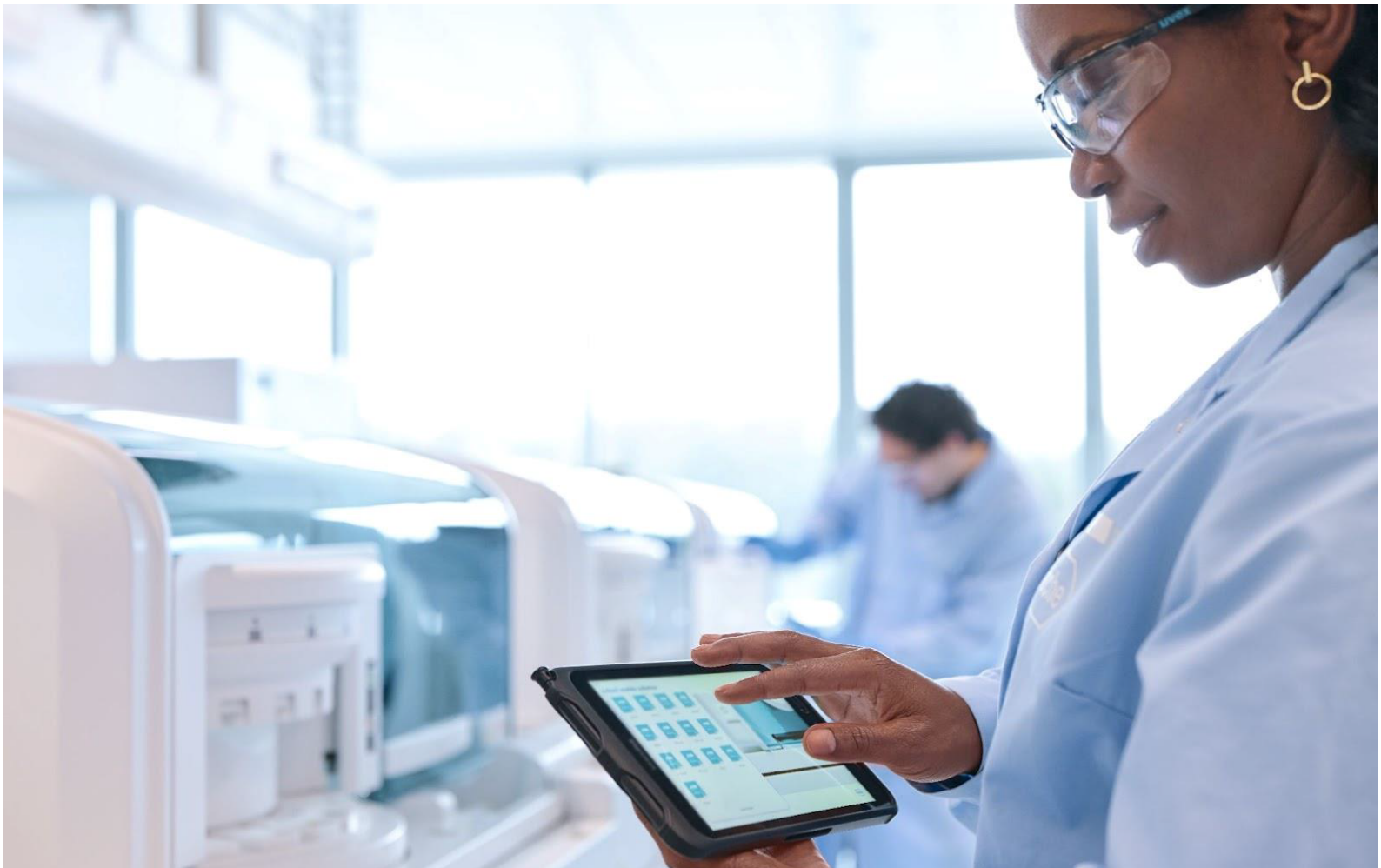
Roche submission to the Senate Standing Committees on Community Affairs

Inquiry into equitable access to diagnosis and treatment for individuals with rare and less common cancers, including neuroendocrine cancer

August 2023



About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics, as well as growing capabilities in the area of data-driven medical insights help Roche deliver truly personalised healthcare. Roche is working with partners across the healthcare sector to provide the best care for each person.

Roche is one of the world's largest biotech companies, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also a world leader of in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. In recent years, Roche has invested in genomic profiling and real-world data partnerships and has become an industry-leading partner for medical insights.

Founded in 1896, Roche has a robust 125-year legacy, focused on the search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. More than thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, anti-malarials and cancer medicines. Moreover, for the twelfth consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2021 employed more than 100,000 people worldwide. In 2021, Roche invested around CHF 14 billion in research and development worldwide, including over AUD 56 million in local pharmaceutical research in Australia. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. Roche's pharmaceutical division in Australia employs over 300 people who are dedicated to pioneering life-changing healthcare for every Australian via the clinical development, registration, sales, marketing and distribution of innovative pharmaceutical medicines. Australian patients have access to around 35 Roche medicines.

Roche's diagnostics division in Australia employs over 200 people and supplies a large range of in-vitro diagnostics covering a broad spectrum of medical conditions including cardiovascular disease, infectious disease, oncology and women's health. Roche Diagnostics concentrates on leveraging advanced scientific knowledge and technological progress to increase the medical value of its diagnostic solutions and supports customers spanning the entire healthcare spectrum - from research institutions, hospitals and commercial laboratories to physicians and patients.

Roche Diabetes Care has been pioneering innovative diabetes technologies and services for more than 40 years. More than 5,500 employees in over 100 markets worldwide work every day to support people with diabetes and those at risk to achieve more time in their target ranges and experience true relief from the daily therapy routines.

Being a global leader in integrated Personalised Diabetes Management (iPDM), Roche Diabetes Care collaborates with thought leaders around the globe, including people with diabetes, caregivers, healthcare providers and payers. Roche Diabetes Care aims to transform and advance care provision and foster sustainable care structures. Under the brands RocheDiabetes, Accu-Chek and mySugr, comprising glucose monitoring, insulin delivery systems and digital solutions, Roche Diabetes Care unites with its partners to create patient-centred value. By building and collaborating in an open ecosystem, connecting devices and digital solutions as well as contextualising relevant data points, Roche Diabetes Care enables deeper insights and a better understanding of the disease, leading to personalised and effective therapy adjustments.

For more information, please visit www.roche-australia.com.

