A new vision for collaborative RWE studies

The OECI Oncology Days
June 16th, 2022

Prof. Gennaro Ciliberto, DIGICORE President
Scientific Director, IRCCS National Cancer Institute
“Regina Elena”, Rome, Italy

THE DIGITAL INSTITUTE FOR CANCER OUTCOMES RESEARCH

U.S. FOOD & DRUG ADMINISTRATION

"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

«Real world» studies from different viewpoints

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

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

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

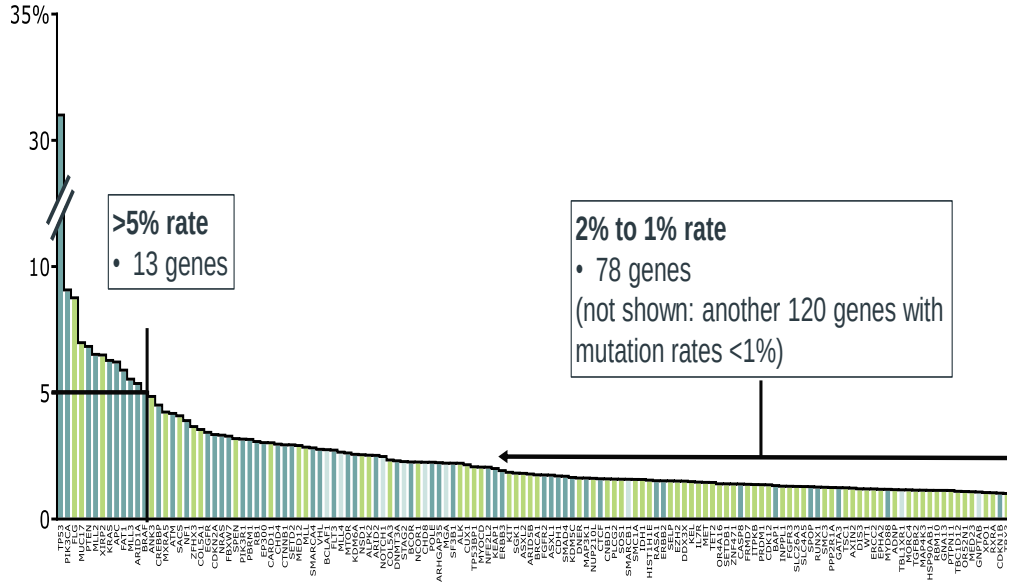
Chart notes: Terminated and withdrawn trials were excluded from the analysis. Trials were industry sponsored and interventional. Diagnostics, behavioral therapies, supplements, devices, and medical procedures were excluded. Phase II includes Phases I/II, II, IIa, IIb. Phase III includes Phase II/III 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

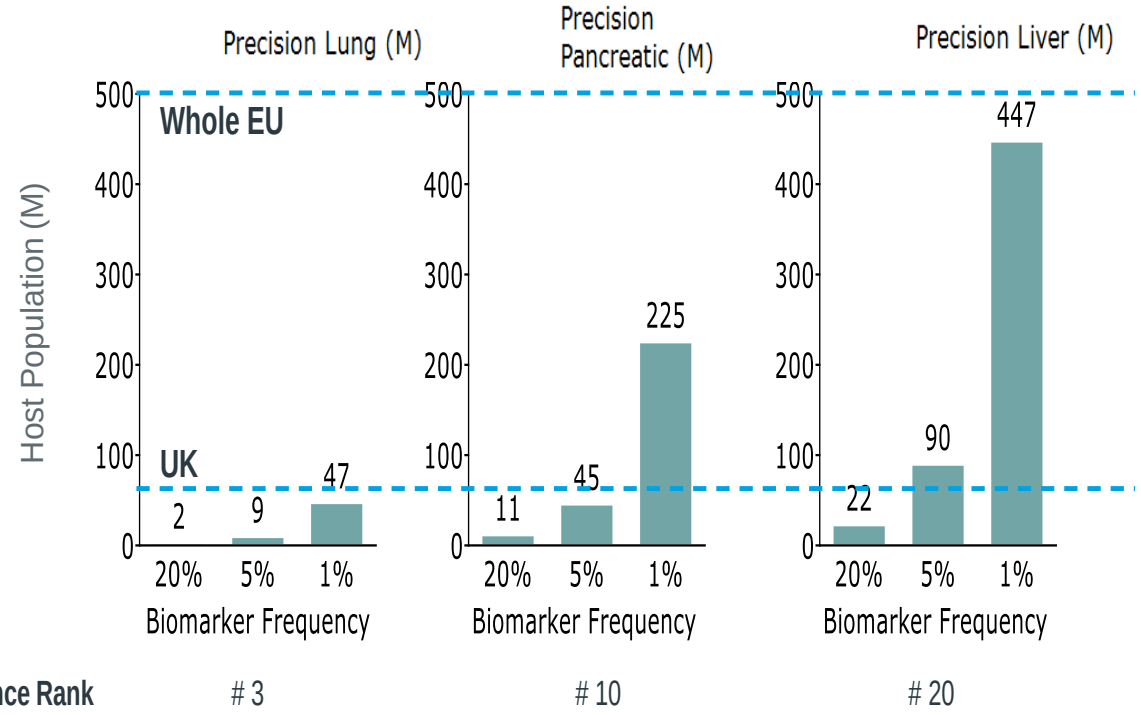
The rarity problem – somatic mutations are rare and require enormous scale to establish meaningful clinical evidence

