

The clinical consequences of not testing

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Consultant medical oncologist

Guy's and St Thomas' NHS Foundation trust, London

DISCLOSURES

-Speaker, consultancy, advisory role (non remunerated)

Apogen, Roche, Mylan, Lilly, Pfizer, Novartis, Medicines for Europe, mAbxience, European Access Academy (EAA)

-Speaker/advisory role (fee)

Astra Zeneca, EAA, Pfizer, CDDF

-Research funding paid to Institution: MSD; Novartis,

-Other roles

Co-chair of the Healthcare Professional Working Party of the European Medicines Agency (EMA), 2022-2025

Member of the EMA Cancer Medicine Forum

Former core member of the EMA Scientific Advisory Group-Oncology (2012-2021)

Past Director of the ESMO Public Policy (2020-2022)

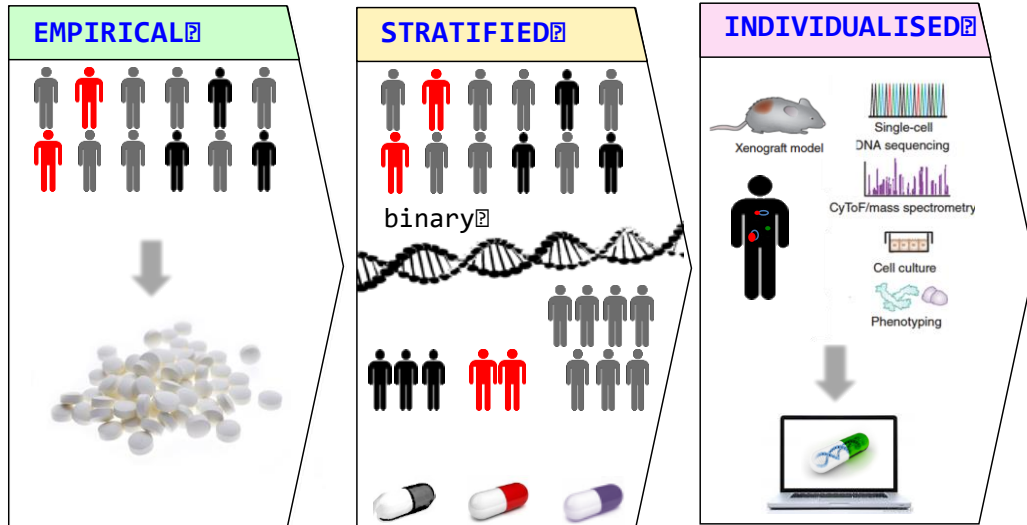
Cancer Drug Development Forum (CDDF) member

EAA faculty member

Access to Oncology Medicines Coalition (ATOM) advisory group member

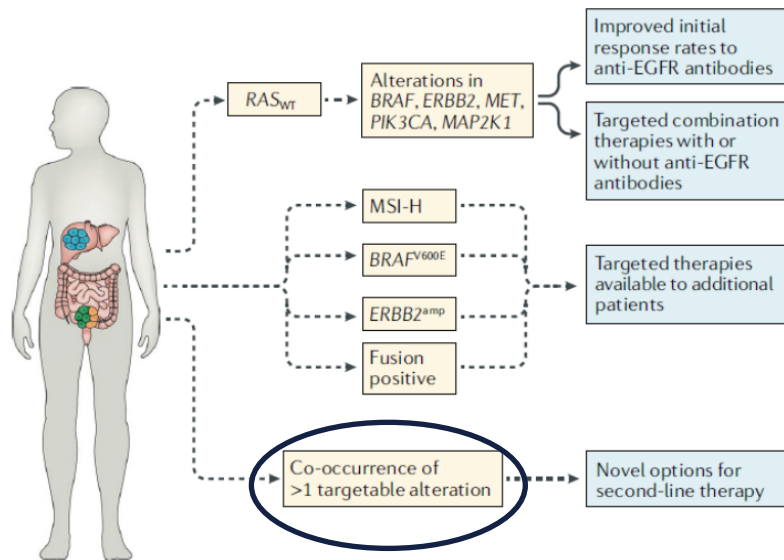
European Coalition for Access to Comprehensive Genomic Profiling (ECGP) member

PARADIGM SHIFT



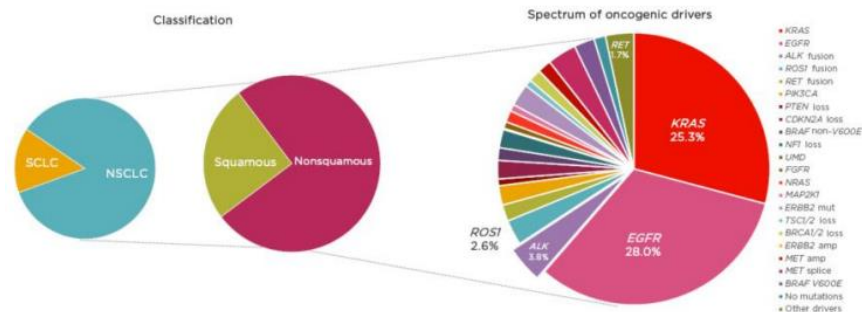
Unselected/poorly selected population, huge numbers to detect marginal differences

The paradigm shift in practice



Prenen, ESMO 2023; Sveen, Nat Rev Clin Onc 2019, Charan M, et al Int J Mol Sci 2020; Jordan EJ et al, Cancer Discov 2017

