NEXT GENERATION SEQUENCING IN ONCOLOGY

AN UPDATE ON THE SWISS MARKET

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Inovigate GmbH, Basel, Switzerland, May 2023

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Glossary

Abbreviation	*Definition*
DNA	Deoxyribonucleic Acid
DRG	Swiss Diagnosis Related Groups
EAPM	European Alliance for Personalized Medicine
ETH	Eidgenössische Technische Hochschule
ECPC	European Cancer Patient Coalition
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicines Agency
ESCAT	ESMO scale for clinical actionability
ESMO	European Society for Medical Oncology
FDA	Food and Drug Administration
FMH	Foederation Medicorum Helveticorum, Professional organization of Swiss physicians
FOPH	Federal Office of Public Health
GDP	Gross Domestic Product
HCO	Healthcare Organizations
HCP	Healthcare Personnel
IARC	International Agency for Research on Cancer
IQN Path	International Quality Network for Pathology
KOL	Key Opinion Leader
MGTO	Molecular Guided Treatment Option
MTBs	Molecular Tumor Boards
NCCN	National Comprehensive Cancer Network
NGS	Next Generation Sequencing
NSCLC	Non-Small Cell Lung Cancer
OECD	Organization for Economic Co-Operation and Development
RNA	Ribonucleic Acid
TARDOC	Replacement for TARMED tariff catalogue
TARMED	Tariff Medical, Swiss medical tariff catalogue
WES	Whole Exome Sequencing
WGS	Whole Genome Sequencing
WHO	World Health Organization

Executive Summary

Next generation sequencing (NGS) has proven its clinical validity and is widely applied in oncology. In order to better understand how it is used in clinical reality and how the different stakeholders in the Swiss oncology environment collaborate, Inovigate conducted a market research in 2022.

Switzerland is among the leading countries in regard to patient access to NGS testing. The technology is available throughout the country and the cost reimbursement policies are in place.

Yet, little is currently known about the supplier and collaboration network. Thus, we developed an oncology collaboration model based on a series of interviews with oncologists, medical personnel, and representatives of medical service providers.

High throughput diagnostic requires a likewise scalable infrastructure and processes as well as experts with the appropriate skills and expertise to analyze and interpret the rich outcomes of NGS testing. Nevertheless, data collection, protocols for pre- and post-processing and other laboratory procedures may differ across laboratories. To utilize the full potential, comparability of the entire processing and analysis chain should be accounted for. In order to maximize the value of NGS testing for patients and in line with recommendations made elsewhere, country wide quality assurance schemes should be considered, and consistency of data and processes be addressed.

To this purpose, continuous stakeholder education is crucial. According to our interviewees, an exchange network in addition to and independent of the commercially driven collaborations is desirable.

Another emerging theme relates to the timing of NGS testing. It was recommended to apply it earlier in the disease in order to optimize treatment, reduce additional burden on patients (e.g., multiple biopsies) and, in turn, increase the likelihood of a successful treatment.

Our analysis revealed that the collaboration network evolves around the big academic institutions and reflects geographic and language constraints. With the growing demand and ongoing investment in this technology in Switzerland, we expect for NGS testing and comprehensive profiling to become the new standard in oncology.

The individualization of every single patient journey through Precision Medicine has the ability to enhance patient outcomes significantly. This approach can be applied to both diagnosis and treatment, with advancements in technology enabling the development of diagnostic solutions that facilitate early disease detection and more effective monitoring during treatment.

Roche, with a focus on oncology, aims to individualize cancer treatment based on patients' unique molecular tumor profiles. Consequently, Roche is interested in understanding the Next Generation Sequencing (NGS) market in Switzerland to further support the development of personalized cancer treatment. Although the adoption of NGS in clinical oncology in Switzerland is not fully understood, comprehending its use, opportunities, challenges, and the collaboration between oncologies and pathologies is critical.

For this reason, Roche Pharma Switzerland, Roche Diagnostics Switzerland and F. Hoffmann - La Roche Ltd have supported Inovigate in its market research on "Next generation sequencing in Oncology".

We thank F. Hoffmann-La Roche AG for supporting us in this project as a sponsor.

1 Introduction

1.1 Background

Advances in Next Generation Sequencing (NGS) technology have provided a significant step forward in personalized medicine and have offered unique opportunities to better understand disease pathology and risk factors. NGS is used for DNA and RNA sequencing as well as variant/mutation detection. It has had a big impact on clinical oncology where it is successfully used to identify treatments, that match genomic driver alterations, known as molecularly guided treatment options GTO) (Horgan et al., 2022).

Objective of this market research

- To understand the use of NGS testing in the Swiss oncology environment and the associated collaboration models.

