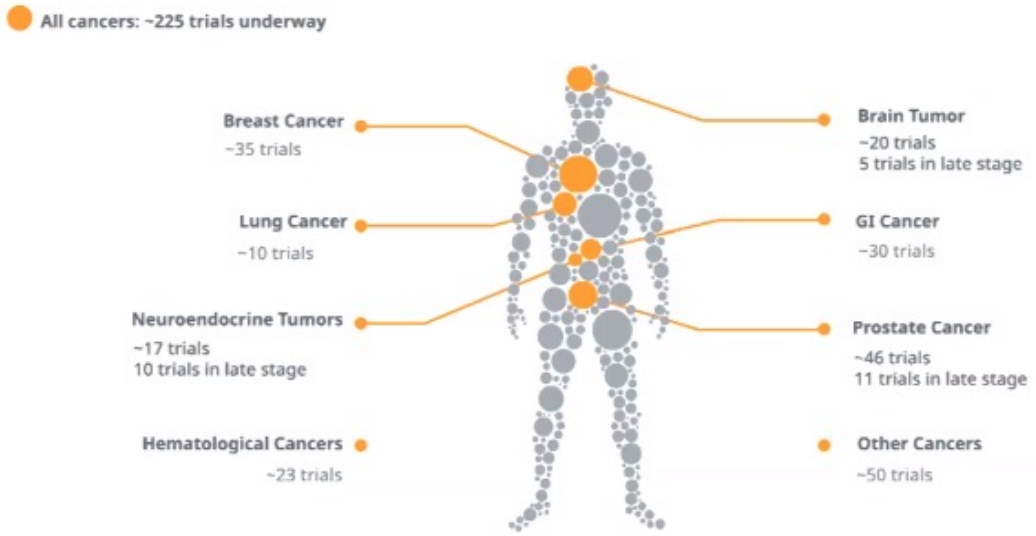
RLTs have shown clinical benefit in advanced GEP-NETs and PSMA-positive metastatic prostate cancer; Several trials are underway for other advanced cancers

Novartis radioligand therapy Lutathera® demonstrated statistically significant and clinically meaningful progression-free survival in first line advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

Sep 29, 2023

European Commission approves Pluvicto® for prostate cancer

The European Commission has approved Pluvicto® as the first targeted radioligand therapy for advanced prostate cancer, based on significant results from the Phase III VISION trial.

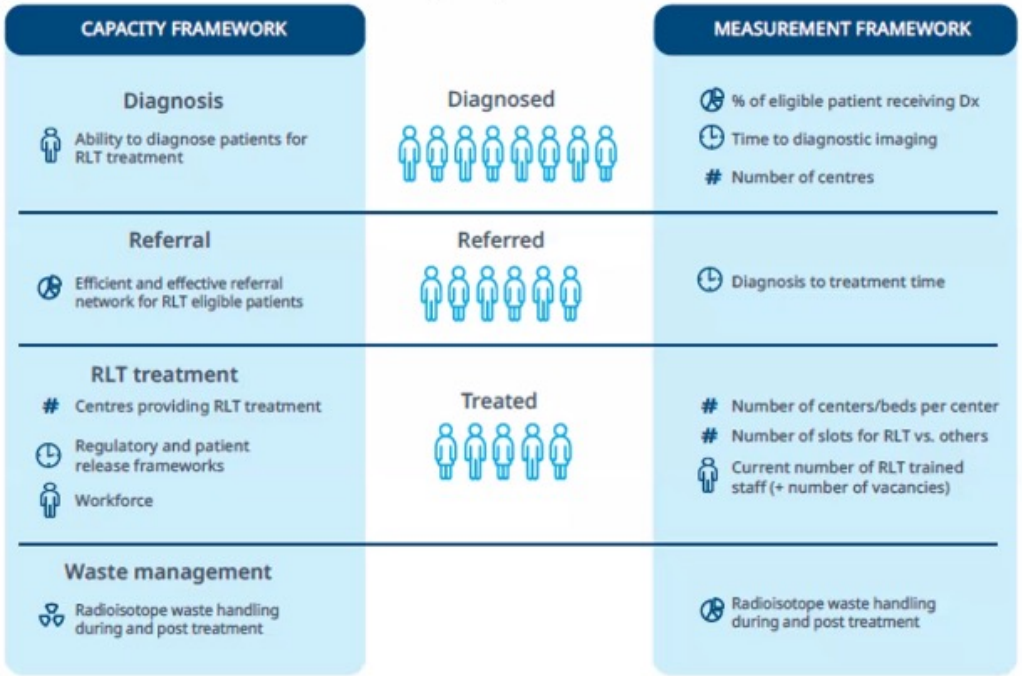


Source: clinicaltrials.gov; company investor reports and portals
Abbreviate: GI= gastrointestinal