Lung Cancer

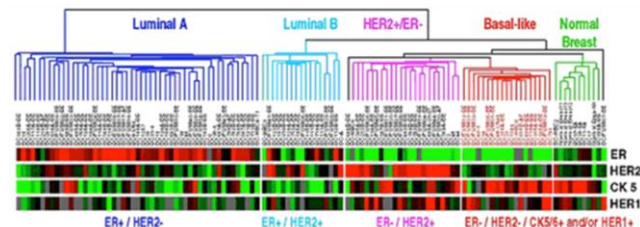


Molecular portraits of human breast tumours

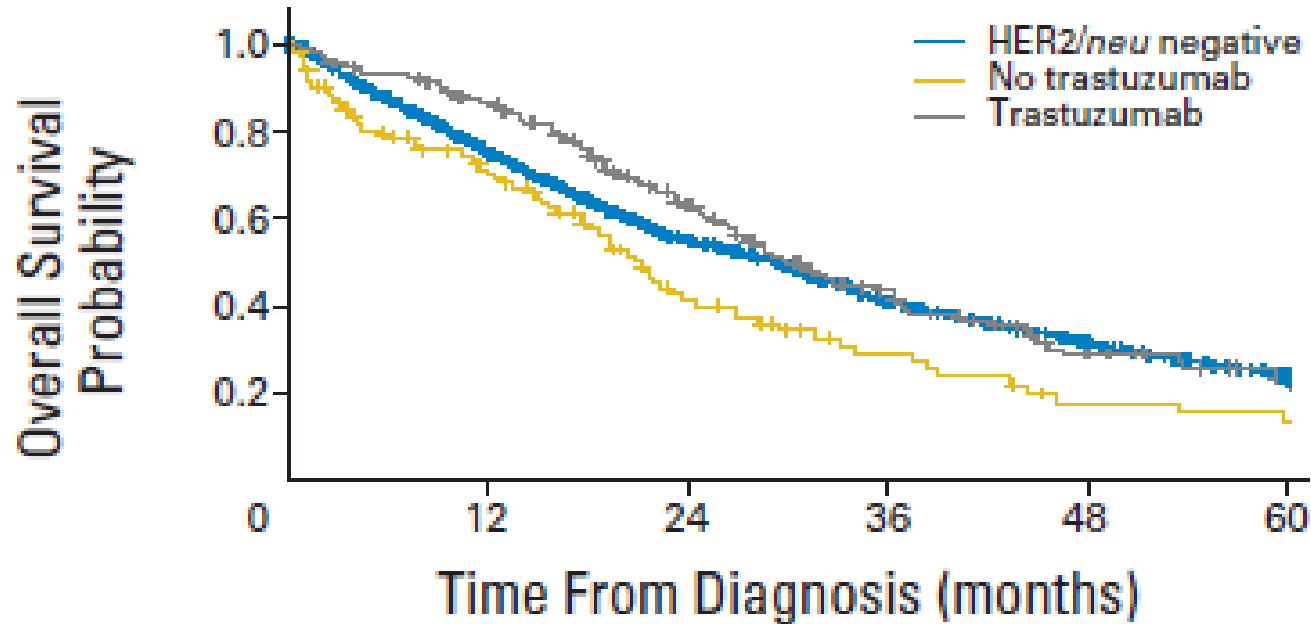
BC is not any more one disease

Charles M. Perou¹, Thorsteinn Sorlie^{1,2}, Michael B. Eisen³, Matt van de Rijn⁴, Stefanie S. Jeffrey¹, Christian A. Rees⁵, Jonathan R. Pollack⁶, Douglas T. Ross¹, Hilde Johnsen¹, Lars A. Akslen⁷, Øystein Fluge⁸, Alexander Pergamenschikov⁹, Cheryl Williams¹, Shirley X. Zhu¹, Per E. Lønning¹, Anne-Lise Børresen-Dale¹, Patrick O. Brown^{1,10} & David Botstein¹

Perou, Nature, 2000

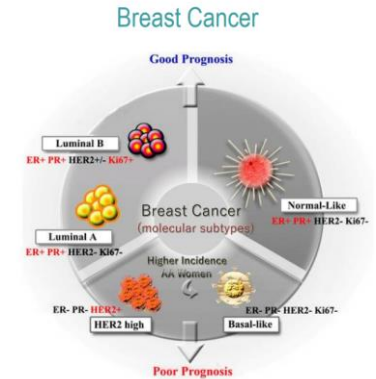


PROGNOSIS BY HER2 STATUS AND H TREATMENT: CHANGE OF NATURAL HISTORY



No. of patients at risk

HER2/neu negative	1,782	1,060	633	348	211	120
No trastuzumab	118	65	31	16	8	6
Trastuzumab	191	155	94	51	25	10



Dawood, JCO 2010

**TREATMENT OPTIONS FOR
METASTATIC BREAST CANCER:
NOT ALL DRUGS ARE CREATED
EQUAL**

Rosa Giuliani

Rachel Payne

Eric Lam

*Department of Oncology
Imperial College*

Large **UNRESECTABLE** MASS in left
supraclavicular fossa
Cytology positive for adenocarcinoma

