2030 Vision for Cancer
Response from Sanofi
6 March 2020

Introduction

Sanofi supports the call from the National Oncology Alliance for the development of a National Cancer Plan for Australia. In doing so, we have addressed the following three themes:

- Equitable and timely access to the best and latest treatments and technologies;
- Understand and measure outcomes for future investments; and
- Key challenges and areas for improvement for clinical trials.

Oncology research is important for Sanofi, with a large percentage of our investment and development is going into this therapeutic area. Greater knowledge of the genetics of various cancers, the emergence of 'checkpoint inhibitors' that can help the immune system defeat a tumour's defense mechanism, and major advances in our understanding of other novel potential targets and delivery mechanisms have vastly expanded the options for researchers.

Over the next decade, with the right policy settings and funding pathway, Australians will benefit from more personalised and individualised oncology therapies. Getting these new medicines to patients in an appropriately timed manner will deliver value to all stakeholders across the healthcare ecosystem, including patients and their carers, healthcare professionals, governments and industry.

While scientific knowledge in relation to oncology is advancing at a rapid rate, we know that bringing the Vision 2030 for Cancer to fruition will not be without its challenges. We believe the likelihood of success will be increased by all stakeholders contributing their views – and ensuring the patient remains central to all policy considerations. With this in mind, we are pleased to present our views on the following priority areas.

Equitable and timely access to the best treatment and technologies

A meaningful National Cancer Plan should include strategies that help facilitate timely and affordable access to the latest innovative treatments for Australians diagnosed with cancer.

At each PBAC meeting, submissions seeking consideration are dominated by oncology. For example, at the November 2019 PBAC meeting, more than a third of the agenda items were for oncology treatments. With this in mind, we need to ensure that the PBAC process is fit-for-purpose.

We question whether the PBAC in its current format is indeed fit-for-purpose. To demonstrate, we would like to consider multiple myeloma. This is the second most common blood cancer worldwide (GLOBOCAN 2018 data). In Australia, 5,345 people were diagnosed with multiple myeloma during a 5--year period from 2010 through to 2014 (Cancer Australia, 2019[1]). The chance of surviving at least 5 years following a diagnosis of multiple myeloma is only 51%.

Multiple myeloma patients have the highest excess mortality risk among blood cancers (19.5--fold compared to the general population) [1]. Prognosis further worsens after each relapse; median overall survival decreases from 48.2 months after first line to 5.8 months after fifth line therapy [2]. In relapsed/refractory multiple myeloma (RRMM) patients who have failed two or more lines of therapies, median overall survival was reported to range from 7.9 to 15.2 months [3, 4]. Approximately one-third of RRMM patients have a poor prognosis and are difficult to treat due to their disease profile, advanced age, and comorbidities [5, 6, 7, 8, 9].

[1] https://myeloma-cancer.canceraustralia.gov.au/statistics

Due to a complex combination of a heavy symptom burden and adverse events/toxicity from multiple treatment regimens, multiple myeloma patients experience a clinically meaningful decline in health--related quality of life [10].

Multiple myeloma is a complex disease to treat. The PBAC have considered treatment options for multiple myeloma during the: (i) 2017 DUSC review; and (ii) May 2018 stakeholder meeting. Despite this, treatment options available to Australians are limited compared with international standards of care. This problem is likely to become worse.

Most multiple myeloma trials are based on new therapies used in combination with an existing medicine. Although these studies show the best outcomes in terms of prolonging overall survival, demonstrating cost-effectiveness will be difficult even at negligible prices for the new therapies, as combination therapy also significantly extends the use of existing medications. Without an appropriate framework to fund new combination therapies for multiple myeloma - and other cancers, Australia risks being left even further behind.

Taking a closer look at multiple myeloma in Australia from registration to PBS listings highlights that not all molecules registered with the TGA are submitted to PBAC. This begs the question why. Is it because the PBAC is not-for-purpose to assess the clinical benefit and budget investment? This analysis was restricted to multiple myeloma. It is possible that this trend will be seen across other cancer treatments.