For any further information in relation to this submission please contact:

Mark Stewart, Policy and Value Manager
Roche Products Pty Limited
Level 8, 30-34 Hickson Road, Sydney, NSW, 2000, Australia
Telephone:
Email:

Executive Summary

Science and technological advancements are changing the way cancer is being screened, diagnosed, and treated, which will provide greater benefits to patients with rarer cancers. In Vitro Diagnostics (IVDs) are increasingly playing a pivotal role in diagnosing patients with cancer, opening up an individual's ability to receive the care that is right for them.

Digital health technologies are increasingly being used to help patients and this includes decision support software which can help healthcare providers access the latest information, and make evidence-based decisions. It also includes digital pathology which provides a critical role in diagnosing cancer cases, reducing the time to make a diagnosis, and assisting with an increase in the demand for pathology.

At the same time cancer treatments are shifting to target specific genetic and molecular characteristics of an individual's tumour, an approach known as precision oncology or personalised medicine. This approach recognises that cancer is a complex disease and will look to address unique genetic mutations and molecular alterations which drive growth and spread.

Meanwhile, the introduction of cell and gene therapies will aim to address the underlying cause of the cancer, intended as an upfront treatment that has the potential to provide durable, preventative and curative effects. These medicines have the potential to revolutionise the treatments of rare cancers which often have limited treatment options.

However, there are barriers which are preventing faster access to these new health technologies and precision medicines. Firstly, there are significant delays in the time to access IVDs on the Medicare Benefits Schedule (MBS), meaning that affordable access to testing in the community is patchy and inconsistent. Additionally, the full value of these tests to cancer care and to health system efficiency is not fully accounted for when the total budget impact is considered, resulting in unrealistic MBS fees.

On top of this, there is no up-to-date Blueprint to inform Australians how genomic testing will be integrated into clinical practice, and there is no ongoing sustainable government funding for genomic profiling initiatives to ensure that patients can receive an early and accurate diagnosis.

For the new precision medicines, there are specific challenges faced through traditional Health Technology Assessment (HTA) decision making processes which results in a lack of subsidised access to patients with these newer options. For cell and gene therapies, there are HTA pathway inconsistencies, undefined timeframes, and funding uncertainties, creating challenges to obtaining reimbursement for these new medicines.

Following this, there are challenges for patients with rarer cancers in accessing treatments through clinical trials. This is due to fewer trial sites when compared to more common cancers, and difficulties in attracting more rare cancer trials to Australia. There are also issues with clinician expertise being primarily located in metropolitan areas, and a general lack of awareness about the availability of rare cancer clinical trial sites by clinicians.

If these barriers and challenges aren't addressed, patients with rarer cancers risk missing out, or having delayed access to, these new health technologies and precision medicines.

Summary of recommendations

To address the barriers to screening and diagnostics Roche recommends:

1. The Government commits to include new In-Vitro Diagnostics on the Medicare Benefits Schedule within 12 months of inclusion on the Australian Register of Therapeutic Goods.

2. The Medical Services Advisory Committee considers its methods to value the full benefits of In-Vitro Diagnostics to inform listing recommendations, as well as the resultant Medicare Benefits Schedule fee, and the total budget impacts.

3. That Genomics Australia prioritise the development of a Blueprint for implementing genomics across the Australian healthcare system.

4. That the Government commit to a national funding framework for genomic screening that is sustainable in the long term. This should begin with a funding framework for genomic screening of cancers, so that projects such as PrOSPeCT can continue beyond their existing timeframes and the Government can look at options for expanding access for all cancer patients.

To address the barriers to accessing appropriate treatment, Roche recommends:

5. For molecular guided therapies, there is increased acceptability of the best available evidence by health technology assessment bodies, or that there is the introduction of interim access mechanisms that enable evidence generation for key uncertainties to be considered.

6. That there is greater consideration of excluding testing costs in health technology assessment for rare cancers or mutations, notably when the testing technology is anticipated to be embedded into the health care process in the near term, or when access to testing is covered through other means.

7. That the Australian Government set up a central registry with minimum data collection standard for rare cancers in line with the recommendations from other key stakeholders.

8. In agreement with The *New Frontier Report*, the Australian Government establish a Centre for Precision Medicine and Rare Diseases within the Department of Health and Aged Care, to ensure that the capacity of the Department of Health and Aged Care is enhanced to provide Australians with timely access to new medicines and novel medical technologies, including cell and gene therapies.

9. That the Government continues to invest in clinical trials through programs such as the Clinical Trials Initiative, and provides regular reporting on how this initiative is addressing rare cancer patient barriers, and is utilising novel approaches to clinical trials design for patients with rare cancers.

Introduction

Roche welcomes the opportunity to respond to the Senate Standing Committee Inquiry into Equitable Access to Diagnosis and Treatment for Individuals with Rare and Less Common Cancers. While Australia has achieved significant improvement in outcomes for cancer patients, as cancer mortality rates continue to drop, cancer still accounts for around 3 of every 10 deaths in Australia.[1]

Rare cancers encompass hundreds of different cancers, and each type affect a small number of people.[2] Rare and less common cancers comprise approximately one-third of all cancer diagnoses and 40% of all cancer deaths, while adolescents and young adults have higher incidence of rare cancers with poorer outcomes.[3]

While definitions may vary, there are well established challenges for less common cancers. This includes challenges in providing timely diagnosis, greater difficulty in developing treatment and providing evidence through clinical trials, and a general lack of knowledge across the clinical community. All of these challenges can lead to poorer health outcomes for patients of rare cancers.

The recent improvements in reduced mortality for cancer patients have in part been driven by advances in science, medicine and technology, which are continually being developed and brought to patients. Roche has been at the forefront of cancer management, with medicines and medical devices including precision medicines, in-vitro diagnostics (IVDs), diagnostic platforms, clinical decision support tools, and biological medicines.

This rapid evolution of advancement in medicines, medical devices and biological medicines is enabling better management of cancer across the healthcare continuum, including screening, prevention, prediction, diagnosis, treatment and monitoring. However, the rapid pace of these scientific, medical and technological advances are outstripping the healthcare system's capacity to respond.

As such, our submission will focus on the new health technologies used in cancer care, and will highlight the key barriers facing these newer technologies. Roche believes that the Government should be leading initiatives to ensure that patients are able to access the best and latest advancements in medicine, science and technology.

Health Technologies - Uses in Cancer

Outlined below are a number of the key health technologies used to help patients with cancer. We should note that by health technologies we refer to medicines, biological medicines and medical devices as regulated by the Therapeutic Goods Administration.