June 1998



February 2008

CHEMOTHERAPY

1 Neo-Adju

7 MBC

RADIOTHERAPY

55 Gy on left SC
fossa
August 2000

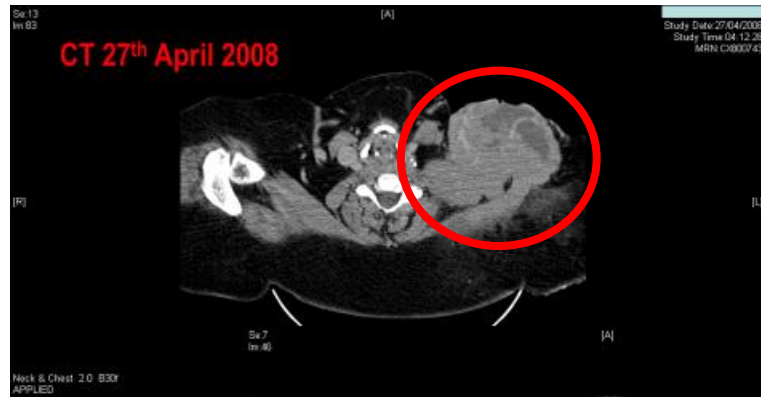
**HORMONAL
THERAPY**

1 Adju

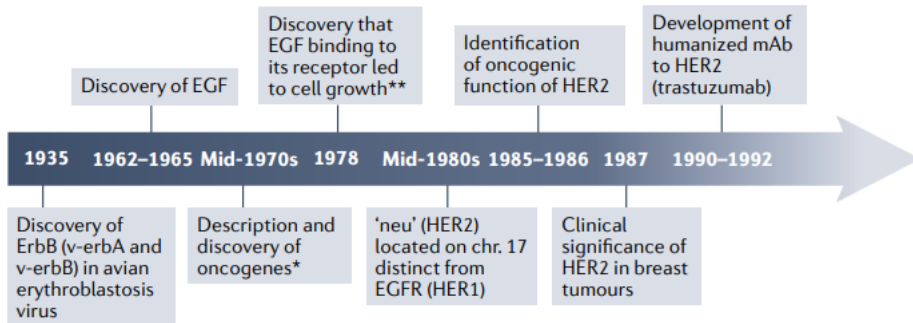
4 MBC

HEAVILY PRETREATED PT





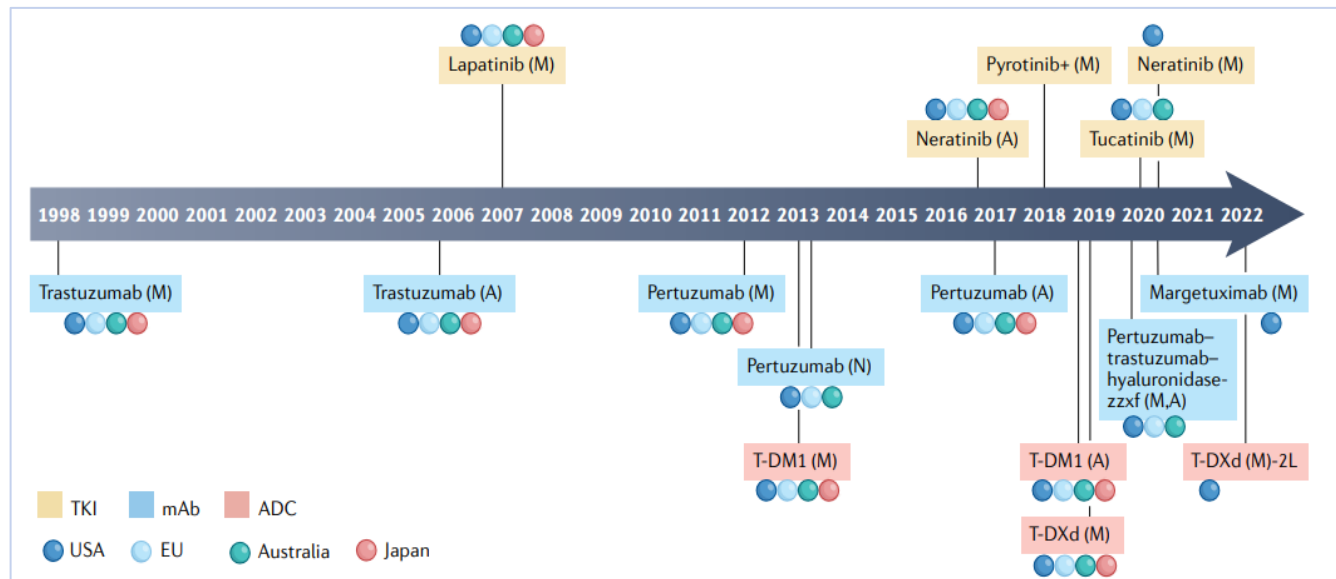
Preclinical



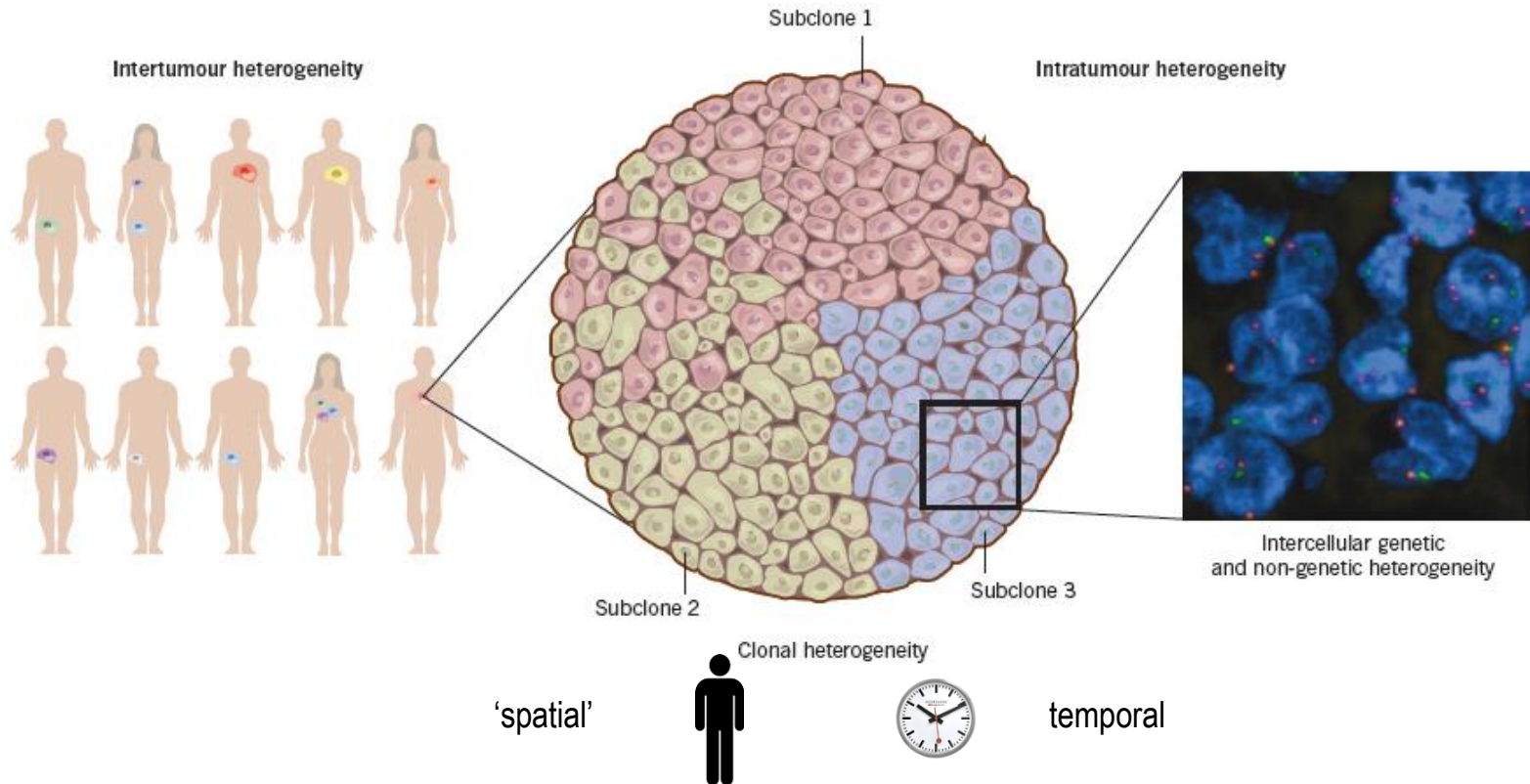
Approval of HER2 directed therapeutics

Adapted from Swain, Nat Rev Drug Discov, 2023

- Breast cancer survival exceeds 90%
- More than 50% de novo MBC
- Significant survival improvement in metastatic setting



Cancer heterogeneity (population→single-cell level): testing once is not enough

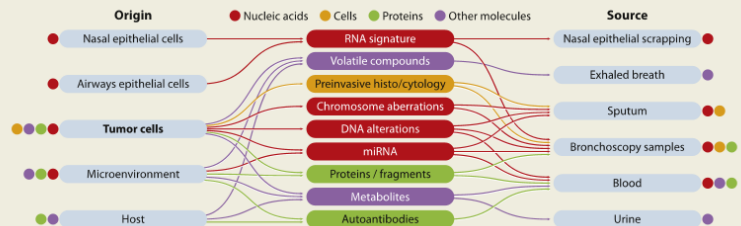


Molecular «chaos» in advanced setting: are we capturing it?

