IDENTIFYING THE KEY CHALLENGES IN THE REIMBURSEMENT OF NEXT GENERATION SEQUENCING AND FUTURE POLICY CHANGES IN EUROPE USING A WEB-BASED PORTAL TO ENGAGE PAYERS

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INTRODUCTION

Next-generation sequencing (NGS) is a massively parallel sequencing technology that can provide results for multiple genomes with high accuracy and sensitivity using relatively minimal tissue. Broad testing ensures that a wider range of genomic alterations are identified facilitating patient selection for precision medicines (PM). Currently in the USA reimbursement of NGS is widespread, however there are challenges associated with EU reimbursement. This research was completed to identify current and evolving public funding considerations for NGS in France, Germany, Italy, Spain, and UK.

METHODOLOGY

A web-based survey was administered through Rapid Payer Response™ online portal (RPR®) to 15 payers with experience in reimbursement decision-making for oncology diagnostics (3 payers per market). Responses were collected through RPR® in 5 days and analysed via Microsoft™ Excel.

RESULTS

In some markets, there is a lack of a clear framework for NGS testing reimbursement. There is large variation in NGS access and uptake due to the different reimbursement pathways in France. In Spain and Italy, there is a significant variation in access to NGS across regions because of the different coverage guidelines and referral pathways. In many cases, PM manufacturer sponsorship may also be required. However, in Germany and the UK, the centralized systems permit infrastructure investment, and these markets demonstrate greater uptake of NGS. As the number of targetable mutations increase, access pathways are expected to evolve to enable broader reimbursement and uptake of NGS diagnostics (Dx) in all markets.

NGS reimbursement pathways

NGS Reimbursement					
	Predominately centralized			*Predominately regionalized*	
Stakeholder levels: Centralized	**Ministry of Health: Inclusion in RIHN**	**EBM: Coverage decision**	NHS pathology/ NCTO: Coverage decision		National fund promoting personalized medicine includes CDx
Regionalized				Regional regulatory bodies/ Regional molecular tumour boards: Coverage decision	Regional regulatory committee: Coverage decision
Local	INCA platforms: Budget control	Hospitals (inEK): Additional funding request	Pathology centers: Budget control	Hospital committees/ oncology units:Evaluation	Hospital committees/ Reference centers: Payment
Current policies/ evaluation process	NGS Dx coverage are assessed by Ministry of Health in order to evaluate their **inclusion in the repository of innovative laboratory tests** (RIHN). The Institut National Du Cancer (INCA) is responsible for the budget control when NGS Dx are required for cancer therapies.	NGS reimbursement is assessed by Einheitlicher Bewertungsmabstad **(EBM): CDx in EBM subchapter 19.4.** Additional funding to hospitals needs to be **requested to the Institute for the Hospital Remuneration System** (InEK), but valid for only 1 year.	For oncology-related NGS Dx, **National commissioning of testing for oncology** (NCTO) together with the NHS pathology are the key stakeholders. The implementation of the **Integrated Care Systems** have also now a higher responsibility controlling pathology services.	**Applications from oncology units of each hospital are sent to regional authorities** which then decide to reimburse or not a new NGS Dx.	**Most regions evaluate NGS Dx** and then if coverage is approved, the committees designate a reference centre. However, **NGS Dx are funded by hospital budgets**, which may or may not have funds available.
Payer perception of level of NGS access (1= very low, 5= very high)	4.0	4.7	4.7	3.0	2.7

High (3.5-5) Moderate (2.5-3.4) Low (1-2.4)

EBM: Einheitlicher Bewertungsmabstad; INCA: Institut National Du Cancer; InEK: Institut für das Entgeltsystem im Krankenhaus; NCTO: National commissioning of testing for oncology; NHS: National Health System; RIHN: Repository of Innovative Laboratory Tests

Figure 1. NGS Dx reimbursement pathways and key stakeholders across five European markets

Key drivers and challenges to reimburse NGS diagnostics in oncology

Key value attributes	France	Germany	Italy	Spain	UK	Importance in influencing the NGS reimbursement in oncology in the future (Very Low (1) – Very High (7))
EMA/MHRA approval of NGS test as CDx	**7.0**	**6.7**	**6.7**	**6.0**	**7.0**	6.7
Test Accuracy / Reliability	**6.0**	**7.0**	**6.3**	**6.3**	**7.0**	6.5
No. of actionable mutations in a tumor site	**6.0**	**5.7**	**6.3**	**5.5**	**5.7**	5.9
Cost	**5.0**	**3.0**	**7.0**	**6.0**	**5.3**	5.3
Inclusion in relevant oncology guidelines	**5.0**	**5.0**	**5.0**	**4.3**	**5.0**	4.9
Availability of labs specialized in NGS	**4.3**	**1.7**	**6.7**	**6.3**	**4.3**	4.7
KOL Support	**4.7**	**2.0**	**4.3**	**5.0**	**4.7**	4.1
Turnaround Time (TAT)	**4.7**	**2.3**	**5.0**	**4.3**	**4.3**	4.1

High Importance (5.5-7) Moderate Importance (4-5.4) Low Importance (1-3.9)