IQVIA INSTITUTE

As demand for RLT use potentially increases, understanding readiness and capacity for diagnosis and treatment will be crucial

An initial estimation of the capacity for RLT diagnosis and treatment was made using public sources and through discussions with industry experts

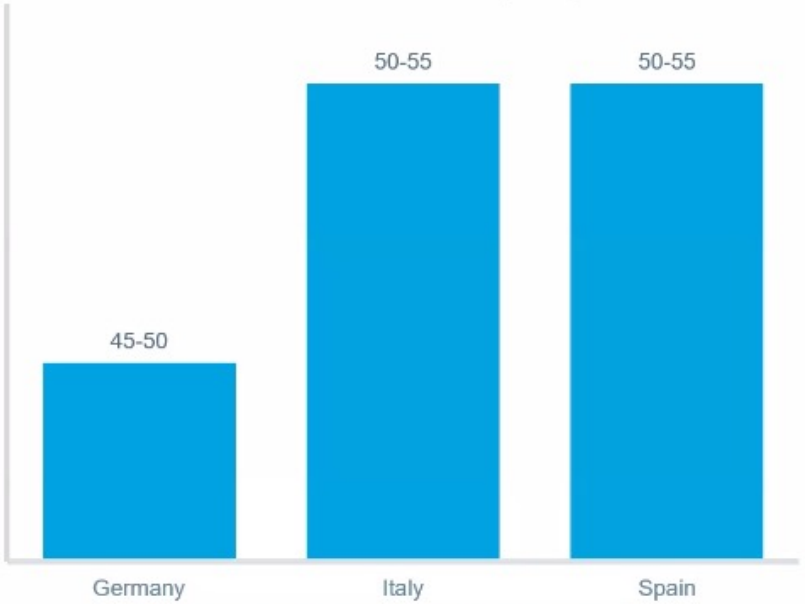


Source: IQVIA research and discussions with industry professionals in each country, and hospital and physician input
Abbreviation: HCS = healthcare system

IQVIA INSTITUTE

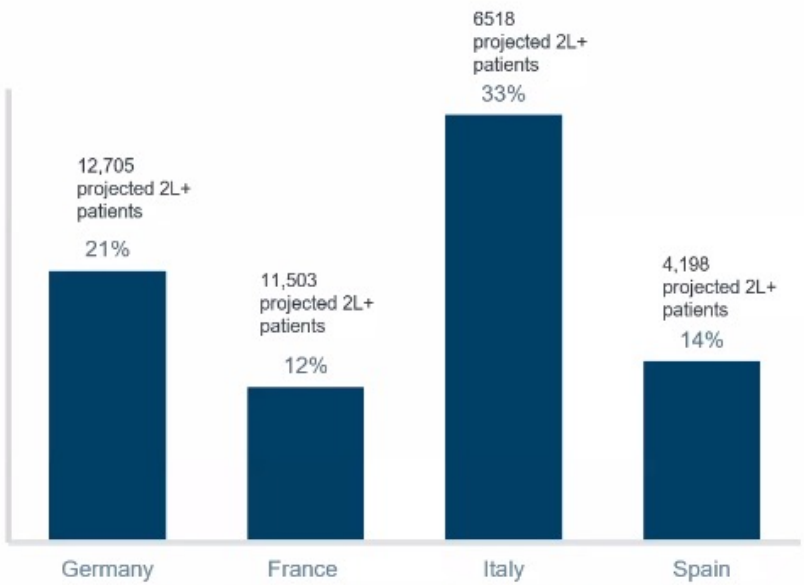
The share of mCRPC eligible patients that receive a PSMA test ranges between 12 and 33% across countries studied

