Real World Data: si possono davvero usare tra Italia e Europa?

Prof. Gennaro Ciliberto – IRCCS Istituto Nazionale Tumori «Regina Elena» – President DIGICORE

DIGICORE is an international consortium that aims to transform and digitise cancer outcomes research in Europe

Members

Academic cancer centres

unicancer

ALLIANCE AGAINST CANCER

Individual cancer centers

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 40 cancer centres today in 17 countries

Benefits and rationale

- For **Cancer Centres**, interoperability of 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

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Key Principles Built Into DIGICORE's Legal Constitution

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

DIGICORE now includes 40 cancer centres in 17 countries – everyone welcome to join!

TAYS Cancer Centre

Vision Zero Cancer

Oslo University Hospital

Edinburgh
Leeds
Trinity St James

Maastricht CCC

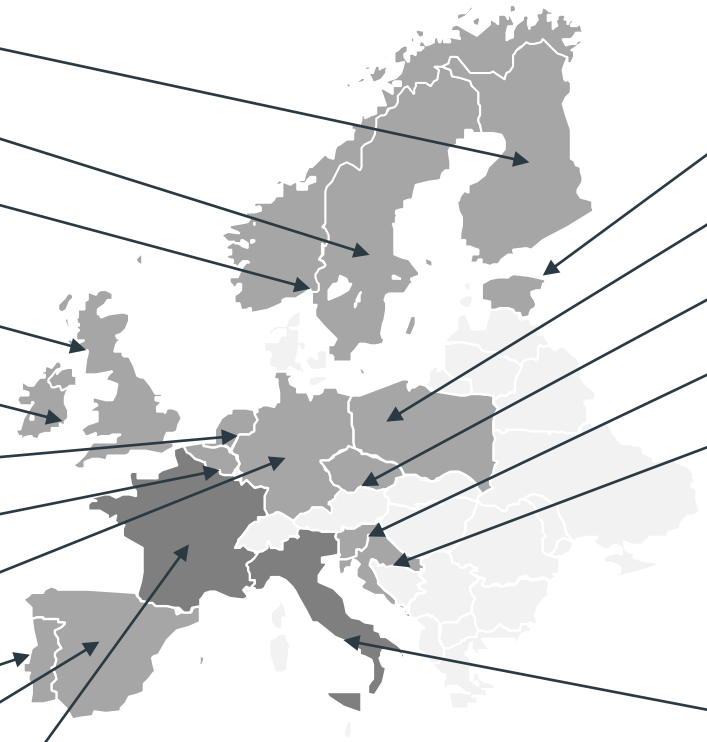
Saint Luc

UCC Frankfurt

IPO Porto

Fundacion Jimenez Diaz
Start Madrid

Unicancer network (4)
Institut Curie,
Centre Léon Bérard,
Centre Jean Perrin,
ICO