NGS as a high throughput technology allows to simultaneously interrogate hundreds and thousands or even millions of targets in a short period of time. In essence, NGS scales well with high and robust quality, enabling analyses which would otherwise be too expensive. For this reason, it has been commonly used for disease diagnosis, prognosis, therapeutic decision and follow-up of patients (Dahui, 2019). For instance, any given tumor may have multiple mutations. When low throughput molecular assays are used in cancer patient care, multiple assays have to be performed for multiple mutations, thus requiring a larger amount of tissue. This also implies that patients have to wait longer for the results and, in some cases, they need to undergo additional biopsies. In contrast, NGS technology allows to interrogate the same targets in one test. This report will focus on its application in clinical oncology only. However, NGS technology is frequently used for the study and diagnosis of rare diseases, noninvasive prenatal testing, infection biology, cardiovascular diseases, and pharmacogenomics (Guan et al., 2012) as well.

Currently it is possible to analyze large gene panels, sometimes referred to as comprehensive genomic profiling, whole exomes (WES) and even whole genomes (WGS). Sequencing information obtained with NGS can be restricted to a pre-specified group of genes (targeted gene panels), focus on the encoding regions of the base pairs of genomes (WES) or involve

the analysis of the entire tumor genome (WGS). The choice between these different methods depends on multiple factors such as the intended application of the tumor testing (i.e., clinical versus research setting), the results required, technical efficiency and cost. In general, targeted gene panels are used preferably in the clinical setting since they provide greater depth of coverage in selected areas of interest, faster turnaround and more clinically relevant data compared to broader genomic profiling by WES or WGS approaches (Malone et al., 2020).

Focus domains for this report

- NGS in Switzerland: explore its application in clinical oncology
- Collaboration model: map out the Swiss oncology network
- Reimbursement: understand implications of payment policy
- Challenges: describe potential obstacles associated with NGS

Adopting the patient journey illustrated in **Figure 1** as the framework of our market research, this report summarizes the research findings around four main areas of interest related to the use of NGS testing in clinical oncology in the Swiss market.

1.2 Obstacles

Despite its profound effects in advancing genomic medicine, NGS technology is associated with a greater likelihood of discovering variants of unknown clinical significance. The larger number of genes being tested may lead to findings that are not relevant to the disease in question such as risk factors for other diseases or to unclassified variants. Specialized and trained experts (i.e., molecular pathologists and clinical geneticists) are required to determine the pathogenicity of the variants identified and differentiate between pathogenic and benign ones (Fahrioğlu, 2018). Thus, the interpretation of genomic analyses is becoming increasingly complex. Following current guidelines, such as the National Comprehensive Cancer Network (NCCN) guidelines in the case of tumor NGS testing, is therefore recommended (Dahui, 2019).

Multiple MGTO have been approved for different tumors by the US Food and Drug Administration (FDA), the European Medicines Agency (EMA) and other regulators (Malone et al., 2020). The NCCN guidelines now recommend multigene panel testing for multiple

tumor types including non-small cell lung cancer, colon, prostate, breast ovarian, carcinoma-of-unknown-primary-origin and bone cancer (Horgan et al., 2022). The European Society for Medical Oncology (ESMO) Precision Medicine Working Group 2020 also recommended NGS for daily clinical practice in several tumor types including non-squamous non-small-cell lung cancer, prostate and ovarian cancers as well as cholangiocarcinoma (Mosele et al., 2020). Swiss guidelines recommend counseling and testing for genetic predisposition to breast, ovarian, pancreatic and prostate cancer (Stoll et al., 2021).

Despite growing support for genomic testing in treatment guidelines, there is no equal access to NGS within and across countries (Horgan et al., 2022; Normanno et al., 2022). In 2021 the European Alliance for Personalized Medicine EAPM-led expert panels including key stakeholders from 10 European countries (i.e., Belgium, France, Germany, Israel, Italy, Portugal, the Republic of Ireland, Slovenia, Switzerland and the UK) identified the challenges associated with the implementation of NGS into routine clinical practice and provided recommendations to overcome them (Horgan et al., 2022). The recognized challenges relate to the demand for NGS tests, which is influenced by factors such as governance, clinical standardization, awareness and education and the supply of tests determined by equitable reimbursement, infrastructure for conducting and validating tests and testing access driven by evidence generation (Horgan et al., 2022; Normanno et al., 2022).

1.3 A patient journey

From a patient perspective, local medical support is as important as access to the best medical care possible. However, local language and family support are essential factors for patients to consider, especially for patients diagnosed with a life-threatening disease.