Biomarkers for screening

H. Robbins, ESMO-IARC webinar on the future of lung screening, Dec 2022

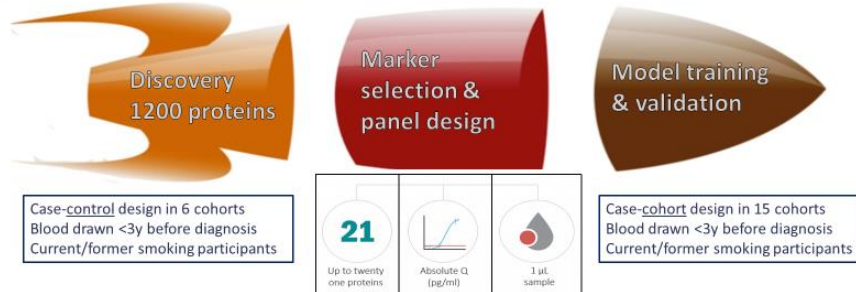
Types of biomarkers proposed for lung screening



Seijo et al, J Thorac Oncol 2019

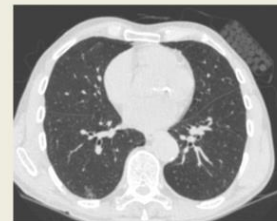
Candidate biomarkers: our INTEGRAL protein panel

A three-stage rocket



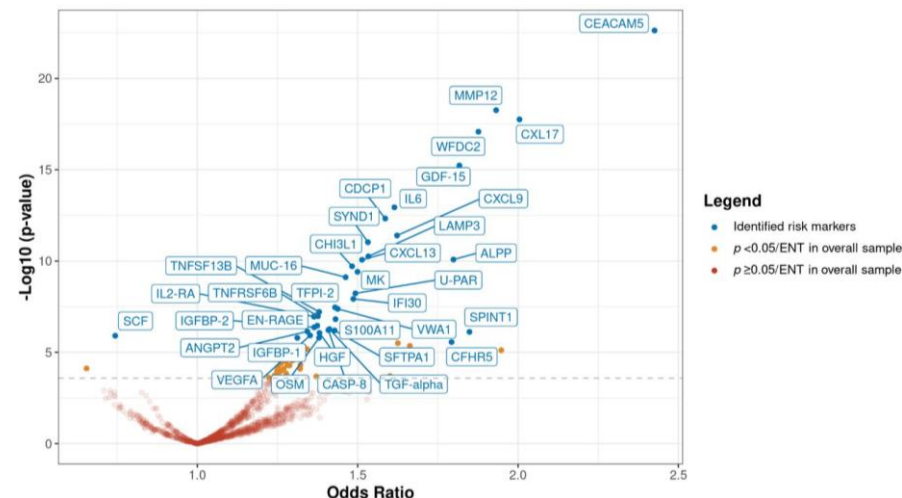
Robbins et al, Annals Epidemiol 2023
The Lung Cancer Cohort Consortium, medRxiv 2022

Will artificial intelligence eclipse the utility of biomarkers when an LDCT image is available?



LDCTs contain a wealth of information about lung cancer risk:

- Nodules: location, size, attenuation, margins, growth over time...
- Emphysema
- Adenopathy, consolidation, and other signs of cancer



ORIGINAL ARTICLE

ESMO study on the availability and accessibility of biomolecular technologies in oncology in Europe

A. Bayle^{1,2,3,4,5*}, J. Bonastre^{3,4}, D. Chaltiel^{3,4}, N. Latino⁵, E. Rouleau^{5,7}, S. Peters^{5,8}, M. Galotti⁵, G. Bricalli⁵, B. Besse^{2,9†} & R. Giuliani^{5,10†}

SIX DOMAINS	AIM
Healthcare organization for biomolecular technologies	Existence of national authorities or initiatives regarding biomolecular testing, from a reference list, and the field reporter's view about the access to these technologies
Availability of biomolecular technologies in cancer	Always, usually, or occasionally in routine practice, only in trial or research, or never
Laboratories or platforms performing the biomolecular testing	To identify the entities (public, private or both) performing the biomolecular testing for each technology
Use of technologies in pre-specified cancer types	Prescription process by techniques and indications -always, usually, or occasionally in routine practice, only in trial or research, or never
Pricing and reimbursement	Pricing (by indicating a range between the minimum and the maximum price) and reimbursement of each technique
Barriers to utilization	In particular for financial, organizational, or ethical aspects

Target: 53 countries in the World Health Organization (WHO) European Region.



- Data submitted between July 2021 and December 2021 by the field reporters through an electronic survey.
- The preliminary set of data was posted on the ESMO website for open peer-review between May 2022 and July 2022, and amendments have been incorporated into the final report.

July-December 2021

On line tool Qualtrics

201 individual reporters from 48 countries
143 oncologists (72%), 44 biologists or pathologists (22%), and 14 other professionals (7%).

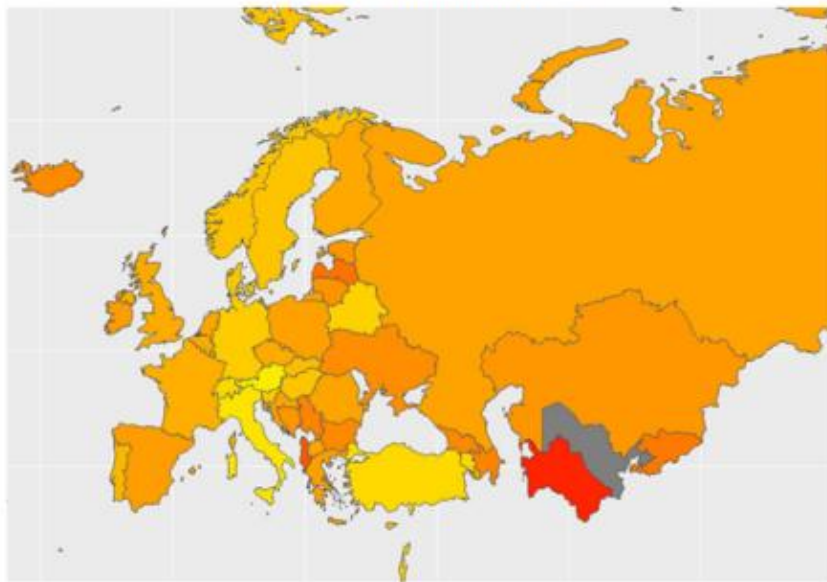
Majority (94%) of field reporters worked in hospitals

Limited size of the oncology supply in non responder countries (e.g. Monaco, San Marino).