Precision oncology is mostly 1% mutation ORFs

Pan-cancer non-silent mutation frequency (%)



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



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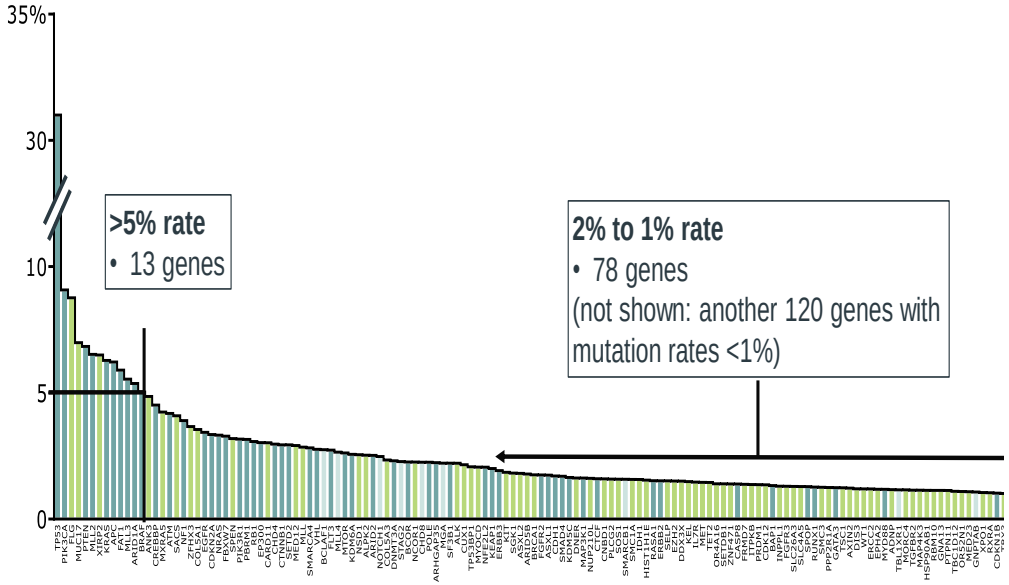