Number of identified diagnostic centers with PSMA capability



■ # of identified RLI centers with PSMA capability

Percentage of 2L+ mCRPC patients tested for PSMA; Q3+Q4 2023



■ % of 2nd Line mCRPC patients receiving PSMA testing

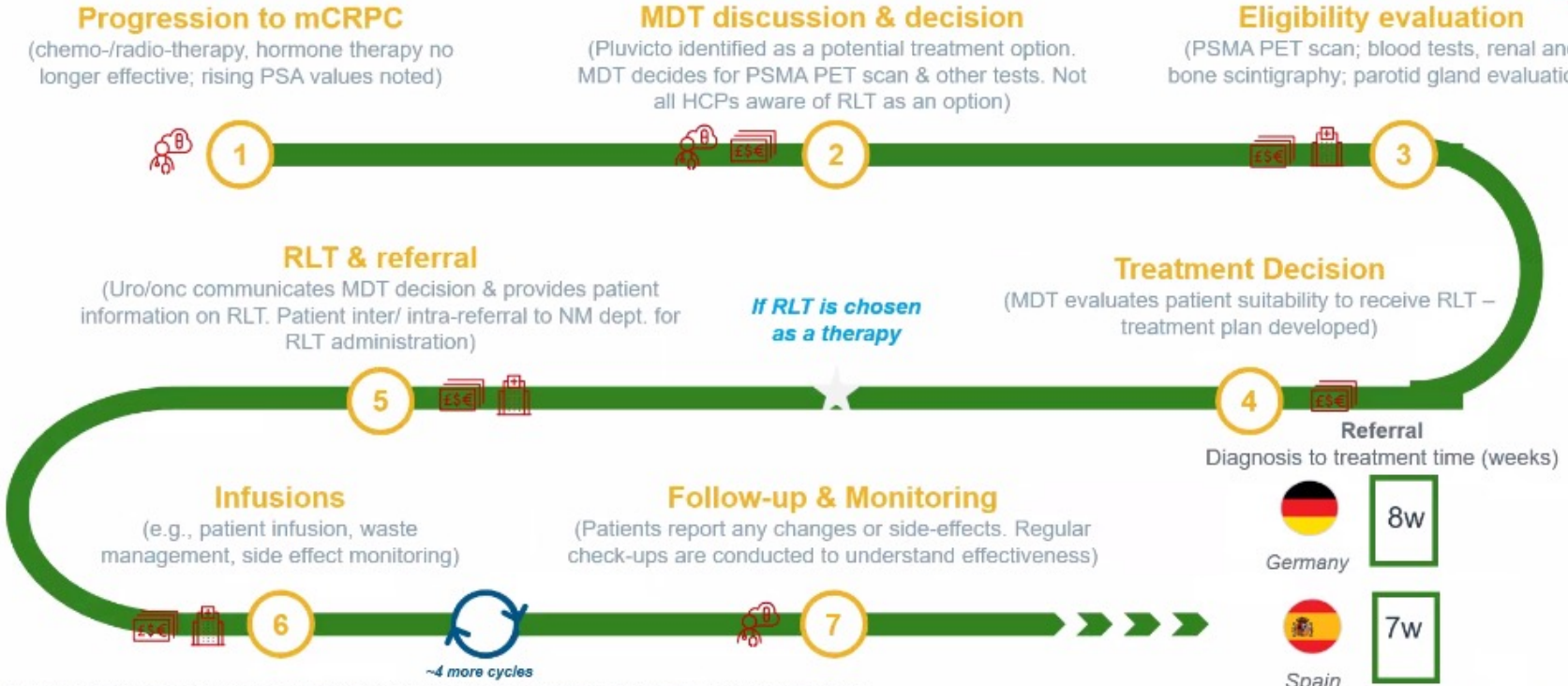
Source: IQVIA research and discussions with industry professionals, and hospital and physician input; IQVIA Oncology Dynamics - Pluvicto Monthly Tracker - MAT Q4 2023
Notes: Mapping diagnostic centers in listed countries is an on-going effort and current number is based on discussions with industry professionals. Overall RLI diagnostics may be understated across all geographies. Data for France is excluded where more recent data is available based on French Capacity Study.
Abbreviation: RLI= radioligand imaging

IQVIA INSTITUTE

In Germany and Spain, time from diagnosis to treatment is estimated at 7-8 weeks

Diagnosis to treatment time for lutetium (^{177}Lu) vipivotide tetraxetan, 2023

Illustrative and simplified



Referral
Diagnosis to treatment time (weeks)

Germany	8w
Spain	7w

Source: IQVIA research and discussions with industry professionals, and hospital and physician input
Notes: Diagnosis to treatment time data not available for Italy and France. This data is based on best estimates from industry professionals.

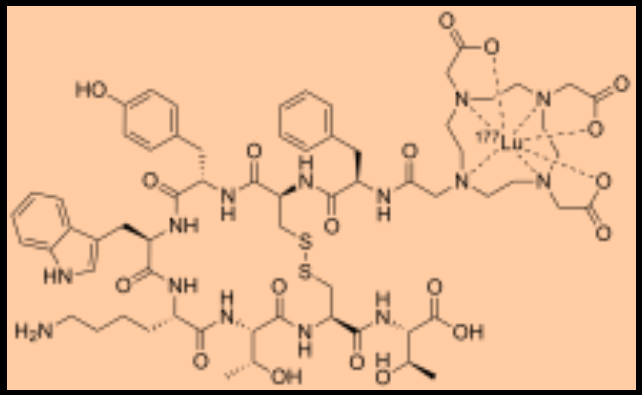
IQVIA INSTITUTE

Lutathera for Neuroendocrine Tumors

Lutathera is a peptide receptor radioligand/radionuclide therapy (approved by the FDA in 2018) specifically for patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs) that have somatostatin hormone receptors (SSTR). The radioisotope is Lu-177 and the ligand is a SSTR on the surface of tumor cells.

