PRECISION ONCOLOGY
CONSULTING

Comprehensive Genomic Profiling (CGP) provides an insight into an individual's cancer, so why is precision oncology still far from the reality for all patients?

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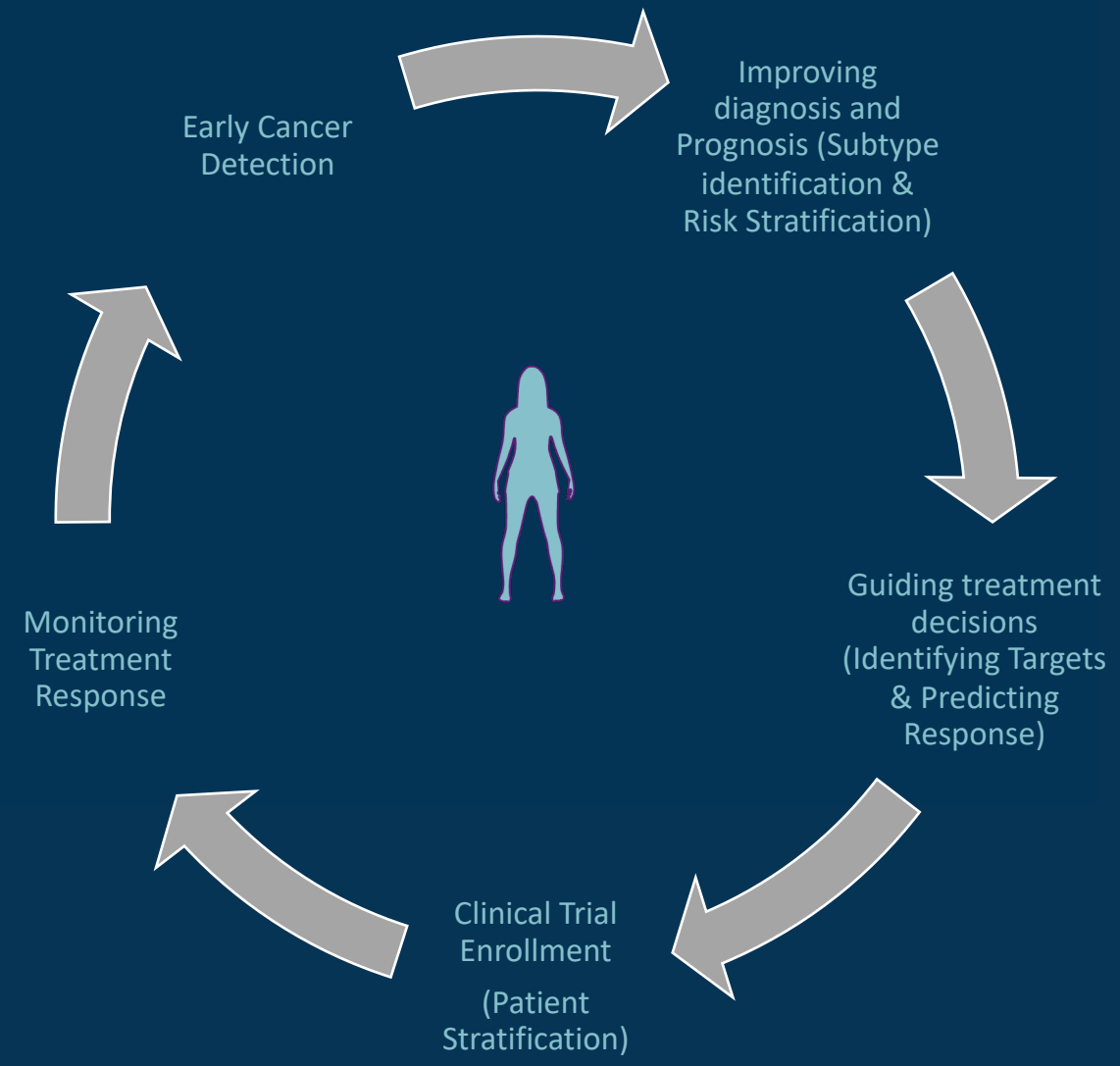
21/10/2024

Disclosures

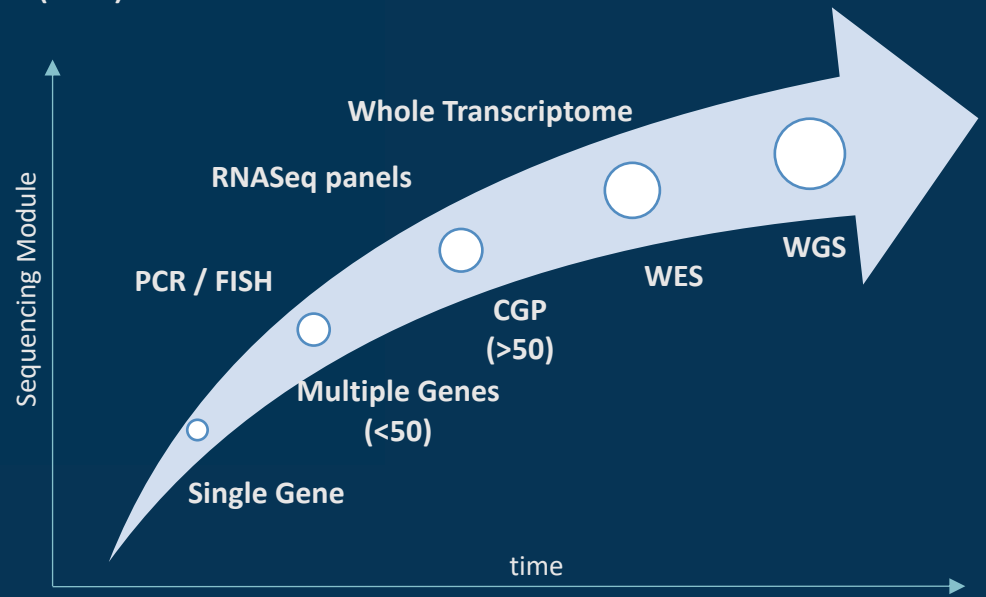
- Advisory role at 2Strands Biosciences

Role of Biomarkers in Precision Oncology



Where does a need for CGP testing come from?

- Evolution of NGS technologies alongside of increasing number clinically relevant biomarkers have led to development of large NGS panels for molecular testing of cancer patients.
- Many studies have shown that cancer patients who are treated with molecularly matched therapy have better outcomes that the ones used with non-matched therapies (1-3).
- There is an increasing number of FDA/EMA approvals for targeted therapies and immunotherapies linked to specific genomic biomarkers
  - A recent analysis highlights that, as of September 2024, the EMA had granted approval for 82 such therapies, spanning at least 20 different solid tumor (4)



