institutCurie

DigiCore

CONNECT TO WIN

November
3rd-5th 2021

In collaboration with
OECI

The Digital Institute for Cancer Outcomes Research

DIGICORE's vision for collaborative RWE

Gennaro Ciliberto

President DIGICORE

Scientific Director National Cancer Institute «Regina Elena» Rome

Executive Board Member of Alliance Against Cancer

Initial Concept:
Back to the pre-pandemic time in 2019

Effective date of DIGICORE's Foundation
April 1st, 2021

THE DIGITAL INSTITUTE FOR CANCER OUTCOMES RESEARCH

DIGICORE's keywords

- Digital Revolution
- Electronic Medical Records
- Molecular Diagnostics Information
- Trial Automation
- Outcomes research
- Care Quality Management

"As the breadth and reliability of RWE increases, so do the opportunities for FDA to make use of this information."

Scott Gottlieb, FDA Commissioner
National Academies of Science, Engineering, and Medicine,
Examining the Impact of RWE on Medical Product Development,
September 19, 2017

"FDA will work with its stakeholders to understand how RWE can best be used to increase the efficiency of clinical research and answer questions that may not have been answered in the trials that led to the drug approval, for example how a drug works in populations that weren't studied prior to approval."

Janet Woodcock, M.D., Director, CDER

https://www.fda.gov/media/120060/download

Challenges:
We need to do more to prove the benefits of innovation

Many new oncology drugs are struggling to demonstrate real-world benefit

Drug was…	FDA 2008-2012[1]	EMA 2009-2013[2]
Approved on surrogate markers	67%	57%
Shown within 5 years to improve survival*	**14%**	**15%**

Sources 1) Kim C et al: JAMA Intern Med2015;359:1992-4 2) Davis C et al: *BMJ* 2017;359:j4530

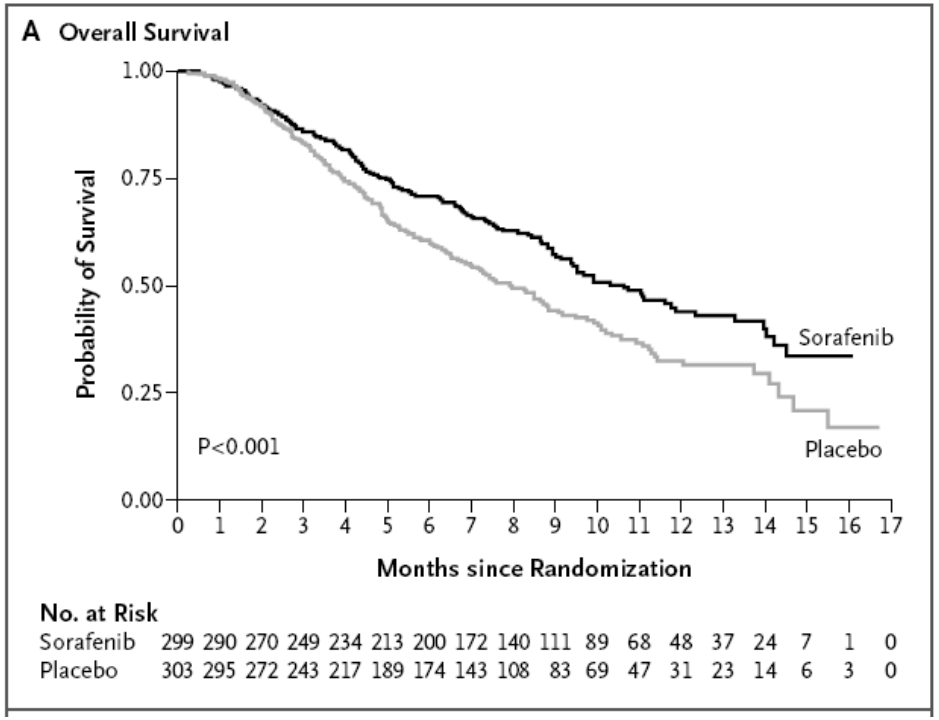
* Vs Standard of care or placebo

The efficacy-effectiveness gap: one example

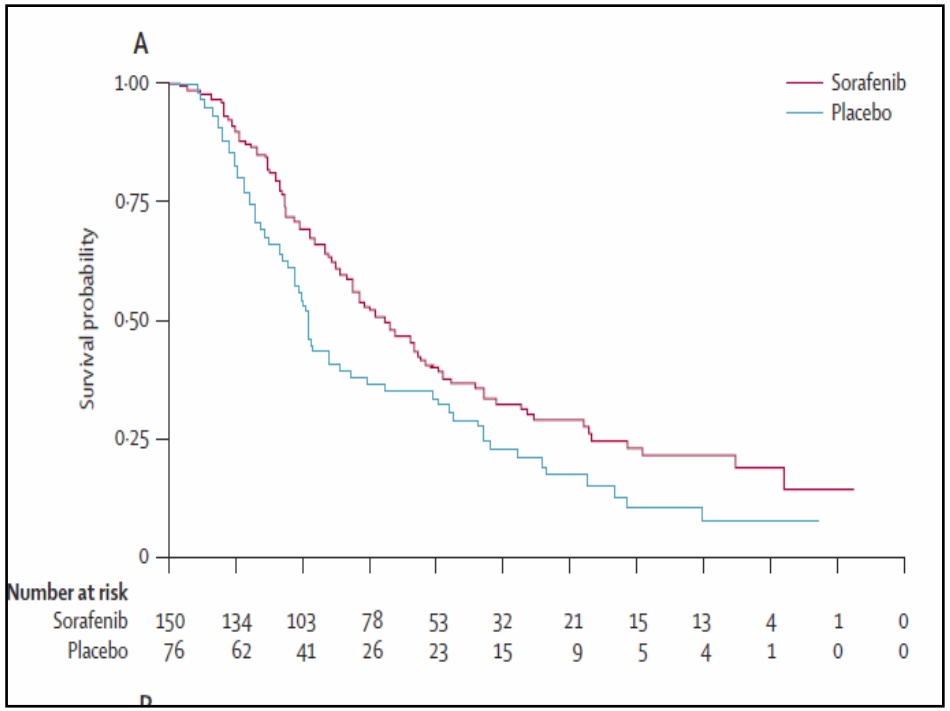
- **Sorafenib** in advanced HCC patients:
  - RCTs versus «out of trial» data