Diagnostics, surgery and first treatment usually take place in hospitals or medical centers with the appropriate infrastructure and technology, like NGS, in reach. Follow-up care, e.g. post-surgery or chemotherapy as well as long term monitoring is handled by local, smaller hospitals or local oncologists.

It is now well accepted that Molecular Tumor Boards (MTBs) play a key role in the implementation of precision oncology in clinical settings. These are multidisciplinary meetings where potential therapeutic strategies are discussed based on genetic evidence and they are crucial particularly for those patients who are not responding to standard of care systemic therapies. While MTBs differ in terms of scope, composition, methods and recommendations worldwide, they are powerful panels in that they help harmonize the interpretation of NGS results, which, in turn, informs clinical management (Horgan et al., 2022). In tumor boards cancer diagnosis and treatment are discussed by oncologists, surgeons, pathologists, and radiologists and are clinical in nature. By contrast, MTBs are also attended by geneticists, bioinformaticians and biostatisticians, thus providing the scientific and technical expertise needed to interpret complex genomic data accurately and meaningfully (Stoeklé et al., 2018).

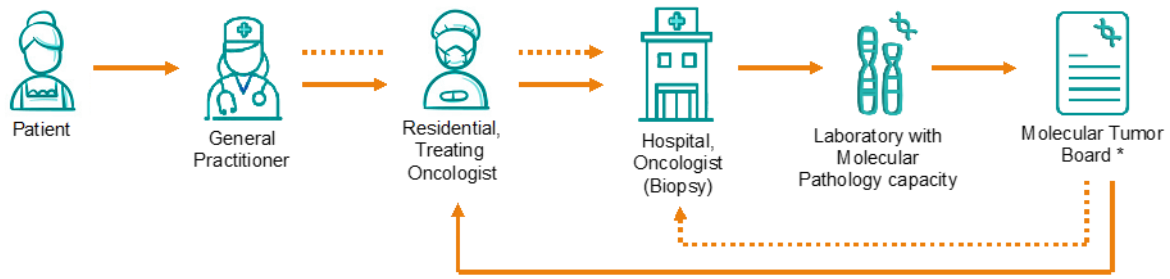


Figure 1: Patient Journey

*The patient is referred to a nearby hospital that may or may not have an embedded Molecular Pathology Laboratory. When this is not the case, the patient is referred to an external Laboratory to undergo NGS testing. Note: Dotted line: General Practitioner can refer the patient to a residential oncologist or a hospital for specialized clinical care. * The comprehensive Clinical Report generated in the previous step is discussed in an interdisciplinary team where decisions about treatment options are taken. Please note that not all hospitals have Molecular Tumor Boards, they are mostly established in larger centers and university hospitals.*

Cancer patients usually go through the stages of the patient journey shown in **Figure 1**. When patients present themselves with suspicious symptoms, the general practitioner refers them to specialists in the discipline for diagnosis and treatment. After referral, the oncologist, either a residential oncologist or a specialist in the cancer clinical team of the chosen institution,

