

Liquid Biopsy reimbursement landscape in Europe: Spain



Rodrigo Toledo

Head, Biomarkers and Clonal Dynamics Group at VHIO Barcelona

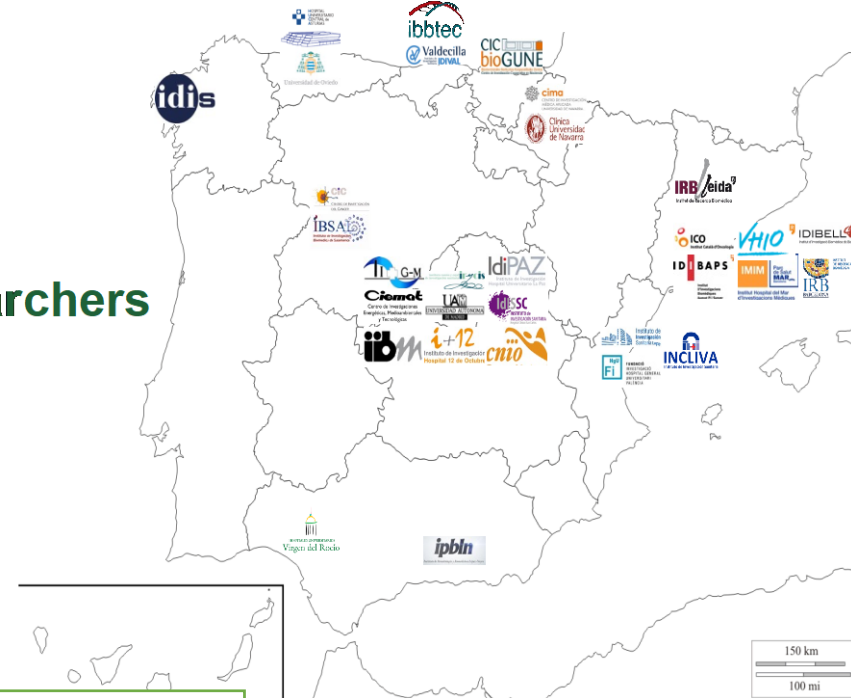
Outline of the talk

1. Liquid Biopsy Working Group in Spain
2. Awareness and access to liquid biopsy in Spain
3. Reimbursement/Funding status of liquid biopsy in Spain
4. Technologies offered

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+ 700 Researchers



The CIBERONC Liquid Biopsy Working Module





TYPE HERE

HOME

ABOUT US

FOR PATIENTS

FOR RESEARCHERS

ECOSYSTEM

EVENTS

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HOME

We are promoting collaborative research to advance the application of circulating biomarkers in the liquid biopsy field to improve cancer management



Collaborations

Ecosystem
Search here for the liquid biopsy

Protocols

EVENTS

26 JAN

VI Simposio de Biopsia Líquida: el camino a la Oncología de precisión

06 FEB

VI Simposio de Biopsia Líquida: el camino a la Oncología de precisión.

PROTOCOLS

Plasma

Serum

leukocytes

CTCs

cfDNA

Exosomes

Platelets



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The Spanish Society of Medical Oncology (SEOM)

- **Priority: Implementation of Precision Medicine in Oncology in the National Health System**

- Dra. Enriqueta Felip Font (*Coordinadora*)
- Dra. Pilar Garrido López (*Coordinadora*)
- Dr. Javier de Castro Carpeño
- Dr. Ramon Colomer i Bosch
- Dra. Carmen Esteban Esteban
- Dr. Juan de la Haba Rodríguez
- Dr. Antonio González Martín
- Dr. Rafael López López
- Dr. Aleix Prat Aparicio
- Dr. David Vicente Baz

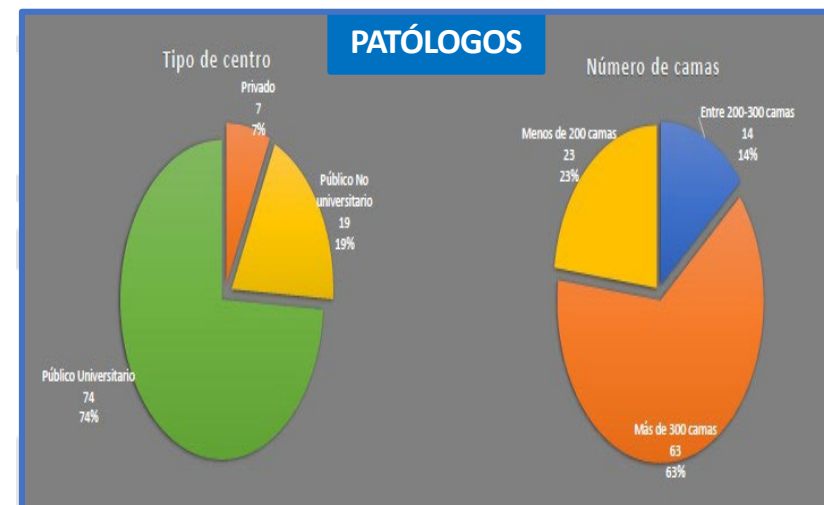
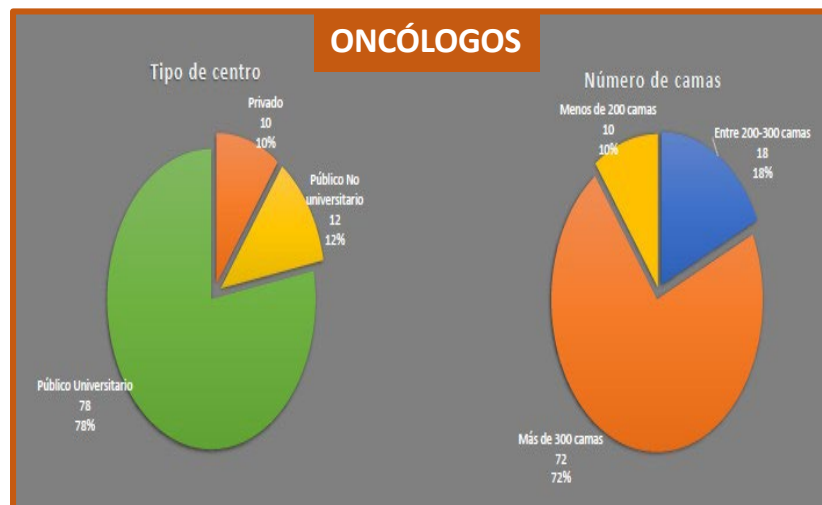
- It is a priority to advance in the organized implementation of precision medicine in Oncology.
- It is necessary to know the current situation in our country and identify the future needs that this incorporation implies
- **For this reason, a survey was carried out in the Medical Oncology and Pathology Services**

1st Precision Medicine Meeting (@2022)

- Aims:
 1. To know the current situation in Spain
 2. To ID future needs to incorporate PM in our clinical practice

N=200 participants (100 Med Oncol and 100 Pathology)