Sorafenib demonstrated a (limited) prolongation of overall survival in advanced HCC

SHARP



Asia-Pacific



	SHARP	Asia - Pacific
Median, sorafenib	10.7 months	6.5 months
Median, placebo	7.9 months	4.2 months
Hazard Ratio (95% CI)	0.69 (0.55 – 0.87)	0.68 (0.50 – 0.93)

Llovet et al. N Engl J Med 2008; 359:378-390
Cheng AL *et al.* Lancet Oncol 2009; 10: 25-34

The Oncologist®

Hepatobiliary

Sorafenib Effectiveness in Advanced Hepatocellular Carcinoma

HANNA K. SANOFF,[a,b] YUNKYUNG CHANG,[a] JENNIFER L. LUND,[a,c] BERT H. O'NEIL,[f] STACIE B. DUSETZINA[a,d,e]

[a]University of North Carolina Lineberger Comprehensive Cancer Center, [b]Division of Hematology/Oncology, [c]Department of Epidemiology, Center for Pharmacoepidemiology, [d]Division of Pharmaceutical Outcomes and Policy, University of North Carolina Eshelman School of Pharmacy, and [e]Department of Health Policy and Management, University of North Carolina Gillings School of Global Public Health, University of North Carolina, Chapel Hill, North Carolina, USA; [f]Indiana University Simon Cancer Center, Indianapolis, Indiana, USA

Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Carcinoma, hepatocellular • Liver neoplasms • Sorafenib • Drug costs • Medicare • Liver diseases • Aged

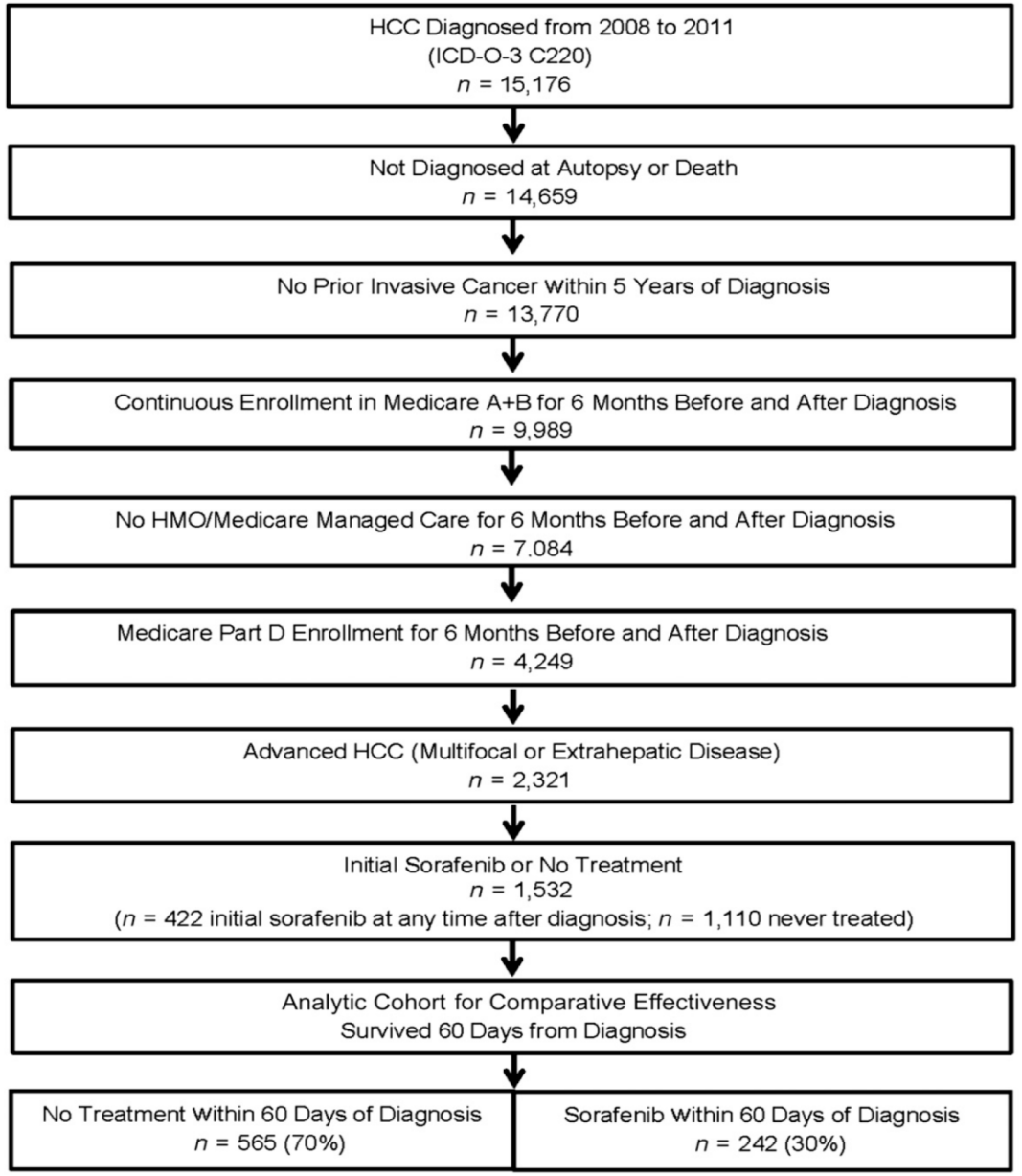
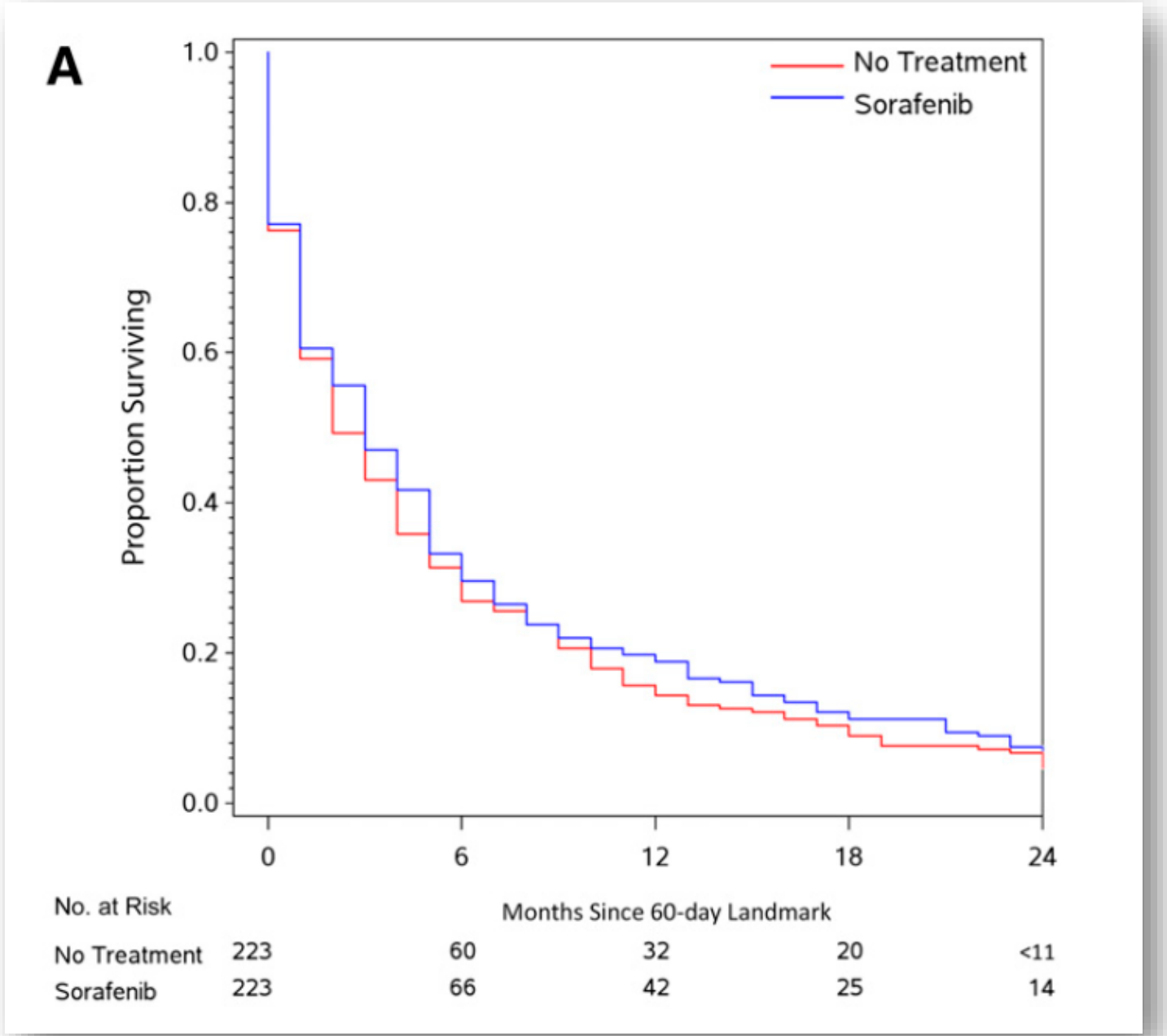