However, the uptake of single NGS tests is poor across EU

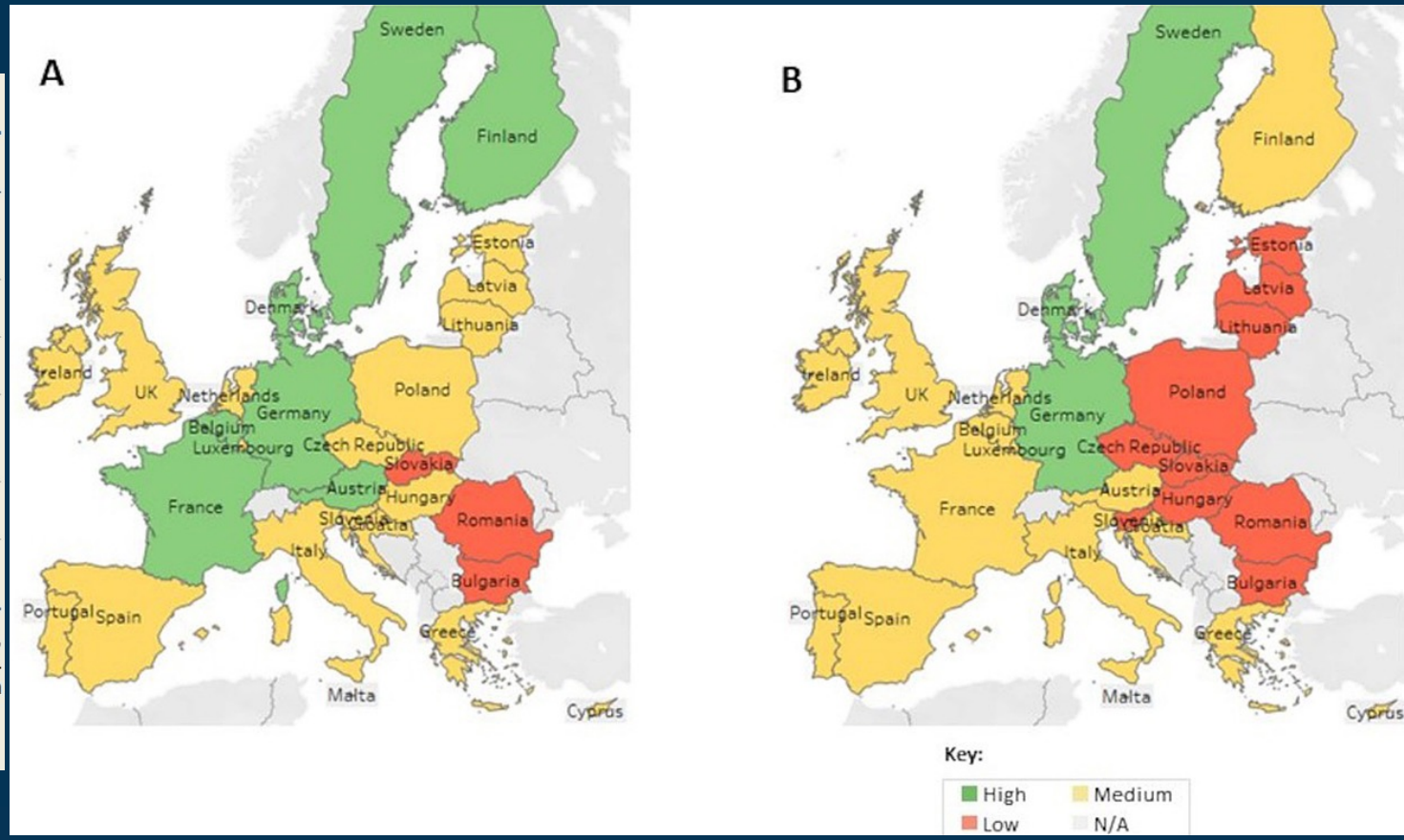
Table 3.2. Biomarker testing with NGS technology varies widely in the EU in 2020

Access dimension	Access level	Country
Uptake (% of all biopsies analysed with NGS technology)	0-24%	Belgium, Croatia, Czechia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Slovakia, Spain, UK
	25-49%	Austria, Cyprus, Portugal, Sweden
	50% or more	Denmark, Netherlands
Average proportion of all existing NGS tests that are publicly reimbursed	<75%	Bulgaria, Croatia, Czechia, Estonia, Greece, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia, Spain
	75-90%	Austria, Belgium, France, Ireland, Italy, Luxembourg, Netherlands, Portugal
	90% or more	Cyprus, Denmark, Finland, Germany, Slovenia, Sweden, UK

Notes: Uptake was calculated as the % of all biopsies analysed with NGS technology. Information for Bulgaria, Estonia, Luxembourg, Romania, and Slovenia only indicated an uptake of less than 50% but not an exact level, and information for Malta was missing. Reimbursement was calculated based on the average proportion of NGS tests reported to be covered by public reimbursement. Information on reimbursement for Malta was missing.

Source: (Normanno et al., 2022[56])

Hofmarcher, T., C. Berchet and G. Dedet (2024), "Access to oncology medicines in EU and OECD countries", OECD Health Working Papers, No. 170, OECD Publishing, Paris, https://doi.org/10.1787/c263c014-en.

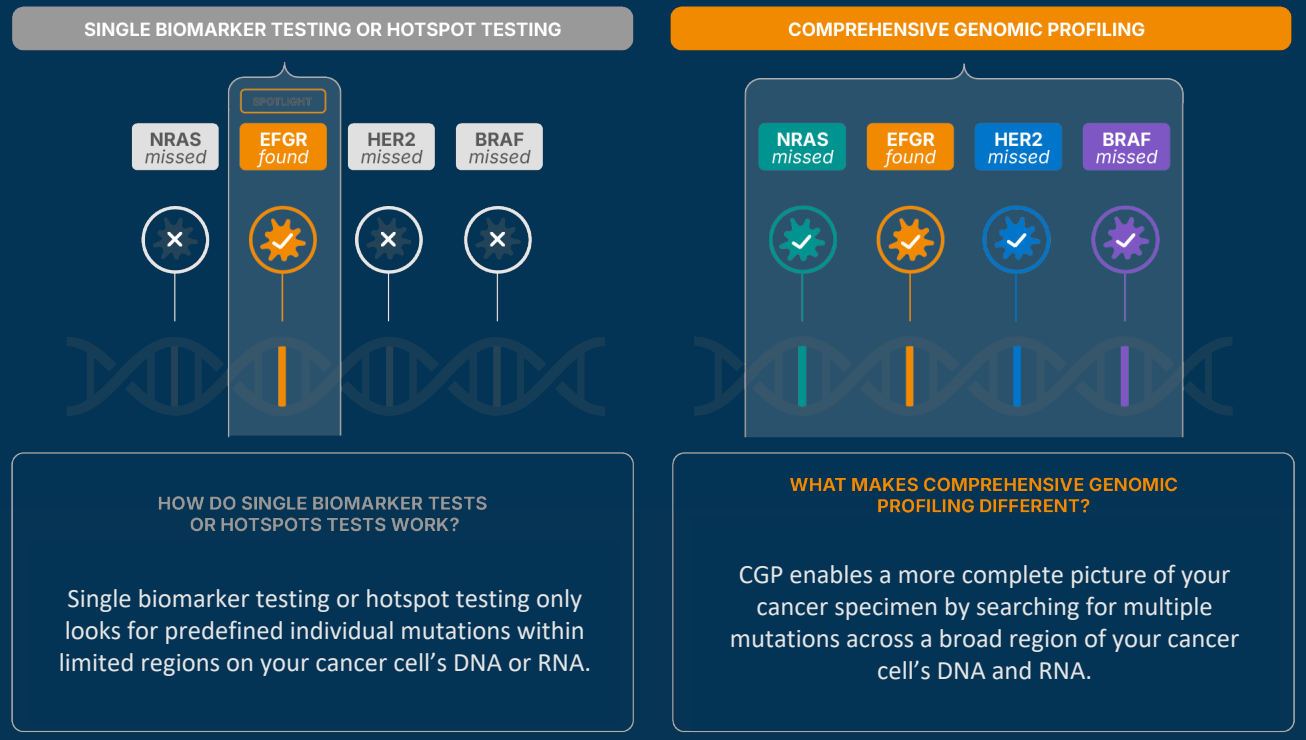


The current status on quality and access to biomarker testing in Europe: (A) Single biomarker test access; (B) multi-biomarker test access. Normanno N. et al. European Journal of Cancer, 2022 Volume 176, 70 - 77

What is Comprehensive Genomic Profiling?

Definition of CGP

It is a genomic assay which enable assessment of distinct genomic aberrations at DNA and RNA level across more than 50 genes*, which typically includes known and emerging biomarkers.



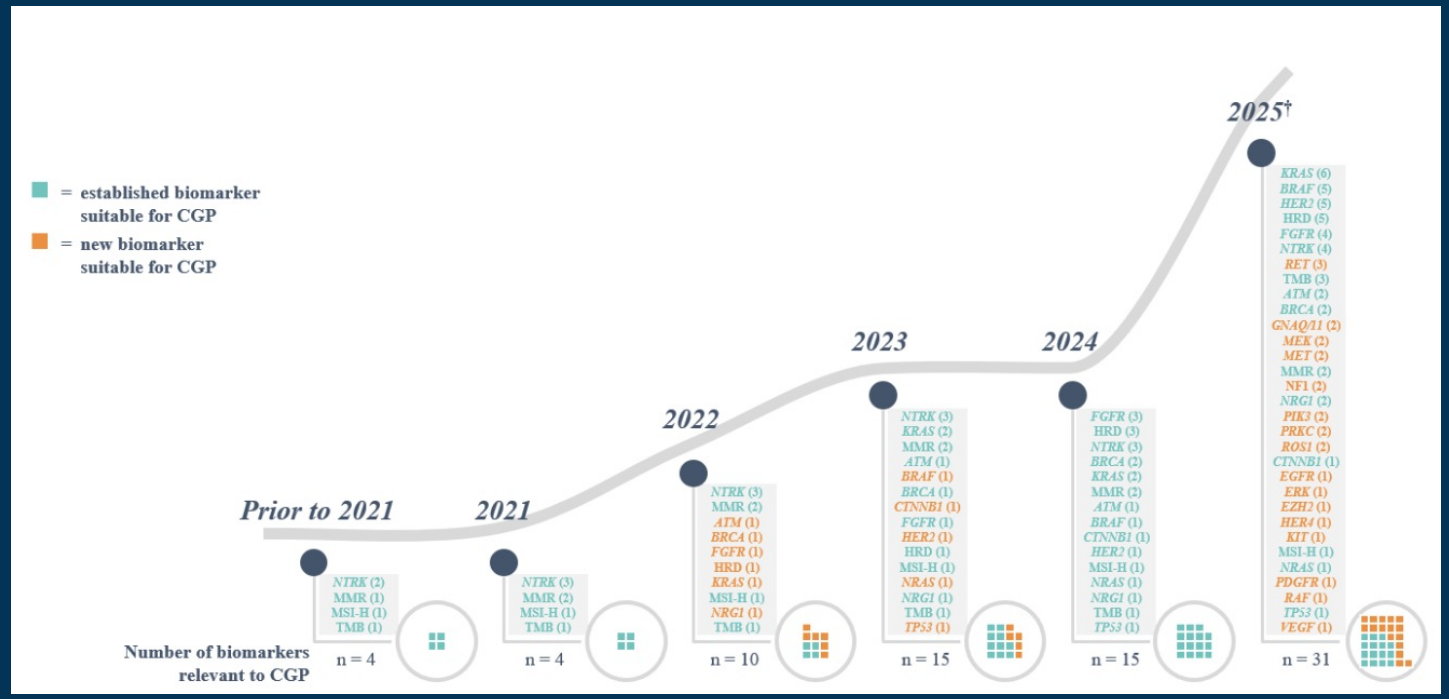
- Multi-gene panels
- Broad gene panels
- Large gene panels

