White Paper

Accelerating Patient Access to Precision Oncology in Asia-Pacific

SIRINTHIP PETCHARAPIRUCH, MSc, Principal, Real World Solutions, IQVIA Asia-Pacific
JUNICE NG, PhD, Consultant, Real World Solutions, IQVIA Asia-Pacific
EEMIN TAN, PhD, Associate Consultant, Real World Solutions, IQVIA, Asia-Pacific

Commissioned by:

Roche

Table of contents

Glossary

Biomarker: A biological molecule found in blood, and other body fluids or tissues, that is an indicator of a normal or abnormal process or of a condition or disease. A biomarker may be used to gauge how well an individual's body responds to treatment for a disease or condition. Also known as molecular marker or signature molecule.

Circulating tumor DNA (ctDNA): Cell-free DNA released by tumor cells and found in the bloodstream. The analysis of ctDNA is known as liquid biopsy.

Comprehensive genomic profiling (CGP): Comprehensive genomic profiling is a next-generation sequencing approach, able to detect both novel and known variants, including all classes of genomic alterations (base substitutions, insertions and deletions, copy number alterations and rearrangements) and genomic signatures (such as tumor mutational burden [TMB] or blood TMB, microsatellite instability and loss of heterozygosity), to provide prognostic, diagnostic and predictive insights that inform treatment decisions for individual patients across all cancer types.

Gene alteration: A mutation that occurs when a DNA sequence is changed in such a way as to alter the genetic message carried by that gene.

Health technology assessment (HTA): A multidisciplinary process that uses explicit methods to determine the value of health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient and high-quality healthcare system.

Microsatellite instability: A genomic alteration in which microsatellites, or short nucleotide repeats, accumulate mutations corresponding to deletions or insertions of a few nucleotides.

Molecular profiling: A form of testing that classifies tumors based on genetic make-up to help diagnose and treat cancer. Also called "tumor genomic profiling."

Multiple-criteria decision analysis (MCDA): A decision-making analysis that evaluates multiple criteria as part of the decision-making process.

Next-generation sequencing (NGS): Deep, high-throughput, in-parallel DNA sequencing technologies that allow for massively parallel analysis of multiple samples at much-reduced cost.

Precision oncology: An emerging approach for cancer treatment and prevention that uses molecular profiling of tumors to identify targetable genomic alterations.

Public-private partnership: A long-term contract between a private party and a government entity for providing a public asset or service in which the private party bears significant risk and management responsibility, and remuneration is linked to performance.[1]

Real-world data (RWD): Data relating to patient health status and/or the delivery of healthcare services that is routinely collected from a variety of sources, such as electronic health records or claims and billing databases.

Real-world evidence (RWE): Clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD.[2]

Risk-sharing agreement (RSA): Arrangements between firms and healthcare payers that allow for coverage of new medicines while managing uncertainty around their financial impact or performance.

Tumor-agnostic therapy (TAT): Genomically-informed treatment strategy that enriches for novel targets regardless of histological origin.

Tumor mutational burden (TMB): A measure of the number of somatic mutations present in a tumor and is an emerging clinical biomarker associated with response to immunotherapy.

Abbreviations

CGP:	Comprehensive genomic profiling
ctDNA:	Circulating tumor DNA
HTA:	Health technology assessment
MCDA:	Multiple-criteria decision analysis
MSI:	Microsatellite instability
NGS:	Next-generation sequencing
PM:	Precision medicine
QALY:	Quality-adjusted life year
RCT:	Randomized controlled trial
RSA:	Risk-sharing agreement
RWD:	Real-world data
RWE:	Real-world evidence
TAT:	Tumor-agnostic therapy
TMB:	Tumor mutational burden

[1] World Bank Group Public Private Partnership Legal Resource Center. What are Public Private Partnerships? Available at: https://ppp.worldbank.org/public-private-partnership/overview/what-are-public-private-partnerships#:~:text=The%20PPP%20Knowledge%20Lab%20defines,remuneration%20is%20linked%20to%20performance%22.

[2] U.S. Food and Drug Administration. Real-World Evidence. Available at: https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence

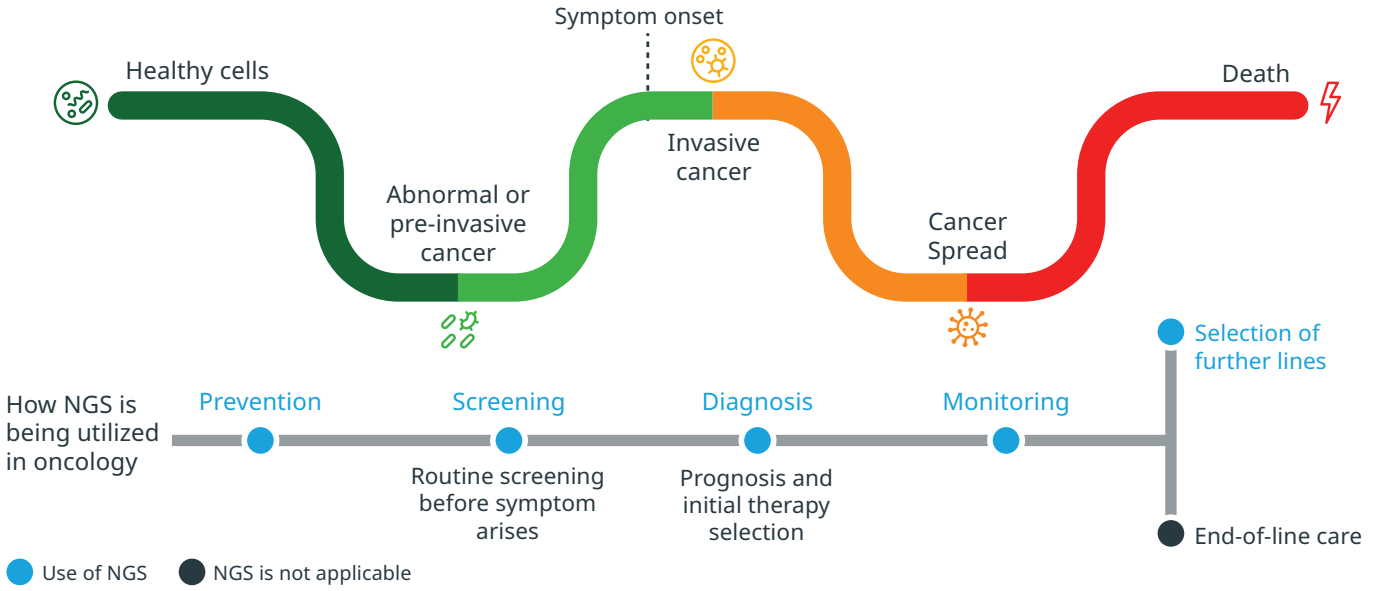
Introduction

A growing knowledge of human genetics has revolutionized cancer diagnosis and treatment over the past decade. By allowing for the characterization of patients at the genomic level, precision oncology ensures that each patient gets the right treatment at the right time.[1] However, challenges to the growth and uptake of precision oncology are cropping up, ranging from health technology assessment (HTA) and reimbursement of precision oncology to clinical and data infrastructure. On the other hand, these challenges could also be a boon for precision oncology if the right strategies are at play. This paper aims to assess the adoption of precision oncology in Asia-Pacific (APAC), delving into comprehensive genomic profiling (CGP) and tumor-agnostic therapies (TAT) as prime examples of diagnostic and treatment innovations that drive the shift towards precision oncology. This paper also highlights the challenges faced in various stages of the precision oncology initiative and proposes potential solutions for sustainable access to precision oncology in APAC.