Skeletal formula of Lu-177

Lu-177 is produced by bombarding the stable isotope Yb-176 (which is found in monazite sand as well as the ores euxenite and xenotime) with neutrons. Yb-176 turns into Yb-177 which is unstable and has a half life of 1.9 hours so it quickly decays into the medical isotope Lu-177.[137]For mass production, it is better to produce Yb-176 through fission reactors. This is the indirect production method and requires elaborate radiochemical separation, purification, and results in large amounts of radioactive waste. The direct method of producing Lu-177 is by performing neutron irradiation on Lu-176 to Lu-177. This is an inexpensive and effective method to produce Lu-177.[138] In the United States, the main place that Lu-177 is produced is the University of Missouri Research Reactor.

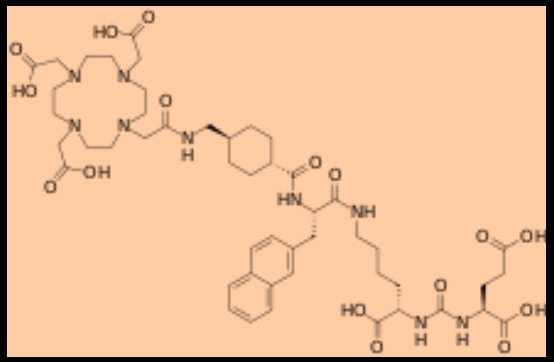


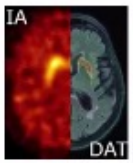
Pluvicto and Xofigo for Prostate Cancer

Pluvicto also uses Lu-177 as the radioisotope (which is a beta emitter that decays to Hf-177) but its ligand is a prostate-specific membrane antigen (PSMA) targeted ligand as this radioligand therapy addresses metastatic prostate cancer.[42] It was FDA approved in 2022. The difference between Lutathera and Pluvicto is shown in the chemical linkages in the images above. The production, transportation, and storage is the same as Lutathera. The therapy is administered intravenously through gravity, syringe, or a Peristaltic Infusion Pump.[43] The major warnings include renal toxicity, infertility in males, and embryo/fetal harm. General side effects of this radioligand therapy include fatigue, nausea, dry mouth, anemia, decreased appetite, and constipation. Regular blood tests and imaging post-therapy are needed to see if the radioligand therapy is working and its side effects.

Chemical structure of Pluvicto

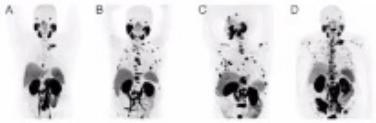
The benefits of Pluvicto include delaying tumor growth, extending life by about 20 months,[44] and destroying tumor cells by damaging the DNA inside those cells.
Xofigo, a radioligand therapy that was FDA approved in 2013, uses Radium-223 dichloride as the radioisotope, but its ligand varies from Pluvicto. Pluvicto only attacks cancer cells expressing PSMA, but Xofigo attacks all bone metastases. Qualified patients are 30% less likely





From Health Data Hub (HDH) partnership …

HEALTH DATA HUB



…to real-world RLT registry

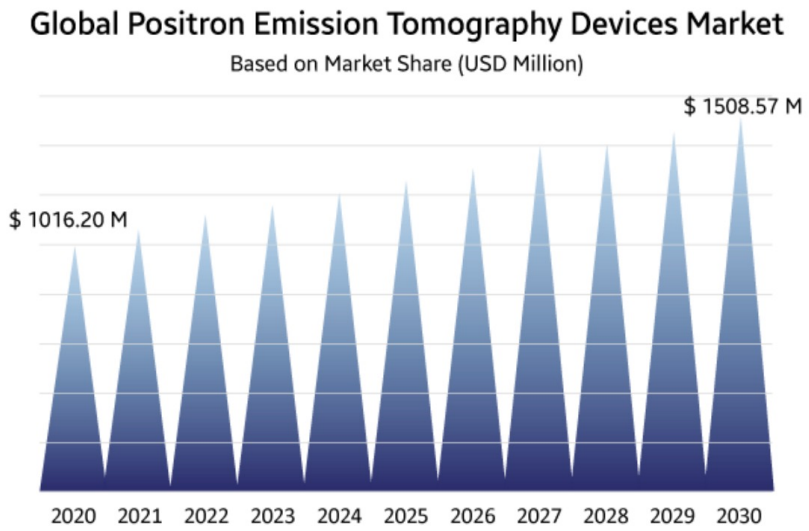
- Major interest for the (re)use of health data, with promising perspectives of AI :
  - for research & innovation, to measure therapeutic effects in real life
  - but also for medical organizations, to improve accessibility and quality of care
- Firstly requiring qualitative collection of health data:
  - Audit of the French Nuclear Medicine Centres Capability
  - National/regional activity survey for nuclear imaging and therapy, coordinated by Prof. O. Couturier, with a response rate >95% for more than 10 years, describing the numbers of examinations and treatments carried out by typology, and associated resources: www.cnp-mn.fr/sfmn-accueil/enquete_nationale_annuelle/
  - Early access program for ^{177}Lu-PSMA:
- The creation in 2019 of the public interest group “Health Data Hub” (HDH) demonstrates a significant French public investment for the reuse of health data and structuring the ecosystem
- SFMN/HDH partnership since 2022, initially for neuroimaging, with the ambition to extend it to RLT, contractually supported by a project manager (Imad Bousaid), a health DPO (Dr Data) and a CRO imaging platform (Pixilib)