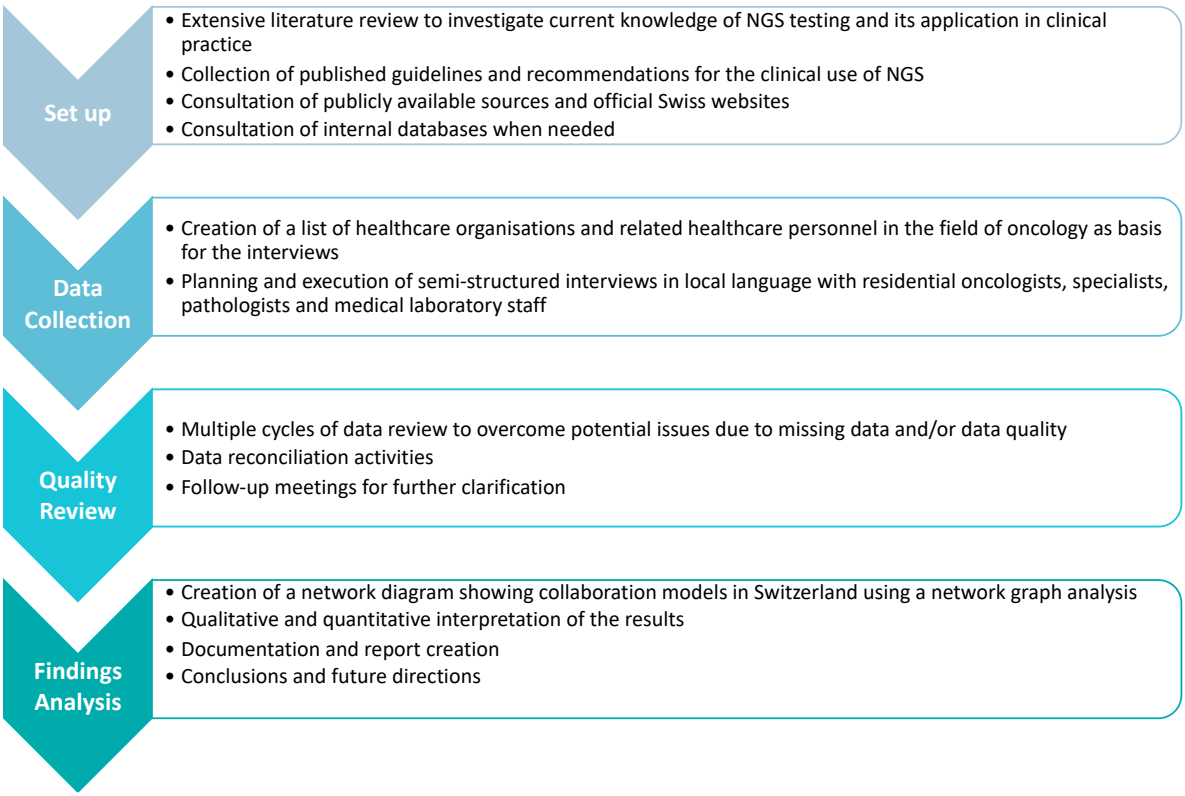
carries out the in-depth diagnosis and may order molecular testing to detect actionable genomic alterations for diagnostic, therapeutic as well as follow-up purposes. In some cases, hospitals have an in-house laboratory with Molecular Pathology capacity, whereas in others, collaborations with external and/or private laboratories exist that allow multigene panel analysis. Once the clinical genomics report is generated, the findings are discussed at multidisciplinary MTBs that ensure all cancer patients receive the best care utilizing genomic data in conjunction with clinical attributes of their disease to create a personalized treatment plan. The gathered information supporting clinical and treatment decisions are then shared with the treating clinicians responsible for the direct care of the patients. It is important to note that not all hospitals are able to incorporate the required expertise for an MTB, in most cases MTBs are established in large centers and university hospitals. The patient journey illustrated in **Figure 1** describes the optimal care management scenario in which MTBs are integrated that combine high-quality clinical and genetic expertise to place NGS results into a clinical context.

2 Methodology

2.1 Desktop Research

This report is based on our market research conducted in 2022, aimed at understanding the use of NGS testing in the Swiss oncology environment and the associated collaboration models.

To generate the insights shared in this report, a wide range of public and official sources were used (BAG, 2022; Comparis, 2022; FMH, 2022; SGMO, 2022; Spitalvergleich, 2022). In addition, 102 interviews were conducted, of which 33 with medical laboratory representatives and 69 with oncologists or medical personnel. Lastly, our findings were confirmed by payer organizations and public administration. Meeting notes and associated documentation were stored and processed according to the Swiss data protection law (Bundesgesetz über den Datenschutz, DSG) from 19th of June 1992 as of March 1st, 2019. Only information, which is relevant for the purpose of this report, was used. This report, its associated data and the network diagram are anonymized and will not disclose any name, email, postal address, or any other information which may disclose such identity.



No financial incentives were awarded to the participants in the study. It was agreed with the participants that they would receive this report, if they showed interest in the outcome of the study.

2.2 Network analysis

The collaboration model was developed based on network graph analysis. Connections between collaborating sites are represented by edges and sites by nodes. A circular layout was chosen as it is well suited to identify group structures. The underlying algorithm creates partitions by analyzing the connectivity structure of the graph. Partitions are placed on separate circles with nodes arranged as radial trees and its root nodes placed on the circles' boundary, see figures below in section 3.1.

The graph was analyzed and visualized with the network editor yEd, Version 3.22 (*YEd - YFiles Graph Visualization Library*, 2022). The program is provided for free by yWorks (https://www.yworks.com/), a company specialized in the development of software solutions for the creation and visualization of graphs, diagrams, and networks.

The collaboration network nodes were classified as hospitals, residential oncologists, laboratories or NGS laboratories, respectively Molecular Pathology Laboratories with NGS capability.
A summary of the stakeholders and network key figures are listed in **Box 1** and **Box 2**.

Connections between nodes are directional. The direction is imposed by the route of a diagnostic test request, a tissue sample, or a molecular pathology analysis request. This chain of requests is also in alignment with the generalized patient journey depicted in **Figure 1**. Nodes and edges are evidenced by our conversations and interviews. Websites were used to complement and verify relations only in cases where the respective information was specific. General statements about collaborations or geographic vicinity alone were not considered.
As a result of this rigid process nine residential oncology sites remain disconnected as stand-alone nodes. Three smaller sub-nets could not be connected to the main collaboration network, too. To reduce visual clutter only the nine stand-alone nodes were omitted from the figures, the three sub-nets are shown in their context.