Advances in Diagnostics – Moving from Single Biomarkers to CGP

Powered by Next-Generation Sequencing (NGS) technology, there has been a shift from evaluating single biomarkers, that is the measurement of single analytes such as DNA, RNA, proteins or metabolites to guide the use of single class of therapy, to hotspot panels that assess for identified gene alterations correlated with effective targeted therapy, and CGP.[2] Unlike conventional testing, CGP uses NGS to rapidly and broadly detect all classes of genomic alterations (base substitutions, insertions and deletions, copy number alterations and rearrangements) and genomic signatures (such as tumor mutational burden or blood TMB, microsatellite instability and loss of heterozygosity) across the genome. It can also simultaneously assess all established and exploratory biomarkers with targeted agents in clinical trials, including single variants and complex signatures, such as microsatellite instability (MSI) and tumor mutational burden (TMB).[3, 4] By providing more comprehensive molecular insights, CGP enables better-informed treatment decisions. While current clinical guidelines, including those from the European Society for Medical Oncology (ESMO)[5] and the National Comprehensive Cancer Network (NCCN),[6] recommend the use of NGS-based assays to determine mutations in a tissue sample of the tumor mainly for therapy selection in late-stage cancer, the field of circulating tumor DNA (ctDNA) analysis is also evolving quickly to address needs along the whole patient journey,[7] as illustrated in *Figure 1*. Genomic profiling should ideally occur as early as possible in a patient's cancer treatment journey to allow doctors to explore the greatest number of available and appropriate treatment options before the cancer progresses.

Figure 1: Use of next-generation sequencing (NGS) in a cancer patient journey



Source: World Health Organization. (2017). Guide to cancer early diagnosis. World Health Organization. https://apps.who.int/iris/handle/10665/254500.

Advances in Treatment – From Histology-Dependent Drugs to Tumor-Agnostic Therapies

The advent of powerful NGS technologies has led to the discovery of tumors with rare genomic signatures across diverse cancer types, making each patient's cancer unique. This has ushered in the development and approval of tumor-agnostic therapies, that is, treatments selected based on the specific variants identified that are agnostic to the tissue of origin.[8] These therapies have transformed the outlook for several deadly cancers that harbor specific molecular alterations, including non-small cell lung cancer, renal cell carcinoma and colorectal cancer.[9] The number of approved TATs is on the rise and could become a major pillar for oncology treatment.[10]

Benefits of Precision Oncology to Patient and Healthcare System

The potential benefits of precision oncology extend beyond direct patient outcomes to healthcare systems with societal and economic impacts.

BENEFITS TO PATIENTS

Cancers are heterogeneous in nature, and tumors that share the same tissue of origin or histology do not necessarily share the same underlying biology. Biomarker-based selection of targeted treatment improves patient outcomes by identifying and treating patients based on their likelihood to respond to existing targeted therapies. Early molecular profiling can select drug candidates with an optimal efficacy and safety profile in the face of a disease with fewer or no standard treatment options.[11] By identifying targetable mutations, these novel technologies also uncover treatment options for patients in underserved disease areas like rare cancers.[12]

BENEFITS TO HEALTHCARE SYSTEM AND BEYOND

The healthcare system will transition from one that is predominantly reactive, treating the sick, to one that is also predictive, preserving the health of individuals. The diagnostic accuracy of precision oncology can improve patient care, as it reduces the possibilities of variations in diagnoses performed by multiple care providers. The use of CGP helps to cut back on unnecessary or repeated testing, allowing clinicians more time to dedicate to other aspects of patient care, such as communicating with patients and ensuring treatment effectiveness and safety.[13]

By informing the use of more effective treatments, precision oncology also allows for more efficient use of healthcare resources, both by reducing the number of emergency room visits and hospitalizations and through allocation of resources to the target population in need.[14] Outside direct health benefits, precision oncology technologies can also enhance the health economy through increased clinical trial activity and medical research. Extensive data collection and analysis enable the healthcare system to continually learn and develop.

Opportunities and Challenges for Precision Oncology in APAC

Cancer is becoming an increasingly important health problem in the APAC region because of aging populations and lifestyle changes associated with economic development and epidemiologic transition.[15] Various governments have recognized the potential of precision oncology and have created specific initiatives to drive it. These initiatives include establishing platforms, such as the Korean Cancer Precision Medicine Diagnosis and Treatment Enterprise (K-MASTER) in South Korea and a nationwide lung cancer genomic screening project (LC-SCRUM) in Japan.

Consisting of a mix of mature and emerging markets, APAC's healthcare systems and development are uniquely diverse. The uptake of precision oncology across APAC remains uneven due to the presence of differing healthcare systems and other healthcare priorities, such as emerging infectious diseases. Besides some developed markets like South Korea, Japan and Australia, the adoption of precision oncology in most APAC markets' remains low due to low awareness and the absence of political support and financial investment.[16]

Outside direct health benefits, precision oncology technologies can also enhance the health economy through increased clinical trial activity and medical research.

While advances in precision oncology create new paradigms in cancer care, they also pose additional layers of complexity, especially when it comes to value assessment. The traditional HTA framework was set up to evaluate single biomarkers or single drugs with specific indications based on tumor types. Innovative technologies such as CGP and TAT present new challenges to the traditional value assessment frameworks.[17] For example, the conventional model of HTA evaluation tethers the cost of a diagnostic to the clinical and economic value of a specific treatment. The challenge arises on apportioning the costs of CGP to one specific treatment when CGP examines multiple genes simultaneously, producing multiple results, leading to differential treatment options, each with distinct short- and long-term clinical and economic trajectories. Additional complexity comes from the evolving value over time as CGP panels change with the addition of new biomarkers, as well as with the availability of new and better drugs. There are several noteworthy challenges in the evidence development for drugs targeting rare mutations. While basket trial is an innovative study design that is particularly useful in the evaluation of rare diseases, this study design comes with its own set of challenges, such as the heterogeneity of the patient population, lack of comparators, small patient cohorts and reliance on surrogate outcome measures. These pose additional barriers, as they make it difficult to perform traditional HTA and predict long-term outcomes with reliability.

Given these opportunities and challenges, there is a clear need for healthcare systems to evolve to accelerate the adoption of and broaden opportunities for precision oncology to materialize our markets' visions.

Methods

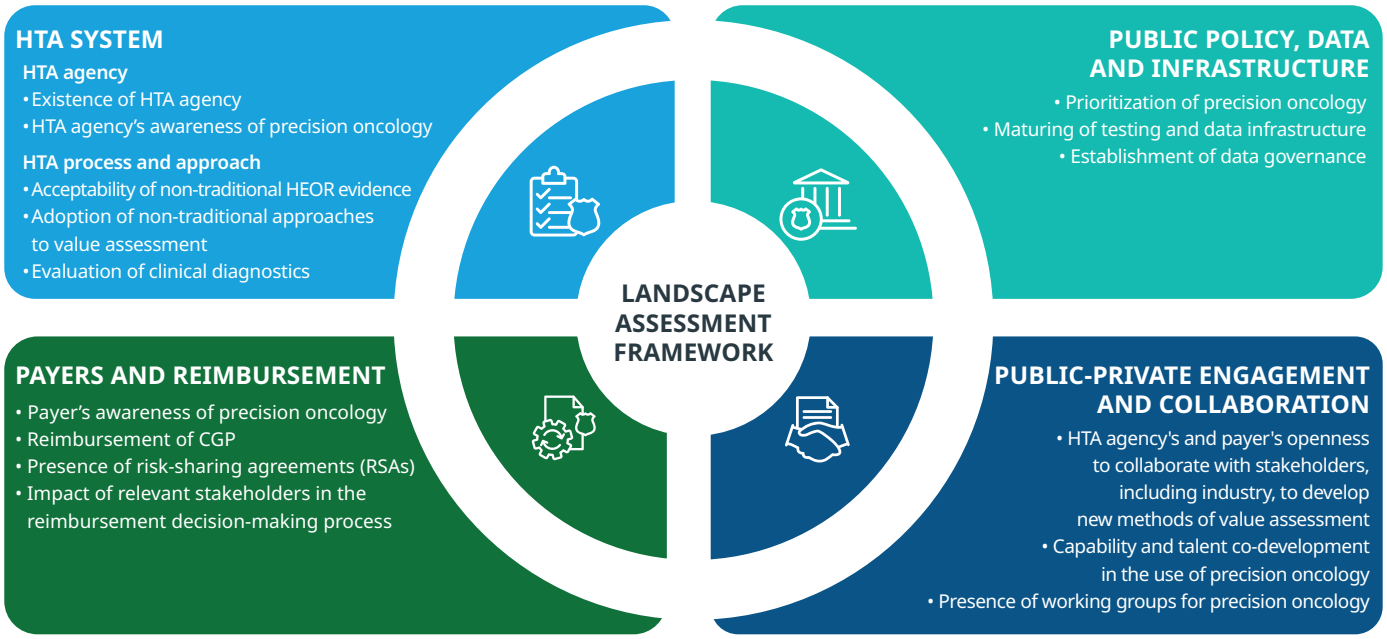
A literature review of peer-reviewed publications, grey literature, such as government reports and policy statements, and white papers which examined the adoption of precision oncology was conducted. Based on the findings from the pertinent literature, a landscape assessment framework was developed. An advisory panel comprising medical oncologists, HTA experts and health economists validated this framework. These domains include HTA agency and payers, HTA process and approach, reimbursement and pricing, public-private engagement and collaboration, and public policy data and infrastructure.