Figure 1. Consolidated Standards of Reporting Trials diagram of cohort assembly.
Abbreviations: HCC, hepatocellular carcinoma; HMO, health maintenance organization; ICD-O-3, International Classification of Diseases for Oncology, 3rd edition.

Sanoff HK et al, Oncologist 2016 Sep;21(9):1113-20



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European Journal of Cancer 130 (2020) 155–167

Available online at www.sciencedirect.com

ScienceDirect

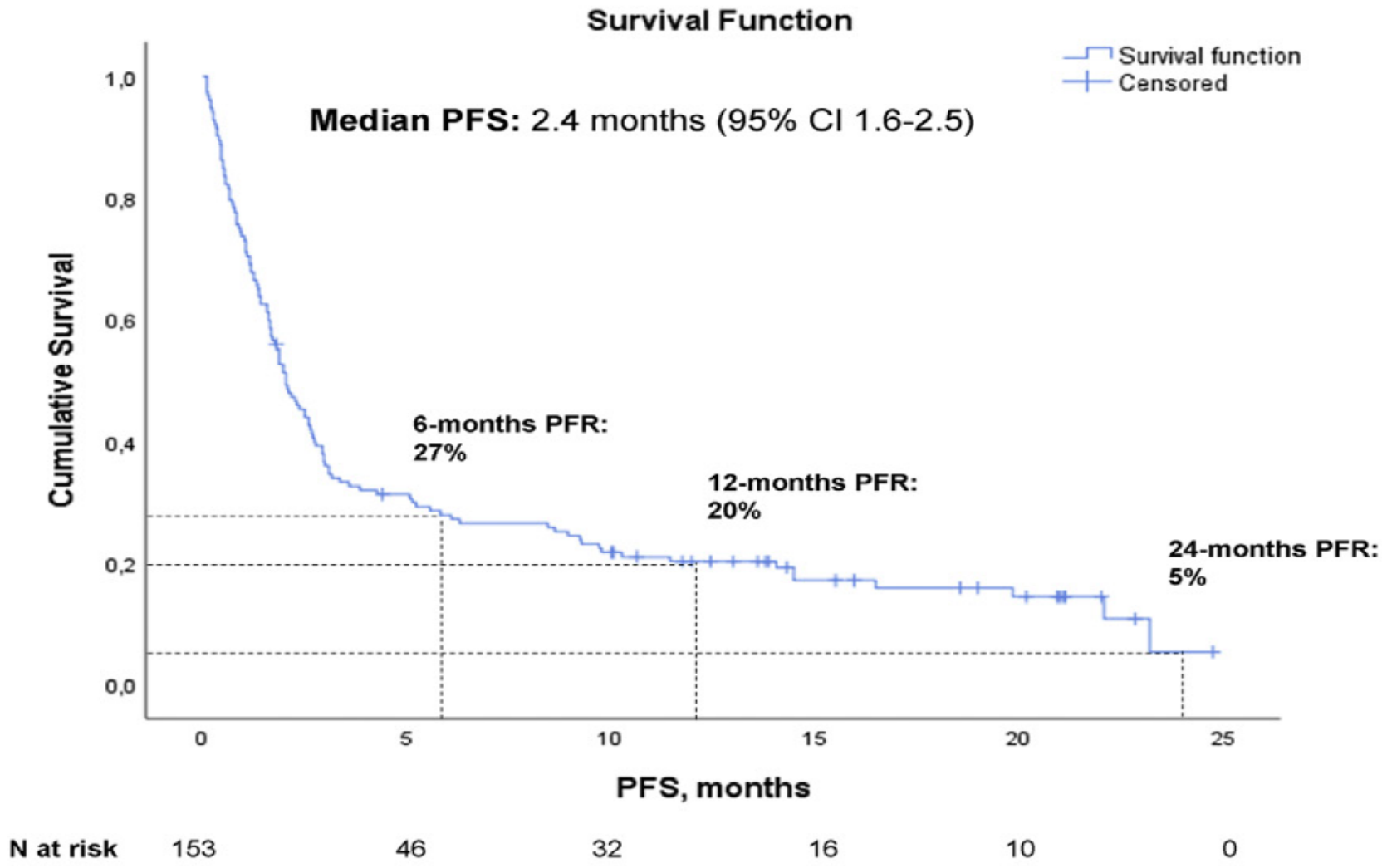
journal homepage: www.ejcancer.com

Original Research

First-line pembrolizumab in advanced non–small cell lung cancer patients with poor performance status

Francesco Facchinetti [a,b,*], Giulia Mazzaschi [a], Fausto Barbieri [c], Francesco Passiglia [d], Francesca Mazzoni [e], Rossana Berardi [f], Claudia Proto [g], Fabiana Letizia Cecere [h], Sara Pilotto [i], Vieri