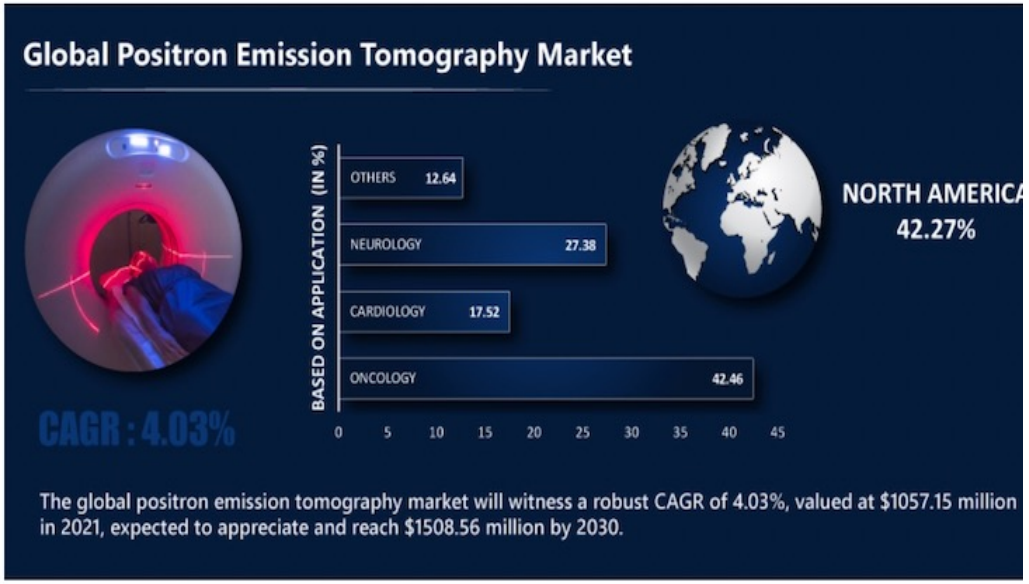
Next step

Implementation of a real-world ^{177}Lu-PSMA registry
as we did for ^{177}LuDOTATATE in endocrine tumours (Epilunet) and meningioma (Melute)