The five domains are composed of several subdomains that are represented at three levels of increasing comprehensiveness or maturity as shown in *Appendix 1*. The subdomains are detailed in *Figure 2*.

A set of interviews with external stakeholders was undertaken to validate market evaluation and recommendations to complement the literature review. Eighteen interviews with medical oncologists and HTA or health economic experts from six markets (China, Australia, South Korea, Taiwan, Malaysia and Thailand) were conducted from July to August 2020. More details on the methodology can be found in *Appendix 2*.

A set of interviews with external stakeholders was undertaken to validate market evaluation and recommendations to complement the literature review. Eighteen interviews with medical oncologists and HTA or health economic experts from six markets (China, Australia, South Korea, Taiwan, Malaysia and Thailand)

Figure 2: Subdomains of Landscape assessment framework



Our Findings and Recommendations

Archetypes and their Description

In applying our landscape assessment framework, we found varied levels of access and adoption of precision oncology, particularly CGP and TAT, in APAC. Rather than over-simplifying and depicting all the markets in unity, we characterized them into three main archetypes — Initializing, Defining and Innovating — with each archetype further along the scale of progressiveness, as shown in *Figure 3*.

THE INITIALIZING ARCHETYPE

The **initializing archetype** is characterized by markets such as China that are embarking on and formalizing their access approach for precision oncology.

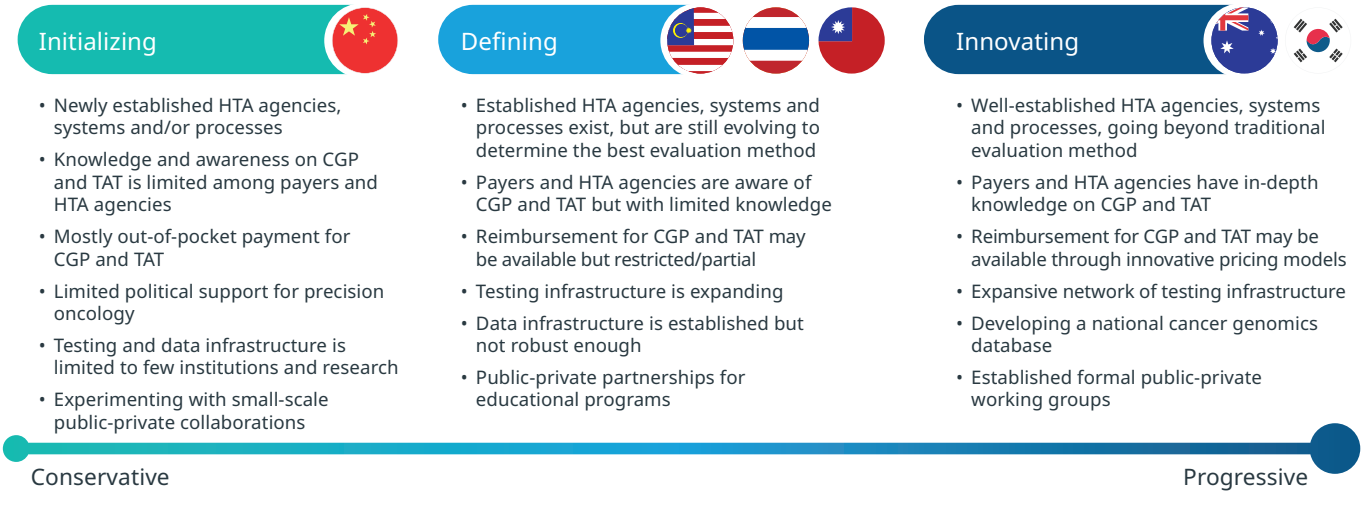
HTA system: As the HTA bodies and relevant systems in this archetype are still in the developmental state, HTA processes are not yet systematically incorporated into healthcare decision making and, if implemented, are focused on evaluating drugs. For instance, the China National Health Development Research Center has been leading the development of HTA in China since 2008. However, standardized methods and processes for HTA are still being refined.[18]

Payers and reimbursement: In this archetype, evaluation of the diagnostics, irrespective of the evaluation methods, is not yet put in place and is still not required for reimbursement decisions. This could intensify the access challenges to precision oncology.

Government support and infrastructure: Limited political support to drive precision oncology in the initializing archetype is evidenced by the unsophisticated healthcare policies and the relatively low financial investments to build the testing and data infrastructure necessary for precision oncology. Coupled with modest awareness of CGP and TAT in these markets, the paucity of testing capabilities leads to a corresponding low uptake of CGP in both specialized and tertiary hospitals. The launch of the Precision Medicine Initiative in China in 2016 has surely but slowly built awareness of CGP and TAT among the HTA body and payers. However, the availability and use of CGP in China remain privy to a few leading institutions, mainly for research or clinical trials.

Public-private engagement: Payers and other public stakeholders of precision oncology prefer an organic approach to designing and customizing its system in accordance with increasing demand, while small-scale collaborations between stakeholders to drive precision oncology adoption in these markets are still being experimented with.

Figure 3: Landscape assessment of oncology-focused PM in selected APAC markets



THE DEFINING ARCHETYPE

Markets in the **defining archetype**, such as Malaysia, Thailand and Taiwan, are in the process of establishing and refining the precision oncology strategy most appropriate to the market priorities.

HTA system: Markets in the defining archetype have established HTA bodies; however, formal HTA processes specific to precision oncology are not yet in place, such as those in Malaysia and Thailand.[16] Due to the limited utility of CGP and TAT in clinical settings, payers and HTA agencies are still building their understanding around these innovative health technologies and their potential benefits to patients, thus the inadequate support for evaluating precision oncology beyond using traditional evidence from randomized clinical trials (RCTs). Such is the case in Taiwan, where formal evaluation of novel technologies is available but a preference for traditional forms of evidence dominates.

Payers and reimbursement: In the defining archetype, payers have limited knowledge of CGP and partial or full reimbursement for CGP is unavailable or limited.

Government support and infrastructure: Despite collaborative efforts among research and clinical institutions to enhance the development of precision oncology, competing healthcare priorities that overshadow the precision oncology endeavor in the market may also dampen industry initiatives aimed at increasing the adoption of CGP and TAT, or at expanding testing and data infrastructure. For example, CGP for clinical applications is only available at select leading tertiary hospitals in Thailand and Malaysia. The data sharing and governance frameworks in the defining archetype tend to allow for genomic data sharing solely for academic research purposes. Data infrastructure available in this archetype is established but not sufficiently extensive yet to enable robust evidence generation. The Taiwan Biobank, for example, has an established genomic database. Nonetheless, genomic data has yet to be linked with other health and phenotypical data in the electronic medical records due to data privacy concerns, and efforts are currently being pursued to develop a governance framework to support the convergence of these databases in Taiwan.[19]

Public-private engagement: Markets in the defining archetype have collaborations between the public and private healthcare sectors to co-develop educational programs that are delivered to a targeted group of specialists, as opposed to being instituted as part of medical training. Formal working groups are still exclusive to academic and scientific institutes, such as the Task Force on The Precision Medicine Initiative for Malaysia, spearheaded by the Academy of Sciences Malaysia to provide strategic recommendations to the government.[20]

THE INNOVATING ARCHETYPE

In the **innovating archetype**, markets such as Australia and South Korea are constantly improving and refining their frameworks for access to precision oncology.