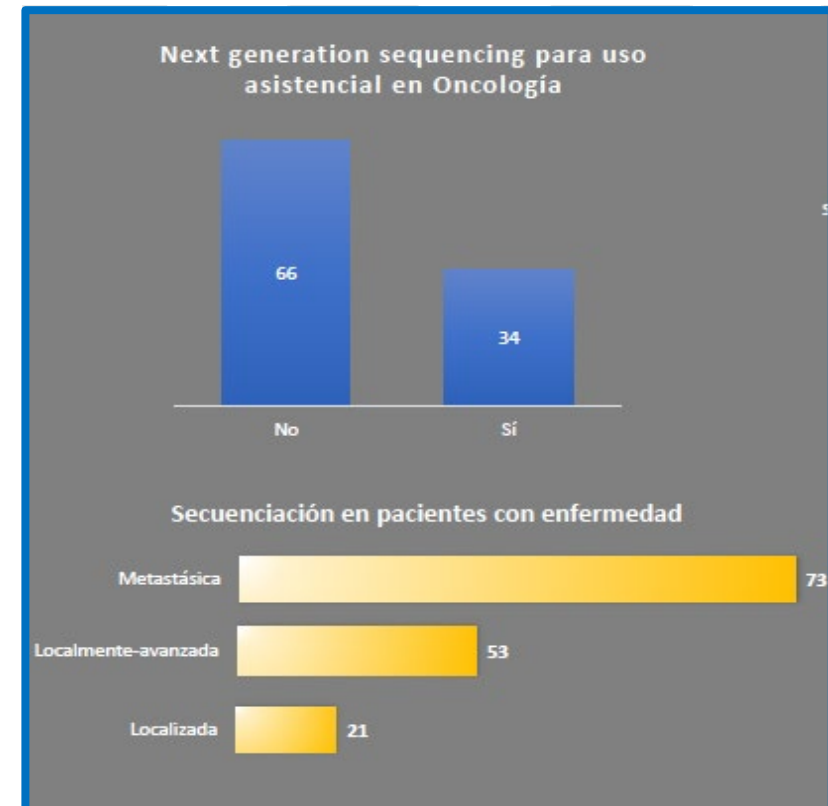
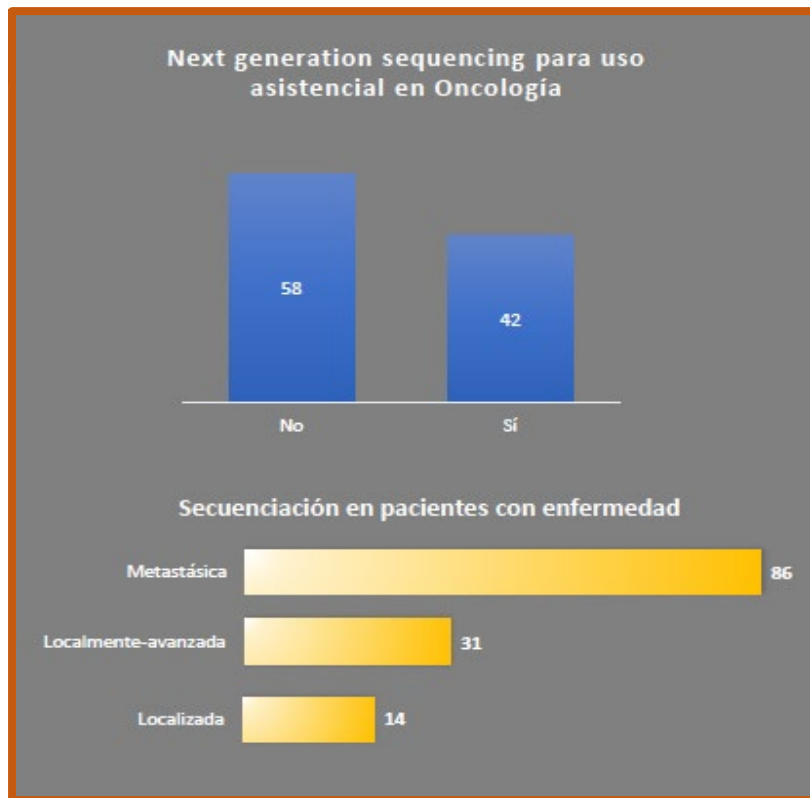
- 76% University Hospitals
- 67.5% >300 beds hospitals
- 12% participants belong to the same institution



1st Precision Medicine Meeting (@2022)

Access by Stage of disease

- **Only 40% have access to the healthcare NGS**
- 80% of the requests are in the metastatic setting & only 18% in localized disease



1st Precision Medicine Meeting (@2022)