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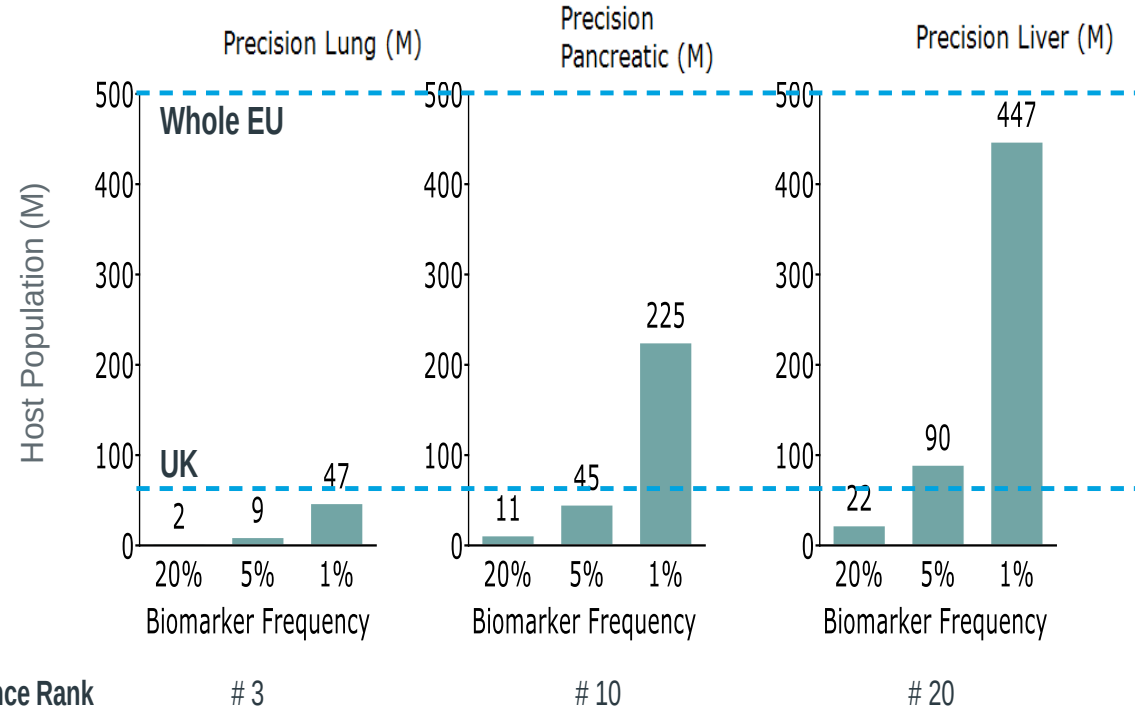


Need to establish a world-class trial recruitment network in precision oncology

DigiCore

DIGICORE is a new international Consortium that aims to transform and digitise cancer outcomes research in Europe

Members

Academic cancer centres

unicancer

ALLIANCE AGAINST CANCER

Other networks to come

Industry

IQVIA

illumina

DIGital Institute for Cancer Outcomes Research (DIGICORE)

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

Independent European Economic Interest Group (like OECI) with 30 cancer centres today

Benefits and rationale

- For **Cancer Centres**, pool cancer data across sites for improved translational research
- For **Patients,** broader trial access and in future better outcomes
- For **Industrial Partners:** drive commercial multi- centre, international RWE projects in precision oncology and drive precision trial recruitment
- Grow clinical evidence base for molecular diagnostic tests in improving outcomes and accelerate reimbursement for all vendors

DigiCore

DIGICORE's keywords

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

DIGICORE came about through 3 years of negotiations between OECI, Unicancer, Alliance Against Cancer and IQVIA

2018

Dec 2018
OECI/IQVIA discussions on digital partnership

2019

Apr 2019
Interested parties agree a new EEIG* partnership solution

Apr 2019 – Nov 2020
Detailed negotiations: Research independence, data protection, legal structure

2020

Apr 2020
First formal meeting of partners and commitment to proceed

COVID delay

2021

Apr 2021
DIGICORE legally founded in Brussels

Nov 2021
First conference: “Connect to Win” in Paris

2022…

Feb 2022
First HORIZON success with *IDEA4RC*

* European Economic Interest Grouping, same legal structure as OECI

Our foundational legal statutes built strong governance and protections for cancer centres

General Assembly
(Meets at least annually, 1 member 1 vote)

Appoints

President & Board
(Meets monthly)

Gennaro Ciliberto	Mario Campone	Xose Fernandez	Roberto Orecchia	Piers Mahon
Alleanza contro il cancro (ACC)	*Institut de Cancérologie de l'Ouest & Unicancer*	*Institut Curie*	*European Institute of Oncology*	*IQVIA*

- **Academic Research Manager** — *Serena di Cosimo*
- **Commercial Research Manager** — *Piers Mahon*
- **Working groups/ research committees**

* For more detail see: [OECI Magazine (December 2020)]