Scotti [j], Sabrina Rossi [k], Alessandro Del Conte [l], Emanuele Vita [m], Chiara Bennati [n], Andrea Ardizzoni [o], Giulio Cerea [p], Maria Rita Migliorino [q], Elisa Sala [r], Andrea Camerini [s], Alessandra Bearz [l], Elisa De Carlo [l], Francesca Zanelli [t], Giorgia Guaitoli [c], Marina Chiara Garassino [g], Lucia Pia Ciccone [j], Giulia Sartori [i], Luca Toschi [k], Filippo Gustavo Dall'Olio [o], Lorenza Landi [n], Elio Gregory Pizzutilo [p,u], Gabriele Bartoli [q], Cinzia Baldessari [c], Silvia Novello [d], Emilio Bria [m], Diego Luigi Cortinovis [r], Giulio Rossi [v], Antonio Rossi [w], Giuseppe Luigi Banna [x], Roberta Camisa [a], Massimo Di Maio [y], Marcello Tiseo [a,z]

Facchinetti et al
Eur J Cancer. 2020 May;130:155-167.



Facchinetti et al.
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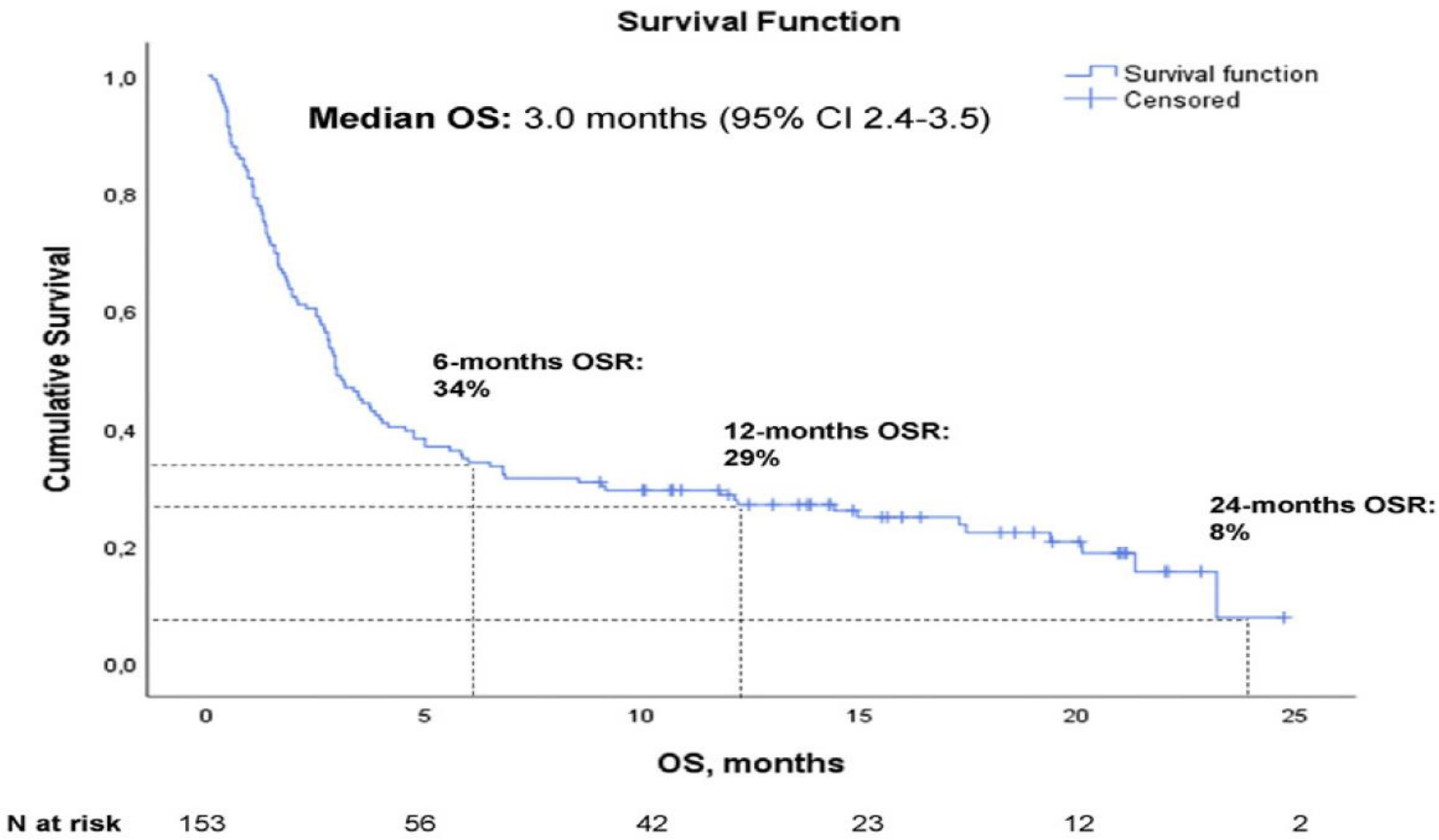