HTA system: These markets have established HTA agencies and processes that seek to go beyond traditional evaluation methods. Nonetheless, there remains the methodological challenge of apportioning the costs of CGP to one specific treatment, given that genomic testing can be used to inform a multitude of management strategies. For example, including the cost of CGP in the economic evaluations of a TAT may significantly impact its cost effectiveness. Therefore, a novel therapy may be "penalized" for innovation, despite spillover effects from genomic testing that informs multiple subsequent therapies. While this challenge may not be unique to the innovating archetype, markets within this archetype are better poised with the technological know-how to direct efforts progressively at going beyond existing methodologies and fine-tuning evaluation strategies appropriate for their healthcare landscape.

Payers and reimbursement: Payers and HTA agencies in this archetype have in-depth knowledge of CGP and TAT and acknowledge the need to explore reimbursement for precision oncology through innovative pricing models, such as risk-sharing agreements (RSAs).

Government support and infrastructure: There is strong government support for precision oncology in these markets, demonstrated by its provision of most of the funds for initiatives related to the development of precision medicine in the market. These markets also have an expansive network of testing infrastructure available. Genomic and clinical data is typically stored within each hospital's database but a central data repository has yet to be constructed to coalesce these data sources, a key step crucial to studying and understanding population health. K-MASTER, operated by Korea University, received 70 million funding from the South Korean government to support three key goals in precision oncology over 5 years.[21] Specifically, these goals are genomic sequencing of cancers, clinical trials for South Korean cancer patients and the development of a cancer genomics database. Beyond championing precision oncology initiatives in South Korea, there are also global collaborations with renowned research organizations, such as the American Association for Cancer Research and the Dana-Farber Cancer Institute, to share the genomic profiling data and advance the development of diagnostic technologies and treatments.

Public-private engagement: Markets in this archetype often have established formal working groups, such as the Precision Medicine Expert Working Group in Australia, comprising members from public and private sectors, to further and align their precision medicine initiatives.

Faced with different sets of opportunities and challenges to accessing precision oncology, each archetype could evolve differently but still arrive at the same goal.

Challenges and Recommendations

Faced with different sets of opportunities and challenges to accessing precision oncology, each archetype could evolve differently to arrive at the same goal. In this section, we detail the challenges and provide possible solutions to advance the archetypes to the next level. Across all archetypes, we submit that expansion of access to precision oncology could be enabled through the following five aims:

I. **Building a flexible HTA pathway which acknowledges emerging evidence**

II. **Enabling payment systems to evolve**

III. **Building nationwide testing and data infrastructure for clinical and genomic information**

IV. **Building data governance frameworks to safeguard data privacy, facilitate data sharing and ensure data quality**

V. **Involving relevant stakeholders in the development of precision oncology**

Focusing on the following priorities would help the archetypes reach these aims and ultimately advance to a more progressive model, as summarized in *Figure 4*.

Figure 4: Focusing on key priorities to advance precision oncology by archetype

GOAL	FLEXIBLE HTA PATHWAY THAT ACCOUNTS FOR NUANCES OF PRECISION ONCOLOGY*	EVOLVING PAYMENT SYSTEMS	NATIONWIDE TESTING AND DATA INFRASTRUCTURE WITH GENOMIC INFORMATION	DATA GOVERNANCE FOR REGULATORY COMPLIANCE AND DATA PROTECTION	INVOLVEMENT OF RELEVANT STAKEHOLDERS IN THE DEVELOPMENT OF PRECISION ONCOLOGY
INNOVATING	• Manufacturer seeks advice from HTA in the early development of technology • Recognize measure of values beyond clinical outcomes	• Co-investment model: governments may absorb certain costs for indirect benefits from private sector	• Analyze genomic information for drug development and population health/ Set up population biobanks	• Regulate data privacy and data sharing to allow industry to access	• Bring together stakeholders from each country to promote collaboration in the region
DEFINING	• Evaluate RWE along with clinical trials • Formal consultation session between manufacturer and HTA	• Innovative payment models/ risk-sharing agreements	• Public-private partnership to expand testing infrastructure • Stregthen current data infrastructure to collect genomic evidence	• Regulate data privacy and data for sharing for academic purpose	• Clinical and non-clinical stakeholders discuss how to prioritize precision oncology in national health and research strategies and devise plans to achieve this goal, to make a convincing argument for the state support
INITIALIZING	• Build capacity in HTA • Separate assessment process for diagnostic/device and medicine	• Engage policymakers/ payers with clinical needs/ values and drive policy/ funding support	• Pilot feasibility studies on testing and data infrastructure with top hospitals	• Publish guidelines for data custodians on data sharing and access	• Break the administrative barriers among policymakers, regulatory and HTA agency • Start a small working group to expand use of precision oncology among clinical stakeholders

Public-private partnership

**Assess if HTA is the most appropriate method for CGP*

(I) BUILDING A FLEXIBLE HTA PATHWAY WHICH ACKNOWLEDGES EMERGING EVIDENCE

With the ever-increasing complexity of diseases, the ways in which breakthrough medicines and diagnostic tests are being developed have evolved tremendously. In the era of precision oncology, where a medicine might only work, albeit exceptionally well, in a small proportion of patients, we are faced with technical challenges associated with evidence generation. For instance, clinical trials of drugs that target rare biomarkers often adopt a basket trial design, but its evaluation is still relatively unfamiliar to many HTA agencies in APAC and the methods for assessing conventional drugs are applied to these innovative drugs. This could result in innovative drugs taking much longer to reach patients.[22]

To reduce uncertainty, it is imperative to continue to track these drugs in the real world to collect more evidence. Therefore, it is crucial to build a flexible HTA pathway that allows for the acknowledgment of new evidence demonstrating the value of precision oncology technologies.

As described earlier, the **initializing archetype** is characterized by markets that are still formalizing their HTA framework and are in the early stages of its precision oncology endeavor. As such, markets in this archetype could focus on building their HTA capabilities and enriching their experience with evaluations of treatments and diagnostics. External expert input could be obtained in building an HTA framework that

Recognizing the potential of real-world data (RWD) and RWE in improving timely patient access to new technologies, there is growing interest within the region to establish collaborations among academics and HTA agencies in this area.

would be best suited to its overarching healthcare policies, priorities and strategies. Markets should also explore the development of a distinct reimbursement pathway for diagnostics or adapt existing pathways that acknowledge and account for the differences between diagnostics and drugs.[23] Evaluation approaches, such as Multiple-criteria decision analysis (MCDA), have been implemented alongside HTA in certain markets.

In the **defining archetype**, markets are in the process of establishing their precision oncology strategy. Hence, formal consultation sessions and open communication between different stakeholders will help to facilitate feedback and refine the existing framework. An ideal framework recognizes the challenges in evidence development for innovative technologies and allows for flexibility in evidence requirements. Evidence requirements for traditional HTAs are still largely dependent on results from RCTs and there is a relative lack of acceptance of non-traditional evidence, such as real-world evidence (RWE). Nonetheless, in many diseases with high unmet needs, such as rare cancers or cancers with rare mutations, it is not always feasible to generate RCTs with enough statistical power within a reasonable period. For example, the clinical effectiveness of TATs is widely observed through real-world studies as part of its post-authorization surveillance. Hence, such evidence should be critically reviewed as a key marker of its effectiveness to reduce uncertainties associated with the use of these new technologies.

Alignment in evidence requirements between regulatory agencies and HTA bodies could help alleviate challenges related to assessing evidence generated from innovative designs. There is also an opportunity to learn and adapt evidence requirements and assessments from other countries. Recognizing the potential of real-world data (RWD) and RWE in improving timely patient access to new technologies, there is growing interest within the region to establish collaborations among academics and HTA agencies in this area. For instance, the REAL World Data In ASia for HEalth Technology Assessment in Reimbursement (REALISE) working group is currently seeking to develop a framework on the use of RWD/RWE to inform HTA decision-making in Asia.[24]

Markets in the **innovating archetype** are continually improving and refining their frameworks for access to precision oncology. To enable improvements to their frameworks and develop a flexible HTA pathway, markets in this archetype could consider developing and recognizing other reliable and acceptable measures of value beyond clinical outcomes. Adopting and including a wider perspective of value would ensure that the actual benefits of the technology are well-represented and considered. For example, adopting a societal perspective would enable additional components of value, such as productivity, to be considered. Markets should also consider using other health outcome measures in economic evaluations and value assessments of precision oncology. The value of TAT extends beyond the commonly used metric of quality-adjusted life-years (QALY) that do not consider the value of reducing uncertainty and imparting the value of hope.