Access by Tumor type

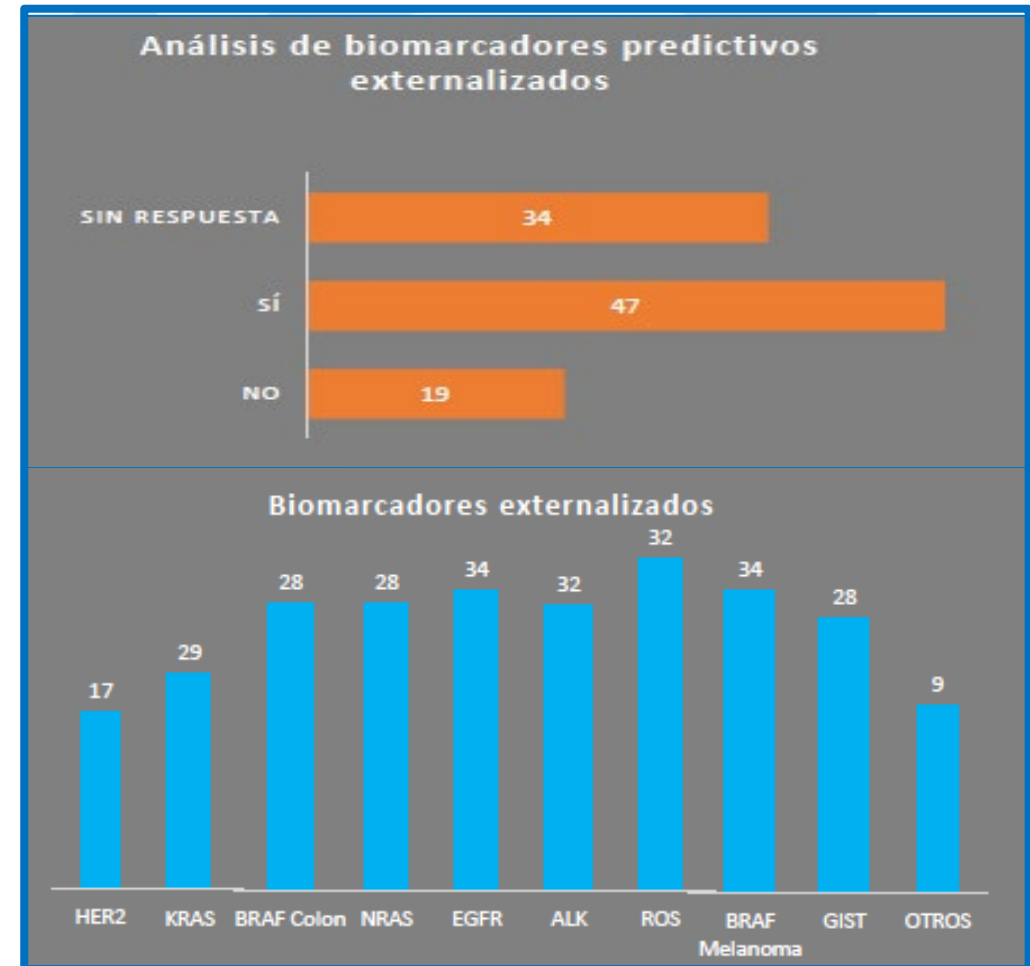
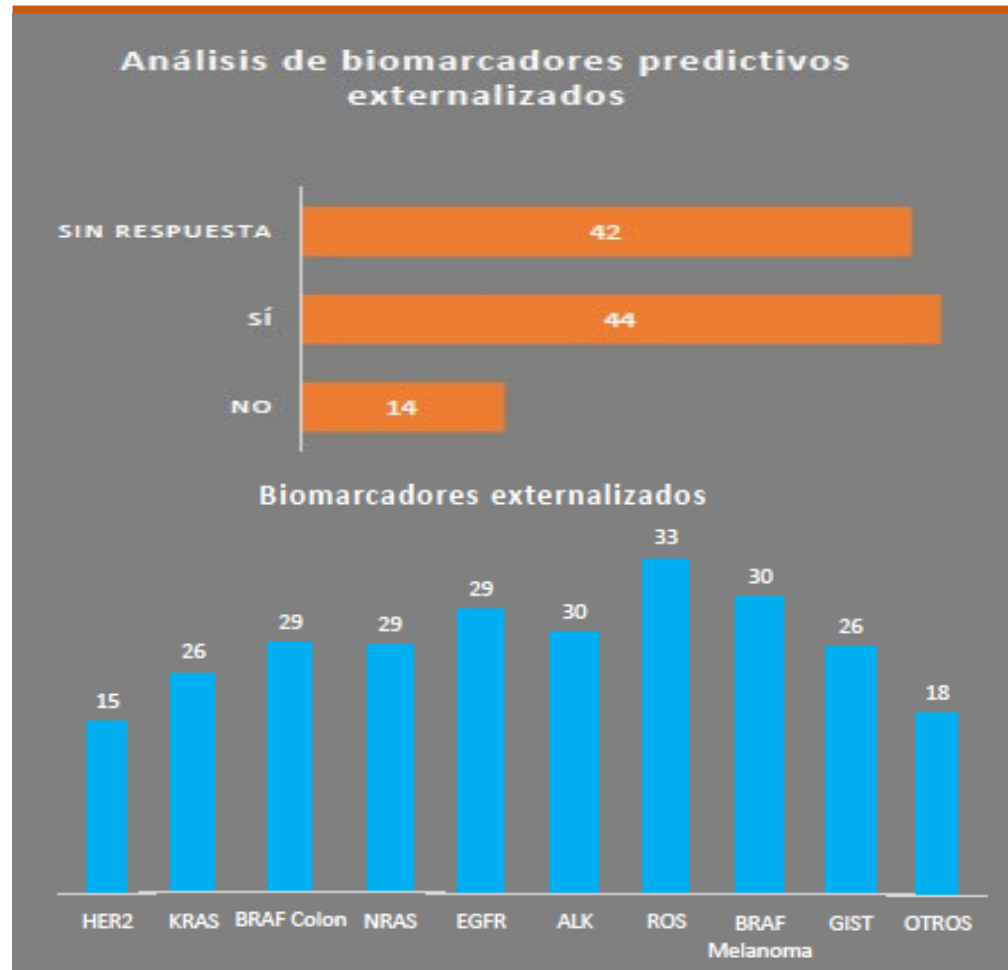
- **Breast, colon and lung** cancer are the tumors in which NGS is requested
- Only 12% of those surveyed requested for all tumors



1st Precision Medicine Meeting (@2022)

Annual volume of biomarker “outsourcing”

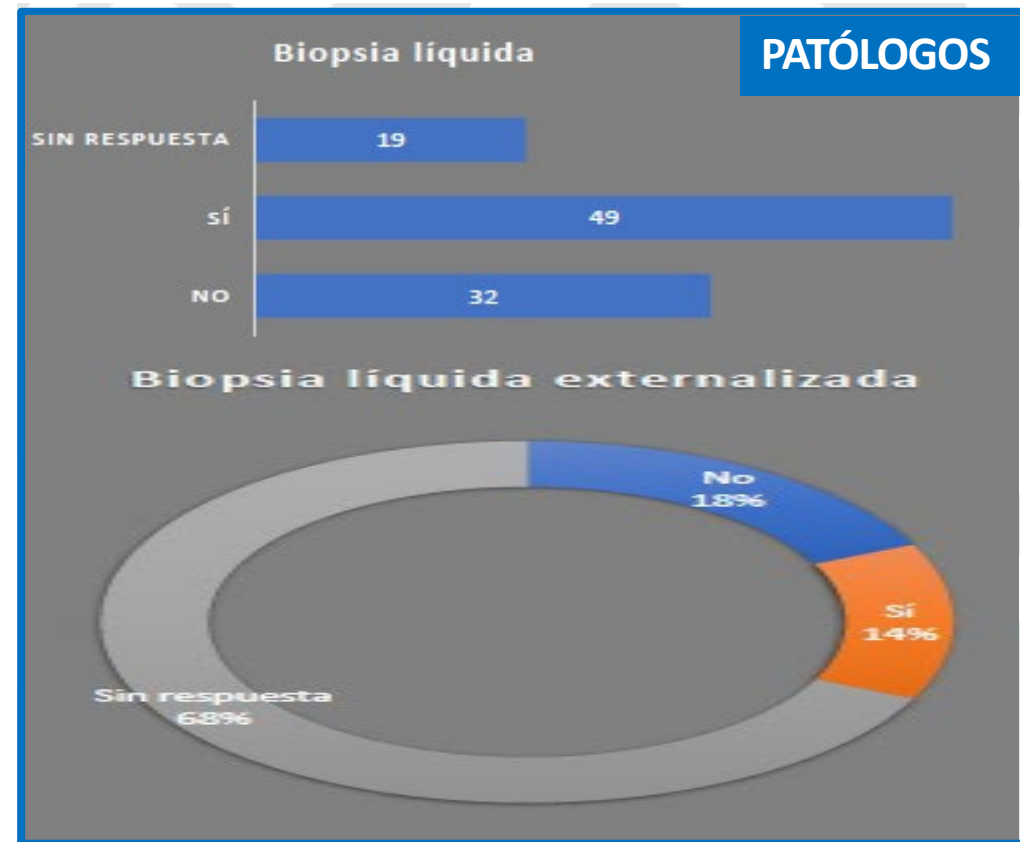
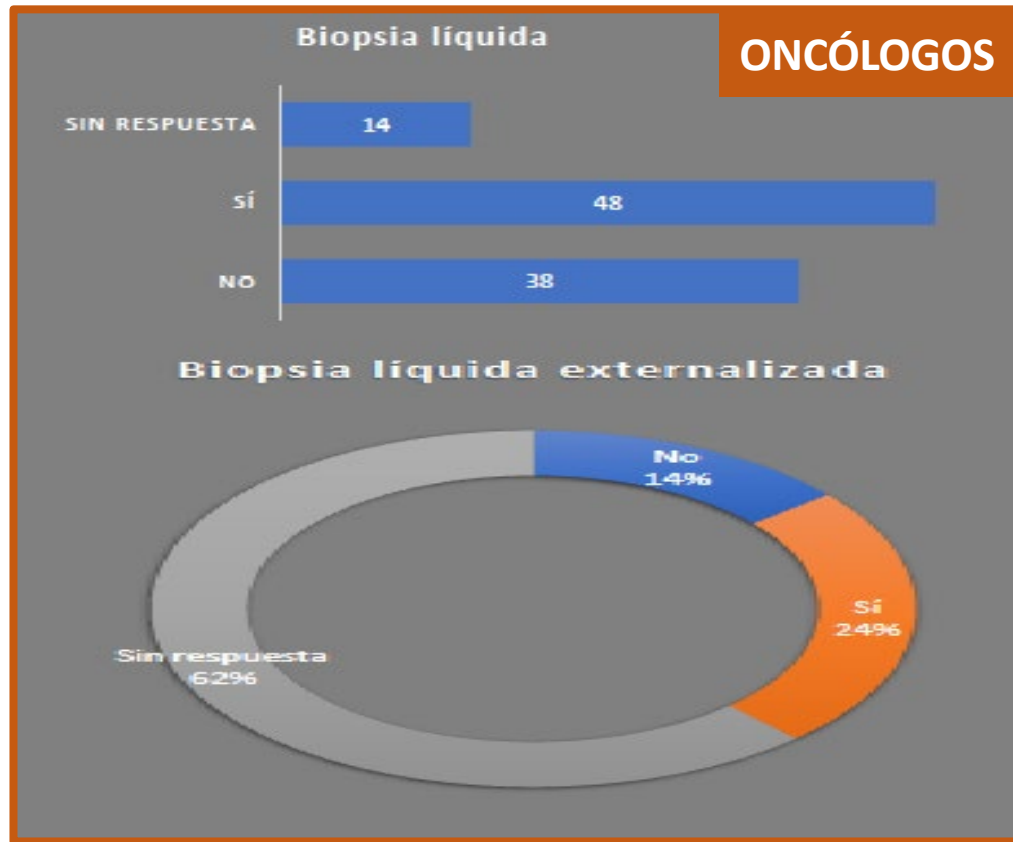
- **45% outsource** predictive biomarker analysis (*access is not universal*)