Facchinetti et al
Eur J Cancer. 2020 May;130:155-167.

Determinants of PS 2

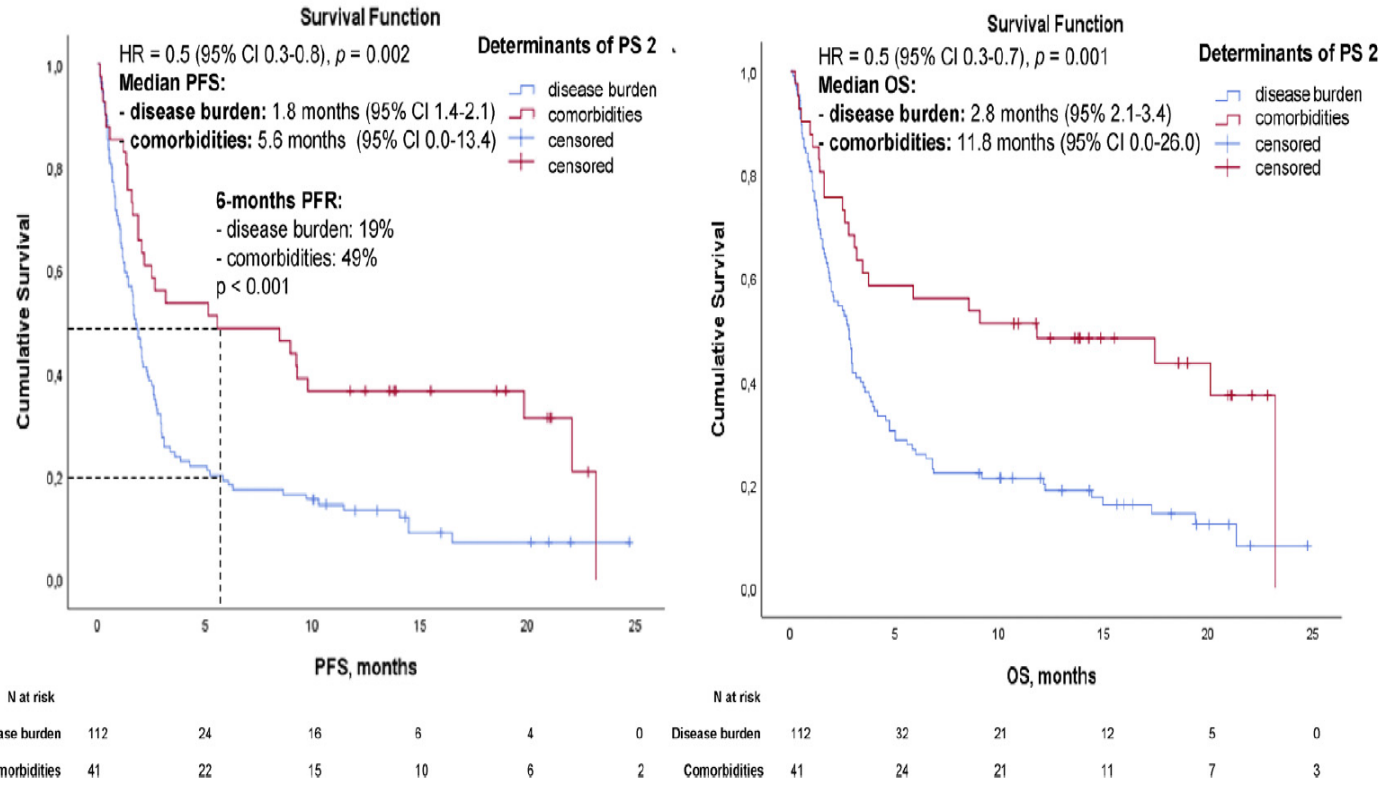

Fig. 2. Kaplan–Meir curves of progression-free survival (PFS) and overall survival (OS) according to performance status (PS) 2 determinant. HR, hazard ratio; 95% CI, 95% confidence interval; PFR, progression-free rate.

Facchinetti et al
Eur J Cancer. 2020 May;130:155-167.

In conclusion, clinical outcomes of PS 2 advanced NSCLC patients receiving immunotherapy as first-line therapy because of PD-L1 $\geq$ 50% were globally poor but strongly related to the reasons conditioning the poor PS. NSCLC patients with PS 2 due to comorbidities had a significantly better prognosis compared with patients whose poor PS was determined by the disease burden, for whom pembrolizumab alone seems to provide very disappointing results. If patients with comorbidities-induced PS 2 may benefit from pembrolizumab mono-therapy, on the other hand, chemoimmunotherapy combinations would be a better choice when the poor PS is due to disease aggressiveness itself.