In-Vitro Diagnostics (IVDs) and genomic testing

IVDs play a vital role in diagnosing patients with cancer as they are involved in almost 100% of cancer diagnoses, opening up an individual's ability to receive the care that is right for them.[4] IVDs are more commonly known as pathology tests or diagnostic tests and are used to measure changes in body fluids or tissues that can indicate disease.

IVDs play a vital role in a cancer patient's entire healthcare journey. They are used in:

- Diagnosis for confirming (or ruling out) cancer.
- Treatment for identifying or optimising treatment to increase effectiveness.
- Prediction for identifying the risk of developing cancer, a response to treatment, or the risk of developing an adverse event due to treatment.
- Screening for identifying cancer before symptoms develop.
- Monitoring for identifying cancer progression and development of resistance to treatment.
- Prognosis for identifying the likely course of a disease.

In cancer, it is widely accepted that an early diagnosis results in better health outcomes at lower costs, as less intensive interventions are required.[5] When coupled with digital health technologies, the value that can be derived from IVD innovation is improved as they can enhance the value of the information generated by the test and the pathology process in the laboratory.

A key innovation in the IVD sector is genomic testing (See Case Study 1). In cancer, genomic technologies are able to identify genetic or biological markers that are driving cancer growth by analysing a tumour or blood sample. Consequently, cancer is being re-classified into an increasing number of subtypes based on the presence of these markers, which is making cancers 'rarer'.

Identifying genetic or biological markers benefits patients with a test identifying if a treatment targeting the marker is available. Recent advances in genomic technology mean that a single test can identify hundreds of genetic or biological markers in a tumour sample, potentially broadening the number of treatments identified. This is particularly important in rare cancers or where patients may have run out of treatment options, while also enabling the classification of misdiagnosed disease, and better clarification of subtypes.

Digital health technologies

Digital health refers to a range of technologies which can be used to treat patients and collect and share a person's health information.[6] This includes some software, apps, wearable devices, remote monitoring tools, electronic health records, telehealth, and artificial intelligence.

Clinical decision support software

Medical knowledge is growing exponentially and this knowledge has been estimated to double every 73 days by 2020.[7] It can be very challenging for healthcare practitioners to keep up to date with the latest developments particularly when coupled with the increasing demand for healthcare services and the increasing complexity of care (see Case Study 2).

Given the complexity of cancer care in the genomic age, decision support software can help address the above challenges as it allows healthcare providers to have access to the latest information regarding clinical trials, scientific and medical literature, and guidelines to make evidence-based decisions. This can be combined with other patient information, including that from diagnostic testing, to decide on the best treatment options for the patient.

Digital pathology

Digital pathology is an innovation increasingly used in anatomical pathology where tissue specimens are examined to help diagnose cancer cases. Given the critical role of anatomical pathology in diagnosing cancer where tissue specimens are available, and the pathologist shortage in Australia, the evolution of digital pathology has many potential benefits for cancer patients because it can reduce the time required to make a diagnosis, particularly in complex cases.[8]

Digital pathology can supplant the use of a traditional microscope to analyse tissue samples on a glass slide by digitising slides which can then be manipulated to enable the tissue to be seen in greater detail than is possible with a microscope (see Case Study 3).[9] Digitisation enables digital tools such as algorithms derived from artificial intelligence to help analyse the virtual slide images for more accuracy and consistency.

Furthermore, digital pathology enables pathologists to collaborate with other medical professionals, including as part of a multidisciplinary care team, and broadens access to pathology expertise in areas where such expertise is not available. This is particularly valuable given the current and growing pathologist shortage[10] at the same time as the rising complexity of testing, increasing the burden on pathologists.

Personalised medicines

The way new cancer medicines are being developed and the way that cancer is being treated is shifting. Historically, cancer was treated by a one-size-fits all approach where medicines were developed with an intended purpose to treat broad patient populations. Most cancer treatments have been developed to treat a cancer type which has developed within a specific organ or tissue, such as breast cancer or lung cancer.

Cancer management is shifting towards treatments that target specific genetic and molecular characteristics of an individual's tumour, an approach often referred to as precision oncology or personalised medicine. This approach recognizes that cancer is a complex and heterogeneous disease, and each patient's cancer may have unique genetic mutations and molecular alterations that drive its growth and spread.

Precision oncology aims to identify these specific drivers and target them with highly specialised therapies to improve treatment outcomes while minimising side effects. Genomic testing is an essential component of precision oncology as it enables the identification of specific molecular abnormalities driving a patient's tumour, such as genetic alterations in key pathways that control cellular growth, differentiation, replication and death.

Once the molecular abnormalities are identified, oncologists can choose precision medicines that are designed to specifically inhibit the action of those mutated genes or proteins. These therapies are often associated with improved outcomes compared to traditional chemotherapy, which can impact both cancer cells and healthy cells.[11]

Precision medicines are increasingly being developed in a tumour agnostic fashion, meaning that medicine is designed to treat cancers harbouring a specific genomic alteration regardless of where in the body it started or the type of tissue from which it developed.[12] Tumour agnostic precision medicines can be used to treat any kind of cancer as long as the cancer has the specific genomic alteration targeted by the medicine.

Taking this approach to treating cancer based on the presence of validated driver mutation is a specific way to target rare cancers and cancers of unknown primary which often have limited treatment options and a scarcity of clinical data. As an example, chromosomal rearrangements in the genes encoding neurotrophic tropomyosin kinase receptors (NTRK or TRK) can induce carcinogenesis (the formation of solid cancers) in a number of different organs.

While NTRK alterations collectively represent under 1% of all solid tumours,[13] they are highly prevalent in rare tumours. Therefore, tumour location agnostic therapies such as the ones targeting NTRK alterations can provide a broader range of treatment options for patients with rare cancers.[14]

And finally, another example of personalised medicine is the development of cell and gene therapies. Cell and gene therapies are increasingly being introduced as a treatment which aim to address the underlying cause of the cancer. Gene therapies that seek to modify, delete, or introduce genes into a patient's body and gene-modified cell therapies that genetically reprogram cells to treat the disease, are intended as an upfront treatment and have the potential to provide durable, preventive or curative effects.[15]

There is a significant advantage of novel health technology development, such as cell and gene therapies compared to that of conventional pharmaceuticals, as their utilisation is modular and platform technologies that can be rapidly reconfigured to treat multiple disease targets such as genetic diseases, cancers and infectious diseases. This may lead to more treatments that are cost effective being available in the future.[16]

In summary, personalised medicines target specific genetic and molecular features of an individual's tumour. Increasingly, these medicines are being developed in a tumour agnostic fashion, meaning that they have the potential to revolutionise the treatment of rare cancers, which often have limited treatment options compared to more common cancers.