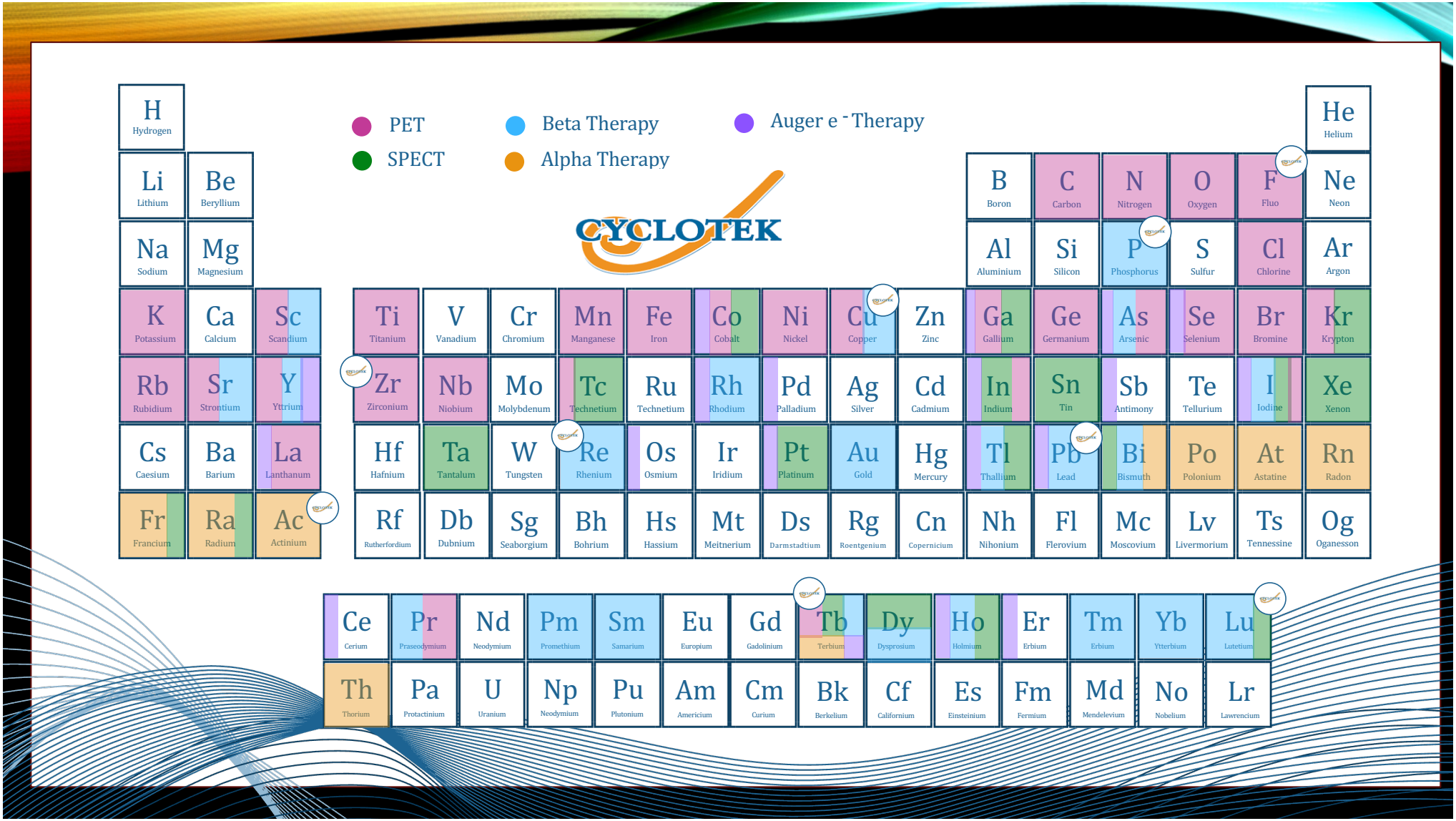
PET CT SCAN OUTLOOK

6 Scan/ 1000 Pop
4.500 average/day



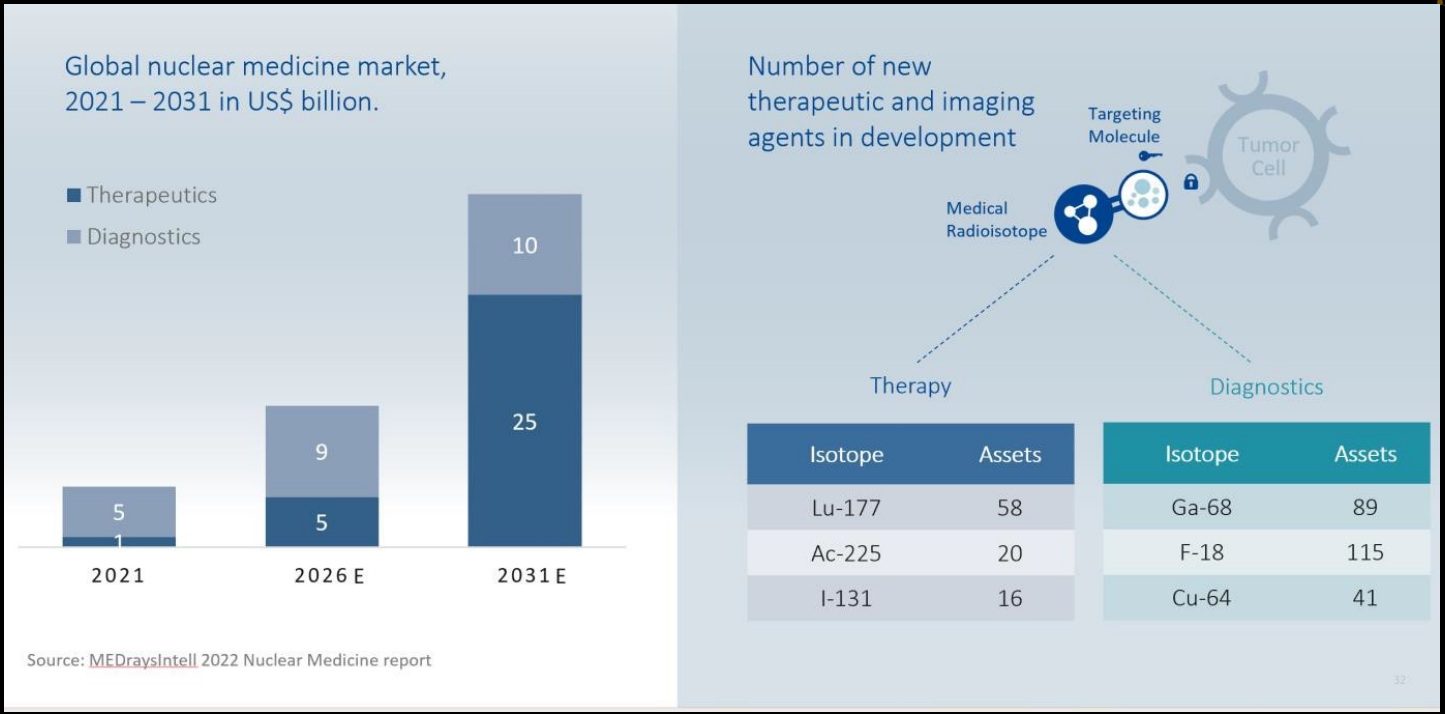


Grandview Research
2021


PET
SPECT
Beta Therapy
Alpha Therapy
Auger e - Therapy
CYCLOTEK
H Hydrogen
He Helium
Li Lithium
Be Beryllium
B Boron
C Carbon
N Nitrogen
O Oxygen
F Fluo
Ne Neon
Na Sodium
Mg Magnesium
Al Aluminium
Si Silicon
P Phosphorus
S Sulfur
Cl Chlorine
Ar Argon
K Potassium
Ca Calcium
Sc Scandium
Ti Titanium
V Vanadium
Cr Chromium
Mn Manganese
Fe Iron
Co Cobalt
Ni Nickel
Cu Copper
Zn Zinc
Ga Gallium
Ge Germanium
As Arsenic
Se Selenium
Br Bromine
Kr Krypton
Rb Rubidium
Sr Strontium
Y Yttrium
Zr Zirconium
Nb Niobium
Mo Molybdenum
Tc Technetium
Ru Technetium
Rh Rhodium
Pd Palladium
Ag Silver
Cd Cadmium
In Indium
Sn Tin
Sb Antimony
Te Tellurium