As the end-users, patients should be involved in the evaluation process of these novel technologies. In Australia, the revised Medical Services Advisory Committee (MSAC) guidelines now incorporate other measures of value that extend beyond the patient to include family, caregivers, the healthcare system and society. The new guidelines allow for qualitative assessment of value measures such as the value of knowing. One way to minimize delay to patient access is by having early discussions on evidence requirements between manufacturers and HTA bodies in the early development of innovative precision oncology technologies and refining the necessary evidence requirements based on feasibility to enable quicker patient access to the relevant genetic tests once regulatory approval is obtained.

EXAMPLE:

The adaptive HTA pathway for drugs focuses on areas of high unmet medical needs by providing earlier access to a novel technology to a smaller group of patients where the benefit-risk balance may be favorable. Clinical trial data could be submitted but is deemed insufficient to make any conclusion. In this case, to maintain the highest standards of benefit-risk assessment, clinical trial data may be supplemented with real-world evidence. Once a positive benefit-risk balance is proven, the access can be expanded to wider patient populations. An adaptive pathway does not lower HTA standards for the evaluation of benefits and risks or the requirement to demonstrate a positive benefit-risk balance.

Although an adaptive HTA pathway has not yet been implemented, steps are taken by the European Union (EU) to realize this potential. The public-private partnership initiative ADAPT-SMART brought together representatives from key European stakeholder groups – regulatory agencies, HTA bodies, pharmaceutical companies, payers, patients and healthcare professionals. This created a platform where the conditions and feasibility of implementing an adaptive pathway within the EU regulatory/legal context could be discussed openly, leading to a better understanding of the issues promoting early access of innovative drugs to patients [25]

Should CGP be subjected to HTA?

The value of CGP is constantly evolving as new biomarkers are uncovered with new prognostic or treatment-related implications. Therefore, current HTA approaches and economic evaluation methods may not fully capture these values and cannot assess the true benefits on population health across multiple cancer types. Across all archetypes, markets should assess whether the existing HTA framework is suitable to address the complexity of multi-biomarker testing with CGP. For example, in the conventional model of HTA evaluation, the cost of a diagnostic test is assessed in conjunction with the clinical and economic value of a specific targeted treatment. However, CGP allows for the simultaneous examination of multiple genes with the potential to inform multiple treatment options in both the short- and long-term. Therefore, a static single-time point evaluation of CGP tethered to a single drug evaluation may not account for the broad and evolving value of multi-biomarker testing enabled by CGP.

EXAMPLE OF ASSESSING THE BENEFITS OF CGP BEYOND COST-EFFECTIVENESS:

CGP is reimbursed in Japan and South Korea for advanced cancer patients. The use of CGP is viewed as a clinical need with potential population and individual health benefits, improving efficiencies in patient-level healthcare, and as an investment for medical research, thus these considerations were prioritized over its cost-effectiveness. This scaled up the usage of CGP, which supported the establishment of the genome information management and system in these markets – a critical step in predicting which patients can effectively be treated with targeted therapies, immunotherapies or TAT and facilitating drug discovery and research.

(II) ENABLING PAYMENT SYSTEMS TO EVOLVE

Changing the value assessment approach for precision oncology technologies should go hand-in-hand with changing the way we pay for value. Given that the value of precision oncology technologies may change with the uncovering of new biomarkers and the availability of newer drugs with better risk-benefit profiles, payment systems will have to evolve with the changing value of multi-biomarker testing. Besides, the value of the drug differs among patients with different indications. The current "one drug, one price" system in most, if not all, markets does not accurately reflect the multi-indication nature of most modern cancer medicines.

For the **initializing archetype**, policymakers and payers could be engaged to drive policy and funding support for precision oncology. In the meantime, mobile-based health savings accounts, low-interest loans and remittances can be used to increase the access and affordability of care for low-to-moderate income populations that might otherwise be difficult to reach. As with any emergent healthcare solution, implementing robust fintech platforms will require extensive research, public-private partnerships and good governance to reach the patients who need them most.

In the **defining archetype**, other than centralized funding and tariff-based approaches, innovative payment models or RSAs could be developed to allow early patient access to precision oncology technologies while acknowledging the uncertainty in clinical benefit of novel treatment or the value of biomarkers due to limited or immature evidence. Conditional coverage with evidence development schemes provides hope and early access to patients with debilitating conditions, especially when no other treatment alternatives are available.

There is a continuous collaboration between the payer/provider and the pharmaceutical industry in the **innovating archetype**. For innovative payment models where guidance may be ambivalent, the archetype could explicitly address them by regulation. Co-investment models may also be developed in the innovating archetypes if the initiative is in line with the government's development plans. If adaptive HTA pathways are adopted, there could also be a need for accompanying adaptive pricing and reimbursement models to accurately reflect drug values for specific indications.

EXAMPLE:

In the U.K., larotrectinib and entrectinib received conditional reimbursement from the National Institute for Health and Care Excellence (NICE) based on the evidence from basket trials. Given its plausible yet uncertain cost-effectiveness, the treatment was financed through a disease-specific fund known as the Cancer Drugs Fund (CDF).[26] The CDF provides a conditional reimbursement pathway, which is critical in enabling early patient access while providing the opportunity to collect further data in clinical practice.

In terms of testing infrastructure, a percentage of the NGS testing cost would be supported by the manufacturer, with the remainder of the costs covered by the National Health Service (NHS). This co-investment model also helped to accelerate NHS England's developments in genomic testing. In more advanced multi-payer markets such as the U.S., there have also been suggestions for payers to explore novel payment mechanisms, such as subscription-based payment or the "Netflix" business model for precision oncology technologies.

Another instance worth highlighting is the registry established by The Italian Medicines Agency to track drugs under RSA. In this web-based registry, clinicians are required to fill in an online prescription, including patient information, indication and dosages for all dispensed medicines under RSA. Subsequently, they are required to record follow-up clinical data and outcomes. The hospital pharmacist can apply for pay-back to the manufacturer, who can accept or reject the proposal (with the latter requiring arbitration) if a patient meets the non-responder criteria set during contract negotiation.[27]

(III) BUILDING NATIONWIDE TESTING AND DATA INFRASTRUCTURE FOR CLINICAL AND GENOMIC INFORMATION

Developing an extensive genomic testing infrastructure is crucial for enabling access to precision oncology, while a robust data infrastructure that allows for the interlinking of databases will allow researchers and policymakers to have a more comprehensive understanding of community and individual health, to study diseases and novel treatments based on genomic and clinical data and to enable better value assessment through the use of real-world evidence.

Markets in the **initializing archetype** could begin focusing efforts on expanding biomarker testing capabilities, including both single biomarker tests and small panels. Alongside, the use of CGP could be piloted in top-tier hospitals or specialized cancer treatment institutions to evaluate the feasibility of introducing more advanced precision oncology technologies. This archetype can also kickstart their data strategy by evaluating the data infrastructure within a microenvironment before scaling up.

The **defining archetype** should focus on efforts that improve the nation's infrastructure for innovation and enhance its overall competitiveness in medical research. Initiatives aimed at increasing the awareness and adoption of precision oncology beyond clinical stakeholders can be implemented through collaborative education and research activities. CGP testing capabilities can also be expanded across the nation through public-private healthcare sector partnerships for selected tumor types with the highest clinical utility. Clinical and genomic information obtained from CGP testing can be harnessed by establishing a common data infrastructure that facilitates trusted data sharing between institutions and facilities.

Markets in the **innovating archetype** could target to expand CGP testing infrastructure and funding for all advanced cancers. In parallel, population biobanks can be set up and utilized for translational research and drug discovery. This is especially useful for studying population health in APAC, where associations between biomarkers, clinical history and lifestyle information are less known. Members of the innovating archetype could also spearhead registries of rare mutations or cancers in the region to understand the molecular pathology of diseases and their epidemiology better. Additionally, the exchange of data from biobanks and registers at the APAC level can increase the study power to detect genetic variations that exist within its population.