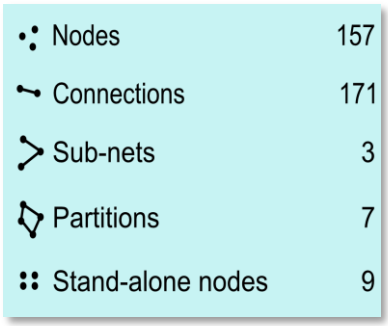
3 Findings

3.1 The Swiss oncology collaboration network

Box 1: Stakeholders

The oncology collaboration network consists, at time of writing, of 157 nodes, 171 connections and seven partitions. Contrasting sub-nets, partitions are connected to the larger network and emphasize group structures. Sub-nets are networks on their own without connections to the larger network. Nodes and connections, but also network topology, are a snapshot in time and will change as the Swiss NGS services environment evolves. Network partitions, i.e., collaboration clusters, were named after network nodes with the most incoming connections from requesting sites.

The circular layout algorithm emphasizes group properties of underlying graphs. It does not take geographic location into account. That means, geographically distant sites could well be assigned to the same partition whereas close by sites could be assigned to different or distant sub-nets. Hence, the network representation in **Figure 2** must also be viewed in context of the Swiss map.



Box 2: Network key numbers

To ease this complementary view, **Figure 3** renders the clipped partitions on top of the Swiss map, next to their geographic center. Language regions are indicated by color, population density by size of the township.

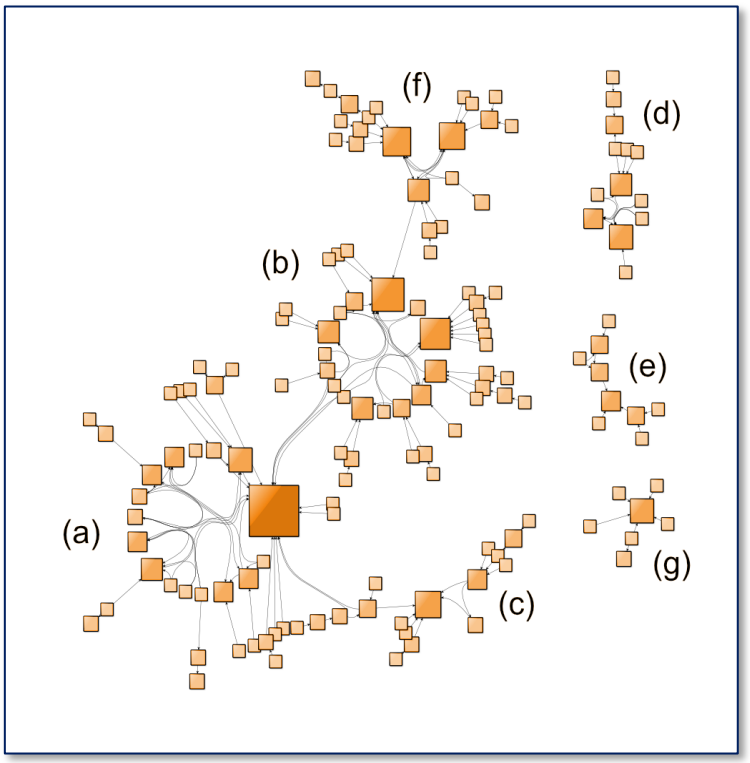


Figure 2: Collaboration network

Number of connections are represented by node size and color intensity.

Main network partitions: (a) Zurich, (b) Bern-Lucerne, (c) Basel, (f) Geneva-Lausanne.

Sub-nets: (d) St. Gallen, (e) Lausanne, (g) Ticino.

The geographic centers of the collaboration clusters coincide with the largest Swiss cities. However, their connected sites are spread across the country.

The five-year prevalence of cancer patients in Switzerland is 230.472 with 60.483 new cases in 2020 (International Agency for Research on Cancer (IARC), 2021). Approximately 73% of the Swiss live and work in urban areas whereas 27% of the Swiss population, nearly 2.4 million, live outside of agglomerations. The number of citizens per township in Switzerland is shown in **Figure 3**, which also indicates the language regions.

It is not surprising that the oncology collaboration network reflects these regional and demographic conditions.