I Iodine
Xe Xenon
Cs Caesium
Ba Barium
La Lanthanum
Hf Hafnium
Ta Tantalum
W Tungsten
Re Rhenium
Os Osmium
Ir Iridium
Pt Platinum
Au Gold
Hg Mercury
Tl Thallium
Pb Lead
Bi Bismuth
Po Polonium
At Astatine
Rn Radon
Fr Francium
Ra Radium
Ac Actinium
Rf Rutherfordium
Db Dubnium
Sg Seaborgium
Bh Bohrium
Hs Hassium
Mt Meitnerium
Ds Darmstadtium
Rg Roentgenium
Cn Copernicium
Nh Nihonium
Fl Flerovium
Mc Moscovium
Lv Livermorium
Ts Tennessine
Og Oganesson
Ce Cerium
Pr Praseodymium
Nd Neodymium
Pm Promethium
Sm Samarium
Eu Europium
Gd Gadolinium
Tb Terbium
Dy Dysprosium
Ho Holmium
Er Erbium
Tm Erbium
Yb Ytterbium
Lu Lutetium
Th Thorium
Pa Protactinium
U Uranium
Np Neodymium
Pu Plutonium
Am Americium
Cm Curium
Bk Berkelium
Cf Californium
Es Einsteinium
Fm Fermium
Md Mendelevium
No Nobelium
Lr Lawrencium