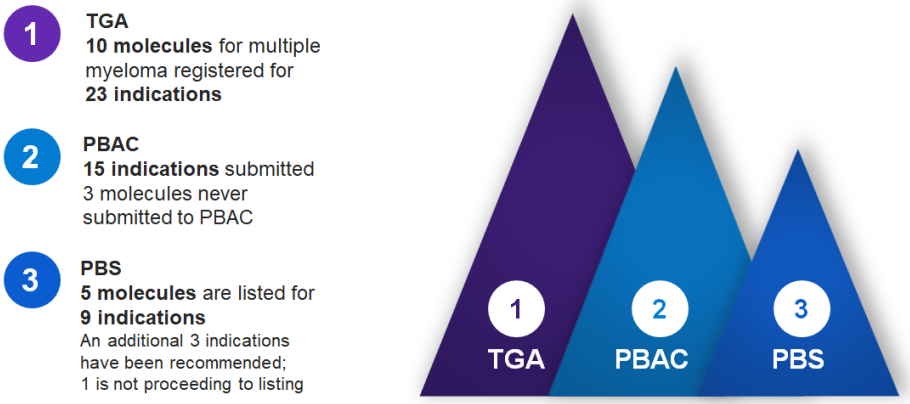


Figure 1. Multiple myeloma in Australia from registration through to PBS listing

The challenges of valuing and paying for combination therapies in oncology has already been identified. A 3-day workshop was held in Sydney last November. The challenge being that add-on therapy to a backbone that is already PBS-listed is not cost-effective even when the add-on therapy is at ZERO price. As mentioned above, combination therapies in oncology often increase the duration of treatment of the backbone. Frequently, the add-on therapy and backbone therapy have different Sponsors with confidential deeds of agreement protecting special pricing arrangements.

Possible solutions, as discussed at the workshop, include:

- **Evidence-based value attribution.** Research is needed into how value could be attributed, and who should be doing it
- **Flexible payments and pricing mechanisms.** The legalities of price negotiations need to be explored.

This challenge is not unique to Australia. The UK published a paper in 2014 titled *'Assessing technologies that are not cost-effective at a zero price.'*[2] And Europe recently released *'Challenges in the value assessment, pricing and funding of targeted combination therapy in oncology.'*[3]

Access to innovative cancer treatments has been improved in countries that have alternative approaches in place that allow earlier funded access. Examples include:

- The AMNOG procedure in Germany where new medicines are reimbursed right after EU approval with assessment 1-year later;
- The Cancer Drug Fund (CDF) in the United Kingdom; and
- Scotland has just introduced an interim funding mechanism like the CDF, where submissions with high uncertainty are funded on an interim basis and re-assessed later.

These pathways enable patients to access effective cancer treatments while additional evidence is generated.

Some countries have reimbursed early access programmes. The French ATU offers free pricing and full reimbursement. The difference from the price negotiated at launch is paid back. Countries with their own unique version include, but are not limited to, Switzerland (Article 71), Israel (29C pathway), Hungary, and Latvia.

Perhaps now is the time to take a closer look at registration pathways to ensure timely reimbursement. The TGA has in place work sharing arrangements. By working with similarly advanced HTA markets, the PBAC evaluation time could be reduced.

Enabling access to new and effective therapies for all Australians with cancer is a key challenge that needs to be addressed through the development of a National Cancer Plan. Whilst broader in its remit, an updated National Medicines Policy should provide the bulwark upon which a National Cancer Plan is based. The current review of the National Medicines Policy presents a timely opportunity to modernise the policy to ensure it encapsulates new ways of treating, and in the future, curing cancer.