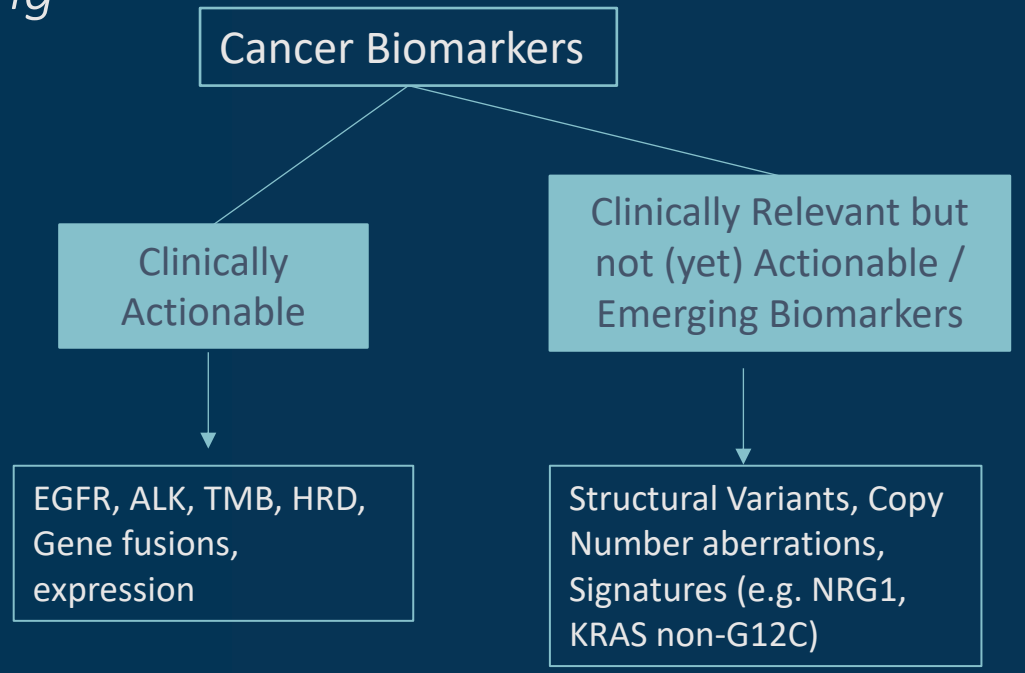
→ All refer to CGP

*No official definition

Why the size matters

Growing number of clinically relevant (EGFR), pan-cancer (HER2) and complex (HRD) biomarkers will drive further the adoption of CGP testing





https://www.genomeweb.com/companion-diagnostics/perspective-accessing-innovation-point-care-comprehensive-genomic-profiling

Some pan-cancer Genomic biomarkers such as TMB and HRD, relevant for therapeutic decision-making (IO and PARP inhibitors) can only (more accurately) be detected using CGP

What Factors drive the adoption of CGP?

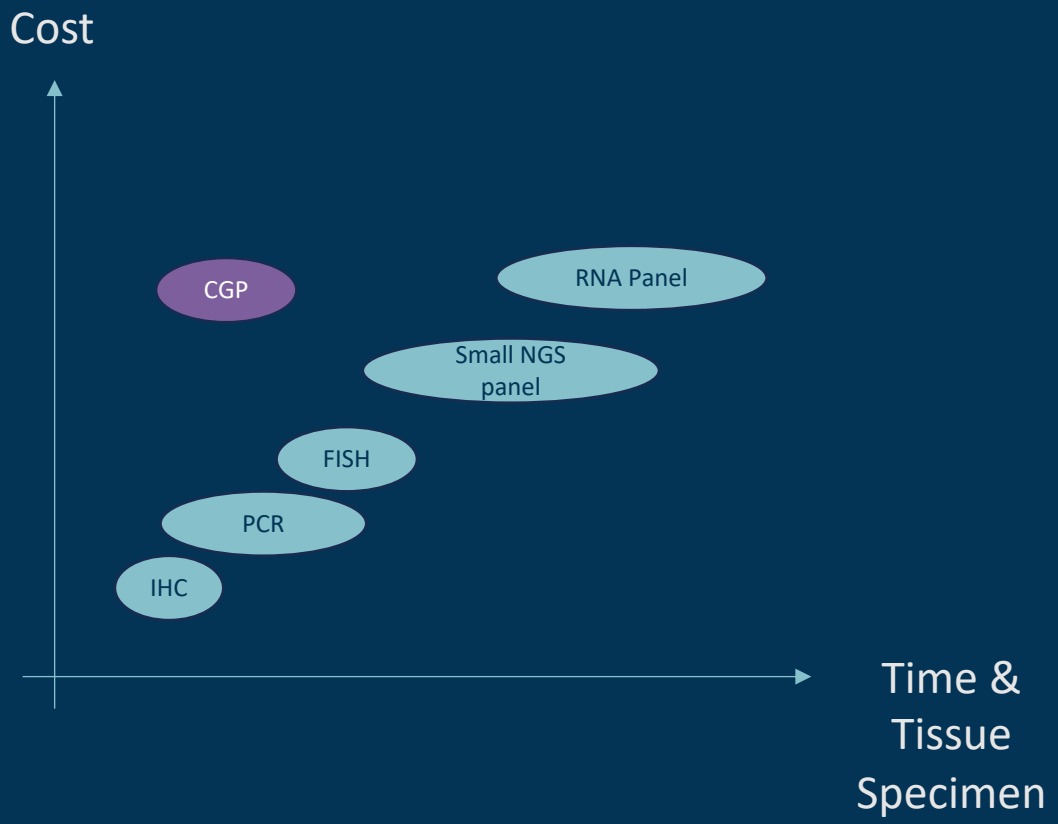
Tumor biology

- Growing number of clinically relevant biomarkers
- Increasing number approved targeted therapies and immuno-therapies
- Complex biomarkers
- Clinical implications of genomic aberrations as SVs, CNVs and gene fusions, will drive transition from small NGS panels to CGP (4)

Operational Efficiency

- Optimal use of tissue biospecimens
- Consolidation of different, traditional molecular methods
- Better use of lab resources (human and financial)
- Competitiveness (access to clinical trials & possibility to offer testing for novel guideline-endorsed biomarkers)
- Freeing-up time of cancer workers

CGP improves operational efficiency



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CGP testing leads to improved patient outcomes

aNSCLC tested with SoC

aNSCLC EGFR/ALK+

aNSCLC EGFR/ALK- (**209** pts)

CGP

64 (30%) pts identified with actionable alterations in following genes:

20: EGFR
15: RET
9: ROS1
7: MET*
6: BRAF
4: ALK
3: HER2

28 (13%) pts received molecularly matched therapy

- Patients with NO actionable alterations detected → **OS 20,1 months**
- Patients with actionable alterations detected but no matched therapy received → **OS 17,1 months**
- Patients with actionable alterations detected and matched therapy received → **OS 66,2 months**

Byeon, S., et al., Benefit of Targeted DNA Sequencing in Advanced Non-Small-Cell Lung Cancer Patients Without EGFR and ALK Alterations on Conventional Tests. Clin Lung Cancer, 2020. ***21****(3): p. e182-e190.*