Terms of Reference

A. barriers to screening and diagnosis, including the impact of factors such as: i. geographic location, ii. Cost, iii. cultural and language barriers, iv. type of cancer, and v. availability of treating practitioners;

As noted above, IVDs, including genomic tests, are critical across the cancer clinical pathway and health continuum. Screening and diagnosis and digital health technologies are helping to enhance the value of diagnostic testing in cancer.

For screening and diagnostics, there are two primary stages where Roche sees barriers to patient access. This is:

- When a health technology is available in Australia (i.e. it is included on the Australian Register of Therapeutic Goods (ARTG)) but is not reimbursed through the MBS or other scheme and is therefore unaffordable.
- Once a technology is available on the MBS or other reimbursement scheme, a patient may still not have access. This may occur for various reasons - geographical, workforce or cost where patients cannot afford out of pocket costs such as the patient co-payment or 'gap' fees.

The barriers, and our recommendations to improve access to these technologies are outlined below.

IVDs and genomic tests

Access to IVD innovation is challenging as international experience shows that adoption of these technologies is slow and that Australia is no exception. However, there are moves afoot internationally that are seeking to accelerate access to these innovations.

Medicare Benefits Schedule (MBS) listing - timely availability of new IVDs

The MBS is a central component of Medicare, Australia's universal health care system and Australians rely on it for subsidised access to medical services, including pathology tests.

Based on research conducted within Roche, once an IVD is included on the ARTG (i.e. it can legally be supplied in Australia) it typically takes more than 8 years to include it on the MBS if a new MBS item is required or a significant change to an existing MBS item is required.[17]

Of the 8 years, 2 years are spent in the assessment process conducted by the Medical Services Advisory Committee (MSAC) and 1.5 years are spent awaiting Government implementation of MSAC's recommendation. This means that for more than 8 years, affordable access to testing in the community is patchy, inconsistent and can result in:

- Reduced equity of access to diagnostics which can reduce the capacity of individuals or certain populations to achieve equitable health outcomes,

- Unnecessary healthcare system costs being incurred where the technology enables more efficient and effective care at a lower cost than existing testing,

- Rendering the use of the test obsolete by the time it is made available. This can occur because the technology is evolving quickly or because scientific and medical knowledge are increasing exponentially, changing the standard of care.

The findings of Roche's internal research are consistent with experience internationally which indicates it takes around 10 years to adopt a new IVD.[18] However, unlike Australia, other countries have recognised the benefits of these technologies and are trialling new ways to accelerate access.

International initiatives to accelerate access to IVDs

The United Kingdom (UK) has developed a Medical Technology Strategy to enable these technologies to support the transformation of the healthcare system, with IVDs identified as a priority.[19] Some key initiatives include developing a clear pathway from pre-registration through to commercial adoption to rapidly progress priority, innovative products and establishing collaboration between the National Health Service (NHS) and the industry to support clinical engagement and encourage innovation in areas of need.

In England, the National Institute for Health and Care Excellence (NICE), is trialling the Early Value Assessment (EVA) Scheme which enables accelerated access by conducting an earlier clinical and cost-effectiveness evaluation of promising technologies in areas of clinical or health system need while real world evidence (RWE) is collected.[20] Based on the website, it appears that the overall time for an early value assessment is well within 12 months.

Furthermore, in May 2023, the World Health Assembly resolved to improve access to diagnostic technologies to support universality of healthcare and equity, outlining actions for the World Health Organisation and Member States.[21] One of these includes prioritising and rapidly reviewing clinical evidence for new diagnostic interventions, services or products for consideration in guidelines and across diseases.

Recommendation:

1. The Government commits to include new In-Vitro Diagnostics on the Medicare Benefits Schedule within 12 months of inclusion on the Australian Register of Therapeutic Goods.

This recommendation recognises the centrality of the MBS to funding IVDs used outside the public hospital sector, the importance of early diagnosis and targeting treatment to the molecular drivers of tumour growth to health outcomes, and the rapid evolution of genomic knowledge and application. This recommendation also helps to align Australia with international efforts that have recognised the critical role IVDs can play to their future healthcare systems.

Initially, a Working Group could be established to consider how existing barriers to faster access can be overcome at the pre-MSAC, MSAC, and post-MSAC stages, how an Early Value Assessment Scheme could be introduced in Australia and a review of the MSAC administrative and assessment processes.

MBS listing - adequate reimbursement levels

If the MBS schedule fee is set too low, not all laboratories will provide the test, despite it being available on the MBS which makes access uncertain and inconsistent from a patient perspective. This is a particular issue for genomic tests where the cost of providing the full service is highly variable as it involves testing and analysis and clinical interpretation of the data.

These variabilities relate to the differences in testing platforms and their capacity for high throughput, which also lead to differences in achieving economies of scale. There are also variabilities in the cost of analysing and interpreting genomic results which depend on the amount of genomic information analysed.

In rare cancers, a comprehensive approach to genomic analysis is generally taken, requiring the analysis and interpretation of a very large amount of data. The MBS fee comprises the cost of the IVD and the cost of delivering the service by the provider, being the laboratory for a pathology test. The MSAC considers the price at which cost-effectiveness is demonstrated but will also then proceed to benchmark the MBS fee to that of other (mostly lower cost) tests available on the MBS.

Cost-effectiveness is assessed following a clinical and economic assessment of the evidence provided by an applicant in a submission to the MSAC. There is a lack of clarity as to how benchmarking of the final MBS fee to other tests available on the MBS is undertaken and what factors are considered.

Typically, the broader elements of value for IVDs are not captured in the primary economic analysis and it is unclear to what extent capturing these elements (qualitatively or quantitatively) influences the MSAC decision. MSAC assessments also typically only adopt a very narrow view of the total healthcare costs associated with IVDs.

This means that where the use of an IVD promotes efficiencies in the healthcare system and results in savings, the full spectrum of savings is not fully accounted for when the total budget impact is considered. Furthermore, the calculation of the total budget impacts is set over a period of 6 years which may not fully account for the longer downstream savings arising from the use of a technology.

A complete account of the total healthcare savings would not only help to justify a more realistic MBS fee, but also accelerate the implementation of an MSAC recommendation by the Government. As noted above, this process takes on average 1.5 years and is tied to the annual Commonwealth Budget process and pricing discussions with the Department of Health.

Recommendation:

2. The Medical Services Advisory Committee considers its methods to value the full benefits of In-Vitro Diagnostics to inform listing recommendations, as well as the resultant Medicare Benefits Schedule fee, and the total budget impacts.