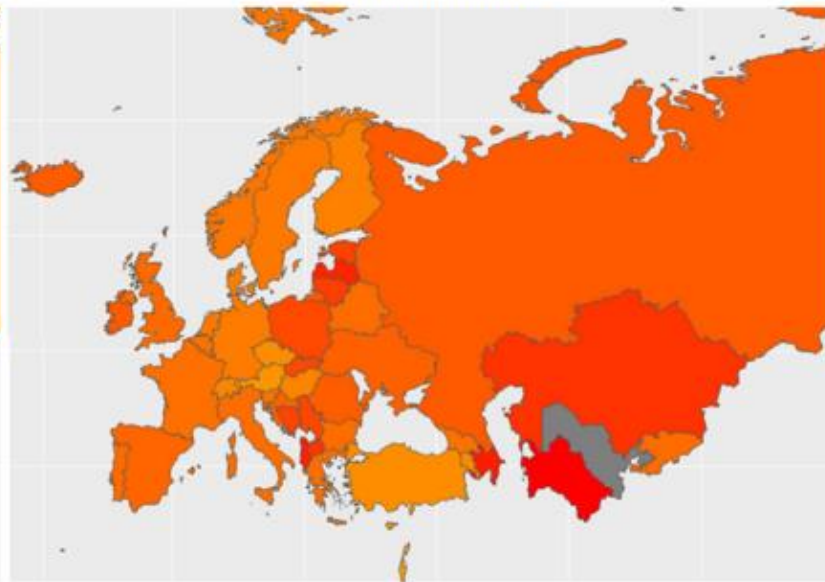
Additional peer-review data were submitted by 120 reporters from 36 countries