*Includes 1 patient with MET amplification and 6 patients with MET exon 14 skipping mutation
Pts,Patients; SoC, Standard of Care; OS, Overall Survival

CGP testing leads to improved patient outcomes

Study	Meng, R., et al. (2024)	Wallenta Law, J., et al (2024)	Zhao, S., et al. (2021)	Peleg H. S., et al. (2022)
Cancer type (nr of patients)	aNSCLC (759)	aNSCLC (3884)	aNSCLC (1166)	Ovarian Cancer (946)
Patients with detected actionable biomarkers	77% (CGP) vs 63% (SP test) ↗ **7%**	32% (CGP) vs 14% (SP test) ↗ **18%**	16.7% Additionally detected by CGP ↗ **16.7%**	52.9% (CGP)
Patients who benefited from targeted therapy	64% (CGP) vs 50% (SP) ↗ **14%**	43% (CGP) vs 38% (SP) ↗ **5%**	20.9% ↗ **20.9%**	48.2% (CGP)
Number of additional patients benefiting from molecularly matched therapy due to CGP findings	**130**	**194**	**243**	**na**
Overall Survival	15.7 (CGP) vs 7 months (SP) ↗ **OS; 15 months**	18 (CGP) vs 10 months (SP) ↗ **OS; 8 months**	46.8 (CGP) vs 30 months (non-matched) ↗ **OS; 16.8 months**	73.4 (CGP) vs 54.5 months (SoC) ↗ **OS; 18,9 months**

Patients profiled with CGP have better outcomes, compared to the ones tested by traditional SoC

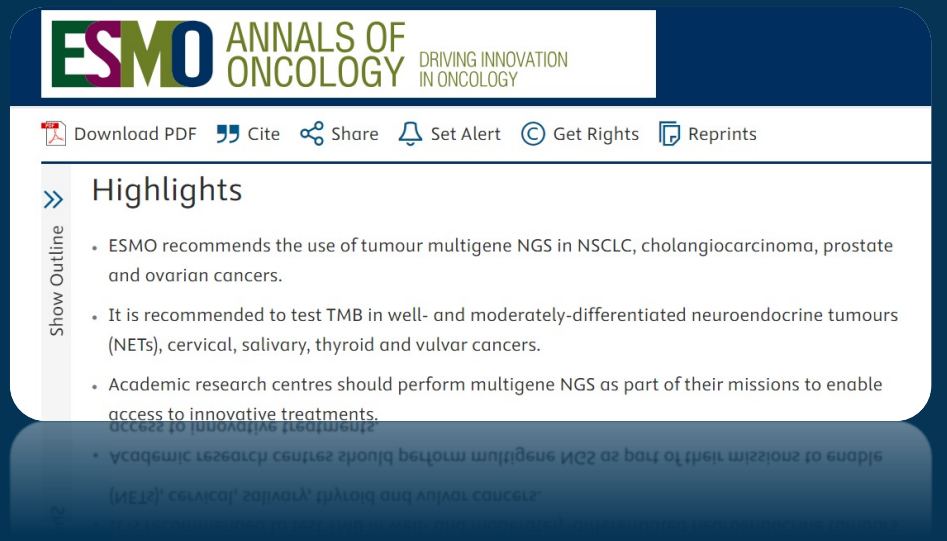
What causes delays in implementing CGP?

Challenges in Implementing CGP

- Access to therapies impacts CGP implementation
  - Long and distinct drug approval processes across EMEA
  - Clinical Guidelines
    - Time lag between endorsment of specific aproaches between international and national guidelines
- Cost and Reimbursement - High costs and varying insurance coverage
  - High Initial Costs
    - Implementation of CGP involves significant upfront investment in technology, laboratory infrastructure, and personnel training.
  - Reimbursement Variability
    - Not all healthcare systems or insurance providers cover CGP testing, leading to financial barriers for both laboratories and patients.
  - Budget Impact
    - The cost-effectiveness of genomic profiling may not be immediately evident, making it difficult for institutions to justify the expense.
- Infrastructure / Operations - Need for advanced technology and trained personnel
  - Technology Requirements:
    - Labs need advanced sequencing technologies (e.g., NGS) and equipment capable of handling and interpreting large datasets.
  - Expertise Shortage
    - A lack of trained personnel (e.g., geneticists and bioinformaticians) to conduct tests and interpret complex genomic data can hinder implementation
  - Standardization
    - Protocol Variability - Many labs follow different procedures for CGP, leading to inconsistencies in test results and interpretation.

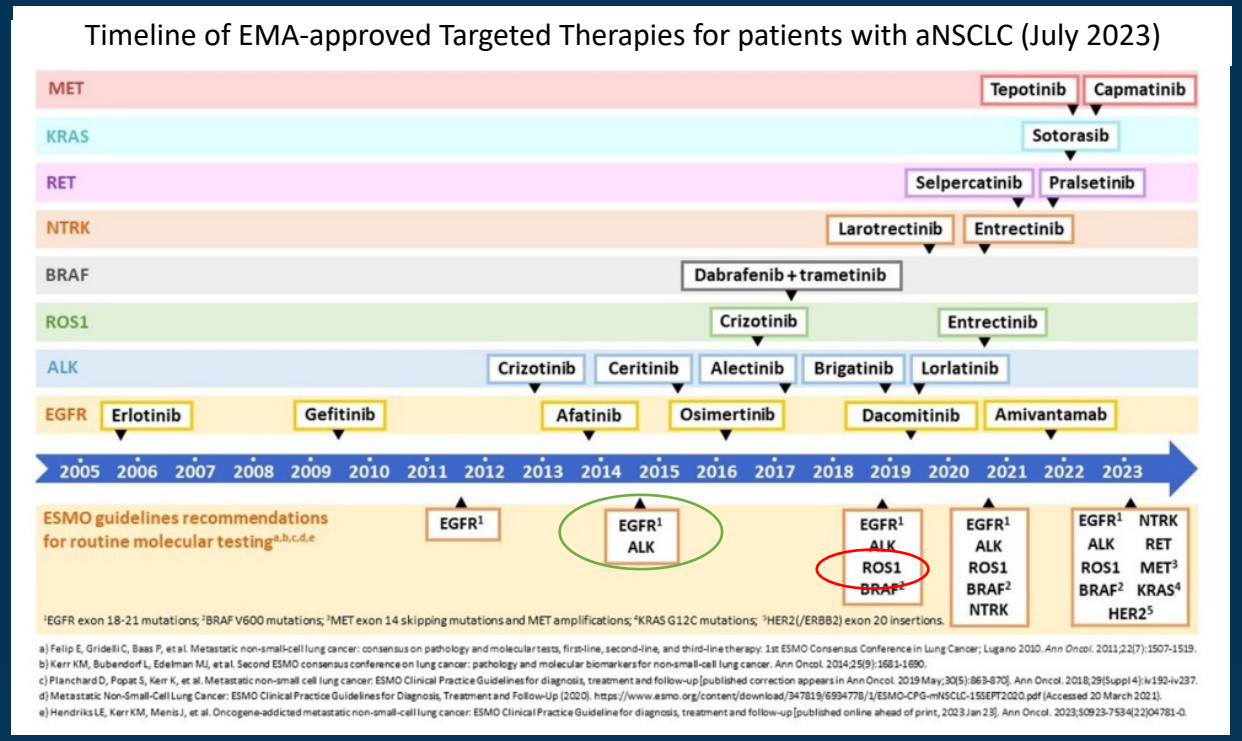
CGP is getting into ESMO guidelines

Cancer type	Stage	ESMO
NSCLC	Advanced	**CGP**
Breast Cancer	Metastatic	NGS
	Recurrent / Adjuvant setting	NGS
Colorectal Cancer	Metastatic	NGS
	Early Stage	NGS
Prostate	Advanced	**CGP**
Gastric cancer	Metastatic	NGS
Pancreatic Ductal adenocarcinoma	Advanced	NGS
Hepatocellular carcinoma	Advanced	NGS
Cholangiocarcinoma	Advanced	**CGP**
Ovarian Cancer	Advanced	**CGP**
	Recurrent setting	NGS
Cancer of Unknown primary (CUP)	Unfavourable CUP	**CGP**