Facchinetti et al
Eur J Cancer. 2020 May;130:155-167.

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European Journal of Cancer xx (2017) 1–3

Available online at www.sciencedirect.com

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journal homepage: www.ejcancer.com

ELSEVIER

EJC

Editorial

Real-world data for efficient health technology assessment

*The clue to why **real-world data** is an important component of any estimation of cost-effectiveness is in the name: the definition of effectiveness, as opposed to efficacy, refers to the measurement of effects in the real-world, rather than under the conditions of experimentation required for the unbiased measurement of efficacy.*

Peter S Hall, European Journal of Cancer 2017

«Real life» studies from different viewpoints

- From a payer's point of view, «*real life*» studies can be useful to define the real effectiveness of a treatment **in a more heterogeneous population**.

- From a clinician's point of view, «*real life*» studies can be useful to describe the outcome associated with use of a treatment **in patients underrepresented in RCTs**.

- From a patient's point of view, *«real life»* studies can be useful to better address the concept of **personalized care**

Challenges:
Clinical Research has to find new ways to optimize costs and timelines

48%

Of sites do not achieve enrollment targets

57%

Of trials experience protocol changes

80%

Of trials are delayed due to slow recuitment

61%

Inclusion and exclusion criteria have grown

Source: Clarivate Analytics Cortellis, Mar 2019; IQVIA Institute, Mar 2019

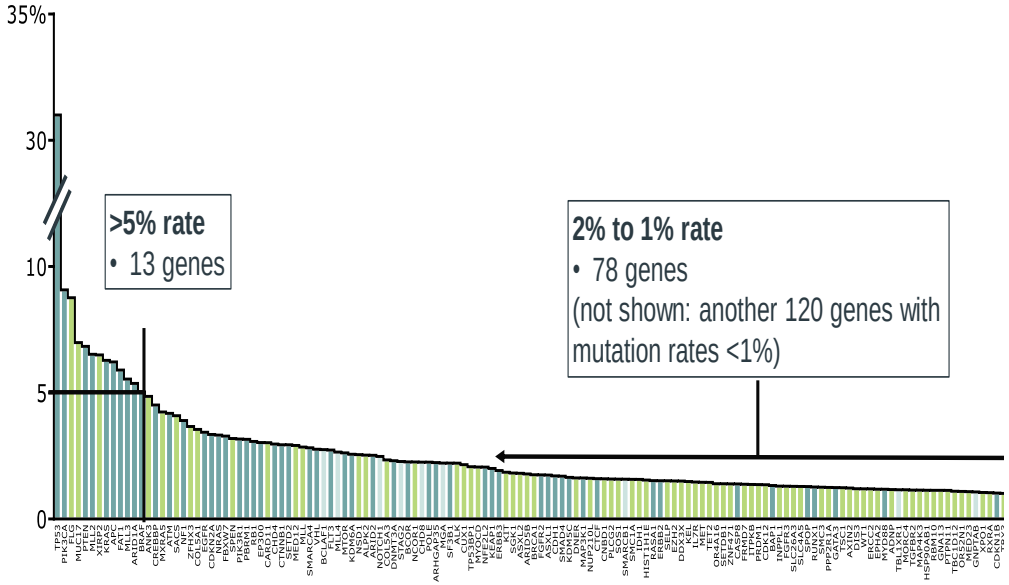
Chart notes: Terminated and withdrawn trials were excluded from the analysis. Trials were industry sponsored and interventional. Diagnostics, behavioral therapies, supplements, devices, and medical procedures were excluded. Phase II includes Phases I/II, II, IIa, IIb. Phase III includes Phase II/III and III. Data shown is weighted average. All TAs = All therapy areas: oncology, immune system, GI/NASH, endocrinology, respiratory, vaccine, infectious disease, neurology and cardiovascular.

Report: The Changing Landscape of Research and Development. IQVIA Institute for Human Data Science, April 2019

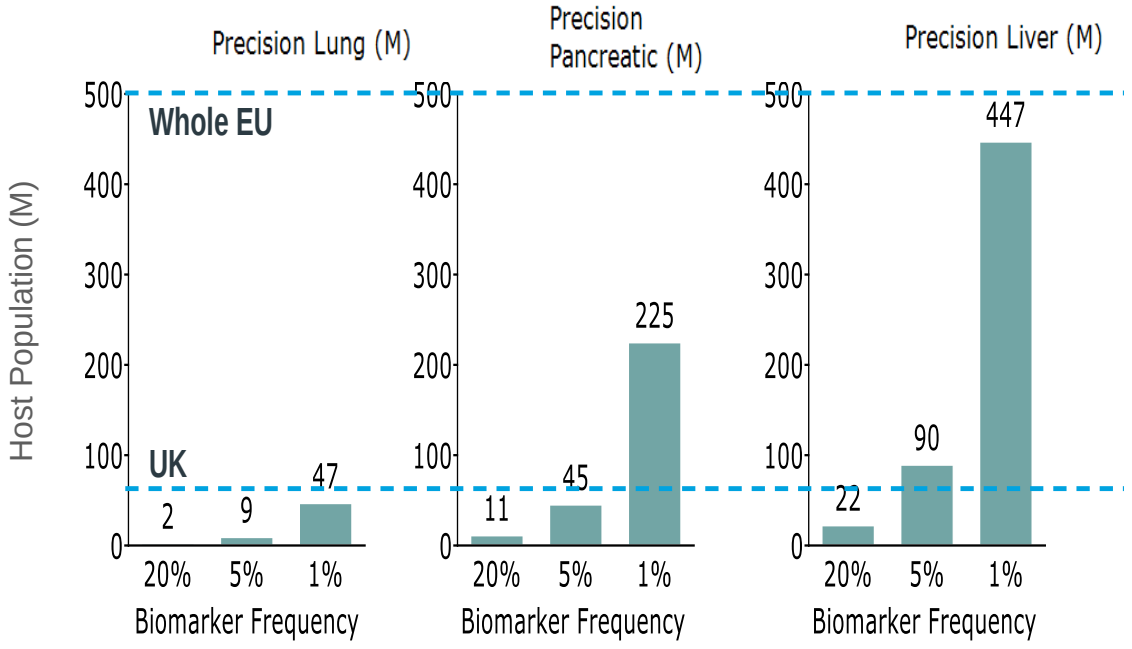
Challenges:
The rarity problem – somatic mutations are rare and require enormous scale to establish meaningful clinical evidence

Precision oncology is mostly 1% mutation ORFs

Pan-cancer non-silent mutation frequency (%)



How big a country needed to recruit 100 pts per year?