1st Precision Medicine Meeting (@2022)

Liquid Biopsy

- **49% of those surveyed have access to liquid biopsy**
- 20% of those surveyed outsourced the liquid biopsy



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Reimbursement/Funding status of liquid biopsy in Spain

- So far, there is no general public funding from the Health system to cover liquid biopsy tests
- **Some Hospitals allocate limited budget** for specific liquid biopsy analyses
- Liquid biopsy analyses, mostly ctDNA-based analyses, are **covered by research funds or by pharma companies**
- **Different technologies** are offered (even to the same test – no consensus)
- ctDNA analyses, when available, are performed **in-house or outsourced**.

Reimbursement/Funding status of liquid biopsy in Spain

- Catalunya:
 - EGFR testing for lung tumors without tissue
 - Vall d'Hebron Hospital: qPCR (Cobas)
 - Hospital del Mar: single gene (Idylla)

THE TECHNOLOGY

Some test has the ISO certification

CIRCULATING TUMOUR CELLS (CTCs)

CELLSEARCH (FDA APPROVED)

CTCs Enumeration

PARSORTIX (FDA APPROVED)

CTCs Characterization
Her2+, PDL1, EGFR

cfDNA/ctDNA ANALYSIS

IDYLLA

-KRAS/NRAS/BRAF/
-EGFR

ddPCR (QX200 BIORAD)

- KRAS/NRAS/BRAF/
- EGFR
- PI3KCA, ESR1
- MET/HER2
- MSI
- ALK

Covered by research funds or by pharma companies

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Barcelona: Vall d'Hebron Institute of Oncology (VHIO)-Guardant Tech-Transfer Agreement

G360 CDx - All NCCN Somatic Genomic Targets with a Single Test

Point Mutations and Indels - 74 Genes - **Complete** or Critical Exon Coverage

<i>AKT1</i>	<i>ALK</i>	<i>APC</i>	<i>AR</i>	<i>ARAF</i>	<i>ARID1A</i>	<i>ATM</i>	<i>BRAF</i>	<i>BRCA1</i>	<i>BRCA2</i>
<i>CCND1</i>	<i>CCND2</i>	<i>CCNE1</i>	<i>CDH1</i>	<i>CDK4</i>	<i>CDK6</i>	<i>CDK12</i>	<i>CDKN2A</i>	<i>CTNNB1</i>	<i>DDR2</i>
<i>EGFR</i>	<i>ERBB2 (HER2)</i>	<i>ESR1</i>	<i>EZH2</i>	<i>FBXW7</i>	<i>FGFR1</i>	<i>FGFR2</i>	<i>FGFR3</i>	<i>GATA3</i>	<i>GNA11</i>
<i>GNAQ</i>	<i>GNAS</i>	<i>HNF1A</i>	<i>HRAS</i>	<i>IDH1</i>	<i>IDH2</i>	<i>JAK2</i>	<i>JAK3</i>	<i>KIT</i>	<i>KRAS</i>
<i>MAP2K1 (MEK1)</i>	<i>MAP2K2 (MEK2)</i>	<i>MAPK1 (ERK2)</i>	<i>MAPK3 (ERK1)</i>	<i>MET</i>	<i>MLH1</i>	<i>MPL</i>	<i>MTOR</i>	<i>MYC</i>	<i>NF1</i>
<i>NFE2L2</i>	<i>NOTCH1</i>	<i>NPM1</i>	<i>NRAS</i>	<i>NTRK1</i>	<i>NTRK3</i>	<i>PDGFRA</i>	<i>PIK3CA</i>	<i>PTEN</i>	<i>PTPN11</i>
<i>RAF1</i>	<i>RB1</i>	<i>RET</i>	<i>RHEB</i>	<i>RHOA</i>	<i>RIT1</i>	<i>ROS1</i>	<i>SMAD4</i>	<i>SMO</i>	<i>STK11</i>
<i>TERT</i> **	<i>TP53</i>	<i>TSC1</i>	<i>VHL</i>			*MSI	** Includes TERT promoter region		

Amplifications – 18 Genes

<i>AR</i>	<i>BRAF</i>	<i>CCND1</i>	<i>CCND2</i>	<i>CCNE1</i>	<i>CDK4</i>	<i>CDK6</i>	<i>EGFR</i>	<i>ERBB2</i>
<i>FGFR1</i>	<i>FGFR2</i>	<i>KIT</i>	<i>KRAS</i>	<i>MET</i>	<i>MYC</i>	<i>PDGFRA</i>	<i>PIK3CA</i>	<i>RAF1</i>

Fusions – 6 Genes

<i>ALK</i>	<i>FGFR2</i>	<i>FGFR3</i>	<i>RET</i>	<i>ROS1</i>	<i>NTRK1</i>
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Microsatellite Instability (MSI) - MSI-High status

Barcelona: Vall d'Hebron Institute of Oncology (VHIO)-Guardant Tech-Transfer Agreement

Covered by research funds or by pharma companies

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- **Different technologies** are offered (even to the same test – no consensus)
- ctDNA analyses, when available, are performed in-house or outsourced
- Liquid Biopsy analysis has been increasingly offered in Spain, but mostly through local initiatives.