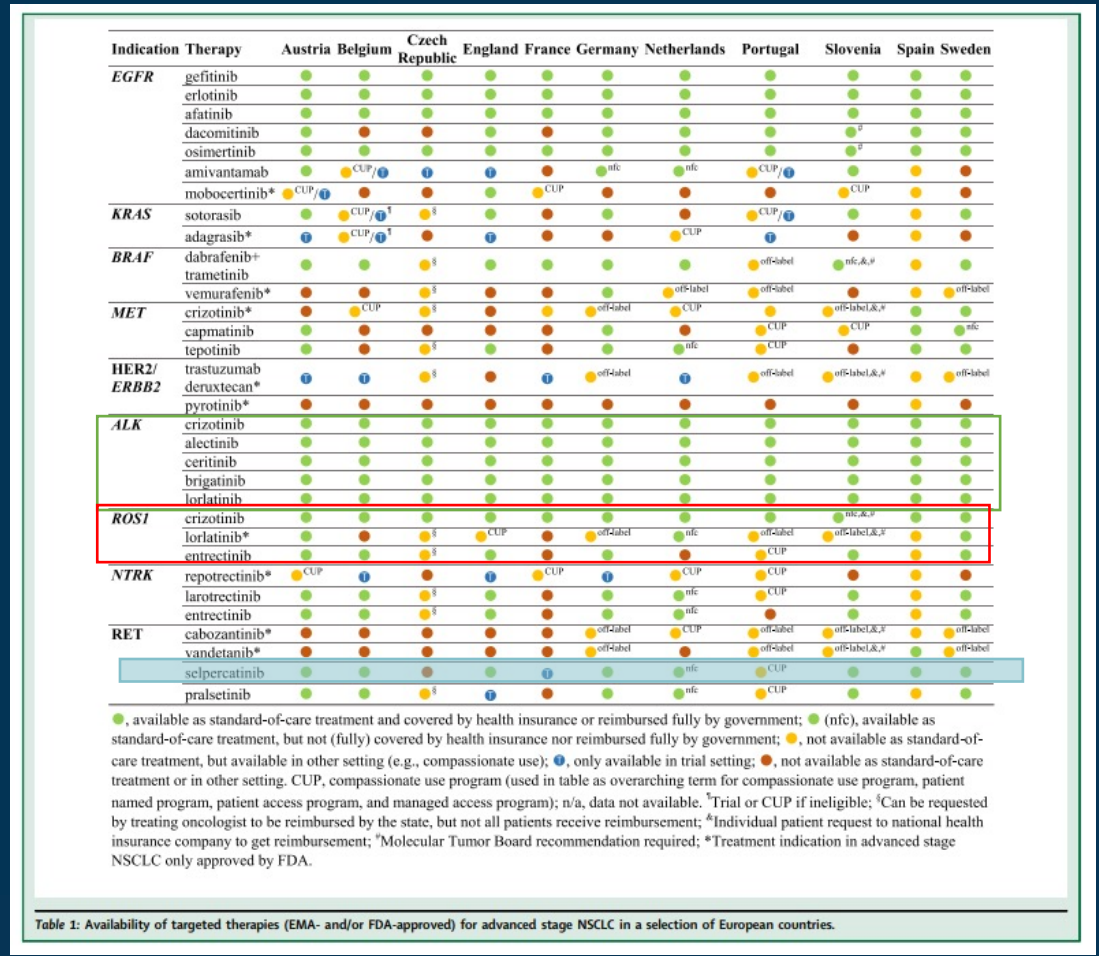


Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group Mosele, F. et al.. 2020 Annals of Oncology, Volume 31, Issue 11, 1491 - 1505

Drug approval and biomarker inclusion into guidelines impact the implementation of CGP



de Jager VD, et al. 2024



Indication	Therapy	Austria	Belgium	Czech Republic	England	France	Germany	Netherlands	Portugal	Slovenia	Spain	Sweden
EGFR	gefitinib	●	●	●	●	●	●	●	●	●	●	●
	erlotinib	●	●	●	●	●	●	●	●	●	●	●
	afatinib	●	●	●	●	●	●	●	●	●	●	●
	dacomitinib	●	●	●	●	●	●	●	●	●	●	●
	osimertinib	●	●	●	●	●	●	●	●	●	●	●
	amivantamab	●	● CUP/ℹ	ℹ	ℹ	●	● nfc	● nfc	● CUP/ℹ	●	●	●
	mobocertinib*	● CUP/ℹ	●	●	●	● CUP	●	●	●	● CUP	●	●
KRAS	sotorasib	●	● CUP/ℹ¶	● §	●	●	●	●	● CUP/ℹ	●	●	●
	adagrasib*	ℹ	● CUP/ℹ¶	●	ℹ	●	●	● CUP	ℹ	●	●	●
BRAF	dabrafenib+ trametinib	●	●	● §	●	●	●	●	● off-label	● nfc,&,#	●	●
	vemurafenib*	●	●	● §	●	●	●	● off-label	● off-label	●	●	● off-label
MET	crizotinib*	●	● CUP	● §	●	●	● off-label	● CUP	●	● off-label,&,#	●	●
	capmatinib	●	●	●	●	●	●	●	● CUP	● CUP	●	● nfc
	tepotinib	●	●	● §	●	●	●	● nfc	● CUP	●	●	●
HER2/ *ERBB2*	trastuzumab deruxtecan*	ℹ	ℹ	● §	●	ℹ	● off-label	ℹ	● off-label	● off-label,&,#	●	● off-label
	pyrotinib*	●	●	●	●	●	●	●	●	●	●	●
ALK	crizotinib	●	●	●	●	●	●	●	●	●	●	●
	alectinib	●	●	●	●	●	●	●	●	●	●	●
	ceritinib	●	●	●	●	●	●	●	●	●	●	●
	brigatinib	●	●	●	●	●	●	●	●	●	●	●
	lorlatinib	●	●	●	●	●	●	●	●	●	●	●
ROS1	crizotinib	●	●	●	●	●	●	●	●	● nfc,&,#	●	●
	lorlatinib*	●	●	● §	● CUP	●	● off-label	● nfc	● off-label	● off-label,&,#	●	●
	entrectinib	●	●	● §	●	●	●	●	● CUP	●	●	●
NTRK	repotrectinib*	● CUP	ℹ	●	ℹ	● CUP	ℹ	● CUP	● CUP	●	●	●
	larotrectinib	●	●	● §	●	●	●	● nfc	● CUP	●	●	●
	entrectinib	●	●	● §	●	●	●	● nfc	●	●	●	●
RET	cabozantinib*	●	●	●	●	●	● off-label	● CUP	● off-label	● off-label,&,#	●	● off-label
	vandetanib*	●	●	●	●	●	● off-label	●	● off-label	● off-label,&,#	●	● off-label
	selpercatinib	●	●	●	●	ℹ	●	● nfc	● CUP	●	●	●
	pralsetinib	●	●	● §	ℹ	●	●	● nfc	● CUP	●	●	●

●, available as standard-of-care treatment and covered by health insurance or reimbursed fully by government; ● (nfc), available as standard-of-care treatment, but not (fully) covered by health insurance nor reimbursed fully by government; ●, not available as standard-of-care treatment, but available in other setting (e.g., compassionate use); ℹ, only available in trial setting; ●, not available as standard-of-care treatment or in other setting. CUP, compassionate use program (used in table as overarching term for compassionate use program, patient named program, patient access program, and managed access program); n/a, data not available. ¶Trial or CUP if ineligible; §Can be requested by treating oncologist to be reimbursed by the state, but not all patients receive reimbursement; &Individual patient request to national health insurance company to get reimbursement; #Molecular Tumor Board recommendation required; *Treatment indication in advanced stage NSCLC only approved by FDA.

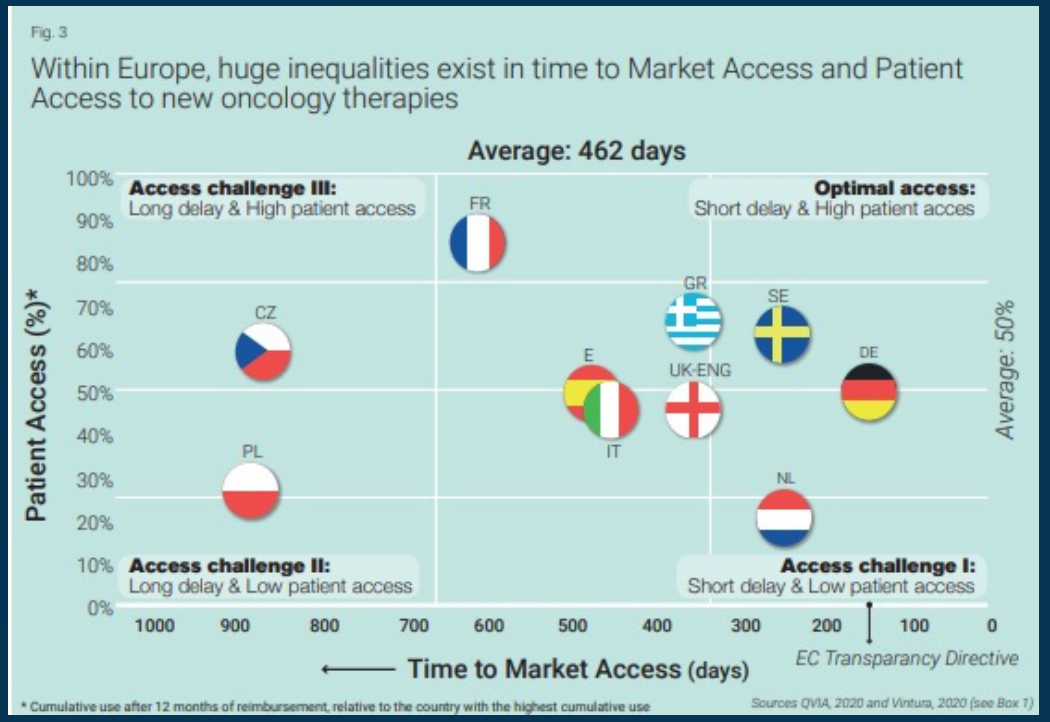
Table 1: **Availability of targeted therapies (EMA- and/or FDA-approved) for advanced stage NSCLC in a selection of European countries.**