Key Principles*

1. **Medical hypothesis neutrality** – no large pharma inside, Surgery & Radio matter
2. Cancer centres retain **full data control** and autonomy over clinical decision making
3. Serve **both academic and commercial research** (later at fair market value)
4. **Institutional research autonomy** – right to refuse any study, or propose one
5. **Equality in research activity** of Associate members and Members
6. Technical solutions will be **federated,** include a **common data model** but do not have to implemented until / unless funded

Current DIGICORE network of 30 centres, 2 national networks and two commercial partners in 16 countries

TAYS Cancer Centre
Vision Zero Cancer
Oslo University Hospital

Edinburgh
Trinity St James

Maastricht CCC
Saint Luc
UCC Frankfurt
IPO Porto
START Madrid

Unicancer network,
Institut Curie,
Centre Léon Bérard,
Centre Jean Perrin,
ICO

Tartu UH
Marie Skłodowska Curie
Masaryk Memorial
Inst of Oncology Ljubljana
Sestre Milosrdnice

ACC network,
IEO,
INT Milan,
Gemelli,
IRST,
Reggio Emilia,
San Matteo,
Humanitas Mirasole,
Istituti Fisioterapici Ospedalieri,
San Raffaele,
IFOM,
INT Pascale

Activities - Connect2Win: Our annual digital research planning conference launched in Paris in November 2021

Connect2Win, Paris 3-5 Nov 2021

Objectives

- Lay out the challenges of delivering digital precision medicine research at scale
- Grow the network, discuss collaborative research in EU Cancer Mission
- Propose a pathway to digital RWE readiness for diverse centres
- Encourage dialogue and collaboration on how to drive international cooperation on these issues

75 delegates

38 cancer centres

19 European countries

Major national centres represented, with 12 institutes joining network as a result

The next Edition of Connect2Win will take place in Milan on November 8-9, 2022

DIGICORE's focus in 2022-2023 is building capacity for digital international comparative cancer outcomes research

1. Mobilise our members for international cancer outcomes research

- Build out our **cancer specific outcome research committees** and support them to seek European and other funding
- NSCLC, NHL, Ovarian initial momentum (others welcome!)

2. Establish Pragmatic Technical Standards for Clinical Informatic Interoperability

- Mapping the digital maturity and systems of centres to develop **a common, practical approach to EHR research**
- Plan out how to make our data "mean the same thing" across Europe

3. Platinum Technology Fund

- Up to €3M available from IQIVA to establish proof of concept on **European federation of oncology EMR data** in OMOP
- Designed to help all DIGICORE members secure follow-on funds

4. IQVIA-DIGICORE Early Career Leadership programme for RWE (IDEAL4RWE)

- **€500K of training in research leadership** & pilot study funding for teams of younger researchers in cancer outcomes research
- **Prepare the next generation for the digital revolution**

1. DIGICORE's research committees' structure is designed to complement national outcome research programmes

Initiation

DIGICORE Board selected 3 research topic - Lung Cancer/ Breast Cancer/ Non-Hodgkin's Lymphoma - and invited members to nominate experts

- **Participation open to all** members and associate members on equal basis
- **In 2022**: Outcome research in a few cancers
- **2023 on**: Broader research topics, member suggestions encouraged

Structure

- At least **5 cancer centres** from at least **3 countries**
- **2 co-chairs** (from 2 different countries)
- **Only clinicians** from cancer centres can co-chair outcome research committees
- **Open and democratic**
- Some **DIGICORE administrative support**

(Over time, some core funding)

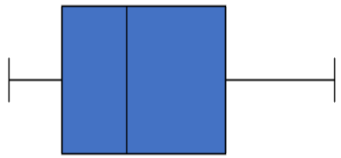
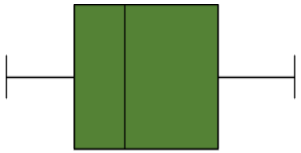
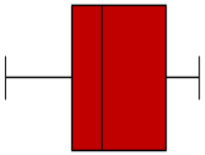
Benefits

- **International RWE research collaboration** among top European RWE experts
- **Attractive to research funders through international scale:**
  - HORIZON/European funds
  - Life sciences industry