Tartu UH

Marie Skłodowska Curie

Masaryk Memorial

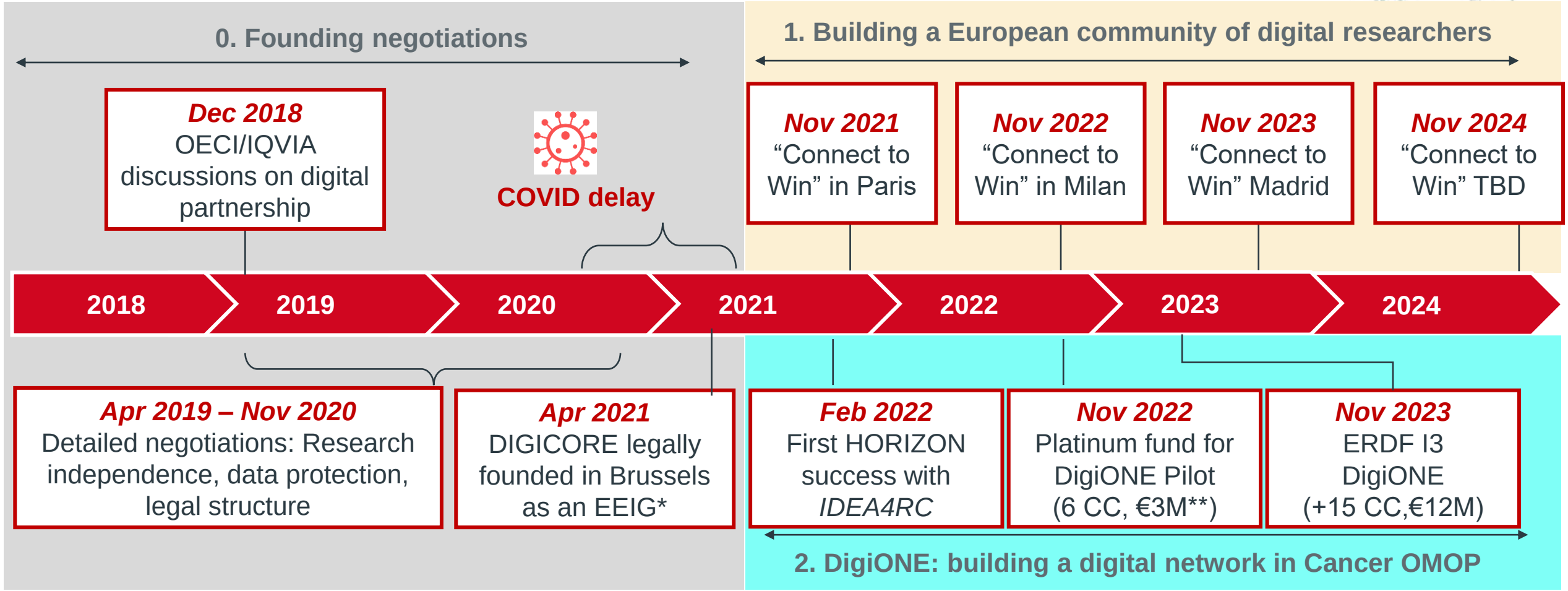
Inst of Oncology Ljubljana

Sestre Milosrdnice

ACC network (12)
IEO
Gemelli,
IRST,
IFOM,
Veneto
INT Milan,
Reggio Emilia
San Matteo,
INT Pascale
San Raffaele
Humanitas Mirasole,
Istituti Fisioterapici Ospedalieri

Key:
Red = joined in 2022-2'23
Black = joined earlier

Three chapters to DIGICORE's story so far



* European Economic Interest Grouping, same legal structure as OECI
** Funded by IQVIA and Illumina

We are participating to 4 HORIZON projects and have started a major internal project (DigiONE) directed to build a Digital infrastructure involving our centers

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IDEA4RC

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

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CAN.HEAL

Building the EU Cancer and Health Genomics platform

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EUonQoL

Quality of Life in Oncology: measuring what matters for cancer patients and survivors in Europe

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DigiONE

DIGItal Infrastructure for ONcology in Europe
Building a European federated digital research network

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CCI4EU

Comprehensive Cancer Infrastructures for Europe

We are 60% through the DigiONE Pilot: €3M for technology proof of concept to automate and federated cancer outcome research under GDPR

Objectives for DigiONE – Funded jointly by IQVIA and Illumina

1. Define a **scalable common international minimum dataset for cancer**, building from French OSIRIS
2. **Achieve interoperability and high data quality** on that dataset between 6 centres across Europe under GDPR
3. **Federate those centres** to allow aggregated statistics like counts and to answer simple research questions, with appropriate information governance and contracting
4. **Link routine molecular and clinical data** (despite the format challenges on molecular PDFs)
5. Work out how to **scale up digitally less mature hospitals** with a **variety of technologies and vendors** in DIGICORE's learning – by- doing community

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Developed frameworks and self-assessment tools to help measure centre RWE readiness and plan improvements