Availability map of single versus multiple genes techniques

Single-gene techniques



Multigene techniques

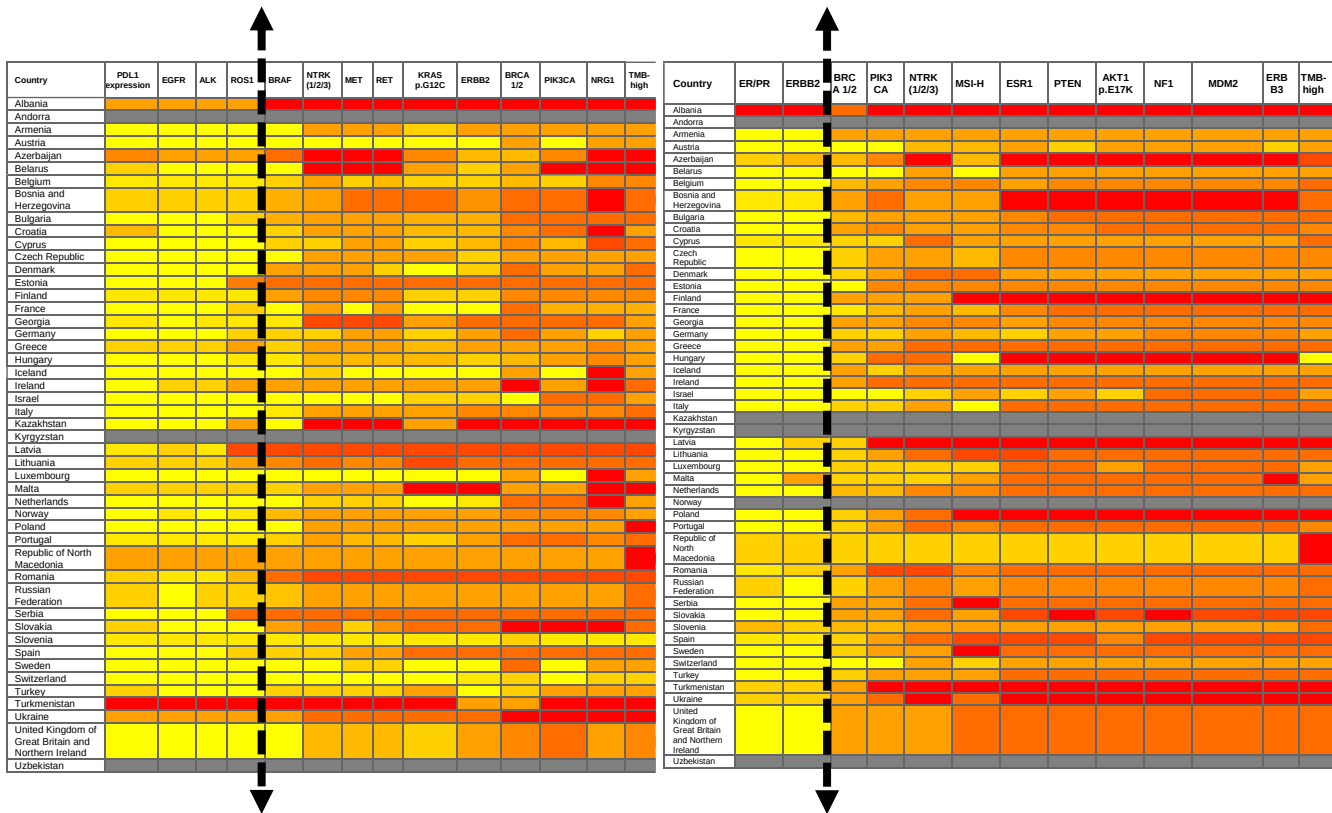


Biomarkers

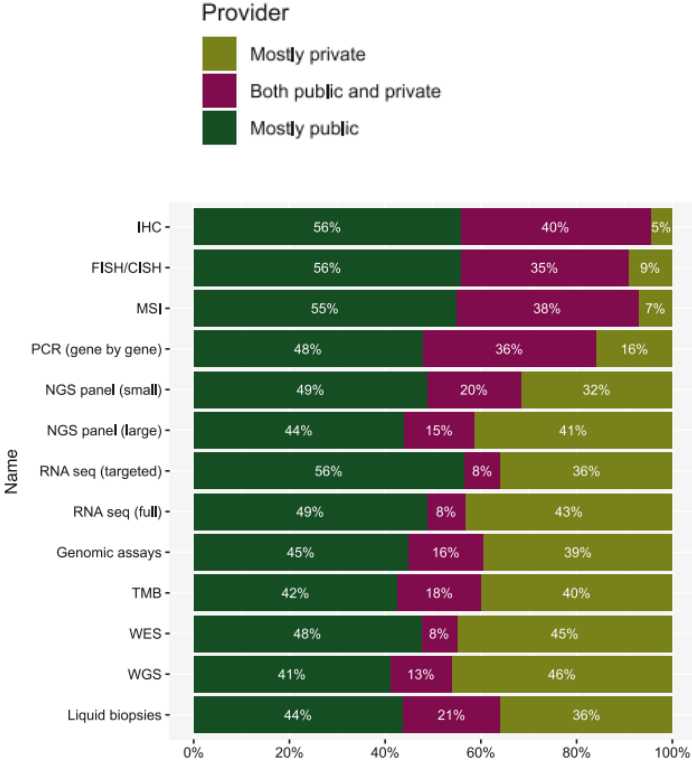
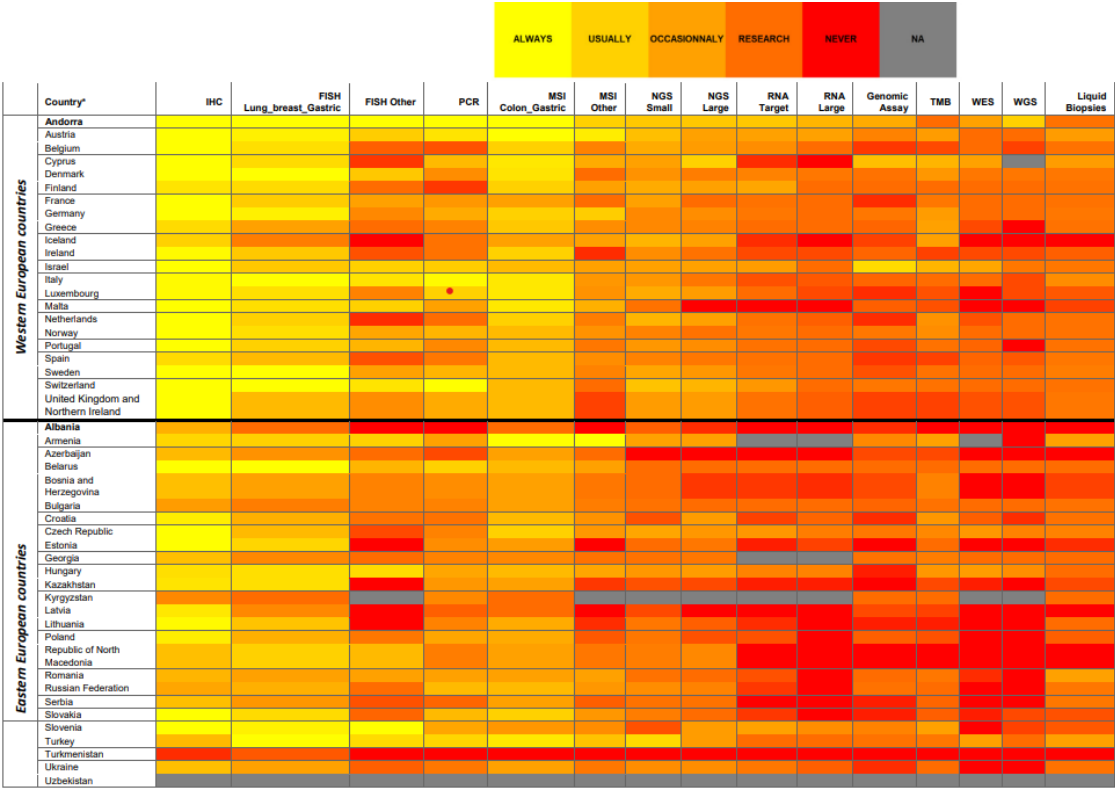
Overall :

Most of the **validated biomarkers** that can be tested using relatively simple techniques, not requiring extensive panels, are **relatively widely tested across countries**.

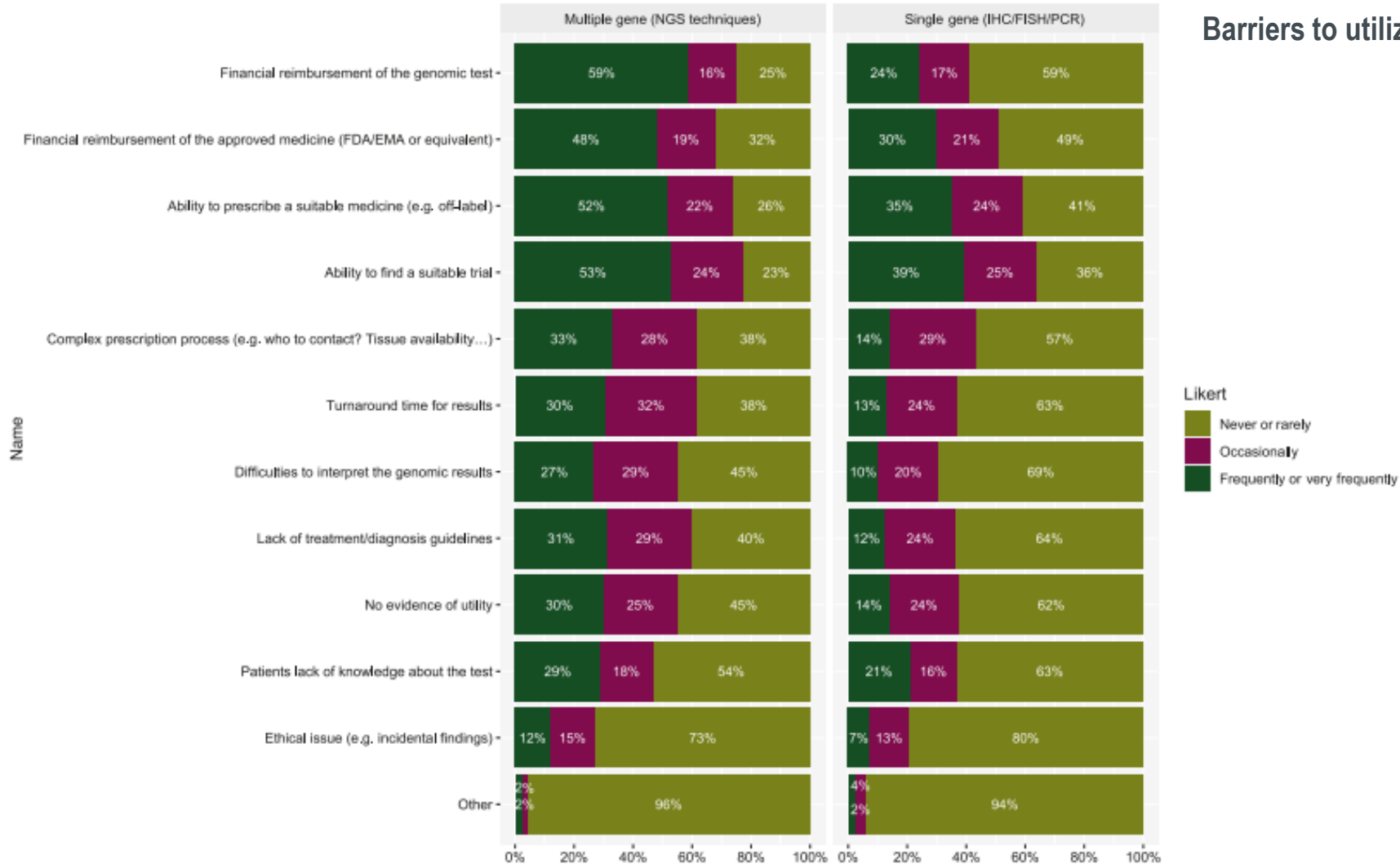
While **more advanced biomarkers** (even some ESCAT 1) are **rarely tested outside clinical trials or research** even accross EU countries and despite available drugs (anti NTRK, anti RET, Immunotherapy for TMB high...)