EXAMPLE:

In Japan, LC-SCRUM is the largest cancer genomic screening consortium, covering more than 200 hospitals.[28] This was pioneered by the National Cancer Center for Japan in cooperation with medical institutions and pharmaceutical and medical device manufacturers. This program has also expanded to Taiwan in early 2019. The industry equips the medical institutions with the testing infrastructure and information databases, as well as providing support for clinical operation. Together with pharmaceutical companies, this nationwide screening system also enables the development of targeted therapies.

(IV) BUILDING DATA GOVERNANCE FRAMEWORKS TO SAFEGUARD DATA PRIVACY, FACILITATE DATA SHARING AND ENSURE DATA QUALITY

There is a need to safeguard health data (both genomic and clinical) privacy given the far-reaching implications of genetic information. Moreover, to harness the potential of genomic databases for the development of biomarkers, drugs and other public health information, it is also crucial to facilitate the interoperability and sharing of data across databases while ensuring data quality. Having safeguards in place to protect health data privacy and regulate data sharing will also provide reassurances to the public to facilitate uptake of genetic tests and the building of clinical-genomic databases.

The government of the **initiating archetype** could address the fundamentals of data governance by first discussing the details and publishing guidelines to assist data custodians in making appropriate decisions related to data sharing and access.

The **defining archetype** could regulate the manner and duration in which genomic data is collected, stored and analyzed for government and academic research. They may also stipulate the necessary preventive measures genomic databases must have against unauthorized access and data use. Such data governance frameworks should also be coherent across other sectors. As previously mentioned, the sharing and linkage of data across multiple databases, such as genomic databases or DNA sequence variation databases with clinical data is critical to harness the full potential of precision oncology. Members of the defining archetype could therefore adopt and implement standards to enhance interoperability of health information systems across the country, followed by integration with genomic databases.

Markets in the **innovating archetype** could expand the data privacy and governance frameworks for data sharing with the private sector to drive research and development of novel treatments. Furthermore, guidelines, such as those put forth by the Global Alliance for Genomics and Health [29] or the Data Working Group in the U.K.,[30] could be implemented to ensure effective and responsible integration of genomic data into the clinical space. It should also be noted that since the identification and understanding of genetic variants underlying diseases is continually evolving, measures to protect individuals and families against genetic discrimination will also be needed.

The sharing and linkage of data across multiple databases, such as genomic databases or DNA sequence variation databases with clinical data is critical to harness the full potential of precision oncology.

EXAMPLE:

In Australia, the regulation of genomic data sharing and use is performed through a combination of levers to promote public trust – Australia's Privacy Act (1998) regulates the collection, use and disclosure of genomic data that meets the definition of personal information, while oversight of genomic research, broadly referring to de-identified genomic data, is maintained by the National Health and Medical Research Council through the National Statement for Ethical Conduct in Human Research (updated 2018) that specifies requirements for research with human genomic data.

The Australia Genomics Health Alliance coordinates the national approach to data federation and analysis that includes developing data standards and processes to capture and use clinical and genomic data, a system to share clinical variant classifications and a national genotype-phenotype database. While these databases are currently in development, the Australia Genomics policy on access to the data collected through their clinical flagship projects stipulates that access and secondary use of the data is limited to bona fide researchers and clinicians (whether internal or external to the Australia Genomics collaboration) for research purposes approved by a relevant ethics committee. Further, access and secondary use of the data is subjected to a data access request that is reviewed and approved by the Data Access Committee.[31]

Discrimination based on genetic status is prohibited under the Disability Discrimination Act (1992), except for the use of genetic status by insurers only with actuarially-justified grounds and with stringent requirements on use by employers to screen for susceptibility to work-related conditions.

(V) INVOLVING RELEVANT STAKEHOLDERS IN THE DEVELOPMENT OF PRECISION ONCOLOGY

The precision oncology endeavor is likely to necessitate a multi-stakeholder strategy to coordinate and facilitate the various stages of the strategy and enhance access to precision oncology in the country. The level of commitment of the stakeholders will define the pace of this development – the more driven and focused they are, the more rapid the progress. This advancement could also be aided by adopting public-private partnerships to develop capabilities and infrastructure. The government could tap into industry expertise to deliver and operate pilot or full-scale projects. At the same time, it is also an opportunity to increase innovation for the private sector, e.g., building synergies and uncovering innovative ways to deliver the infrastructure required to meet the outcomes.

Markets in the **initializing archetype** could convene a multi-stakeholder working group to expand the use of precision oncology among clinical stakeholders. By involving policymakers, regulatory and HTA agencies, this working group may also serve as an opportunity to break the administrative barriers among them.

The **defining archetype** could establish a coordinating workgroup that comprises clinical and non-clinical stakeholders to discuss and prioritize the precision oncology strategy in the context of other national health and research strategies and devise plans to achieve this goal.

The **innovating archetype** could take the lead to bring together relevant stakeholders across APAC to open doors for cross-border collaborations and alliances. Such a platform (e.g., workshops or forums) can be used to cross-pollinate ideas and discuss specific action points for spurring development. Existing platforms like HTAsiaLink could also be leveraged to tap current networks of stakeholders.

EXAMPLE:

All Nordic countries have national strategies on personalized medicine.[32] The Joint Committee of the Nordic Medical Research Councils (NOS-M) is a collaborating body aimed at promoting Nordic cooperation in the medical research area. In 2014, it published a white paper to give specific recommendations to advance personalized medicine in the Nordic region. This has been followed by a series of regular workshops and symposiums to unite and align research efforts and map action plans. There are also several ongoing initiatives addressing the sharing of clinical data and big data generated from genomic projects.

Conclusion

The advances in molecular profiling tools coupled with developments in novel cancer therapeutics have led to the era of precision oncology, where the management of cancer is enhanced by the identification of actionable genomic alterations. Additionally, the incorporation of advanced diagnostics, such as CGP, could aid early diagnosis, treatment selection and disease surveillance monitoring, leading to improved patient outcomes and more efficient use of healthcare resources.

Through our interviews with various clinicians, health economists and HTA experts, we found a varied and differentiated landscape of precision oncology in APAC, with different sets of challenges and opportunities within each archetype. Based on the assessment framework, we carved out three archetypes of markets – initializing, defining and innovating. By considering and using the appropriate archetype, strategic initiatives to incorporate precision oncology into the healthcare system can be better tuned from conceptualization, implementation and translation.

Briefly, we propose a few recommendations to spur the development of precision oncology in the APAC region:

- Acclimatizing HTA pathways to new ways of evidence generation, demonstrating the values of precision oncology.
- Developing, testing and fine-tuning alternative and flexible payment systems based on informed judgments to accommodate a changing reimbursement landscape.
- Building nationwide testing and data infrastructure to collect clinical and genomic information is the precursor to understanding population and individual health.
- Establishing a robust data governance framework as an essential safeguard for the public interest.
- Building collaborations among relevant stakeholders to co-create and co-invest new strategies and solutions.

The precision oncology endeavor encompasses innovative technologies that push the frontier of cancer treatment and require concerted development of many facets of the healthcare system to enable access to it. Our research underscores the fact that countries have choices regarding how they position themselves while pursuing new initiatives to advance the use of precision oncology for better patient outcomes in a sustainable manner.

Through our interviews with various clinicians, health economists and HTA experts, we found a varied and differentiated landscape of precision oncology in APAC, with different sets of challenges and opportunities within each archetype. Based on the assessment framework, we carved out three archetypes of markets – initializing, defining and innovating.