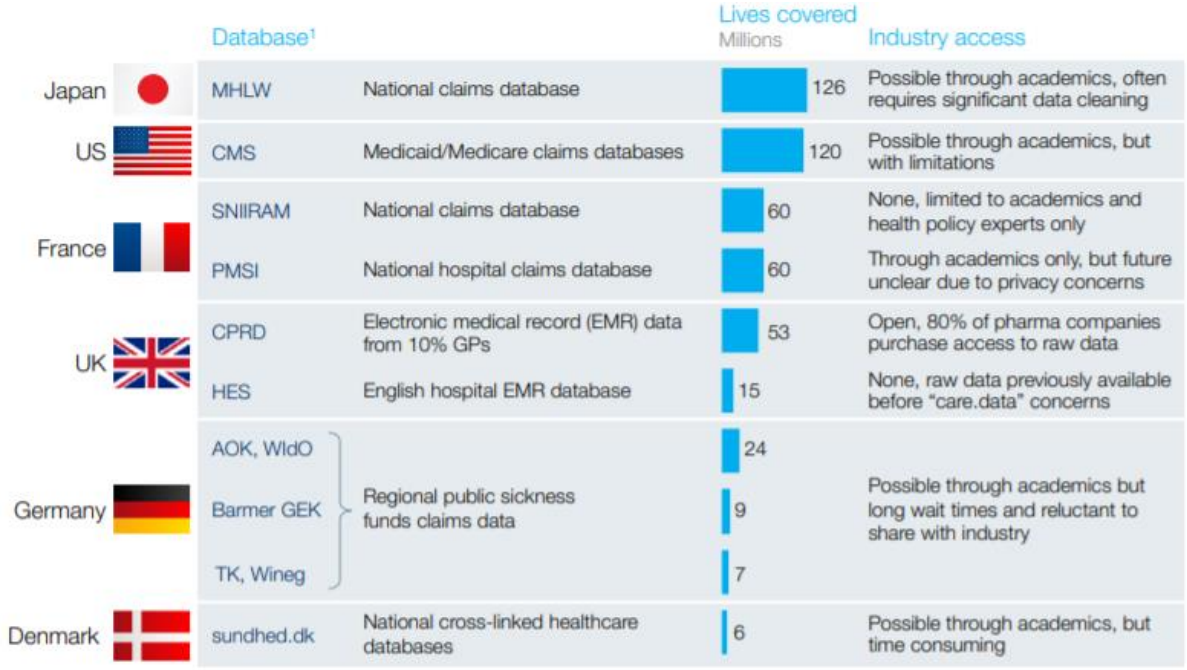
A final consideration is the role of the Australian Government in enabling access in a timely and equitable manner to cancer treatments. It is not the role of the Government, as opposed to the PBAC, to show an increased willingness to pay for these treatments?

Understand and measure outcomes for future investment

There is no formal framework for the use of real-world evidence (RWE) in Australia, as there is in other markets. While a few developed countries have accumulated large datasets containing information about several hundred million patients[11] (see figure below) the approach to collecting, evaluating and using RWE around the globe is inconsistent.

[2] https://www.ncbi.nlm.nih.gov/books/NBK310371/pdf/Bookshelf_NBK310371.pdf

[3] https://www.sciencedirect.com/science/article/pii/S0168851018304597?via%3Dihub#!



	Database[1]		Lives covered (Millions)	Industry access
Japan	MHLW	National claims database	126	Possible through academics, often requires significant data cleaning
US	CMS	Medicaid/Medicare claims databases	120	Possible through academics, but with limitations
France	SNIIRAM	National claims database	60	None, limited to academics and health policy experts only
	PMSI	National hospital claims database	60	Through academics only, but future unclear due to privacy concerns
UK	CPRD	Electronic medical record (EMR) data from 10% GPs	53	Open, 80% of pharma companies purchase access to raw data
	HES	English hospital EMR database	15	None, raw data previously available before "care.data" concerns
Germany	AOK, WIdO	Regional public sickness funds claims data	24	Possible through academics but long wait times and reluctant to share with industry
	Barmer GEK		9	
	TK, Wineg		7	
Denmark	sundhed.dk	National cross-linked healthcare databases	6	Possible through academics, but time consuming

1 CPRD (Clinical Practice Research Datalink), HES (Hospital Episode Statistics), MHLW (Ministry of Health, Labour, and Welfare), PMSI (Le Programme de médicalisation des systèmes d'information), SNIIRAM (Système National d'Informations Inter Régimes de l'Assurance Maladie), WIdO (Wissenschaftliches Institut der AOK).