Improve certainty about the integration of genomics into healthcare

The barriers to access noted above relate to MBS listings which can apply to any IVD, not only genomic testing. However, there are more ecosystem level activities that can be undertaken to improve access to genomics beyond the MBS listing challenges by creating a shared vision and preparing the infrastructure required for adopting genomics in Australia.

Australia is in the process of establishing Genomics Australia to lead the integration of genomics into clinical care in Australia. Meanwhile, Cancer Australia is developing a National Cancer Plan which encompasses genomics.

In Roche's submission to the National Cancer Plan consultation, Roche outlined the need for a strategy for rare cancer patients to have timely access to advanced genomic diagnostics (e.g. comprehensive genomic profiling). Roche recommended specific actions to enable rapid and universal access to new and existing next-generation sequencing (NGS) technologies such as comprehensive genomic profiling (CGP), as a blueprint to foster innovation leaps to future technologies.

Roche also put forward support for an overarching policy and implementation framework for genomic technologies which encompasses the use of genomics more broadly in cancer including preventative screening, prognosis, and advanced diagnostics. While Australia has a Genomics Health Policy Framework, it has expired and no public reporting of progress against the actions in the Framework is available.

There is currently no up-to-date Blueprint to inform Australians how genomics will be integrated into clinical practice, especially its role in primary and secondary care. This would be of value for all healthcare system stakeholders who need to prepare for the significant changes that genomics and precision medicine will bring.

This not only applies to cancer but also rare diseases and complex chronic conditions such as diabetes. An early opportunity for Genomics Australia is to develop a Blueprint which will:

- Communicate a clear vision of the use of genomics across primary and secondary care, including in cancer.
- Outline the key activities that need to be undertaken to achieve this vision, building on activities conducted nationally to date, and the timelines.

Recommendation:

3. That Genomics Australia prioritise the development of a Blueprint for implementing genomics across the Australian healthcare system.

Incentives for public-private partnerships in genomics

As outlined above, genomic technologies are able to identify genetic or biological markers that are driving cancer growth by analysing a tumour or blood sample. Consequently, cancer is being re-defined into an increasing number of subtypes based on the presence of these markers, which is making cancers 'rarer'. This is particularly important in rare cancers or where patients may have run out of treatment options.

Roche is a committed foundational partner in Omico's landmark program, the Precision Oncology Screening Platform Enabling Clinical Trials (PrOSPeCT).[22] PrOSPeCT will give 20,000 Australians cutting edge screening and comprehensive genomic profiling of people with cancer and unmet clinical need, to efficiently link them to clinical trials for novel biomarker-dependent treatments.

It is estimated that PrOSPeCT will result in considerable savings for the healthcare system in terms of avoided health interventions, including medicines, tests and additional hospital costs.[23] It will also provide significant direct investment in locally-based clinical trials, and is expected to generate over 650 jobs including new opportunities for research scientists involved in genomics.

Recommendation:

4. That the Government commit to a national funding framework for genomic screening that is sustainable in the long term. This should begin with a funding framework for genomic screening of cancers, so that projects such as PrOSPeCT can continue beyond their existing timeframes and the Government can look at options for expanding access for all cancer patients.

B. barriers to accessing appropriate treatment;

Currently there are a number of different factors which can become barriers to patients accessing appropriate treatment in Australia. For access to treatments of rare cancer in Australia, there are barriers for patients at three key points in the healthcare system. This includes:

- When a medicine and health technology is available in Australia (i.e. it is included on the ARTG) but is not reimbursed through the Pharmaceutical Benefits Scheme (PBS), MBS or other scheme, and is therefore unaffordable.
- Once a technology is available on the PBS, MBS or other reimbursement scheme, a patient may still not be able to access the treatment, which may occur for various reasons - geographical, workforce or cost where patients cannot afford out of pocket costs such as the patient co-payment or 'gap' fees.
- Patients are unable to access a clinical trial that may offer therapies where no funded therapies are available.

The barriers, and our recommendations to improve access to these technologies are outlined below.

Health Technology Assessment (HTA) pathways and reimbursement mechanisms

Current Government reviews of regulatory and reimbursement processes

It should be acknowledged that there have been a number of reviews completed, or currently underway which address timely access to new medicines and medical technologies. Throughout this section Roche will refer to these reviews.

Australia applies a rigorous assessment process for the registration of a new treatment to ensure it meets the standards for quality, safety and efficacy to gain market entry through the TGA. Once registered with the TGA, another rigorous assessment process for cost-effectiveness is required prior to reimbursement, and this is the HTA approach employed by the Medical Services Advisory Committee (MSAC), and the Pharmaceutical Benefits Advisory Committee (PBAC).

This process served Australia well for the blockbuster medicines brought to market which serve larger patient populations, but they are now being challenged by the rapid evolution of precision medicines technologies alongside the growing trend towards smaller patient populations, including those who suffer from a rarer cancer.[24,25]

The *New Frontier Report* recommended that the Australian Government should establish a Centre for Precision Medicines and Rare Diseases within the Department of Health.[26] The recommendation noted that this Centre should provide Australians with timely access to new drugs, ensure the HTA process aligns with this outcome, provide horizon scanning for new medicines and technologies, and should provide advice to Government on the establishment of a dedicated HTA pathway for cell and gene therapies.

Recommendation 2 in this report noted that this Centre should establish a clear and certain pathway for cell and gene therapies, and that the Australian Government should prioritise and simplify regulation of cell and gene therapy pathways for clinical trials in Australia.[27] Recommendation 29 also specifically called out the Health Technology Assessment Review (HTA Review), and noted that it should reassess relevant aspects of the process to ensure there are future pathways for treatments and therapies that do not fit neatly into the current system such as rare cancers.[28]

The Terms of Reference for the HTA Review, which is due to report at the end of 2023, outline an examination of the assessment of technologies, such as those for rare diseases. The TOR outlines an examination of clinical and economic uncertainty, and how this may be addressed through evidence from relevant sources other than randomised controlled trials, and arrangements for post-market assessment and decision making.[29] Roche is actively participating in the consultation process for this review, and awaits considering the recommendations.

Personalised medicine

As outlined above, cancer treatments are shifting towards molecular-guided treatments, often referred to as precision medicine or personalised medicine. These treatments target specific molecular characteristics of a patient's tumour and are increasingly being developed in a tumour agnostic fashion.

These products are trialled in 'basket trials', where a targeted therapy is evaluated for multiple cancer types that have common molecular alterations.[30] Basket trials are useful for studying rare cancers and cancers with rare genetic changes.[31]

However, as basket studies are commonly non-comparative studies, with small patient numbers (as an overall study and even smaller numbers when broken down by tumour type), the evidence may not exist at the time of reimbursement submission to provide a robust estimate of comparative effectiveness and cost-effectiveness.