2. We have set up a Clinical Informatics Interoperability WG to map our members' digital readiness

Increasing Centre maturity

1 = Rudimentary — Excellent = 5

		Early Insights (Directional N=10)
Precision oncology research maturity		Many centres have large panel, but can't access the data. We have "MDX snapshots only" – biopsy and test at single point in patient journey is the norm
Clinical data digital research maturity		We are OK at managing structured data collectively **BUT** weak at managing unstructured or getting to a common data model or reference data management
Pragmatic outcomes maturity		OK at date of diagnosis, line of therapy and death **BUT** weak at progression, RECIST, A.E. and PROs
Information governance & RWE delivery maturity		While some are well on the journey to strong Information governance post GDPR, many have not started to solve the legal and operational issues

2. This year we aim to develop the fact base that allows members to co-create our technical solutions

Activities for clinical informatics interoperability Working Group:

Mapping the IT vendors and systems in DIGICORE members – e.g. who has what type of chemotherapy dosing software or EHR or access to NLP tools

Mapping individual centre readiness to use the data – what maturity of information governance, data teams, experience in direct for EHR research etc

Assess feasibility of internationalising OSIRIS: Convene a sub-group of international experts to review that minimal model, with extensions for haematological malignancies

in the second half of the year **use the working group to define common technical priorities**

Outputs expected in 2022:

Prepare a **briefing on our collective digital maturity and readiness** for September Board

Provide a simple benchmarking report back to centres that participate – score vs DIGICORE peers

Recommendation to the December board as to next steps

If N high enough, **a paper on comparative national "digital readiness"**

3. Significant funding for digital infrastructure investments is becoming available, but proof of concept needed

Potential source of funding next 5 years	Total funding (estimate)	Of which digital infrastructure (estimate)
Recovery and resilience facility	€100bn	**€12bn***
Cancer mission	€2.6bn	**€0.1 to 0.2bn****
IHI + life sciences industry	€500bn	**€1.5 to 2bn*****

* Digital transition in healthcare funding estimates
**5 to 10% total
*** IHI and in-house research programme funding vs. global R&D spend in Cancer
Source: European Commission Recovery and Resilience Scoreboard, Dec 2021

"What you have got to [in DIGICORE] is very impressive, you are very close to having what everyone needs and have de-risked the partnership side of these collaborations substantially. We realise we have to go external [innovation] now in cancer. ***But you still have technology and study proof of concept to do****, and it will be hard to convince my colleagues to invest without that"*

– Top 5 Pharma Global Head of Scientific Partnerships

3. DIGICORE will fund up to €3M for technology investment in proof of concepts – half cash, half in-kind via the Platinum Technology Fund

Objectives for the Platinum Fund

1. Create **digital interoperability** between 6 centres in 6 different countries; quickly to help secure follow-on funds
2. Agree a **common minimum dataset** that describes cancer; building from French OSIRIS
3. Build **GDPR-compliant research data repositories** (or “nodes”) in Platinum centres, using **Cancer-OMOP**
4. **Federate those nodes** to allow automated counts, trial planning and to answer simple research questions with appropriate controls

DigiCore

Technology solutions need to recognise that health data today is "messy"

1. MOST EHRS TODAY ARE REALLY "PAPER IN DISGUISE"

2. AS A RESULT WE WILL NEED SOLUTIONS FOR UNSTRUCTURED TEXT & PDF

Typical EHR *(some are much more structured)*

i) **Structured or semi-structured** data

ii) **Electronic free text** (most medical notes and observations in core EHR)

iii) **Image or PDF based information**

- PDF text, e.g. scanned referral letters, laboratory test reports, molecular diagnostic test results
- Images e.g. radiology, digital pathology

DigiCore

3. Platinum fund will support the development of a proof of concept network for advanced RWE research

Who?	• Digitally-ambitious cancer centres needing investment
What?	• An investment programme for **advanced RWE technology** – **up to €3M** • **€250K cash - €250K in-kind** tech for 6 centres
How?	• **Individual cancer centres express interest**, access funding details, training materials, get bid prep support and advice • **Submit bids** outlining their plans for needed upgrade
When?	• **Expressions of interest** end of June 2022- Full appl Sep 2022 • **Deployment start in** December 2022 • **Concludes** November 2023
T&Cs?	• Any OECI or similar can apply, but **to receive funding** - Must become a member or associate of DIGICORE - Must be willing to contract for commercial RWE

4. We will need a new generation of outcome researchers to digitise cancer control

The Platinum fund will build “a better digital microscope” for cancer outcomes research..