Agenda: 1st Regulatory WG Meeting of 2023

July 13th, 4 – 6 PM CEST

Work Package Leads: Klaus Pantel, Ariane Hallermayr

LB reimbursement landscape in Europe: impulse presentations

Stefano Indraccolo, University of Padova and Veneto Institute of Oncology IRCCS, Padova, Italy

LB reimbursement in Italy (2023)

Italy has a two-level policy of reimbursement:

- 1 Nation-wide reimbursed tests
- 2 Regionally reimbursed tests



Nation wide reimbursed tests in Italy (2023)

- Some molecular tests on cfDNA are reimbursed in every Italian region, following rules and values set by the Ministry of Health (LEA), including:
- EGFR/NSCLC (according to the recommendations of the Italian scientific societies AIOM-SIAPEC-IAP 2020): ~500 Euro/test
- NGS profiling: new funds available for NGS testing in NSCLC and cholangiocarcinoma from 2023 (LB possible if tissue is not available): 1150 Euro/test

Regionally reimbursed tests in Italy (2023)

- In the case of lung cancer, BRAF, ALK, ROS1, NTRK, RET, MET, HER2, KRAS can also be tested in cfDNA in individual cases, pending multidisciplinary board prescription (reimbursement by the regional budget)
- In the Veneto region, cfDNA CPG can be requested by the institutional Molecular Tumor Board (MTB) for selected cases when tissue is not available: ~2300 Euro/test
- Note: Within MTB, LB can be requested also for tumor types other than lung cancer
- Several regions are going to activate MTBs and propose reimbursement fees for NGS tests (either on tissue or cfDNA)
- In some regions, reimbursement fee may depend on the number of genes tested (i.e. Emilia Romagna 3-tier system)

Limitations of LB testing in Italy (2023)

- Reimbursement fee does NOT distinguish between tissue and plasma testing
- Identification of regional (inter-regional) reference labs still largely to be done
- Still no reimbursement for MRD testing, i.e. in stage II CRC
- Upcoming medical need: assessment of KRAS/NRAS/BRAF/EGFR mutations in cfDNA from CRC patients to guide rechallenge anti-EGFR mAbs (CHRONOS trial and other ongoing trials)

KEY objective: to move LB from being a tool to search for actionable mutations to disease monitoring

- Role of ESMO recommendations
- Role of patients advocacy groups

Role of ESMO recommendations

- Italian Ministry of Health seems to adopt ESMO guidelines/recommendations (i.e. Mosele et al. 2020): Example Decreto 22A06125 30-09-2022 on NGS tests in lung cancer



REVIEW ARTICLE

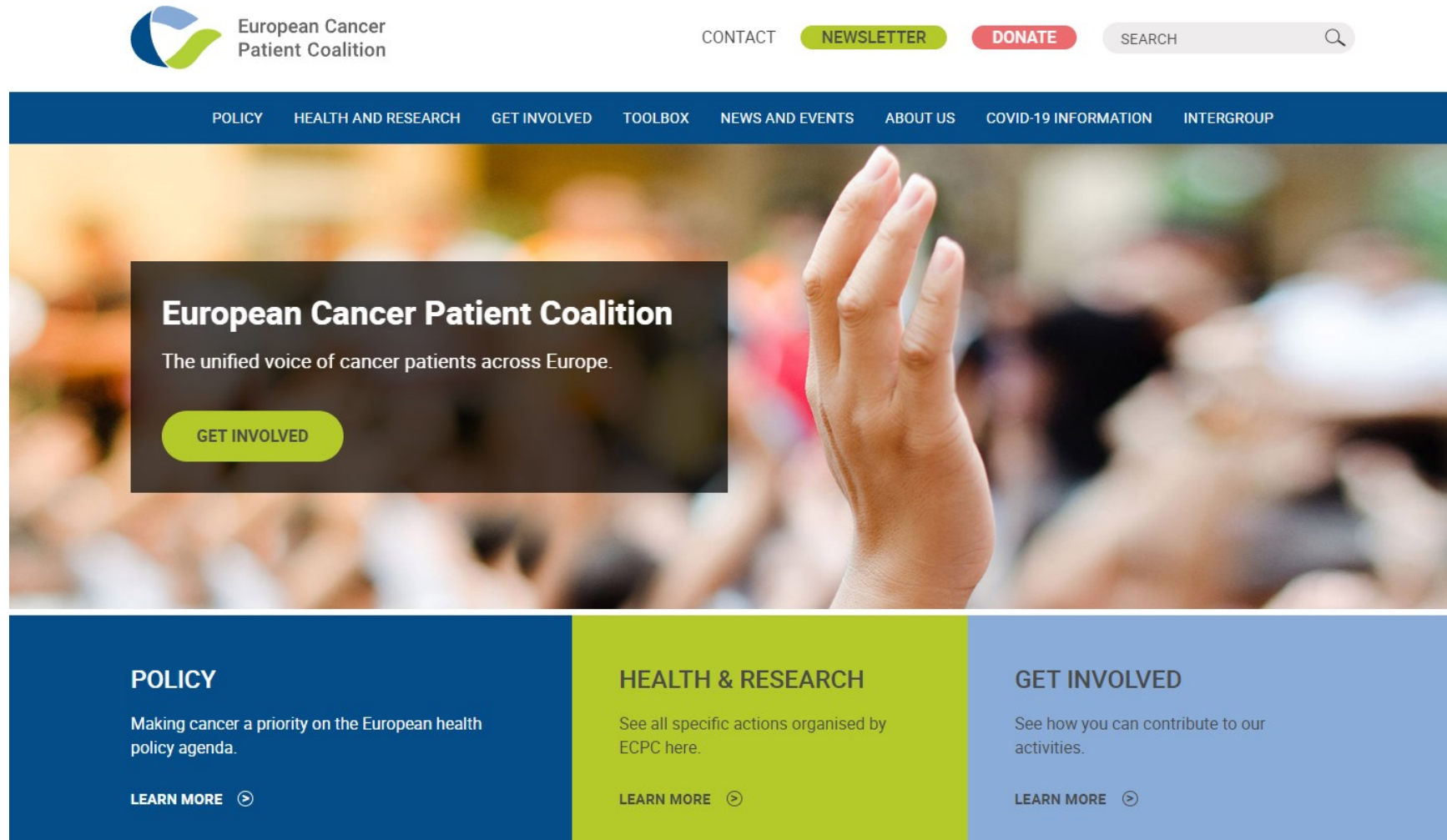
Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group

F. Mosele¹, J. Remon², J. Mateo³, C. B. Westphalen⁴, F. Barlesi¹, M. P. Lolkema⁵, N. Normanno⁶, A. Scarpa⁷, M. Robson⁸, F. Meric-Bernstam⁹, N. Wagle¹⁰, A. Stenzinger¹¹, J. Bonastre^{12,13}, A. Bayle^{1,12,13}, S. Michiels^{12,13}, I. Bièche¹⁴, E. Rouleau¹⁵, S. Jezdic¹⁶, J.-Y. Douillard¹⁶, J. S. Reis-Filho¹⁷, R. Dienstmann¹⁸ & F. André^{1,19,20*}