Availability of techniques across countries by region



Barriers to utilization



AVAILABILITY AND PRICE

Large NGS panels (and more) remain largely inaccessible in clinical routine:

- for clinical trials or basic research (even in EU countries) only
- with **cost differences** that are greater as the technique becomes more extensive

BIOMARKERS

“Simple validated biomarkers” (simple techniques, not requiring extensive panels) are relatively widely tested across countries

“More advanced biomarkers” are rarely tested outside clinical trials or research

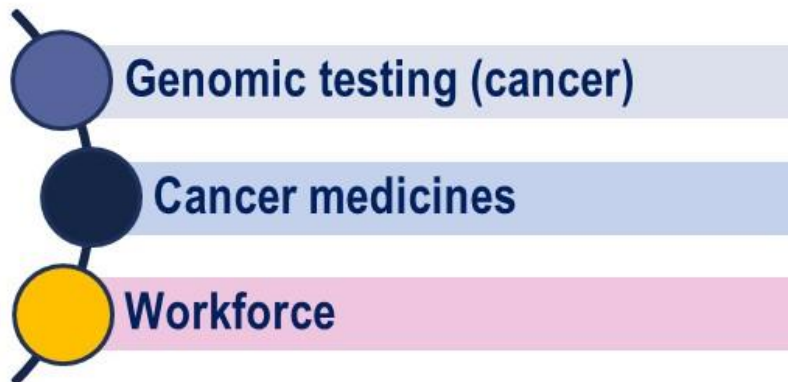
- Even in EU countries
- Even for some ESCAT 1 biomarkers despite available drugs (anti NTRK, anti RET, Immunotherapy for TMB high...)

BARRIERS:

TWO MAIN BARRIERS:

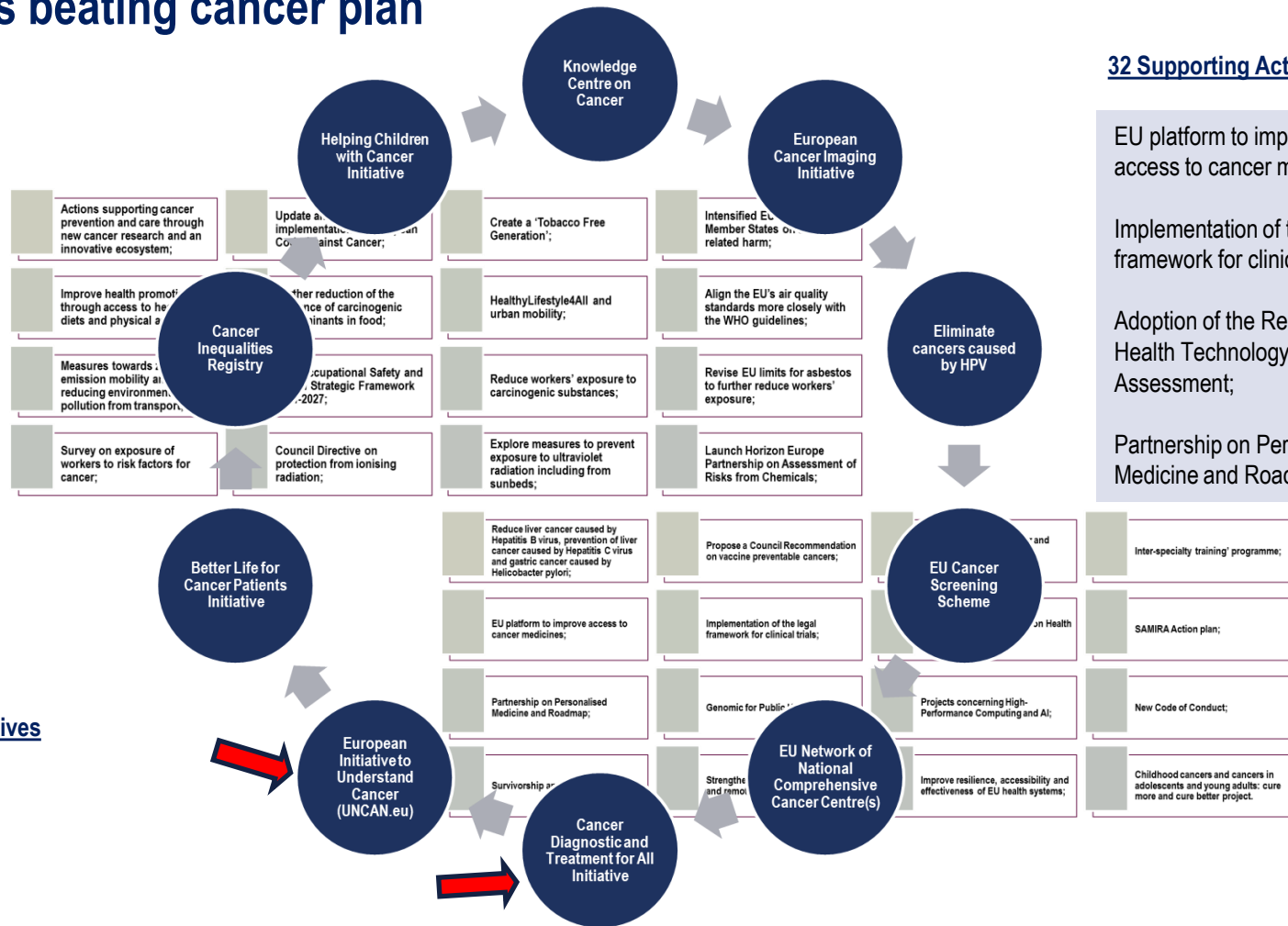
- **Financial reimbursement** of the biomolecular test
- **Availability** of a suitable drug

The cost of



The cost of
NOT

The Europe's beating cancer plan



An EU Commitment towards UNderstanding CANcer: UNCAN.eu



The Goal

Launch **UNCAN.eu** (UNderstand CANcer) as a sustainable European initiative that identifies **critical research challenges** and provides researchers in Member States with a **centralized platform** that fosters collaboration and exchange of cancer knowledge and data.



The Need

Generate new breakthroughs on cancer that enhance **cancer prevention, early diagnosis, and treatment strategies**, ultimately providing a basis for saving millions of lives and improving the quality of life of cancer survivors and their caretakers.