Figure 2. Key drivers for the public coverage of NGS Dx in oncology

Key drivers:

- Approval of an NGS test as a CDx is highly impactful as it expedites reimbursement decision within the context of the related PM
- The NGS Dx accuracy/ reliability is a crucial attribute due to solid evidence proving the quality of this Dx methodology: detecting multiple mutations with small samples efficiently
- The number of actionable mutations detected is another key driver for NGS Dx coverage due to its direct impact on its cost-effectiveness
- In Germany, cost, labs specialized in NGS, KOL support and TAT are not key drivers as those are not obstacles for NGS Dx access
- In contrast, in Italy and Spain, budget and infrastructure required for wider NGS access is lacking, hence cost and lab availability are critical

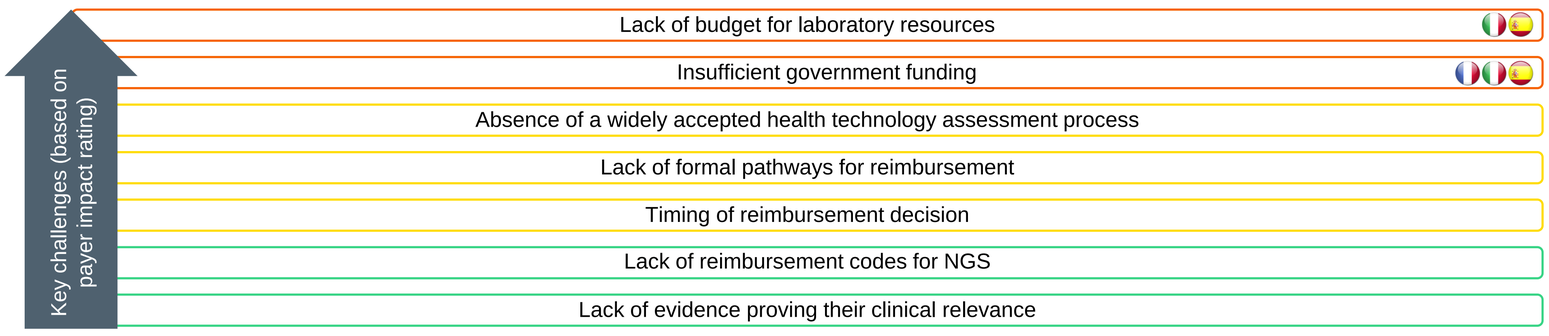

Figure 3. Key challenges for the public coverage of NGS Dx in oncology

Key challenges

- Insufficient budget for lab resources is particularly a challenge in Italy and Spain as labs will be competing for resources in hospitals or regions
- Lack of a central government budget specifically dedicated to NGS Dx is a concern in France, Italy and Spain since it slows down its reimbursement, which also delays use of new precision medicines
- With exception of the UK where the National commissioning of testing for oncology assesses NGS Dx required for cancer therapies, there is no specific HTA or/and reimbursement pathway for NGS Dx in remaining scope markets
- The delay in NGS Dx reimbursement decision in some cases is seen as an obstacle for commencing the use of new cancer therapies requiring a NGS Dx

Recommendations and potential policy changes concerning NGS reimbursement

Recommendations for manufacturers of precision medicines (PMs) to improve the likelihood of NGS coverage

- ✓ Provide RWE proving the economical value of using NGS Dx instead of single analyte tests
- ✓ Provide case studies of successes where the usage of NGS Dx in oncology was cost-effective
- ✓ Collaborate directly with regional stakeholders in Italy and Spain to design a formal reimbursement pathway specifically for PMs-related NGS Dx
- ✓ Be prepared to pay most or all costs related to NGS Dx required for PMs (sponsorship contracts) since the existing budgets for NGS Dx are limited
- ✓ Collaborate with stakeholders responsible for relevant oncology guidelines (e.g. ESMO) to highlight the benefits of NGS Dx both in terms of healthcare resources and cost-effectiveness
- ✓ Collaborate with cancer patient advocacy organizations to educate decision makers on benefits of NGS and create new reimbursement pathways and funds

Potential changes in policies concerning NGS reimbursement

- ✓ Creation of specific budgets for NGS Dx required for recently approved precision medicines
- ✓ Country guidelines including recommendation for using NGS Dx in a wider group of tumours
- ✓ Inclusion of NGS in the catalogue of covered services at the national level
- ✓ Investment to increase the number of laboratories providing NGS Dx

No changes in policies are expected in Germany since the current process for the reimbursement of NGS Dx in oncology is perceived to be very efficient. For instance, there is a national programme (nNGM Lungenkrebs) which offers NGS testing for lung cancer patients via a network of 15 university cancer centers.

Figure 4. Recommendations and potential policy changes concerning NGS Dx reimbursement

CONCLUSION

For manufacturers, the key challenge is to ensure that once EMA or MHRA approves a PM, its coverage is followed by the timely reimbursement of the related NGS test. They must learn how to navigate through the existing complex frameworks for public coverage of NGS tests relating to their EMA/MHRA approved PMs and anticipate future policy changes.