Lorlatinib is still only approved by FDA

ALK Inhibitors are approved in most European countries (testing for ALK fusions has been in guidelines since 2014)

Patient access to innovative therapies and CGP are tightly connected

- **Drug Approval Processes:** Drug approval times vary significantly between the FDA (US), EMA (Europe), and individual countries within Europe. This creates inconsistency and delays.
- **Guideline Updates:** National guidelines for using precision oncology are often slow to be updated, hindering adoption of the latest advancements.
- **Limited Patient Access:** Even when therapies are approved, patients may face barriers to accessing them, such as high costs or limited availability.



https://www.vintura.com/wp-content/uploads/2020/08/White-paper-every-day-counts-improving-time-to-patient-access-to-innovative-oncology-therapies-in-europe_from-EFPIA_and_Vintura.pdf

Why does this matter?

- Does your national Society of Med Oncology endorse immediately ESMO's recommendations ?
- How efficient and frequent does your national Society of Med Oncology updates their NGS recommendations?
- What recommendations are considered by your local payers / Health Technology Assessment (HTA) bodies?

If you need to asses only 5 simple biomarkers in your aNSCLC patient, you do not have a strong case for CGP implementation in your institution

What is the status of CGP reimbursement across EU?

Cost-effectiveness of CGP

- **Cost of therapeutics** is still significantly higher than cost of diagnostics
- **The average cost of diagnostic** workup for NSCLC is in range of €3000-€4000 (De Castro, J., et al 2020) to which need to be added:
  - Hospitalization
  - Sample Acquisition (repeat biopsy?!)
  - Management of side effects
- **Upfront cost for implementation of CGP** is higher, which is justified by long-term benefits (TBD)

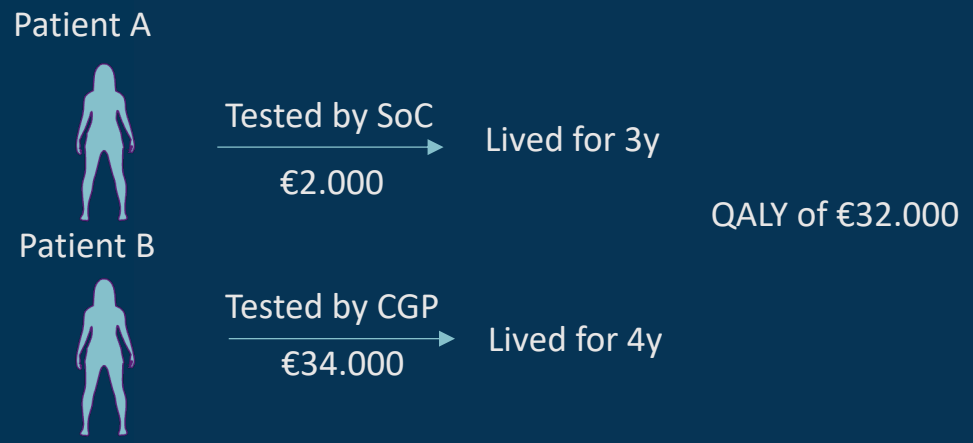
Type of treatment / stage	Cost Estimates / procedure and stage
Cost Estimate of the lung cancer treatment pathway – Stage IA	€37,295
Cost Estimate of the lung cancer treatment pathway – Stage IIIA	€81,222
Chemotherapy	€6,634 per month (initial), €2,753 (continuing)
Targeted/Immunotherapy	€10,189 per month (initial), €5,764 (continuing)
Chemotherapy + Targeted/Immunotherapy	€13,672 per month (initial), €6,983 (continuing)

De Nijs, K., et al.,. 2024

Testing Method	Cost Range (USD)	Advantages	Disadvantages
Single Gene Testing	$100 - $2,000	Least expensive; Targeted analysis of specific gene(s)	Limited genomic coverage; May miss other relevant alterations
Small NGS Panels	Few hundred - few thousand	Broader genomic coverage than single gene testing; More cost-effective than CGP	Limited coverage compared to CGP; May miss less common or novel alterations
CGP	$3,000 - $6,000+	Most comprehensive genomic analysis; Identifies wider range of actionable mutations; Potential for cost savings in long run	Most expensive upfront cost; May identify variants of unknown significance (VUS)

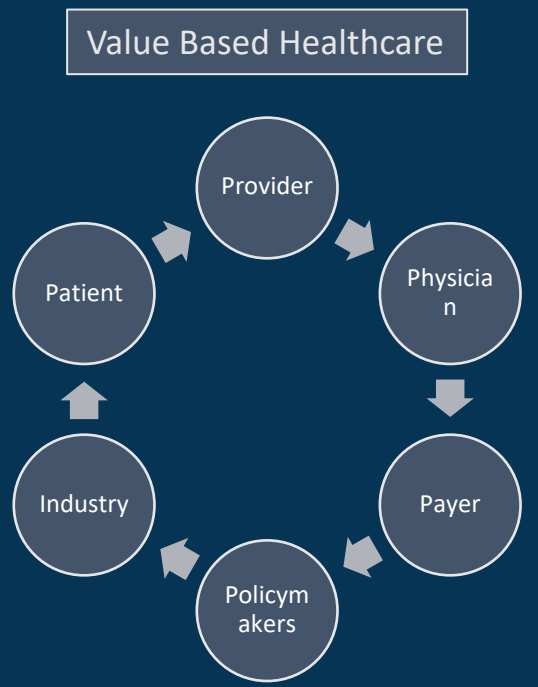
Evidence for cost-effectiveness of CGP is growing

Study	Cancer Type	Comparison	Key Findings
Ode et al. (2021) Netherlands	Metastatic NSCLC	CGP vs. Standard diagnostic testing	□ CGP is cost-effective compared to standard testing, with an ICER of €32,000 per QALY gained. □ CGP led to improved survival and reduced costs associated with ineffective treatments.
Van der Velden et al. (2020) Netherlands	Various solid tumors	CGP vs. Standard diagnostic testing	□ CGP is cost-effective in certain tumor types, with ICERs below the willingness-to-pay threshold. □ CGP improved survival and quality of life for some patients.



To take into consideration:

- The specific ICER threshold for what's considered "cost-effective" varies between countries and healthcare systems.
- ICERs calculated over a short period (e.g., 1 year) might not capture the full long-term benefits or costs of an intervention like CGP.
- The choice of "standard testing" as the comparator can influence the ICER. Different standard testing approaches have varying costs and effectiveness.