..But to use it well will need new research skills and leadership inside cancer centres

Solution

DIGICORE Early Career Leadership Programme for Real World Evidence (IDEAL4RWE)

DigiCore

4. IDEAL4RWE will address a skills gap and support proof of concept research involving emerging research leaders

Who?	• **Under 45,** clinicians, data scientists etc. Interested in **outcome research** and ambitious to lead digital revolution in RWE
What?	• Training on both **technical and leadership skills** for RWE • Based around an international **proof-of-concept** study
How?	• **Mix of training styles:** Face-to-face and virtual • Full programme **involves "test" application – funding available**
When?	• **Started** in Q2 2022 - free "taster" programme • **RWE studies start in Q4 2022/Q1 2023** • **Concludes** H1 2023
T&Cs?	• Open to **multi-centre teams** of early career researchers • **Must have support of their centre** for some research time • Their centre must **join DIGICORE** • 80% study funds spent in centres contracted with IQVIA

Current involvement in EU research bid - won

HORIZON-HLTH-2021-TOOL-06-03

Project

- Intelligent Ecosystem to improve the governance, the sharing and the re-use of health Data for Rare Cancers (IDEA4RC)

Objectives

- Establish a ‘Rare Cancer Data Ecosystem’ to make possible the re-use of existing data (e.g. registries, biobanks, etc)
- Improve data system interoperability and leverage AI approaches to facilitate research in rare cancers and improve equality of care

DIGICORE role

- Engagement, definition of research and market needs and validation of approaches developed

Project coordinator:
Istituto Nazionale dei Tumori di Milano

Current involvement in EU research bid - submitted

Call: EU4H-2021-PJ2

Building the EU Cancer and Public Health Genomics platform

- **Coordinator**: **SCIENSANO**
- **DIGICORE Role**: **Partner**
- **DIGICORE Activities** :
  - ✓ **WP 10**: ***Data integration and Dissemination***
  - ✓ **WP 13**: ***Educational activities***

Call: EU Mission 02-02: QoL of patients and survivors

- **Coordinator: Fondazione INT**
- **DIGICORE Role: Leader WP5 -** ICT Platform and Data Analysis, SW development, digital toolkit

Benefits to centres from participating in DIGICORE

Drive better research in Europe

- **Innovate collaboratively** to develop new methods and digital infrastructure
- Access **cutting edge methods**, IP and tools that increase your competitiveness
- **Statistical power for rare subgroup analysis** e.g., 1% mutations
- **Collaborate in precision oncology** and making large panels “the EU normal”

Access new funding streams

- Secure **EU collaborative grant income** – for digital infrastructure, digital tools, specific studies
- Drive **commercial research** via IQVIA – advanced RW studies, precision trials
- Access **global philanthropy investment** via IQVIA – e.g., paediatric oncology
- Propose **academic studies** to the grouping

How to join DIGICORE

Contact DIGICORE (info@digicore-cancer.eu) for application information and introductory briefing (if required)

Submit application form (https://digicore-cancer.eu/Page.aspx?name=JOIN)

Website instructions

Join Now

DIGICORE – EEIG Membership Application

Instructions and Form

Each Institution that wishes to apply for Membership in DIGICORE-EEIG must fill-out the ***DIGICORE Application Form***

Prior to filling in this form, the Applicant Institution shall verify that it meets the relevant requirements for membership set forth in the ***DIGICORE-EEIG Statute***, and that it agrees to comply with the rules outlined in the DIGICORE-EEIG Statute.

Submitting procedure

1. Fill in the form (page 3-4 below) as clear and legible as possible. Once completed, please make a copy of the document and preserve it for your own records. The original signed form must be sent to:

Prof. **Claudio Lombardo**
c/o SOS Europe Srl
Via delle Campanule, 74
16148 Genova - Italy

2. Please send an electronic copy of the signed form to *info@digicore-cancer.eu* along with a copy of the Statute of the cancer centre/institute/organisation/company

Thank you!