3.2 Collaboration network in the Swiss environment

Switzerland is a multilingual country with four national languages. 62.3% of the 8.7 million Swiss citizens are German speakers, followed by 22.8% French and 8% Italian speakers

(Bundesamt für Statistik (BFS), 2022). The Romansh language is spoken by 0.5% of the Swiss people.

Figure 3 shows the collaboration network partitions in language and geographic context. The network in Swiss Romande, partition (e), and Ticino, partition (g), are only sparsely reaching into other partitions of the German speaking regions.

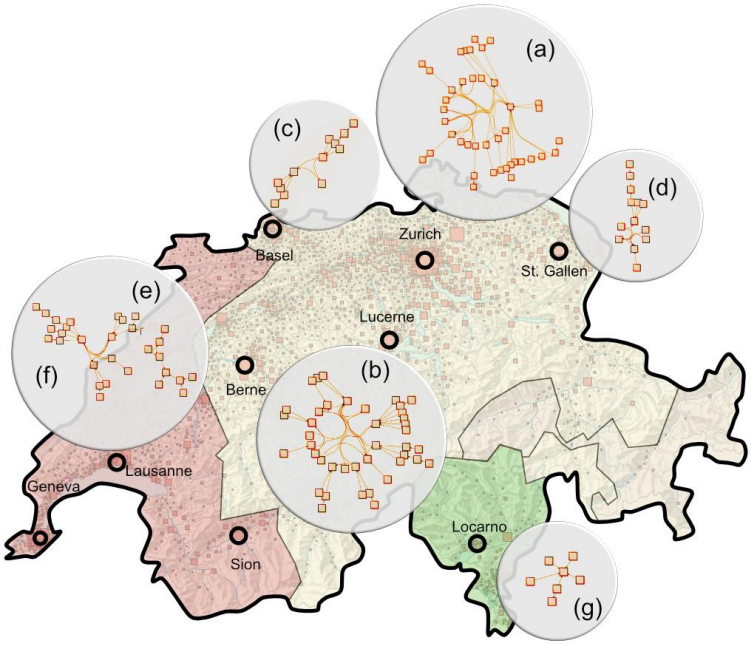


Figure 3: Partitions of the Collaboration Network in the geographic context

Color code indicates language regions: German (beige), French (red) and Italian (green). Population density is indicated by size of the township.

Main network partitions: (a) Zurich, (b) Bern-Lucerne, (c) Basel, (f) Geneva-Lausanne.

Sub-nets: (d) St. Gallen, (e) Lausanne, (g) Ticino.

The graph also reflects differences in the interactions regarding affiliation, e.g., public, or private hospitals. Likewise, patterns of business constraints such as policies which set forth the rules of engaging with internal vs external NGS service providers can be seen.

For instance, the two closely located Swiss Romande partitions (e) and (f) are not connected. The likely reason being that (e) consists of private sector sites, whereas partition (f) represents the Geneva – Lausanne – Sion public sector collaboration network.

This pattern indicates that public and private sector NGS requests are dealt with separately. The general picture, however, does not show such clear separation. It even seems that collaboration and interaction between the two sectors are on the rise.

The St. Gallen partition (d) appears to be disconnected from the Swiss collaboration network. The underlying evidence for a connection at least into the Zurich partition is not sufficient; hence it was omitted.

3.3 The Swiss reimbursement policy

Swiss health expenditures in 2019 measured as share of Gross Domestic Product (GDP) were as high as 11.3%, following the US and Germany with 16.8% and 11.7% GDP, respectively. The average for the 38 countries included in the Organization for Economic Co-Operation and Development (OECD38) was 9.8% GDP for that year. Regarding the number of practicing doctors per 1000 citizens, Switzerland and Germany are par, Greece (6.1), Austria and Portugal (both at 5.3) were ahead of the curve. OECD38 average was 3.6 doctors per 1000 population (OECD, 2021).

In 2021, medical care services were provisioned in 276 hospitals (104 general hospitals and 172 specialized clinics, e.g., psychiatric, rehabilitation and others) with a total capacity of 37845 beds. The density of 52.3 hospitals per million citizens in Switzerland compares well with 51.4 hospitals per million in France but is much higher than, for instance, in Italy or in the Netherlands (23.2 and 13.1 per million citizens).

The Swiss Federal Office of Public Health (FOPH) is responsible for the coordination of health policy. Among other tasks, it supervises compulsory health insurance and is involved in the pricing and reimbursement of medical treatments and products (Kunzler et al., 2022).