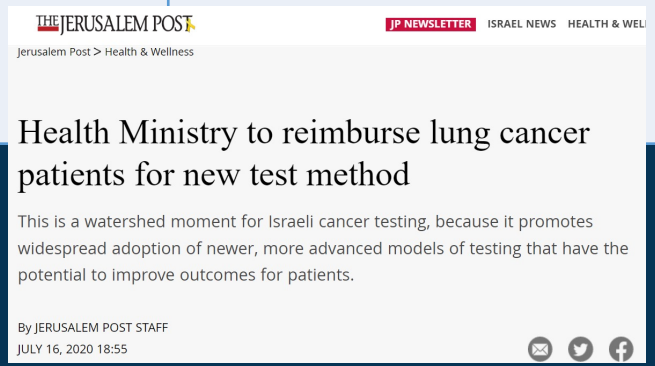


Status of NGS-based biomarker testing across EU

	Italy	Spain	Germany	France
Status	• In Italy, the inclusion of NGS into healthcare at the national and/or regional levels is under development. • An HTA-based approach for NGS is needed in Italy to show the medical and cost effectiveness of NGS (under development). • **The principal barrier for NGS adoption is lack of standardisation and the significant regional variation in reimbursement procedures**.	• Spanish healthcare is highly decentralised, without national reimbursement mechanisms for NGS - Funding is provided by a mix of public payers, private insurance, and the pharmaceutical industry. • Spanish guidelines recommend NGS testing for lung cancer, cholangiocarcinoma, gynaecological cancers, and rare tumours like sarcomas. • NGS is considered valid for identifying CRC mutations in young patient and is used for therapy selection in lung cancer • Additionally, NGS is used in head-neck cancers or challenging cases without a clear relationship with a specific treatment. • **Main challenge is decentralized system with NGS assays being funded by hospital budget.**	• Statutory reimbursement generally covers NGS testing if used per guideline and is limited to 25 kb - longer sequences requiring additional approvals by a health insurance company. • Reimbursement is straightforward for NSCLC but challenging to obtain for other indications . • **Main barrier for wider adoption of NGS is lack of published evidence showing the local impact of NGS on QoL, survival, and resource use and lack of tumour boards in smaller hospitals.**	• NGS is implemented in health and other relevant plans, and it is periodically evaluated for optimization. • There is a national and/or regional investment plan for NGS in healthcare (France Genomique) that incorporates innovation according to opportunities and international developments. • **The cost of NGS to hospitals is the primary hurdle to its adoption in France, as only half of the testing costs are covered.**

Rates	• Sequencing of 400bp €115.97
	• Local Panel (>200 genes) €1247.76
	• Small panel (limited number of genes) €1026.60
	• NGS (Lombardia only) €2072.74
		• NGS molecular tests are reimbursed in Catalunya with four different levels:
		  • Hereditary cancer testing €380
		  • Haemato-oncology and solid tumours EUR €600–680
		  • Paediatric cancer €900
			• Largest panel €2771.40 -€6527.92	• Small Size Panel (< 20 kb) €882.90 Somatic & Germline
				• Medium Size Panel (< 100 kb) - Somatic & Germline €1503.90
				• Large Size Panel (< 500 kb) Somatic & Germline €2205.90

- Israel is the only country in EMEA which currently covers CGP to all NSCLC patients as of 2020.


THE JERUSALEM POST JP NEWSLETTER ISRAEL NEWS HEALTH & WEL

Jerusalem Post > Health & Wellness

Health Ministry to reimburse lung cancer patients for new test method

This is a watershed moment for Israeli cancer testing, because it promotes widespread adoption of newer, more advanced models of testing that have the potential to improve outcomes for patients.

By JERUSALEM POST STAFF

JULY 16, 2020 18:55

Cost and inconsistent reimbursement processes for biomarker testing prevent widespread adoption of CGP

Inconsistent Funding

- A major barrier to CGP testing is the lack of consistent public funding. This varies significantly across and even within countries

Regional Variation

- Decentralized healthcare systems (e.g., Spain, Italy) often have regional differences in test reimbursement, creating unequal access for patients

Patchwork Funding

- Even when public funding exists, it often comes from multiple sources (hospital budgets, lab budgets, grants), leading to inconsistent coverage and administrative burdens.

Delays and Out-of-Pocket Costs

- Funding issues can cause delays in testing and force patients to pay out-of-pocket

Pharmaceutical Dependence

- Lack of reliable public funding makes pharmaceutical companies key sponsors of CGP testing, in some countries – this can create bias and limit test choice.

Relying on inconsistent funding models hinders the widespread adoption and integration of CGP testing into routine cancer care.

A variety of decision-makers is involved in reimbursement processes across EU- clinical and economic efficiency of NGS tests is crucial for all of them

	Regionalized Health Systems (1)		Centralized Health Systems		
	Spain	Italy	Germany	France	UK
Type of Funding	General taxation	General taxation	Statutory health insurance	Statutory health insurance	General taxation
Centralized	National fund promotes personalized medicine, including CDx		EBM within Statutory health insurance	Ministry of Health: Inclusion in RIHN	NHS / NCTO: Coverage Policy
Regionalized	Regional Regulatory committee coverage decision	Regional Regulatory bodies / Regional MTBs coverage decision			
Local	Hospital Committee / Reference Centers make payment decision	Hospital Committee / Oncology Dep do evaluation	Hospitals : additional funding request	INCA platforms: Budget control	Pathology Centers: Budget Control
Evaluation processes & Current Policies	• Regions evaluate NGS test • if coverage is approved, the committee designates reference centers • NGS assays are funded by hospital budget	• Oncology dep. of each hospital sends application for NGS test reimbursement to regional authority	• NGS reimbursement is assessed by EBM • Additional funding to hospitals needs to be requested to the Institute for the Hospital Remuneration System (InEK) and is valid for only 1y.	• NGS testing coverage is assessed by MoH in order to evaluate their inclusion in the repository of Innovative laboratory tests (RIHN) • INCA is responsible for the budget control when NGS tests are required for cancer therapies	• NCTO together with NGS Pathology evaluate NGS tests, as well as Integrated Care Systems.

Rates	• NGS molecular tests are reimbursed in Catalunya with four different levels:
	  • Hereditary cancer testing €380
	  • Haemato-oncology and solid tumours EUR €600–680
	  • Paediatric cancer €900
		• Sequencing of 400bp €115.97
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		• NGS (Lombardia only) €2072.74
			• Largest panel €2771.40 -€6527.92	• Small Size Panel (< 20 kb) €882.90 Somatic & Germline
				• Medium Size Panel (< 100 kb) - Somatic & Germline €1503.90
				• Large Size Panel (< 500 kb) Somatic & Germline €2205.90
					• NA

The context in which drug reimbursement decisions are made also differs significantly between European countries

- Criteria taken into account when reimbursing innovative therapies differs across EU – some systems put more emphasis on clinical aspects (France, Italy) and other on budget impact (Sweden, Norway), while others on both (Spain, Netherlands)

Variation in market access processes and reimbursement decisions for innovative therapies has a direct impact on biomarker testing uptake

European Coalition for Access to Comprehensive Genomic Profiling (ECGP)

ECGP aims to ensure that the political commitment of Europe's Beating Cancer Plan and EU's Cancer Mission to "leave no stone unturned to take action against cancer" is met at the Member State level, where decisions on funding and reimbursement are made. The European Parliament has called on EU Member States to increase access to genomic testing by earmarking financing and creating clear pathways for fast and efficient reimbursement and facilitating equal and rapid access to advanced diagnostics alongside personalised therapies.[3]

https://www.vintura.com/wp-content/uploads/2020/08/White-paper-every-day-counts-improving-time-to-patient-access-to-innovative-oncology-therapies-in-europe_from-EFPIA_and_Vintura.pdf

How effective is biomarker testing in Europe?

Access to Biomarker testing across EMEA

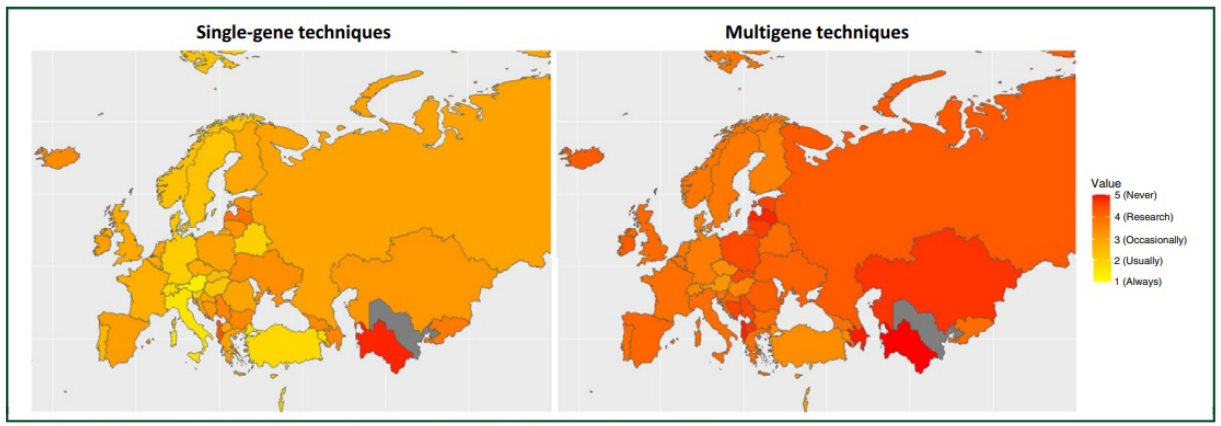


Figure 1. Availability map of single versus multiple genes techniques (all countries, $n = 48$).