Incidence Rank	# 3	# 10	# 20

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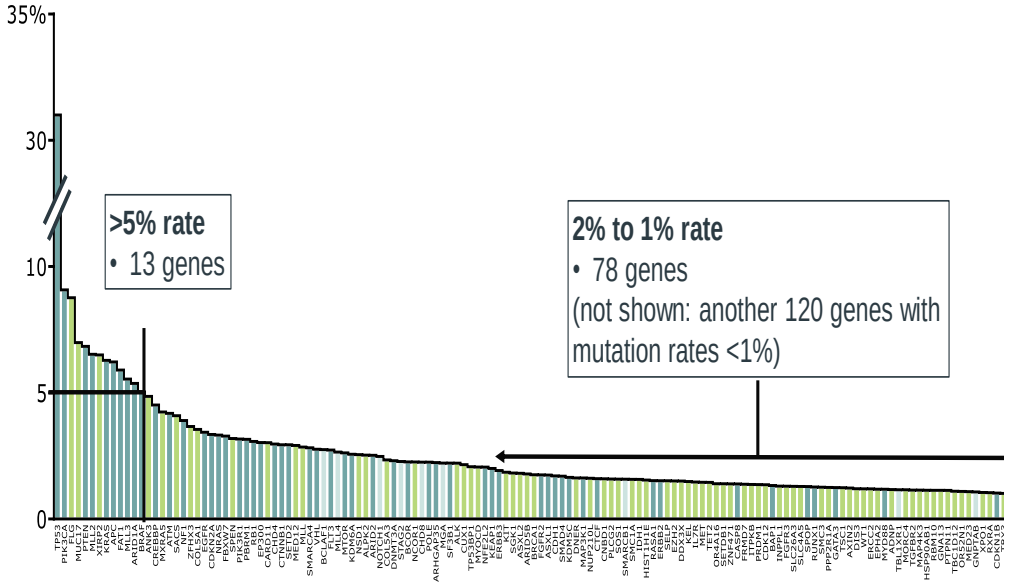

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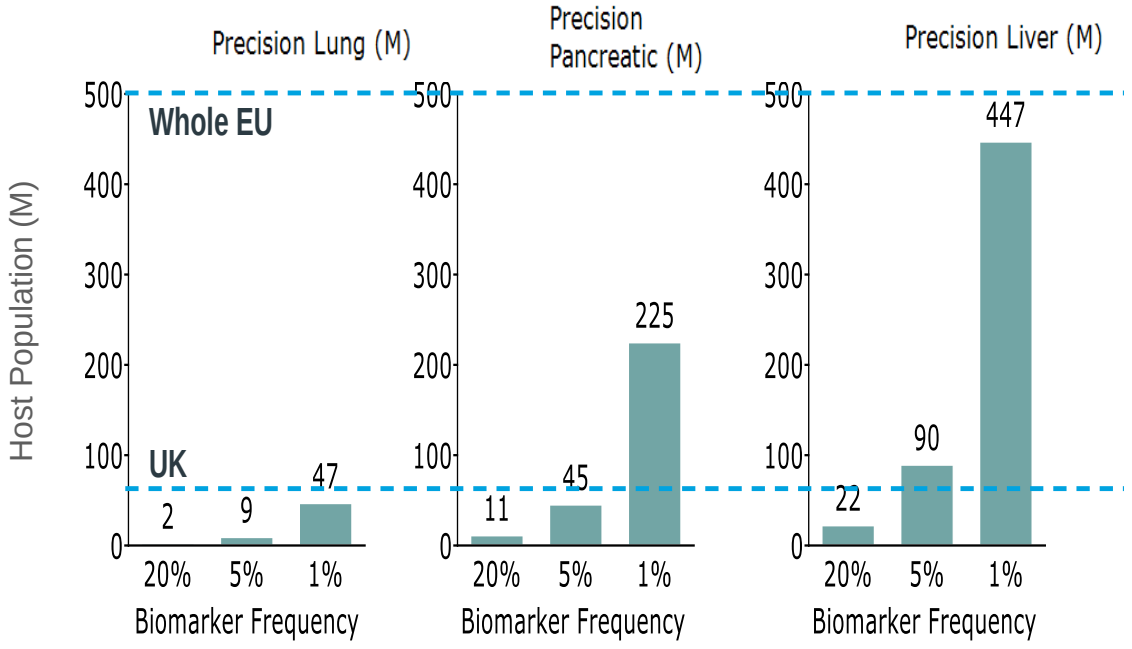


Need to establish a world-class trial recruitment network in precision oncology

DIGICORE: a large Public-Private Partnership in European Cancer Real World Evidence

Members

Industry

IQVIA

Illumina

Academic cancer centres

unicancer

ALLIANCE AGAINST CANCER

16 Cancer Centers already + Others to join hopefully soon

DIGital Institute for Cancer Outcomes Research (DIGICORE)

Pan-EU research collaboration to study cancer outcomes, capitalizing on increase in **precision oncology**

Goal: "Network of networks" with >150 cancer centres

Benefits and Rationale

- For **Cancer Centres**, **pool cancer data across centres for improved translational research**
  - Improving patient outcomes #1
  - Academic research/ publication #2
  - More efficient trials #3
- For **Patients: Broader trial access** and in future **better outcomes**
- For **IQVIA**, **drive commercial multi-centre, international RWE projects** in precision oncology and **drive precision trial recruitment**
- For **MDX major**, **grow clinical evidence base for MDX tests** in improving outcomes and **support MDX test reimbursement for all vendors**