¹Department of Medical Oncology, Gustave Roussy, Villejuif, France; ²Department of Medical Oncology, Centro Integral Oncológico Clara Campal (HM-CIOCC), Hospital HM Delfos, HM Hospitales, Barcelona; ³Clinical Research Program, Vall Hebron Institute of Oncology (VHIO) and Vall d'Hebron University Hospital, Barcelona, Spain; ⁴Comprehensive Cancer Center Munich and Department of Medicine III, University Hospital, LMU Munich, Munich, Germany; ⁵Department of Medical Oncology, Erasmus MC Cancer Center, Rotterdam, the Netherlands; ⁶Cell Biology and Biotherapy Unit, Istituto Nazionale Tumori, 'Fondazione G. Pascale' — IRCCS, Naples; ⁷ARC-Net Research Centre and Department of Diagnostics and Public Health — Section of Pathology, University of Verona, Verona, Italy; ⁸Breast Medicine and Clinical Genetics Services, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York; ⁹Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston; ¹⁰Department of Medical Oncology, Dana-Farber Cancer Institute and Harvard Medical School, Boston, USA; ¹¹Institute of Pathology, University Hospital Heidelberg, Heidelberg, Germany; ¹²Department of Biostatistics and Epidemiology, Gustave Roussy, University Paris-Saclay, Villejuif; ¹³Oncostat U1018, Inserm, University Paris-Saclay, labeled Ligue Contre le Cancer, Villejuif; ¹⁴Department of Genetics, Institut Curie, Paris Descartes University, Paris; ¹⁵Cancer Genetic Laboratories, Department of Medical Biology and Pathology, Gustave Roussy Cancer Campus, Villejuif, France; ¹⁶Scientific and Medical Division, European Society for Medical Oncology, Lugano, Switzerland; ¹⁷Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, USA; ¹⁸Oncology Data Science Group, Molecular Prescreening Program, Vall d'Hebron Institute of Oncology, Barcelona, Spain; ¹⁹Inserm, Gustave Roussy Cancer Campus, UMR981, Villejuif; ²⁰Paris Saclay University, Orsay, France

Role of patients advocacy groups in supporting LB testing

President:
Prof. Francesco De
Lorenzo, former Italian
Ministry of Health





Barbara, Colorectal cancer survivor

What ECPC adds

ECPC works in partnership with leading organisations in this field, such as the Cancer Drug Development Forum, the European Alliance of Personalised Medicine – of which ECPC is a founding member, and the International Quality Network of Pathology, to ensure patients have a central role in policy developments concerning personalised medicine. A joint Patient Survey in 2016 revealed very low awareness about cancer molecular testing and biomarkers. Therefore, ECPC undertook a strong role in patient education, with the launch of the infographic and video animation on biomarkers, and the launch of the first Personalised Medicine Awareness Month.



ECPC works to raise awareness amongst policy-makers at the EU level about the need for harmonised regulatory frameworks and policies to create enabling environments for access to personalised medicine across Europe. ECPC has organised policy events in the European Parliament in partnership with CDDF on biomarkers and the role of Health Technology Assessment, and hosts a patient track every year at the EAPM Annual Congress.

Downloads

Choose language ▼

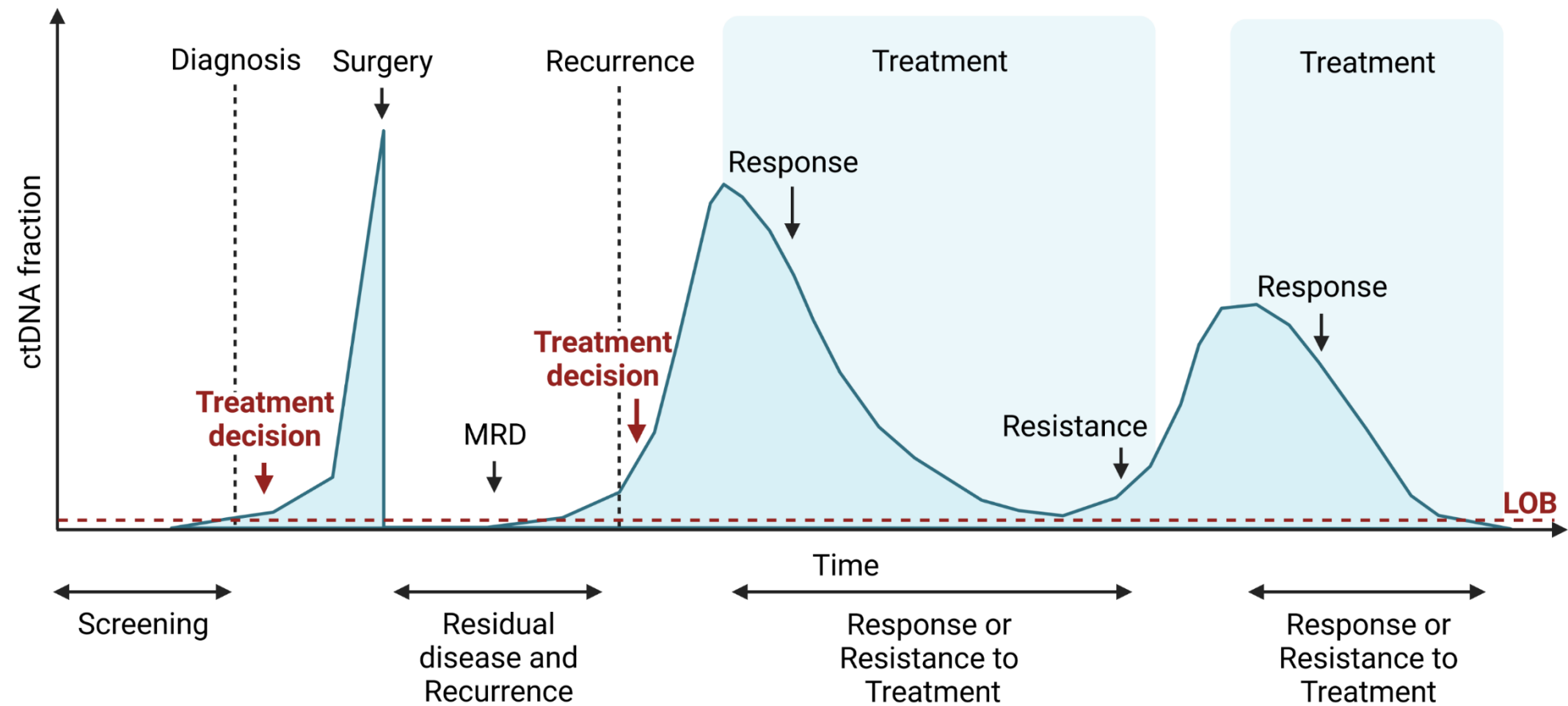
[- Cancer Biomarkers in the Era of Personalised Medicine - \(PDF\)](#)