	Bronze Cancer Centres	Silver Cancer Centres	Gold Cancer Centres
1. Precision oncology research maturity	**MDX testing below NCCN guidelines** • Testing almost all “IHC + some Sanger” • Very limited local precision expertise • Don’t recruit to Biomarker driven trials	**Testing at / above NCCN guidelines** • Small panel the norm only in NSCLC • Some but limited precision expertise • Recruit rarely for SoC biomarker trials	**Large Panel MDX standard of care** • Molecular tumour board pilots • Lots of precision trials underway, especially in “new biomarkers”
2. Routine clinical data digital research maturity	**No Data Warehouse, but core EMR exists** • Siloed Clinical Systems, very partial data • Unstructured Data often paper based • No Data Standardisation • Traditional eCRF obs. studies only	**Basic clinically focused Data Warehouse** • Core Clinical Systems integrated • Identifiable Data, some standardisation • Unstructured Data is digital, un-mapped • Taking first steps in Database Research	**A research ready local Data Warehouse** • All cancer data in (chemo, radio, path), with strong master data management • Strong privacy norms (pseudo etc) • Multi-site database research routine
3. Pragmatic outcomes maturity	**Minimal routine outcomes in EMR** (death in hospital, ER admissions only) • Manual research processes established for date of death, but frequency of routine scans confounds RECIST	**Outcomes interested but gaps remain** • Some communities of care track key outcomes, often outside of EMR • Progression only well tracked where easy to measure (e.g. CA125 in ovarian)	**Preparing for outcomes research at scale** • EMR captures progression and death • Experimenting with routine digital outcomes – PROs tools, AI on scans etc • Maybe pilots in liquid biopsy for relapse
4. Information Governance & Delivery Maturity	**Not systematic on GDPR research reuse** • Very basic patient notifications on data, often limited to clinical use • eCRF processes use traditional pathways of study specific consent • Very limited capacity to support planning or commercial projects	**GDPR foundations based on notification** • High Quality Patient Notification and Opt-out process cover research • Aggregated data released without consent, consent needed for patient level • Some spare capacity, but tends to be cancer specific and easily saturated	**Strong secondary use consents the norm** • Secondary consents routine, and provide a broad basis for processing • Strong processes for privacy management on patient level releases • Large central data science teams with spare capacity for commercial studies

DIGICORE takes a highly compliant approach to GDPR that adapts to individual hospital legal circumstances

Main Principles

- **Hospitals in control** – which studies to run, with what technical methods
- Recognise different hospitals have **different rules**
  - Some with routine consent to research on most patients
  - Some with strong notification and opt-out
  - Some with no well established legal basis beyond study specific consent (they are in DIGICORE to learn)
- Research only takes place within a **protocolised paradigm**