Depending on the individual insurance model, the patient can either choose the practitioner or must follow a prescribed procedure. In Switzerland, there are two different reimbursement pathway options i.e., ambulatory (outpatient tariff structure) or stationary (inpatient tariff structure). The NGS analysis for outpatients is reimbursed via the ambulatory pathway, which is based on the so-called TARMED tariff structure, a uniform tariff for outpatient services throughout Switzerland (BAG, 2022). For stationary patients Swiss Diagnosis Related Groups (DRG) tariff structure is being used throughout Switzerland. The actual reimbursement

(service-related flat rate tariff) per "case group" results from multiplying item-associated "cost weight" with a "base rate". Since NGS testing is one item in a specific case group, cost constraints need to be considered when selecting e.g. large versus small gene panels.

The first TARMED version was introduced in 2004. Since an agreement on a complete revision of the TARMED tariff in the past years could not be achieved, the Swiss Medical Association FMH and the insurance association Curafutura submitted a first version of a new tariff revision project in July 2019, called TARDOC tariff structure, for approval by the FOPH. Although the Federal Council has not yet approved the proposed changes, a new version should be published by the end of 2023. Thus, TARDOC is expected to replace TARMED (BAG, 2022).

3.4 Potential challenges associated to NGS testing

NGS testing in oncology is an accepted step in the cancer pathway and has been recommended for some cancer types by published guidelines (Horgan et al., 2022; Mosele et al., 2020; Stoll et al., 2021). One might ask to perform multigene NGS testing with the majority of diagnosed cancer patients or be tempted to apply it at early stages of the disease. The ESMO Precision Medicine Working Group puts forward words of caution to when and where NGS testing is indicated (Mosele et al., 2020). First, the outcome must be actionable in clinical practice and for the patient's benefit. Simply knowing an alteration in a gene sequence is not sufficient and may lead to false expectations and increased cost. The ESMO Scale for Clinical Actionability, for instance, ranks the match between a drug and a genetic alteration according to its actionability (Mateo et al., 2018).

A couple of initiatives exist to support MTBs with automated report generation and interpretation of the NGS testing outcomes and its implications. Thus, in 2018, a collaboration of the Clinical Bioinformatics Unit of Eidgenössische Technische Hochschule (ETH) Zurich NEXUS and the University Hospitals Zurich and Basel, introduced the first comprehensive high-throughput sequencing based molecular profiling workflow in Swiss clinics (Singer et al., 2018). MTPpilot is one example of how MTBs can be supported in their meeting and decision-making process. MTPpilot was developed in close collaboration with clinicians, oncologists, and pathologists (Kahraman et al., 2022).

4 Conclusions and identified themes

Patient access

- NGS testing for diagnosis and treatment is accessible throughout Switzerland and covered by the medical service catalog

Initially, we believed that accessing NGS testing in Switzerland would be difficult and limited. However, our research revealed otherwise. Firstly, the NGS testing network is available throughout Switzerland, implying that the testing is accessible across the country.

Secondly, and more importantly, several interviewees stated that NGS testing is covered by the medical service catalog. Unlike other countries where access to new technologies like NGS testing may be restricted due to cost, this is not the case in Switzerland.

Also, most of the cost is attributed to the treatment rather than diagnostic. For instance, for non-small cell lung cancer (NSCLC) only 13% of the total treatment cost accounts for the diagnosis (both, NGS or single gene testing), whereas 87% are attributed to the therapy cost (Zou et al., 2022).

The question is not whether NGS testing is reimbursed, but rather whether NGS testing, and the subsequent therapy are reimbursed. Hence, the access to innovative therapies is linked to the availability of high-quality biomarker tests, such as multigene NGS testing.

A recent comparison showed a wide variety in the uptake of multigene NGS testing between the 27 European Union countries plus the UK (Normanno et al., 2022). Equally the access to EMA approved precision medicines (36 EMA approved medicines for the treatment of NSCLC) is limited in many of the investigated countries. Switzerland belongs to the group of leading countries in Europe given the general availability of NGS testing and the reimbursement of oncology therapies (Reimbursement of 33 out of the 36 EMA approved medicines).

Need for data comparability

- Comparability of data across laboratories is desirable but not always possible
- Country wide quality assurance schemes are recommended

The assessment of NGS testing is governed by country-specific legislation and regulatory models (e.g., instruments, reagents, kits) to ensure valid and safe test procedures. One of the challenges with NGS testing concerns the variability of technical parameters applied to the pre-processing laboratory procedures (e.g., sample preparation, sample handling, depth of sequencing). These essential factors, combined under the term of *analytical validity*, determine testing accuracy and robustness (Mosele et al., 2020). It has been stated during interviews that comparability of data across laboratories is highly desired but not always possible.