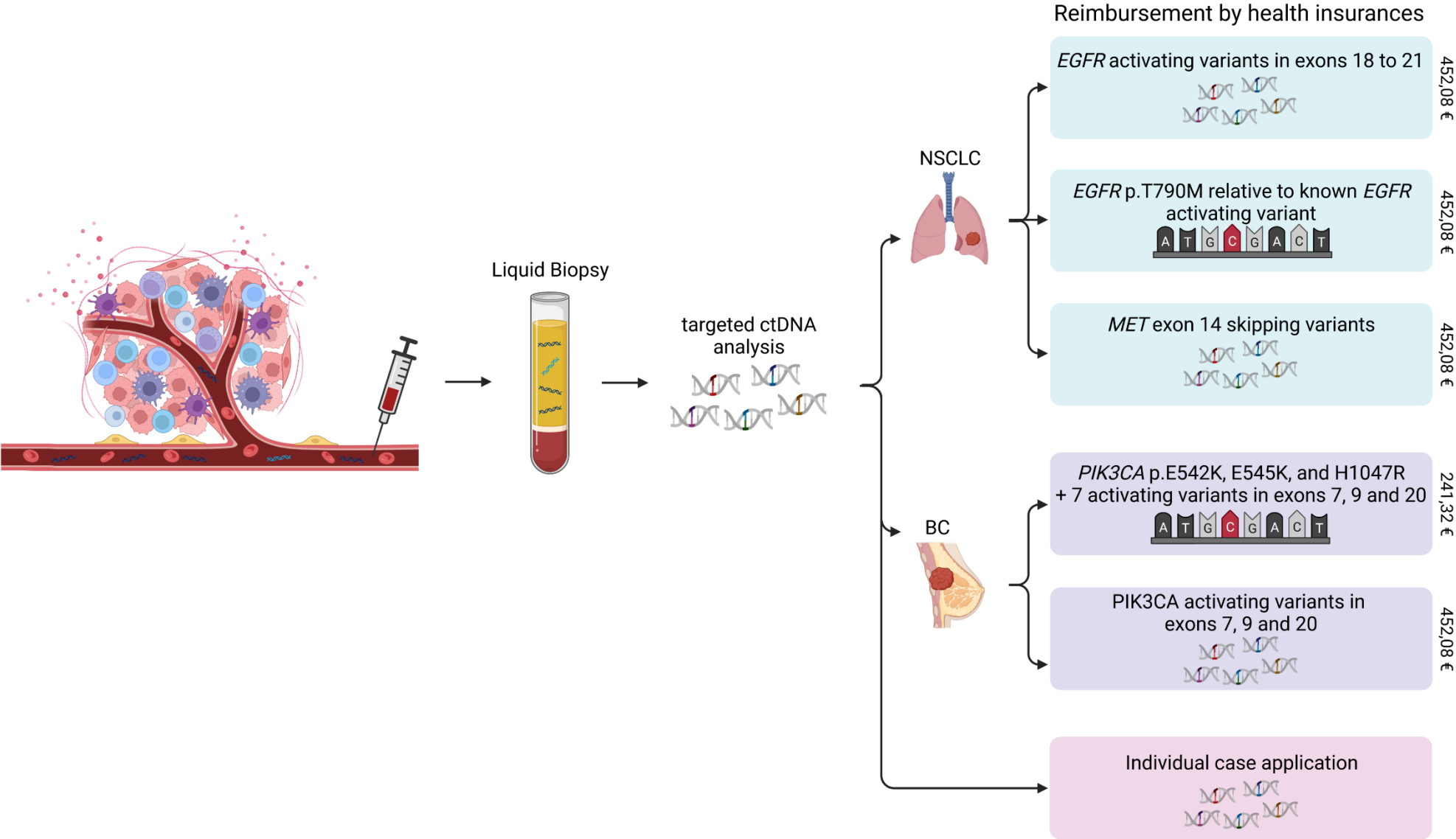
[- Patient Awareness on Biomarkers Across Europe - \(PDF\)](#)

Current challenges in the introduction of liquid biopsy into routine clinical practice