Traditional HTA decision-making approaches, which value certainty, are challenged by the evidence underpinning the registration of tumour agnostic therapies and co-dependent technologies. The low tolerance for uncertainty, combined with Australia's co-dependent framework, accentuates the challenge of providing a robust assessment of the incremental clinical effectiveness and cost-effectiveness for new therapies.

Breakout Box 1: Barriers for tumour agnostic therapies

- In a tumour type which has a biomarker prevalence of 1%, (that is a Number Needed to Treat (NNT) of 100, i.e. 100 patients are needed to be tested to identify one positive case), and a testing cost of $3,000, a simple estimation of the cost of testing to identify a positive patient is $300,000.
- At a willingness to pay of $100,000 per Quality-Adjusted-Life-Year (QALY), a therapy would need to be able to confidently demonstrate an improvement of 3 QALYs (i.e. extend life by greater than three years) to substantiate the cost of testing only, let alone the cost of the medicine.
- Thus, it might not be feasible to achieve reimbursement for highly effective therapies with low biomarker prevalence due to this issue.

Consequently, the assessment of tumour-agnostic therapies may result in a lack of subsidised access to patients with proven treatment options. This is further compounded by the absence of funded CGP. To enable precision medicine for rare cancers, wider access to genomic screening for known mutation targets is required.

One solution that has been proposed to address this challenge is a central registry for rare cancers, with minimum data collection standards, that could facilitate evidence collection, and experience

sharing between HCPs. It could additionally provide a mechanism for life-cycle evaluation of early HTA decisions based on uncertain evidence.

Recommendations:

5. For molecular guided therapies, there is increased acceptability of the best available evidence by health technology assessment bodies, or that there is the introduction of interim access mechanisms that enable evidence generation for key uncertainties to be considered.

6. That there is greater consideration of excluding testing costs in health technology assessment for rare cancers or mutations, notably when the testing technology is anticipated to be embedded into the health care process in the near term, or when access to testing is covered through other means.

7. That the Australian Government set up a central registry with minimum data collection standard for rare cancers in line with the recommendations from other key stakeholders.

Cell and gene therapies

Cell and gene therapies are often developed to treat rare or uncommon conditions, including rare cancers, and highlight a number of current challenges, The Australian experience to date is that cell and gene therapies can follow three different HTA pathways depending on the therapeutic area, the current standard of care (comparator), and the location of treatment delivery (public hospital inpatient or outpatient).

The different pathways are inconsistent in their timelines and methodology, which impacts on patient access. There are also differences in timelines, with the MSAC process requiring the additional application form step for protocol development, no guaranteed timelines for progressing from the protocol development to the submission stage, and undefined timeframes for the outcomes and minutes following MSAC meetings.

While the individual differences between the PBAC and MSAC processes are not all problematic, they lead to inconsistencies in the way new health technologies are evaluated for public funding. Even when HTA pathways are clarified upfront, a narrow approach to value assessment results in a number of challenges to obtaining reimbursement for precision medicine technologies, including the following:

- Related to the upfront costs and curative potential of these therapies, the 5% discount rate applied in Australia is high by international standards and erodes the value of treatment in economic models with a longer term duration.

- The lack of guidance for the inclusion of societal benefits and costs that are relevant for serious, progressive conditions requiring additional care by family members, professional carers, and allied health.

- With the progressive and life-limiting severity of the conditions being treated, the clinical evidence base may be considered uncertain due to the use of historical or shorter-term control data, and limited longer-term follow-up at the time of initial submissions for registration and reimbursement.

For cell and gene therapies that are recommended by the PBAC or MSAC, there are differences in the funding source and processes required before the treatment can be delivered to patients. Treatments recommended by the PBAC, usually classed as medicines, are funded federally through the PBS.

Treatments recommended by the MSAC are currently funded 50:50 by the Commonwealth and States and Territories under the 2020–25 National Health Reform Agreement (NHRA 2020-2025). The National Blood Authority which provides the framework for patients to access blood products is funded by the Australian Government (63%) and by the States and Territories (37%), with the funding provided by each state and territory determined by the quantity of product provided to each particular state and territory.[32]

The requirement for Sponsors to secure funding agreements with each state health department has led to delays in access in some states. The Evohealth April 2023 report[33] on CAR T-cell therapies indicated that some State and Territory Governments received only short notice that a CAR T-cell therapy would be recommended for public funding by the MSAC, but with no funding allocation set aside, faced pressure to secure funding to cover 50% of the cost of delivering CAR T-cell therapy to eligible patients.

While the funding mechanisms are peripheral to the current HTA review, it is relevant to note that the current disparities in the three potential pathways for patient access are causing delays and inequities in patients' access to treatments. As noted in the National Health Reform Agreement - Addendum 2020-25, all governments have a responsibility to ensure that systems work together effectively and efficiently to produce the best outcomes for people, including interfaces between health, aged care and disability services, regardless of their geographic location.[34]

Recommendation:

8. In agreement with The *New Frontier Report*, the Australian Government establish a Centre for Precision Medicine and Rare Diseases within the Department of Health and Aged Care, to ensure that the capacity of the Department of Health and Aged Care is enhanced to provide Australians with timely access to new medicines and novel medical technologies, including cell and gene therapies.

Challenges with clinical trials

When compared to standard cancer treatment options, generally there are fewer options for patients of rare and less common cancers. While this is also true for clinical trials, they are an important means for access to treatment options for patients with rarer cancers.

This need is recognised in the Australian Government's *Clinical Trials Activity Initiative*[35] which will help Australian researchers and patients test new treatments through national and international clinical trials.

Roche supports the objective of this initiative to increase clinical trial activity in Australia to:

- improve the evidence base supporting clinical care,
- help patients access trials relevant to their health circumstances, and
- enable researchers to bring international trials to Australian patients.

Compared to more common cancers, there are fewer clinical trial sites and smaller studies, and this can result in limited data to support registration and reimbursement. This leaves patients with fewer treatment options and subsidised medicines options.

There is a need for novel approaches to clinical trial designs that can be used to study new treatments for patients with rare cancers, thereby addressing a significant unmet need. To this end, Roche has a number of clinical trials that are focusing on targeted therapies either in a basket (where the focus is on the target and more agnostic to tumour type) or umbrella (where the focus is on a single tumour type) design.