Source: Interviews with industry and other thought leaders; press releases; publications; websites

Despite investment of more than AU$1 billion, the 2012 launch of Australia's Personally Controlled Electronic Health Records (PCEHR), now called My Health Record, has yet to deliver significant dividends for patients. The intent of the program was to make the health system more agile and sustainable and allow healthcare organisations to have faster, easier access to more health information for improved treatment decisions. However, widespread adoption and use of the system is still a way off, with concerns about usability and patients' online literacy thought to be impacting uptake[12].

Without the ability to access 'big data', via linking and integration of data sets, the opportunities for Australian RWE are hampered by inadequate sample sizes, timeframes and costs. To truly harness the benefit of RWE, investment is needed in RWE expertise, capability, and governance across the healthcare ecosystem to elevate the science and methodology. Finally, we believe the inclusion of appropriate and validated patient-reported experience measures (PREMs) and patient-reported outcome measures (PROMs) in randomised controlled trials (RCTs) is important, and can also be implemented in real world evidence, such as observational studies.

Key challenges and areas for improvement for clinical trials

<u>Adequate resourcing for clinical trials teams in public hospitals:</u>

We are entering a phase of very complex trial designs targeting very specific and small patient populations. This implies that a lot of pre-screening activity must be undertaken at sites to identify the very few potential patients that will be eligible for a clinical trial. The shortage of staff to do this pre-screening activity at some sites leads to delayed patient identification and unmet recruitment targets. To overcome these challenges, adequate funding for clinical trial teams is needed. Further, ensuring clinical trials are valued as a part of the healthcare system will potentially help to incorporate industry-led clinical trials as a part of the public healthcare system.

Lack of uniform electronic health records:

Many public hospitals still use a hybrid electronic health records system (e.g. scanned paper + EMR). As a result, clinical trial staff cannot sort and identify potential patients for a given trial but must wait for the patient to visit the clinician to be able to discuss the trial. Investment in a robust uniform electronic health record, which the clinical trial teams onsite can access to sort patient data based on trial requirement, will help the site team to identify potential patients. This will eliminate the need for the site team to manually review extensive medical records.

Potential impact on long-term investment in R&D

As global clinical guidelines evolve to reflect therapeutic advances, a lack of funding for backbone therapies that are deemed 'standard of care' can impact the attractiveness of Australia for investment in global R&D for novel combinations. Further, as major regulators, such as FDA and EU, seek to utilise RWE from large connected health datasets to support earlier registration Australia risks being left behind. In particular, the newer registration pathways, such as provisional registration that are critical for cancer patients to gain early access to promising therapies, may no longer be viable if RWE becomes accepted in other jurisdictions and equivalent Australian data cannot be generated. A comprehensive National Cancer Plan should seek to avoid such as scenario from occurring, as this would have negative health, social and economic impacts for the Australian population.

Ethics and research governance:

One of the biggest challenges for Australia is the prolonged start-up period. At a time when we have moved well into mutual recognition of HREC approvals across states, we have moved a step backward by mandating that all NSW sites must get approval from Bellberry for a Phase-1 trial. This will delay start-up timelines for early phase trials, which have multi-state sites. The local research governance process is extensively delayed in most public hospitals. This leave our sites disadvantaged with shorter recruitment windows when we have global competitive recruitments.

Involvement of remote sites in global clinical trials:

We believe greater emphasis should be placed on a process to encourage tertiary institutions to involve rural sites in clinical trials. This could include active use of the tele-trials so that patients that are in remote suburbs and towns are able to benefit from novel medications via clinical trials. The Australasian tele-trial model has been developed by the Clinical Oncology Society of Australia (COSA) Regional and Rural Group in consultation with clinical trial sponsors, clinicians, health administrators and regulatory bodies. Familiarisation and promotion of this model across states will be a great step for patients and should be considered as part of the development of a National Cancer Plan.

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