References

1. Precision Oncology: Who, How, What, When, and When Not? 2018: American Society of Clinical Oncology Educational Book 37 (160-169).
2. Kamps, R., et al., Next-Generation Sequencing in Oncology: Genetic Diagnosis, Risk Prediction and Cancer Classification. Int J Mol Sci, 2017. 18(2).
3. Chung, J.H., et al., Prospective Comprehensive Genomic Profiling of Primary and Metastatic Prostate Tumors. JCO Precis Oncol, 2019. 3.
4. Fang, W., et al., Comprehensive Genomic Profiling Identifies Novel Genetic Predictors of Response to Anti-PD-(L)1 Therapies in Non-Small Cell Lung Cancer. Clin Cancer Res, 2019. 25(16): p. 5015-5026.
5. Mosele, F., et al., Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group. Ann Oncol, 2020.
6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Non-Small Cell Lung Cancer. Version 3.2019.; Available from: www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.
7. Siravegna, G., et al., How liquid biopsies can change clinical practice in oncology. Ann Oncol, 2019. 30(10): p. 1580-1590.
8. Looney, A.M., Nawaz, K., and Webster, R.M., Tumour-agnostic therapies. Nat Rev Drug Discov, 2020. 19(6): p. 383-384.
9. Lavacchi, D., Roviello, G., and D'Angelo, A. Tumor-Agnostic Treatment for Cancer: When How is Better than Where. Clin Drug Investig, 2020. 40(6): p. 519-527.
10. Naito, Y., et al., Japan society of clinical oncology/Japanese society of medical oncology-led clinical recommendations on the diagnosis and use of tropomyosin receptor kinase inhibitors in adult and pediatric patients with neurotrophic receptor tyrosine kinase fusion-positive advanced solid tumors, cooperated by the Japanese society of pediatric hematology/oncology. Int J Clin Oncol, 2020. 25(3): p. 403-417.
11. Le Tourneau, C., et al., Treatment Algorithms Based on Tumor Molecular Profiling: The Essence of Precision Medicine Trials. J Natl Cancer Inst, 2016. 108(4).
12. Groisberg, R., et al., Clinical Next-Generation Sequencing for Precision Oncology in Rare Cancers. Mol Cancer Ther, 2018. 17(7): p. 1595-1601.
13. Phillips, K.A., et al., Genomic sequencing: assessing the health care system, policy, and big-data implications. Health Aff (Millwood), 2014. 33(7): p. 1246-53.
14. Krzyszczyk, P., et al., The growing role of precision and personalized medicine for cancer treatment. Technology (Singap World Sci), 2018. 6(3-4): p. 79-100.
15. Shin, H.R., Carlos, M.C., and Varghese, C., Cancer control in the Asia Pacific region: current status and concerns. Jpn J Clin Oncol, 2012. 42(10): p. 867-81.
16. Chong, H.Y., Allotey, P.A., and Chaiyakunapruk, N., Current landscape of personalized medicine adoption and implementation in Southeast Asia. BMC Med Genomics, 2018. 11(1): p. 94.
17. Thomas, M., Vora, D., and Schmidt, H., Preparing health systems for tumour-agnostic treatment. 2017, AT Kearney.
18. Wang, H., et al., Driving factors and mode transformation regarding health technology assessment (HTA) in China: Problems and recommendations. Biosci Trends, 2019. 13(2): p. 110-116.
19. Lin, J.C., et al., Taiwan Biobank: making cross-database convergence possible in the Big Data era. Gigascience, 2018. 7(1): p. 1-4.
20. Precision Medicine Initiative for Malaysia [cited 2020 25th November]; Available from: https://www.akademisains.gov.my/studies/sig/precision-medicine/.
21. Building a 10,000-genome cancer database. [cited 2020; Available from: https://www.nature.com/articles/d42473-019-00097-5.
22. Sharpe, E., et al., From patent to patient: analysing access to innovative cancer drugs. Drug Discov Today, 2020. 25(9): p. 1561-1568.
23. Petcharapiruch, S. and Wong, C., The Evolving Health Technology Assessment for Medical Devices and Diagnostics in the Asia Pacific Region and Key Considerations for Value Assessment Frameworks. 2020, IQVIA.
24. Lou, J., et al., Real-world data for health technology assessment for reimbursement decisions in Asia: current landscape and a way forward. Int J Technol Assess Health Care, 2020: p. 1-7.
25. ADAPT-SMART: Accelerated development of appropriate patient therapies: a sustainable, multi-stakeholder approach from research to treatment-outcomes. 2015 [cited 2020 14 December]; Available from: https://www.infographic.adaptsmart.eu/.
26. Cancer patients to benefit from new histology independent treatment. 2020 [cited 2020 27 November]; Available from: https://www.nice.org.uk/news/article/cancer-patients-to-benefit-from-new-histology-independent-treatment.
27. Garattini, L. and Casadei, G., Risk sharing agreements: what lessons from Italy? Int J Technol Assess Health Care, 2011. 27(2): p. 169-72.
28. Kuo, C.-H.S., et al., Initial results of lung cancer genomic screening project for individualized medicine in Asia: LC-SCRUM-Asia. 2019: Annals of Oncology Abstracts Thoracic Tumours, Metastatic Volume 30, Supplement 9, IX174-IX175, .
29. Knoppers, B.M., Framework for responsible sharing of genomic and health-related data. Hugo J, 2014. 8(1): p. 3.
30. Thornton, D.J., 100,000 Whole Genomes Project. 2013, EMBL-European Bioinformatics Institute (EBI): London, United Kingdom.
31. Australian Genomics Policy on Data Access and Sharing for Secondary Use. 2019, Australian Genomics Health Alliance: Australia.
32. Personalised Medicine in the Nordic Countries. NOS-M Report with Conclusions and Recommendations for Joint Actions in Personalised Medicine in the Nordic Countris 2018, Joint Committee of the Nordic Medical Research Councils (NOS-M).

Appendices

Appendix 1: Market mappings based on the landscape assessment framework of oncology-focused personalized medicine

DOMAIN	SUBDOMAIN	LEVEL		
HTA agency and payers	Existence of HTA agency	Does not have dedicated HTA agencies	Newly established HTA agencies	Well-established HTA agencies
	HTA agency's awareness of personalized medicine in oncology	HTA agency is not aware of CGP and TAT	HTA agency is aware of CGP and TAT but with no in-depth knowledge	HTA agency is aware of CGP and TAT with in-depth knowledge
	Payer's awareness of personalized medicine in oncology	Payers are not aware of CGP and TAT	Payers are aware of CGP and TAT but with no in-depth knowledge	Payers are aware of CGP and TAT with in-depth knowledge
HTA process and approach	Acceptability of non-traditional HEOR evidence (basket trials, RWE etc.)	Formal evaluation of novel technologies is still not in-place	Formal evaluation of novel technologies is in place; considers all types of evidence, but still prefer traditional form of evidence	Acceptance of non-traditional evidence and novel methodology in the assessment for novel technologies, with non-preferential consideration of the type of evidence and methodology
	Adoption of non-traditional approaches to value assessment	Strong inclination towards traditional approaches and questions the need for non-traditional approaches	Considers the use of non-traditional approaches, such as MCDA to value assessment	Currently using non-traditional approaches to value assessment
	Evaluation for clinical diagnostics	Formal evaluation for clinical diagnostics is still not in-place	Formal evaluation for clinical diagnostics is being considered or under discussion	Formal evaluation of clinical diagnostics is in place, and methods or processes of HTA or funding pools are different from therapeutics
Reimbursement and pricing	Reimbursement of CGP	Out-of-pocket or covered by private insurance for CGP testing	CGP reimbursement (partial or full) is limited to only a few disease areas or patient groups	CGP reimbursement (partial or full) is available to multiple disease areas, with tiered reimbursement based on severity or staging
	Reimbursement of TAT	Out-of-pocket or covered by private insurance for TAT	Partial reimbursement for TAT for selected indications or patient groups	Full reimbursement for TAT
	Risk-sharing agreements (RSA)	No engagement on innovative pricing models or RSA for novel therapies (i.e. Outcomes based pricing and/or value-based healthcare models)	Clear & communicated engagement of multiple stakeholders (e.g. payers, HCPs and patient advisory groups) to establish innovative pricing models or RSA for novel therapies	Appropriate innovative pricing models or RSA are systematically available for novel therapies
	Impact of relevant stakeholders in the reimbursement decision-making	No mechanism to receive inputs from patients, manufacturers and the clinical community	Mechanism to receive inputs from certain stakeholders is in place, with limited impact on decision-making	Structured mechanism to receive inputs from patients, manufacturers and the clinical community, with significant impact on decision-making