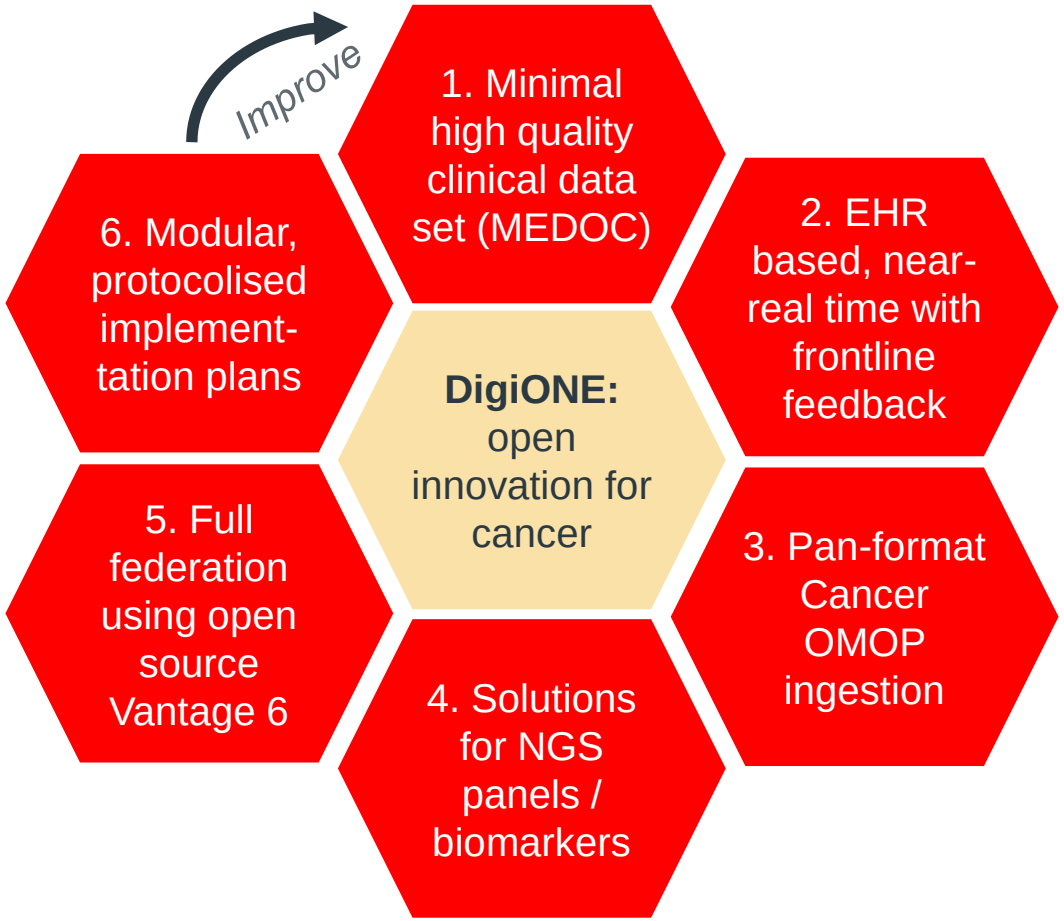
Current approaches

- **"Large N studies"** use methods designed to be GDPR compliant **without specific consent**
- "Low N studies" typically use traditional approaches of specific consent, anonymisation or consent waiver

Future approaches (funding dependent)

- Help hospitals upgrade their local legal basis for processing to broad routine secondary use consent

The main focus in 2023 has been to get to a technical design for our network for high quality Cancer OMOP studies with 6 local builds underway



Digital Oncolgy Network for Europe (DIGIONE)
(6 abstracts at OHDSI Europe – posters outside)

1: **Minimal Essential Description Of Cancer** (MEDOC)

2: **Near-real time frontline feedback loops** to improve data

3: **Pan-format Cancer data ingestion**. Not just ETL also NLP

4: **GDPR recital 34 privacy conserving solutions for NGS**

5: **Full federation with open source Vantage6** to allow statistical analysis equivalent to centralised data, but without data pooling

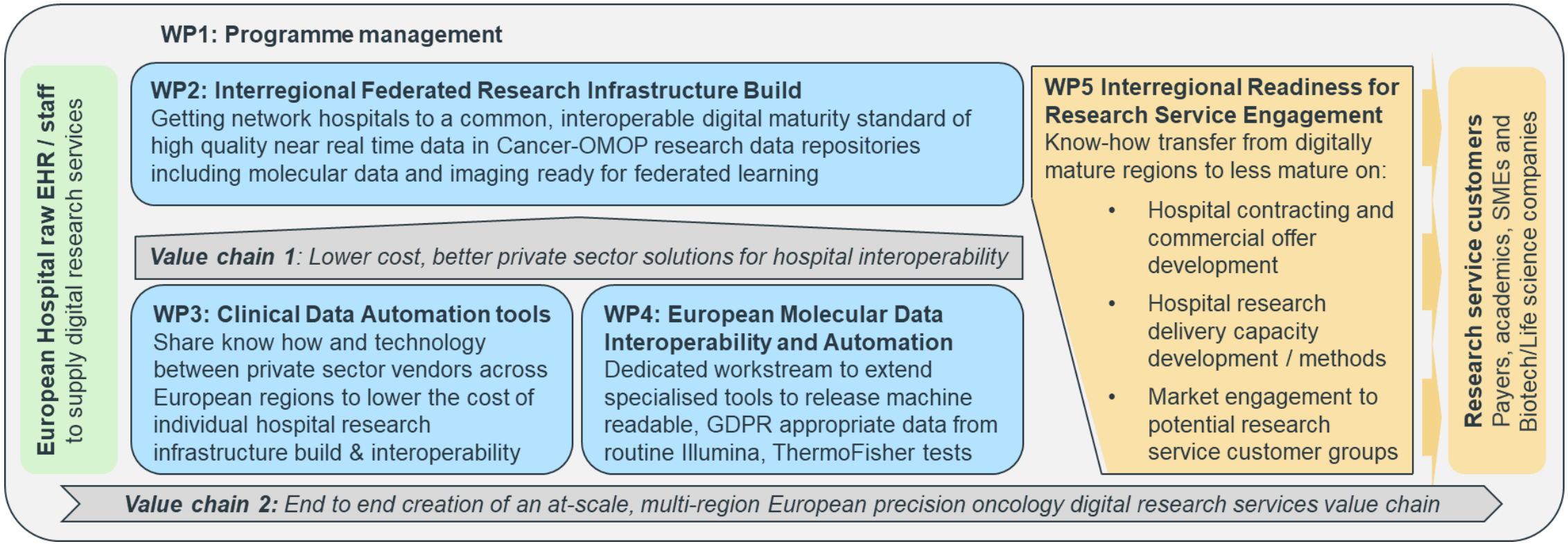
6: **Modular, protocolized implementation plans** to solve for limited data normalisation skills in most hospitals