DIGICORE – FOUNDERS

1. ALLEANZA CONTRO IL CANCRO
2. FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS
3. ISTITUTO EUROPEO DI ONCOLOGIA
4. INSTITUT CURIE
5. INSTITUT DE CANCEROLOGIE DE L'OUEST
6. IQVIA

DIGICORE – ASSOCIATE MEMBERS

1. UNICANCER
2. CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD
3. AZIENDA UNITA SANITARIA LOCALE - IRCCS DI REGGIO EMILIA
4. FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI
5. FONDAZIONE IRCCS POLICLINICO "SAN MATTEO"
6. HUMANITAS MIRASOLE SPA
7. IRCCS ISTITUTO ROMAGNOLO PER LO STUDIO DEI TUMORI "DINO AMADORI" – IRST S.r.l.
8. ISTITUTO FIRC DI ONCOLOGIA MOLECOLARE - IFOM RI
9. ISTITUTI FISIOTERAPICI OSPEDALIE
10. OSPEDALE "SAN RAFFAELE" SRL
11. INSTITUTE OF ONCOLOGY LJUBLJANA
12. MARIE SKLODOWSKA-CURIE MEMORIAL CANCER CENTRE
13. MASARYK MEMORIAL CANCER INSTITUTE
14. PORTUGESE ONCOLOGY INSTITUTE OF PORTO (IPO PORTO)
15. UNIVERSITY CANCER CENTER (FRANKFURT)
16. ILLUMINA NETHERLANDS BV

DigiCore
The DIGital Institute for Cancer Outcomes REsearch

What sorts of science will DIGICORE support?

1. Real World Evidence & outcomes research	• Use routine EMR to drive outcomes research and advanced real world evidence such as external comparators (controls to single arm trials)
2. Digital precision trial screening	• Semi-automate trial screening to make it easier to recruit to trial, especially in precision oncology and so democratise trial access
3. Biomarker validation and clinical benefit research	• Drive large scale Mendelian randomisation research and decision impact studies on large NGS panels linked to clinical data
4. Biobanks & Discovery Research	• Drive large scale collection of well annotated samples with deep clinical records for discovery and diagnostic development programmes
5. Pragmatic digital trials	• Ultimately, drive pragmatic platform trials in precision oncology

Next steps

Define an operating plan for the next 2-3 years

(Main outcome of the Connect to Win meeting)

Items to discuss for our Operating Plan

1. Shape the rules and define priorities

2. Plan joint infra-structure & secure funds

3. Access commercial RWE options

4. Develop academic RWE programs

We are looking to collaborate with cancer centres in cancer bids in response to EU Cancer Mission

DigiCore

Launch UNCAN.eu
Large scale basic research to understand cancer, such as ICGC ARGO

Polygenic Risk Score
EU-wide research program to improve genetic screening and analysis

Effective Cancer Prevention Strategy
Public health programs & comparative research across EU and member states

Screening and early detection
Develop more cost-effective programs in more cancers with better patient uptake

Personalized Medicine
Develop the evidence base (esp. outcomes) for broad use of personalised medicine

Diagnostic & Minimally Invasive TX
Develop right downstream TX for early detection (avoid over-treatment)

Survivorship Quality of Life
Research focused on improving QoL for long term cancer survivors

European Cancer Patient Digital Centre
A virtual network of patient-controlled (national) health data infrastructures

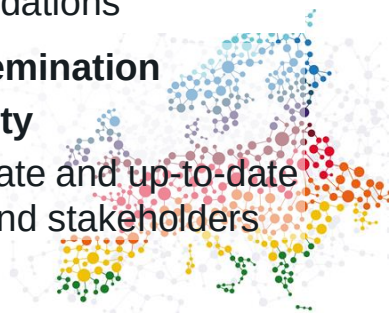
Cancer Health Equity (Policy)
Overcome inequities of quality / access to cancer treatment across member states

Comprehensive Cancer Infrastructure
Set up accredited Comprehensive Cancer Infrastructures in and between all EU members

Childhood and Adolescent Cancer
Generate the evidence needed to advance diagnostic, treatment and survivorship support (fit depends on centres in network)

Oncology-focused Living Labs
Cross-sector research, knowledge-sharing & implementation of new technologies not covered by other recommendations

EU-wide Cancer R&I Dissemination and Communication Facility
Support the uptake of accurate and up-to-date knowledge across Europe and stakeholders



Key: High DIGICORE priority | Medium DIGICORE priority | Lower DIGICORE priority

Together we have the option to bid on Cancer Mission and other funds from the European Commission

DigiCore

European Commission

Mission area: Cancer

Example use of funds

1. **Tech infrastructure at centres**
   - On-site data repositories
   - Common technology & common international data models
2. **Cancer centre data teams**
   - Support protocolized research
   - Convert local data into protocolized insights
3. **Large panel testing**
   - ‘Centres choose the test’ principle
   - Test data standardization follows to create interoperability
4. **Methods development and innovative science programs**
   - Academics in network showcase new digital approaches and methods that can make research more efficient and faster

Major Challenges

- Digital maturity:
  - Variable degree of «digital» readiness of our members
- Ethical and Legal:
  - Participation to retrospective RWE trials may be rendered difficult (if not impossible) by restrictive interpretations of GDPR
- Commitment:
  - Uneven interest of medical oncologists in RWE studies
- Resources and Culture:
  - Newly established and heterogeneous international group

DIGICORE's present dimension not yet ideal

Need to increase membership in order to reach the desired critical mass!

To Formally Join DIGICORE:

- Complete simple DIGICORE membership application form
- Connect with DIGICORE General Manager, Claudio Lombardo

To address questions on how DIGICORE will deliver research contact:

- Serena Di Cosimo, DIGICORE's Academic Research Manager and
- Piers Mahon, DIGICORE's Commercial Research Manager