Normanno N, et al 2022

Table 3. Availability of techniques across countries by region

Bayle, A. et al. 2023

ALWAYS | USUALLY | OCCASIONNALY | RESEARCH | NEVER | NA

	Country*	IHC	FISH Lung_breast_Gastric	FISH Other	PCR	MSI Colon_Gastric	MSI Other	NGS Small	NGS Large	RNA Target	RNA Large	Genomic Assay	TMB	WES	WGS	Liquid Biopsies
Western European countries	Andorra															
	Austria															
	Belgium															
	Cyprus															
	Denmark															
	Finland															
	France															
	Germany															
	Greece															
	Iceland															
	Ireland															
	Israel															
	Italy															
	Luxembourg															
	Malta															
	Netherlands															
	Norway															
	Portugal															
	Spain															
	Sweden															
	Switzerland															
	United Kingdom and Northern Ireland															

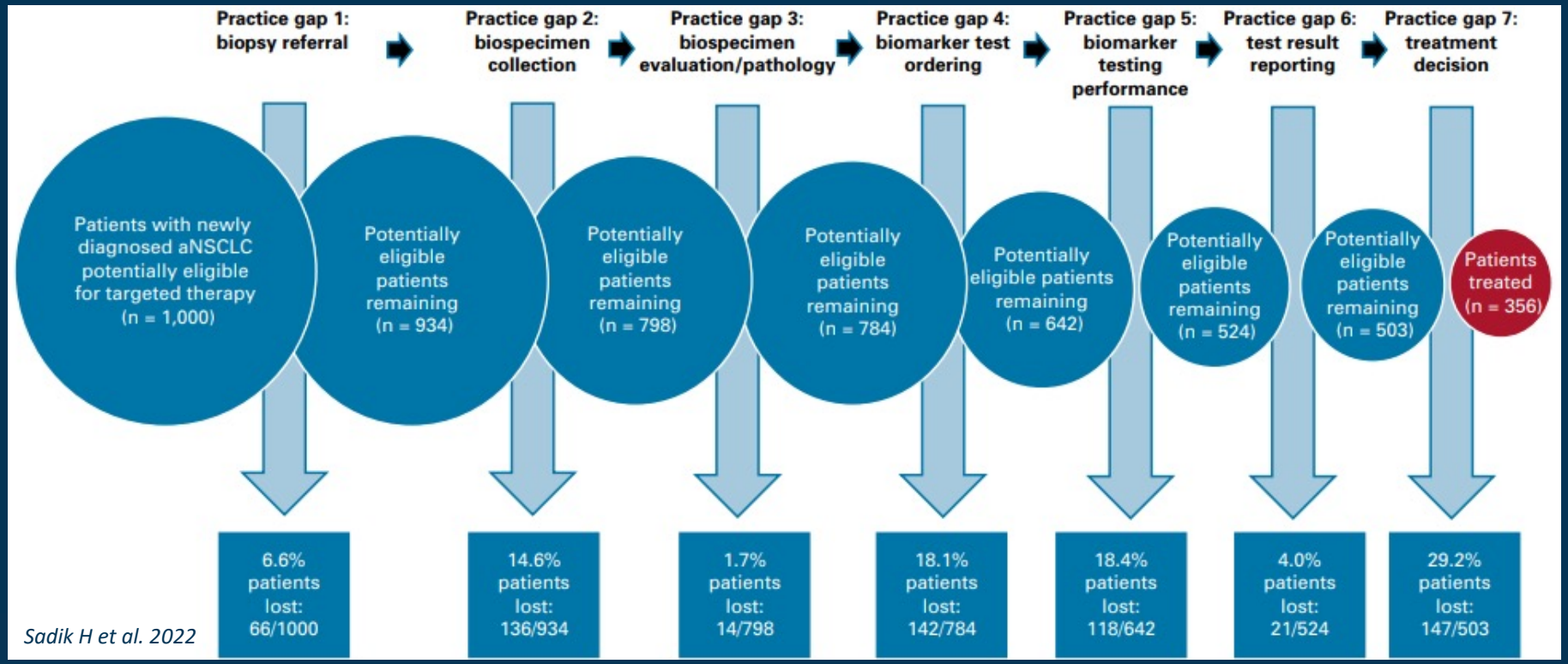
- Even in high-income countries, large NGS panels remain largely unavailable in routine practice, and are limited to clinical trials or research, preventing the search for additional biomarkers in daily practice even though targeted therapies already exist.
- The lack of adequate infrastructure in some Central and Eastern European countries and more generally the presence of inadequate budgets with regional differences in reimbursement policies, make access to tests difficult for many patients.

- In spite of NGS testing being recommended by societies such as ESMO, ASCO and NCCN, the latest ESMO survey shows poor adoption of NGS-based testing in most frequent indications (e.g. Lung, Breast cancer) across Western Europe.
- Across Europe, the adoption of NGS varies from 0-50%.

Many patients are lost to sub-optimal operational aspects

Operational aspects lead to patient lost related to biomarker testing:

- Biopsy referral
- Biospecimen collection
- Biospecimen evaluation/path
- Biomarker test ordering
- Biomarker testing performance
- Test results reporting
- Treatment decision
    - Access to therapy



Sadik H et al. 2022

Up to 45% of aNSCLC patients do no benefit from molecular testing due to a variety of operational hurdles

Data Interpretation and Integration

- Complexity of genomic data
  - Large Data Volume
    - CGP generates massive amounts of data that must be accurately analyzed and interpreted.
  - Variant Classification
    - Determining the clinical significance of variants (benign vs. pathogenic) remains a significant challenge, with ongoing debate over criteria.

- Need for bioinformatics support
  - Need for Advanced Tools
    - Effective bioinformatics tools are essential for managing and interpreting genomic data
  - Resource Allocation
    - Adequate funding for bioinformatics research and development is often lacking, leading to bottlenecks in data handling.

- Integration with clinical decision-making tools
  - Electronic Health Records (EHR)
    - Integrating CGP results into EHRs remains challenging, hindering access to personalized treatment options for healthcare providers.
  - Decision Support Systems
    - Development of clinical decision support systems that can interpret CGP results and suggest therapies is still in its infancy.

Will AI-based tools help us with interpretation & integration of CGP data with the rest of omic and clinical data?

Regulatory and Ethical Concerns

- Regulatory hurdles associated with CGP
  - Approval Processes
    - CGP tests must meet strict regulatory standards for approval, which can slow down the introduction of innovative tests.
  - Variability Across Countries
    - Different countries have disparate regulatory frameworks, which complicates the cross-border implementation of CGP.

- Ethical Considerations
  - Informed Consent
    - Patients must fully understand what CGP entails and the implications of potential findings, especially regarding incidental findings.
  - Confidentiality and Data Privacy
    - Safeguarding patients' genetic information is paramount, raising concerns about data sharing and privacy regulations.

- Public Perception and Education
  - Misunderstanding of Genetic Information
    - The public may have misconceptions about genetic testing and its implications, leading to resistance to CGP.
  - Education Initiatives
    - There's a need for ongoing education for both healthcare professionals and patients about the benefits and limitations of CGP.

Future perspectives on Expanding CGP implementation

Increasing number of FDA and EMA-approved therapies will continue to generate the demand for CGP testing

- To fulfil this need, 1) establishing consistent and efficient Health Technology Assessment (HTA) processes, 2) ensuring consistent insurance coverage across different regions, 3) integrating biomarker testing into healthcare systems and 4) providing sufficient funding and infrastructure development is needed.

Industry / CGP providers

- European market wants distributed CGP solutions; Develop push-button sample-to-report, HCP friendly AI-based solutions, while complying with IVDR regulations
- Generate additional macro-economical / budget impact evidence which will support inclusion of CGP into local guidelines and will accelerate reimbursement in close collaboration with local HTAs/payers
- Engage early with key stakeholders (HCPs, HTAs, payers and policy makers)

Leverage Existing Success stories across EU

- National Studies like BALLET (Belgium)
- Nation-wide CGP coverage for NSCLC patients (Israel)

Education of HCPs, patients and caregivers is essential for broader NGS adoption across different clinical and socioeconomic settings.

- Greater awareness around clinical and economic benefits of CGP testing

Summary

- There is a growing evidence that CGP has significant positive impact on patient outcome measures.
- There is no sufficient emphasis on the operational effectiveness and related costs-savings from CGP usage.
- Biomarker reimbursement landscape is very fragmented, there is no dedicated diagnostics budgets across most of EU countries and lack of access to innovative therapies leads to under-usage of NGS testing.
- CGP manufacturers and pharmaceutical industry should establish early strategies for clinical and economic evidence generations, while taking country-specific differences, and IVDR-requirements into account.

Thank you

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