Despite efforts to improve clinical trial access in regional and rural locations, most cancer experts and cancer centres are located in metropolitan areas in Australia, meaning patients living outside of these areas may have additional challenges in participating in these trials. This creates geographical issues for patients who need to travel and spend time away from their jobs, families, and support systems.

When considering the issues more specifically for rarer cancers, there is a need to increase awareness of clinical trials and what they can offer. There is a lack of information and knowledge regarding the available rare cancer clinical trials amongst clinicians, and the general public may not have the knowledge or the means to do this research, while companies cannot promote these available trials to the general public.

There is also the issue of sourcing the right clinical expertise in the health system for trials, such as tumour agnostic trials which require broad pan-tumour expertise. And from a site perspective, it can be difficult to support trials that are slow to recruit if the necessary infrastructure is not in place.

On top of this, there are a number of barriers to attracting more international trials to Australia. Due to Australia's relatively small population size, there can be reluctance at a global level to place clinical trials here given the great challenge of patient recruitment and ensuring that there are enough patients with the tumour type or genomic profile either eligible or willing, and logistically able, to participate in a clinical trial.

Roche believes initiatives such as PrOSPeCT are vitally important in raising Australia's profile as an attractive destination for clinical trial placement. Ensuring that we have a nationally coordinated approach to genomic screening and the infrastructure to link the genomic analysis to clinical trial therapies, increases international confidence that Australia can make significant patient recruitment contributions and deliver on these trials (see Case Study 4).

Recommendation:

9. That the Government continues to invest in clinical trials through programs such as the Clinical Trials Initiative, and provides regular reporting on how this initiative is addressing rare cancer patient barriers, and is utilising novel approaches to clinical trials design for patients with rare cancers.

C. the adequacy of support services after diagnosis;

Roche believes that there needs to be strong support services for patients of rare cancers after diagnosis. As outlined in the Australian Cancer Plan Consultation Draft, people diagnosed with cancer often face significant anxiety and stress when navigating their treatment, care, and support needs within a complex health system.[36]

Patient-centred cancer care navigation models that will integrate the network of available support offered across the system will be crucial to enhancing the patient experience. Cancer care navigators for rare cancers may not be as abundant as for support navigators for more common cancers, and the co-designing of a national framework to oversee development of these navigation models must include these considerations.

D. the adequacy of Commonwealth funding for research into rare, less common and neuroendocrine cancer; and

Roche supports continuous funding of rare cancer research, including through the Medical Research Future Fund (MRFF). To test the adequacy of the funding, Roche suggests a Government-led review of the funding alongside the outcomes, identifying where there could be improved focus on conversion of research insights into standard of care.

This could include pathways to translation of the outcomes of the research to improvements in clinical practice, improvements in decision making with respect to reimbursement decisions, movement of advanced genomics diagnostics from the research setting to fully reimbursed or national funded pathways. Roche would be supportive of a review which also looks at the current funding arrangements, and outcomes where there is clinical unmet need, and where there are still poor outcomes for disease.

Conclusion

Roche appreciates the opportunity to make a submission to the Senate Standing Committee and supports further review of the systems and Government programs to improve rare and less common cancer patients' access to diagnostics and treatments.

References

1. Australian Institute of Health and Welfare, 2022. Cancer. Web article. Viewed 14 August 2023: https://www.aihw.gov.au/reports/australias-health/cancer

2. Rare Cancers Australia. 'What is a Rare Cancer?' Available: https://www.rarecancers.org.au/page/159/what-is-a-rare-cancer

3. Cancer Australia 2022. The Australian Cancer Plan Consultation Draft.

4. Royal College of Pathologists of Australasia 2022. Pathology the Facts. Viewed 14 August 2023: https://www.rcpa.edu.au/getattachment/e3203b5f-fa65-421e-8762-fbc2f1750c75/Path-Fcts-Booklt.aspx

5. Deloitte Centre for Health Solutions. The Future of Diagnostics Technology driven personalised and preventive healthcare in Europe.

6. AIHW. (2020). Digital Health Snapshot. Accessed June 2022. https://www.aihw.gov.au/reports/australias-health/digital-health

7. Densen, P. Challenges and opportunities facing medical education; Transactions of the American Clinical and Climatological Association 122: 48–58. (2011).

8. Vodovnik 2016. Diagnostic time in digital pathology: A comparative study on 400 cases. Journal of Pathology Informatics 1:4.

9. Aeffner, F., et al. Introduction to Digital Image Analysis in Whole-slide Imaging: A White Paper from the Digital Pathology Association. Journal of pathology informatics, 10, 9. (2019)

10. The Royal College of Pathologists of Australasia. (2018): Pathologist and Senior Scientist Workforce Modelling. KBC Australia. pp. 23, 51, 55.

11. Kateo et al 2020. Real-world data from a molecular tumor board demonstrates improved outcomes with a precision N-of-One strategy. Nature Communications 11:4965.

12. Roche data on file: Tumour agnostic therapy

13. Hsiao SJ, Zehir A, Sireci AN, Aisner DL. Detection of tumor NTRK gene fusions to identify patients who may benefit from tyrosine kinase (TRK) inhibitor therapy. Journal of Molecular Diagnostics 2019;21:553–71.

14. Cocco E, Scaltriti M, Drilon A. NTRK fusion-positive cancers and TRK inhibitor therapy. National Reviews Clinical Oncology 2018;15:731–47.

15. Regenerative Medicine Catalyst Project consortium. Australia's Regenerative Medicine Global Pipeline Tracker. 2021. Available: https://www.ausbiotech.org/documents/item/673

16. House of Representatives Standing Committee on Health, Aged Care and Sport, 2021.The New Frontier - Delivering better health for all Australians. Parliament of Australia. Page 229.

17. Roche data on file: Research included analysing MSAC applications for IVDs from 2016 - 2022 to derive the average time from MSAC application to MBS listing and reviewing the ARTG listing dates for Roche's products that were the subject of an MSAC application.