As the study focus has been on the elucidation of the oncology collaboration network and not on test quality, we consider these comments with caution. However, the situation about data quality compares with what has been described for the 27 European Union countries plus the UK. Recommendations for NGS improvement were put forward such as ESCAT level I recommendations regarding actionability of treatment options, participation in external quality assurance programs, or reporting standards (Mosele et al., 2020; Normanno et al., 2022; Radke et al., 2020).

Community building

- Need for continuous education of stakeholders
- Establish an intellectual network on top of commercially driven collaborations

One of the main objectives of this report was to better understand the collaboration models in cancer patient care. The proposed network is described following the patient journey when a request for NGS testing is made. Therefore, while we could say that the network is primarily commercially driven, our interviewees acknowledged the need of building an *intellectual network* on top, meaning a community with educational and informative purposes where the exchange of ideas and thoughts would meaningfully contribute to foster progress and

professional relationships intra- and inter-regions. The need for continuous education of all stakeholders matters. This is in fact in line with one of the outcomes and short-term recommendations which were put forward in the report of the public private Initiative, namely the importance of education and training (*Unlocking the Potential of Precision Medicine in Europe*, 2021).

Future directions

- Comprehensive genomic profiling opens treatment options early in the disease
- Demand from the clinics and patients is increasing
- Swiss hospitals are investing in building NGS

Our findings provide further evidence that the use of NGS in clinical oncology is now widely accepted. Although NGS testing can be used in the context of different diseases (e.g., cardiovascular diseases), NGS testing is considered a valuable method for accurately exploring the molecular underpinnings of individual tumors. As NGS testing opens possibilities for extensive cancer profiling, more oncologists will gain the diagnostic insights to make better treatment decisions for patients.

As the field progresses, the number of valid biomarkers and actionable recommendations are increasing. Yet, as a general rule, molecular testing is ordered when it may impact clinical management and, in many cases, NGS is only done after failure of several lines of treatment. One clinically relevant theme that emerged from our interviews with experts in the field relates to the potential benefits that NGS testing may have when ordered early in the patient's journey. In fact, for some patients earlier NGS testing may open additional therapy options early in the disease, which, in turn, could have a positive impact on survival. Furthermore, cancer is a heterogeneous disease with unique genomic features that differ between individual patients and even among individual tumor regions. The tumor mutation heterogeneity contributes to the generation of different cell populations during tumor development and progression and may help explain therapeutic failure in some patients. Therefore, in cancer patient care, multiple gene mutations should be monitored in the follow-up.

NGS based genome testing is predicted to replace the different combinations of single gene tests (Vanderpoel et al., 2022; Zou et al., 2022). It is the comprehensiveness of NGS readouts, the simultaneous analysis of thousands of genes (mutations, rearrangements, amplifications) and the reduction of re-biopsies which subsequently leads to a better evaluation of treatment options for patients living with cancer. For example, in Europe, less than 10% of tissue specimens from NSCLC patients requiring the molecular testing are currently analyzed with NGS (Normanno et al., 2022). The authors also report that in many European countries a fraction of 50% NSCLC cases is currently subject to NGS testing at time of diagnosis – this number being consistent with numbers from community hospitals in UK and being confirmed by a global survey on molecular profiling in lung cancer (Smeltzer et al., 2020). We can assume that the corresponding Swiss numbers are in a similar range, presenting room for improvement.

Closing remarks

During this market research we learned a lot about the heterogeneity of the Swiss NGS market and collaboration network, caused by multiple factors, for example cantonal set-up being one of them. So did we learn about the complexity of NGS testing in clinical oncology and the sometimes-simplified view on the matter.

We also strongly believe that this technology together with targeted therapies will be both, beneficial for patients and cost-effective.

5 About Inovigate

5.1 Inovigate

Inovigate is an independent strategy and management consulting company operating in the European Life Science and Healthcare industry, specialized in helping clients to innovate and navigate through an increasingly complex health ecosystem. We strive to achieve better outcomes for our clients by utilizing our deep sector knowledge and experience.

At Inovigate we value the diversity and talents of individuals and how they contribute to the capabilities of our team. We bring our passion and enthusiasm to reap the benefits of every project for our clients, our company, and our team.

We believe that our approach of working closely with the clients' management team creates value for both our clients and us. To that end we embed ourselves in the client organization to become part of the day-to-day interactions on every project we do.

Our experience gained through our many strategy and transformation projects allows us to consolidate multiple methodologies and tools into a unique Inovigate approach that is tailored to the specific client need. Our focus is on actionable outcomes and results that can be implemented immediately.

In our client engagements we also utilize a network of experts and partners with complementary skills. This helps us to mobilize the right team for every single engagement. Our network includes thought leaders, key opinion leaders and other experts from different fields within the health ecosystem.

For more information, please visit our website at https://www.inovigate.com.

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