RADIOPHARMACEUTICALS AND THERANOSTICS

- FASTEST GROWING MAINSTREAM CANCER CARE SOLUTION



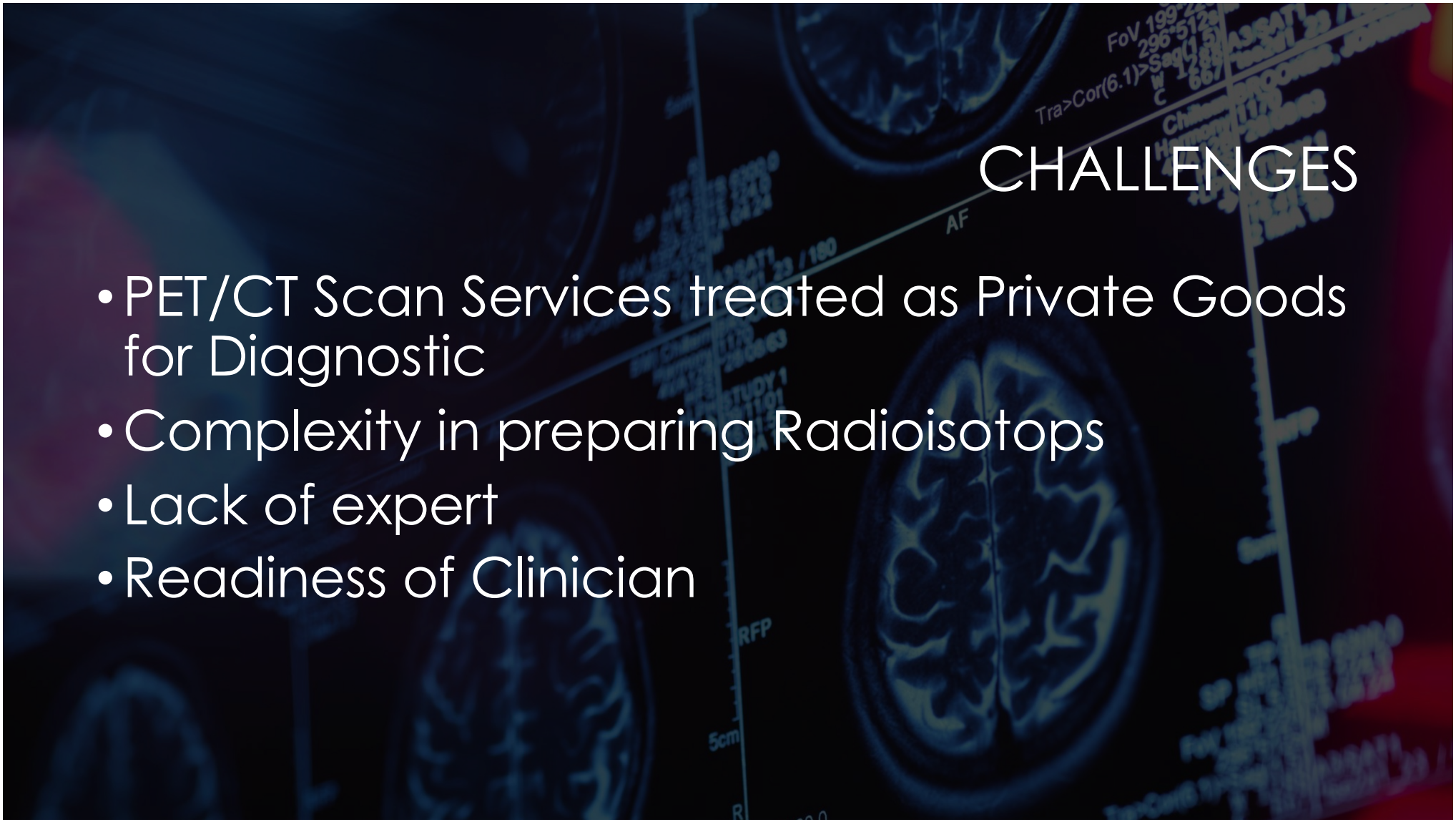
Isotope	Assets
Lu-177	58
Ac-225	20
I-131	16

Isotope	Assets
Ga-68	89
F-18	115
Cu-64	41

Global evolution of radiopharmaceutical market

THE FACTS

Parameter	Indonesia	Australia
Procedures Price (AUD)	1.300-2.300	900-1.100
Downtime	20%	<10%
Investment Cost PET Scan (AUD)	+/- 10.000.000	3.500.000
Average Volume/ Day	+/- 2-6	+/- 10-20



CHALLENGES

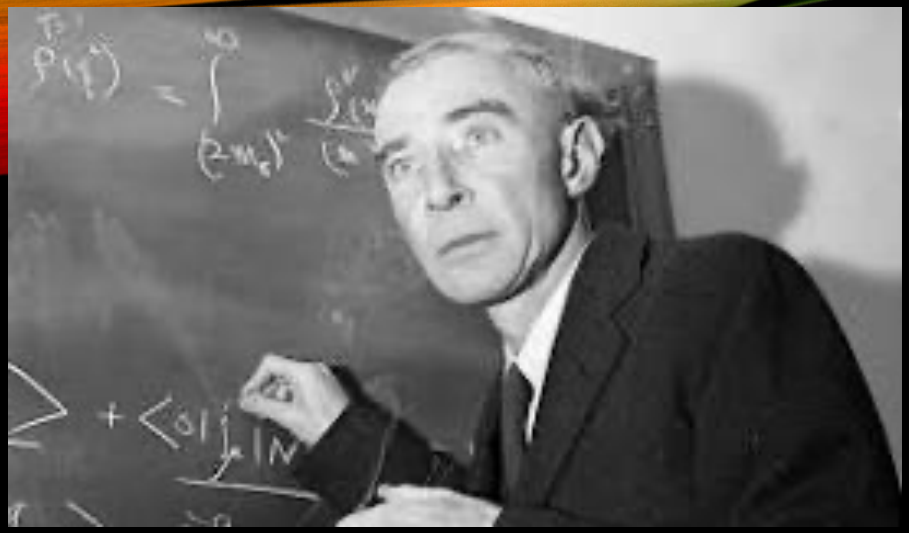
- PET/CT Scan Services treated as Private Goods for Diagnostic
- Complexity in preparing Radioisotops
- Lack of expert
- Readiness of Clinician

IMPACT

- Quality and Innovation for cancer care are low.
- Late Staging initial Diagnostic → Cost of Healthcare dominantly for Complication Treatment
- Mortality High
- Capital outflow

STRATEGIZING

- Build Precision Med **Ecosystem**
- Screening, Diagnostic, Monitoring Therapy
- Outsourced Radioisotops Supplies



It is Harder to Heal rather than to Kill

J. Robert Oppenheimer