DOMAIN	SUBDOMAIN	LEVEL		
Public-private engagement and collaboration to leverage expertise and support	Payer's openness to collaborate with stakeholders including industry to develop new methods to value assessment	Payer does not recognize the need to collaborate 	Payer is keen to develop new methods, but has limited collaboration to develop new methods of value assessment 	Formal or extensive collaboration to develop new methods of value assessment 
	Capability and talent co-development in the use of PM	No programs in place	Co-develop educational programs that are delivered to targeted groups of specialists 	Co-develop educational programs that are instituted as part of medical training
	Working groups on PM	No formal working groups 	Formal working groups set up, but only limited to academic and scientific institutes 	Formal working groups, comprising members from public and private sectors 
Public policy, data and infrastructure	PM as national health priority	No policy support from government 	PM is a national priority and policies related to PM are in place 	Government provides majority of the funding related to PM and its development 
	Testing infrastructure	CGP is limited to few institutions or research 	Few diagnostic centers but scaling up 	Well-established CGP infrastructure with expansive network 
	Data infrastructure (EMR, registry etc)	Limited electronic data sources available for oncology 	Growing data sources available for oncology (established data sources but without extensive genomic data) 	Established and good quality data sources available for oncology, including biobank 
	Data governance for regulatory compliance and data protection	Current data governance does not provide any room for health data sharing or use 	Data governance provides some room for health data sharing but limited to academic research purposes 	Robust data governance in place that allows industry access and use of ex-markets' high quality health data 

Appendix 2: Methods

PHASE 1: LITERATURE REVIEW

Secondary research was conducted to gain understanding of the HTA landscape in several APAC countries and their readiness to adopt precision oncology. Additionally, we looked into the challenges around adoption of CGP and TAT, the endeavors of conducting economic evaluations for these advanced technologies, and examples of how CGP and TAT from countries around the world are adopted and reimbursed.

PHASE 2: ASSESSMENT FRAMEWORK

Based on the findings from the pertinent literature, an initial landscape assessment framework was developed. The five domains of this framework include (I.) HTA agency and payers, (II.) HTA process and approach, (III.) Reimbursement and pricing, (IV.) Public-private engagement and (V.) Collaboration and public policy data and infrastructure. The five domains are composed of several subdomains that are represented at three levels of increasing comprehensiveness or maturity.

PHASE 3: EXPERT INTERVIEWS

Insights from the search were validated through virtual semi-structured interviews (~60 minutes) conducted with medical oncologists and HTA / health economics experts. At least 1 oncologist and 1 HTA expert each were recruited from Australia, China, South Korea, Taiwan and Thailand. Discussion guides for oncologists and HTA experts were developed surrounding key themes (adoption / value assessment of precision oncology, reimbursement and funding of precision oncology, and future perspective of patient access to precision oncology) to fill any gaps in knowledge from the literature review. Experts were sent the interview guide in advance of the interview, together with a pre-read and a short questionnaire. Experts' informed consent was requested at the start of the interview for their participation, as well as for their permission for the interview to be recorded.

PHASE 4: MAPPING FINDINGS

Based on the experts' responses, the current landscape of precision oncology adoption of these markets was used to refine the framework before mapping their responses onto the framework. Each of the 17 sub-domains carries a score ranging from 1-3. The more advanced the subdomain the higher the score for its corresponding level. For each market, the scores were summed and subsequently categorized into one of the three archetypes based on score cut-offs: Innovating (≥ 40 points), Defining (30 to 39 points) and Initializing (< 30 points). The characteristics of each archetype were explored. Briefly, markets that fall under the initializing archetype hold characteristics such as newly established HTA agencies/systems and processes with limited awareness on CGP and TAT among payers and HTA agencies. CGP and TAT are mostly paid out-of-pocket by patients, and the testing infrastructure is limited to a few healthcare institutions or for research purposes. For markets that belong in the defining and innovating archetypes, the characteristics mentioned above grew increasingly advanced.

PHASE 5: ADVISORY BOARD MEETING

A virtual advisory board meeting was organized with key experts from various backgrounds such as researchers, clinicians and policymakers. Most of the experts were identified from Phase 3 based on their knowledge and experience around the access of precision oncology. One HTA expert from Malaysia was also invited to provide insights. Meeting discussions dove deep into the gaps uncovered during the primary interviews and discerned the appropriate approaches for addressing challenges surrounding precision oncology value assessment in APAC. First, we reviewed the framework mentioned above for CGP and TAT. This was followed by reviewing the level of CGP and TAT adoption within the APAC region. The discussion circled around ways to best assess the values of PM and increase CGP and TAT adoption levels. Lastly, the panel provided practical recommendations on the way forward for sustainable access to precision oncology.

About the Authors

SIRINTHIP PETCHARAPIRUCH, MSC
Principal, Real World Solutions,
IQVIA Asia-Pacific

Sirinthip leads and manages the Health Economics and Outcomes Research (HEOR), Real World Evidence, HTA, and market access business for IQVIA, Asia Pacific with a focus on South East Asia market. With over 12 years of extensive experience in roles generating HEOR and Real World Evidence to support product strategy and HTA submissions, her areas of expertise lie in developing pricing and market access strategies, aligning data to evidence requirements in the HTA market, and usage of Real World Evidence to support health care decision making. Sirinthip is a pharmacist by training and she holds a Master's degree in Healthcare Research from Queen Mary, University of London, and a Postgraduate Certificate in International HTA, Pricing and Reimbursement from the University of Sheffield.

EEMIN TAN, PHD
Associate Consultant, Real World Solutions, IQVIA Asia-Pacific

Eemin is a HEOR associate consultant with IQVIA Real World Solutions team in Asia Pacific. She provides support in HEOR and market access project management and delivery. Eemin has over 7 years of experience in the life sciences and healthcare industries involving drug development, health policy and HEOR. Her expertise lies in stakeholder engagement for market access strategies, observational study design, secondary data analysis and holds ISMPP-certified medical publication professional license. Besides, her area of expertise involves translational medicine (genomics, signaling pathways and small molecule inhibitors). Eemin holds Bachelor's degree in Bioengineering from Queen Mary, University of London and a PhD from Yong Loo Lin School of Medicine, National University of Singapore.

JUNICE NG, PHD
Consultant, Real World Solutions,
IQVIA Asia-Pacific

Junice is a HEOR consultant and epidemiologist with IQVIA Real World Solutions team in Asia-Pacific. She is a subject-matter expert in outcomes research and public health. In her current role, Junice delivers various types of outcomes research studies involving databases and cross-sectional surveys, and is involved from conceptualization to research delivery. She has various publications in peer-reviewed journals. Junice is a pharmacist by training and she holds a PhD, Public Health from the National University of Singapore.

OTHER CONTRIBUTORS

Ariosto Matus, Policy & External Affairs Lead, Asia-Pacific, Roche

Dr.Hang Le, Foundation Medicine Access Lead, Roche

Dr.Dony Patel, Associate Principal, Real World Solutions, IQVIA Asia-Pacific

Callix Wong, Former consultant, Real World Solutions, IQVIA Asia-Pacific

Qi Qing Ng, Analyst, Real World Solutions, IQVIA Asia-Pacific

Prof. David Thomas, Head, Genomic Cancer Medicine, Garvan Institute of Medical Research, Australia

George Papadopoulos, Director & Partner, Lucid Health Consulting, Australia

Prof. Kim Kyu-Pyo, Oncology specialist, Asan Medical Centre, University of Ulsan College of Medicine, Korea

Prof. Asrul Akmal Shafie, Director Institutional Planning and Strategic Center Universiti Sains, Malaysia

Prof. Raoh-Fang (Jasmine) Pwu,Adjunct Assistant Professor, Taipei Medical University, Taipei, Taiwan; Board of Director, ISPOR.

Prof.Rungpetch Sakulbumrungsil, Dean, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Thailand

We would like to extend our heartfelt gratitude to all reviewers from IQVIA and Roche for their constructive feedback and insightful comments. We would also like to thank all participants for their active contribution.

CONTACT US
iqvia.com/contactus

LOCATION
79 Anson Road #19-01
Singapore 079906
iqvia.com