7. **All in open standards and vendor agnostic**

4 multi-centre cancer OMOP studies are underway to test that technology, and we would welcome other centres to join them

	Pan cancer / C19	mNSCLC	Breast Cancer	Ovarian cancer
PI	**Elin Hallan Naderi**, Oslo University Hospital, Norway	**Åslaug Helland**, Oslo University Hospital, Norway	**Cédric van Marcke**, Cliniques Universitaires Saint-Luc, Belgium	**Geoff Hall**, Leeds Teaching Hospital NHS Trust, UK
Title	Impact of COVID-19 on cancer care in European centres based on number of new diagnoses and 12-month survival	A disease natural history and outcomes study with care quality assessment (DINASTY) in patients with metastatic NSCLC	DINASTY in patients with HR positive HER2 negative metastatic breast cancer	DINASTY in patients with epithelial ovarian cancer (EOC)
# centres committed	5 *(X with data @ 10 Nov)*	5	4	4
Estimated cohort size	124,000	9,500	3,000	1,500
# Ethics approvals	5	2	*Not yet submitted*	*Not yet submitted*
Contact point	Project Manager: Rosie McDonald, IQVIA, **rosie.mcdonald@iqvia.com**			

We have secured ERDF funding to scale up the network with an additional 15 host via the €12.5M DigiONE I3 project - with 15 hospitals, 12 other partners



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

The DigiONE effort 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 **E**arly **C**areer **L**eadership **P**rogramme for **R**eal **W**orld **E**vidence (IDEAL4RWE)

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In 2023 we completed our first a multi-centre study methods training program for early career researchers – IDEAL4RWE

The story in numbers

- **47 participants** signed up for phase 1
- **4 seminars** delivered on RWE technical content
- **4 teams** self-organised and working on studies
- **3 teams** awarded funding by IQVIA (LAB decision)
- **2 "leadership retreats"** in Paris (Sept '22) and Frankfurt (March '23)
- **2** conference abstracts submitted
- Overall **feedback** received
  - "How likely to recommend?" **8.8/10**
  - "Net promoter score" **62%**

> *…a real opportunity to foster skills we are not used to using in daily practice*
>
> **Clinician**

> *I'm very impressed with the programme… I have learned a lot about myself and how I relate to others in meetings and my work environment*
>
> **Data Scientist**

> *the topics [covered]…made it possible to think critically through our own project/process*
>
> **Clinician**

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You will hear later from some of the participants and studies that program created over the last 2 years and see their early results

Indication (team size)	Countries represented	# patients	Study title
Breast (8)	BE, IT, UK, FR, CZ, Poland, Portugal, Slovenia	780	The Causes and Consequences of Incomplete Paclitaxel Administration during the Neoadjuvant treatment of Early Triple negative and HER2 positive breast cancer (CIPNETH)
Colorectal (6)	CZ, IT, Croatia, Poland	980	CO(r)RECT Me- metastatic COloREctal Cancer Treatment Pathway
Head and neck (5)	Slovenia, Portugal, Norway, IT, Spain	530	Immunotherapy in recurrent/metastatic head and neck cancer: real-world data from six European countries (2017-2022)
Prostate (9)	NL, DK, Spain, FR, UK, IT	1,010	Treatment patterns and survival outcomes for metastatic castration sensitive prostate cancer: real world evidence from five different European countries.

Supported by

Leadership retreats | Peer learning sets | 1:1 coaching | Technical seminars

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Conclusions

- DIGICORE is growing as a large network of cancer centers across Europe for the conduct of digitalized RWE studies using a federated model
- Agreement on a minimal data set to define cancer patients
- Ensured financial support to federate 6 to 15 cancer centers in the next 2 years
- Compliance with GDPR, adaptation to individual hospitals legal basis
- Initial projects delivering first promising results