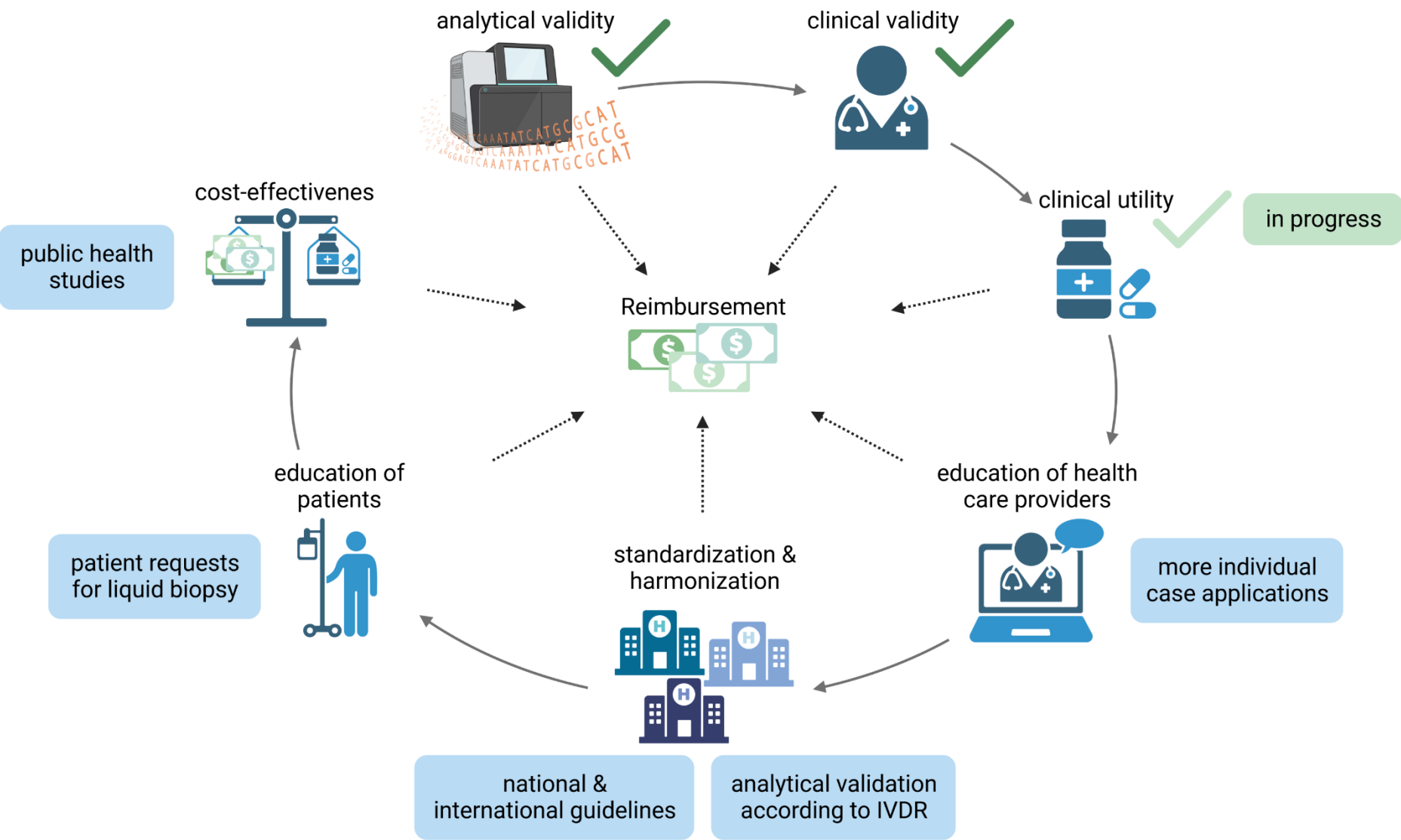
Regulatory WG Meeting – 13.07.2023

Ariane Hallermayr, PhD





Challenges hindering reimbursement of Liquid biopsy diagnostics



education of health
care providers



education of patients



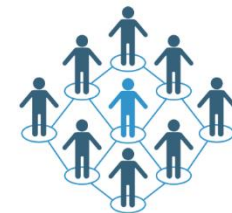
information distribution



conferences



patient initiatives



Implementation of
clinical guidelines
into practice



Improved patient
management



Companion diagnostics

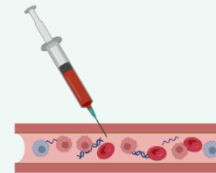
diagnosis



not feasible
long TAT
low quantity / quality

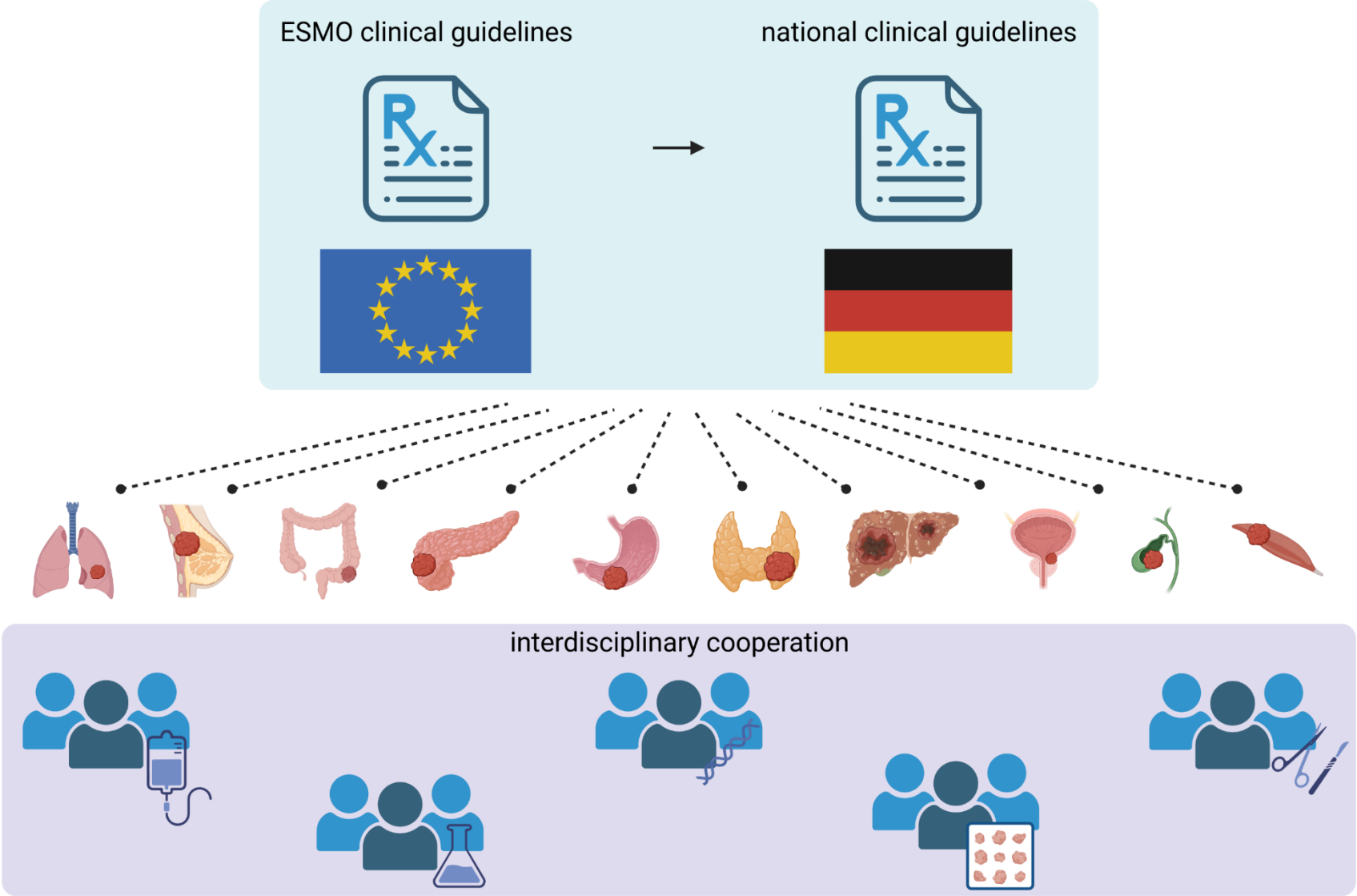


targeted
treatment



actionable variant detection

Requirement of efforts to overcome challenges

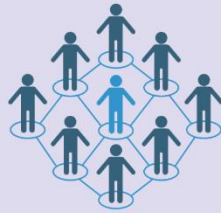


European and national efforts for implementation of liquid biopsy

European efforts



interdisciplinary networking of
research, clinical and industry



international collaboration on
large clinical utility studies



standardization &
harmonization



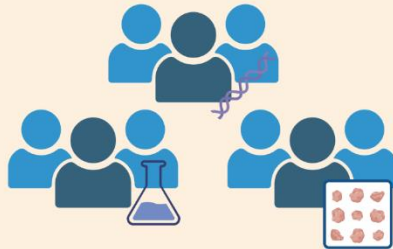
implementation of LB to
european oncology guidelines



national efforts



collaboration of national
specialist societies



transfer to
national guidelines

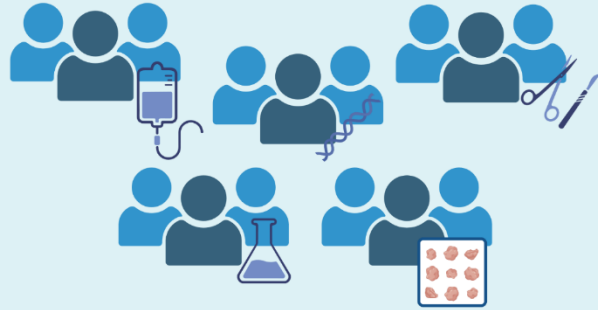


education of health
care providers



education of
patients





Identify medical specialist societies currently working on introduction of liquid biopsy into guidelines?

Are joint efforts to address the challenges beneficial and desired?



Could ELBS provide a platform for required cost-effectiveness studies to improve the reimbursement of liquid biopsy on a national level?



Could ELBS pave the way to patient initiatives, e.g. with flyers and suitable slide deck, and thus inform patients directly about liquid biopsy?

Liquid Biopsy Team



Dr. Ariane Hallermayr



Dr. Thomas Keßler



Dr. Verena Steinke-Lange



Prof. Dr. Elke Holinski-Feder



**EUROPEAN
LIQUID BIOPSY
SOCIETY**