18. British In Vitro Diagnostics Association 2023. The Value of IVDs https://www.bivda.org.uk/The-IVD-Industry/The-Value-of-IVDs

19. United Kingdom Department of Health and Social Care 2023. Medical technology strategy. Viewed 14 August: https://www.gov.uk/government/publications/medical-technology-strategy

20. National Institute for Health and Care Excellence 2023. Early Value Assessment (EVA) for medtech. Viewed 14 August 2023: https://www.nice.org.uk/about/what-we-do/eva-for-medtech

21. World Health Organization, 2023. Seventy-sixth World Health Assembly - Daily update: 27 May 2023. Viewed 17 August 2023: https://www.who.int/news/item/27-05-2023-seventy-sixth-world-health-assembly---daily-update--27-may-2023

22. Omico 2023. The Precision Oncology Screening Platform Enabling Clinical Trials (PrOSPeCT). Viewed 28 August: https://www.omico.com.au/prospect/

23. Ibid.

24. Williamson, R., Anderson, W., Duckett, SJ. et al. 2018. The Future of Precision Medicine in Australia. Report for the Australian Council of Learned Academies. Available: www.acola.org.au

25. MTP Connect 2019. Precision Medicine Roundtable White Paper. Available: https://www.mtpconnect.org.au/images/2019%20Precision%20Medicine%20White%20Paper.pdf

26. House of Representatives Standing Committee on Health, Aged Care and Sport, 2021.The New Frontier - Delivering better health for all Australians. Parliament of Australia. Recommendation 1.

27. House of Representatives Standing Committee on Health, Aged Care and Sport, 2021.The New Frontier - Delivering better health for all Australians. Parliament of Australia. Recommendation 2.

28. House of Representatives Standing Committee on Health, Aged Care and Sport, 2021.The New Frontier - Delivering better health for all Australians. Parliament of Australia. Recommendation 29.

29. Australian Department of Health, 2023. Health Technology Assessment Policy and Methods Review.

30. Schiller et al 2023. Challenges and Solutions for the Benefit Assessment of Tumor-Agnostic Therapies in Germany. Value Health.

31. Haslam A, Olivier T, Tuia J, et al. Umbrella review of basket trials testing a drug in tumors with actionable genetic biomarkers. BMC Cancer. 2023;23(1):46.

32. NBA Australia. National Blood Authority. Overview and Role of the NBA. Available: https://www.blood.gov.au/about-nba. Downloaded 29 May 2023. 2023.

33. Evohealth. CAR T-cell therapy: Is Australia ready, willing and able? Available from: https://evohealth.com.au/media/reports/2023_CAR-T_Ready_Willing_Able.pdf, accessed 25 May 2023 2023.

34. NHRA. Addendum to National Health Reform agreement. Available from: https://federalfinancialrelations.gov.au/sites/federalfinancialrelations.gov.au/files/2021-07/NHRA_2020-25_Addendum_consolidated.pdf Downloaded 25 May 2023. 2020-2025.

35. Australian Government Department of Health 2023. Clinical Trials Activity initiative. Viewed 28 August 2023: https://www.health.gov.au/our-work/clinical-trials-activity-initiative

36. Cancer Australia 2022. The Australian Cancer Plan Consultation Draft 2022.

37. 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. European Society of Medical Oncology. pp. 1491, 1492, 1494. (2020).

38. John, A. et al. Value of Precision Medicine in Advanced Non-Small Cell Lung Cancer: Real World Outcomes Associated with the Use of Companion Diagnostics. The Oncologist 2020; 25:e1743-e1752 (2020).

39. Cancer Australia. (2020). Report on the Lung Cancer Screening Enquiry. p. 5.

40. Wolff, A. et al. HER2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update Summary. Journal of Oncology Practice, 14(7), 437-441. (2018)

Appendix

Case Study 1: The value of genomic testing in lung cancer

Genomic testing using next generation sequencing (NGS) techniques to analyse a patient's tumour sample can provide insights into the molecular drivers of the cancer's growth or other molecular information and identify the best treatment option for the patient.

In lung cancer, identification of the molecular drivers of tumour growth has unlocked a number of high impact treatments for patients, greatly improving their prognosis and long-term outcomes. International cancer guidelines now recommend the routine use of NGS in lung cancer given the large number of molecular alterations that are able to be targeted for treatment by an approved medicine.[37]

The benefit of adopting a molecularly-guided treatment approach is shown by a recent study which found that patients with lung cancer who received molecularly-guided treatment as their first line of treatment were likely to survive three times longer than those who did not.[38] This improved survival is significant in light of Australian data which shows that survival for lung cancer patients was only 18.6% at 5 years compared to 69.2% for all cancers combined.[39]

Case Study 2: Laboratory and Clinical Decision Support Software

The results from genomic tests can be extremely complicated, with long read outs of genomic information which need to be interpreted to identify the genomic variations of clinical significance. This is a time consuming process as it relies on the interrogation of numerous data sources to determine the clinical significance of numerous (thousands) of genomic variations.

Software assists laboratories to accurately and efficiently analyse the clinical significance of thousands of the most common variations to enable concise reports to be provided to the treating clinician on the clinically relevant findings and potential treatment options.

Software is also available to assist discussions across multidisciplinary teams to share the genomics report and other relevant information about the patient, identify clinical treatment options and identify clinical guidelines, literature reports and clinical trial matches that can also inform treatment. This makes decision making faster, more collaborative and maximises the value of the initial genomic test by truly personalising the patient's care.

Case Study 3: Digital pathology and image analysis algorithms in breast cancer

Breast cancer diagnosis is a complex process, requiring assessment and scoring of multiple high-medical value assays.[40] These assays can be complex and difficult to assess manually, and can require second opinions and/or further confirmatory testing, increasing the turnaround time for the patient to receive their results.

A critical element in reaching a breast cancer diagnosis is determining an individual's HER2 gene amplification status. One specific test may require a blinded second opinion to be obtained in some of the more difficult cases. Second opinions can easily be obtained utilising digital pathology platforms, reducing the time taken to obtain the second opinion.

Furthermore, the use of image analysis algorithms in complex cases can assist to improve diagnostic accuracy and resolve discrepancies in results between pathologists by providing an automated, consistent count of HER2 gene copy signals within the cells.

Case Study 4: TAPISTRY Study

One of the key Roche clinical trials being placed in the PrOSPeCT model is the novel platform umbrella study TAPISTRY. TAPISTRY (NCT04589845) is a phase 2, global, open-label, multi-cohort study evaluating the efficacy and safety of targeted therapy or immunotherapy, as single agents or in combination, in patients with unresectable, locally advanced/metastatic solid tumours. Patients are assigned to treatment according to eligibility criteria for biomarker-defined cohorts. Paediatric patients may also be enrolled if age-appropriate formulations/dosages are established.

This clinical trial was placed in Australia on the basis of the national approach to genomic screening and Roche has the opportunity to explore many trial delivery experiments within this framework including teletrial options and opening a clinical trial site in Darwin - a first for Roche.

The data coming out of PrOSPeCT is also invaluable to future trial design and delivery. Not only do we gain insights into the prevalence of biomarkers, but also the geographic spread of these patients. Increasingly successful trial placement and delivery on patient numbers and data quality, will ensure our ongoing reputation as a world class destination for clinical trial placement.