The Way

Create a pivotal framework that supports **ambitious European research consortia** and enables the **collection and analysis of cancer data at an unprecedented scale** leveraging artificial intelligence and computing capacities in Member States.²

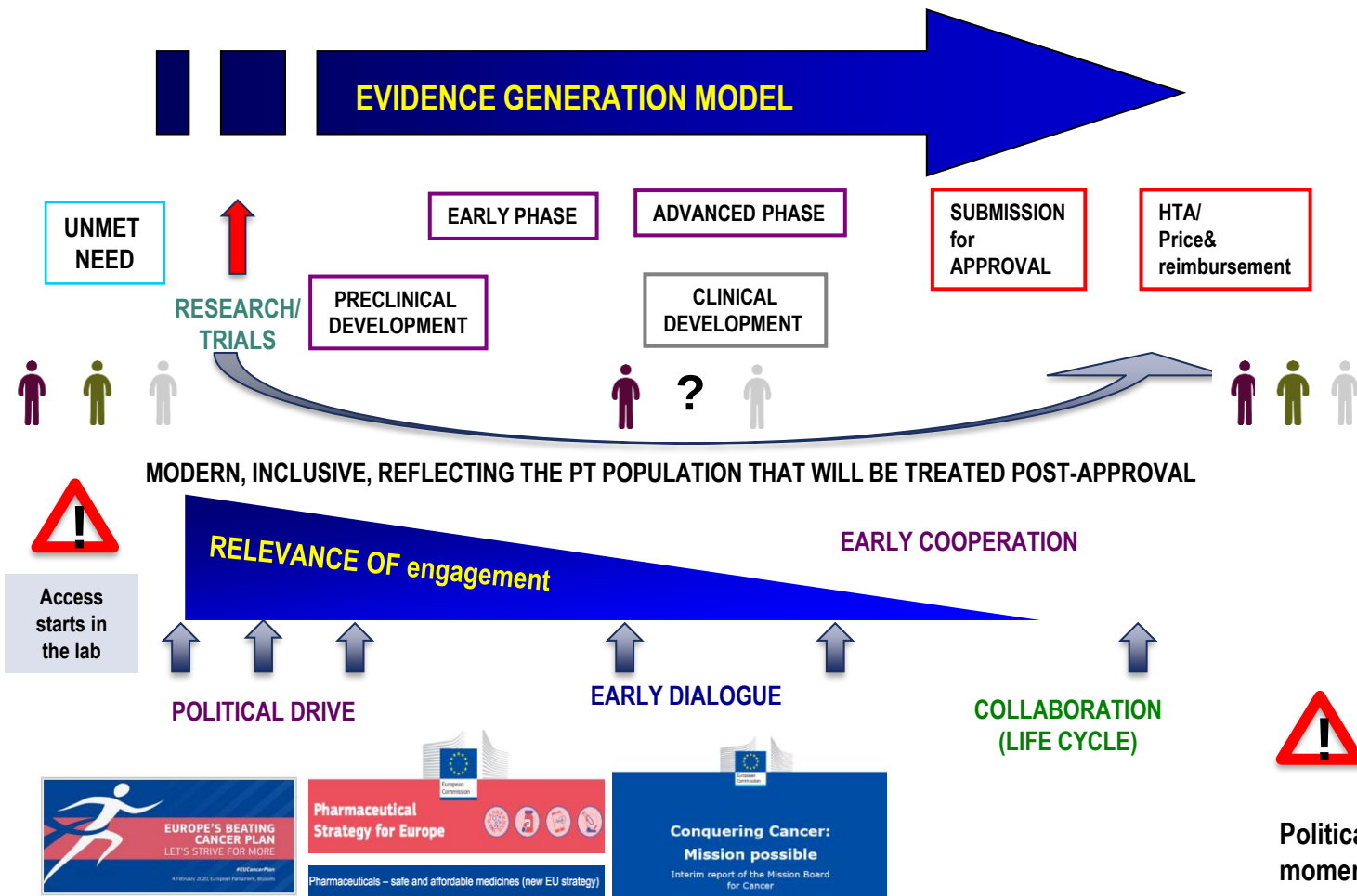
Core Partners



Blueprint to be presented to the European Commission: November 14, 2023

<https://uncan.eu/>
uncan@ecpc.org

ACCESS TO INNOVATION and CANCER CARE (incl Dx)



Historically focused on cancer medicines, in “isolation” for each drug/Dx...the value of panels not adequately captured: Dx left out

Historically focused on Approval, and not what’s happens after approval (this is Rosa moaning time: none is interested in my clinical practice....)

Historically neglecting what – happens-next (mechanisms of resistance)



RATIONAL DRUG DEVELOPMENT

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graph TD; A[RATIONAL DRUG DEVELOPMENT] --> B1[CANCER TYPE/ MOLECULAR TARGET]; A --> B2[PATIENTS SELECTION]; A --> B3[STUDY DESIGN]; B1 --> C1["-MECHANISMS Of PROGRESSION/ RESISTANCE -TIME"]; B1 --> C2[PATHWAYS]; B1 --> C3[Spatial and temporal HETEROGENEITY]; B2 --> C4["TARGETS<br/>DRIVERS vs PASSENGERS"]; B2 --> C5[BIOMARKERS]; B2 --> C6[Access to testing]; B3 --> C7["CLINICAL DEVELOPMENT<br/>TAILORED TO MOLECULAR PHENOTYPES"]; B3 --> C8[INNOVATIVE TRIALS]; B3 --> C9[Complexity of study design];
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**CANCER TYPE/
MOLECULAR TARGET**

**-MECHANISMS
Of PROGRESSION/
RESISTANCE
-TIME**

PATHWAYS

**Spatial and temporal
HETEROGENEITY**

PATIENTS SELECTION

TARGETS
DRIVERS
vs
PASSENGERS

BIOMARKERS

Access to testing

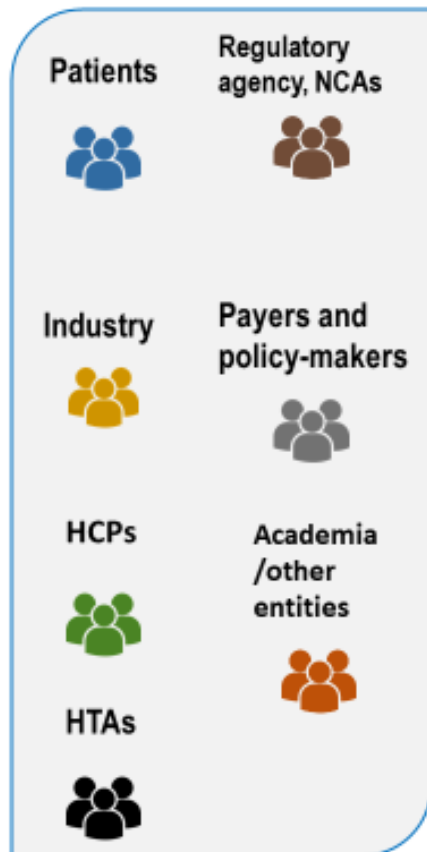
STUDY DESIGN

**CLINICAL DEVELOPMENT
TAILORED TO MOLECULAR
PHENOTYPES**

INNOVATIVE TRIALS

**Complexity of study
design**

Key Actions: Engage, Plan, Time





Happy to continue the discussion

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