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Mind the gap: An analysis of foregone health gains from unfunded cancer medicines in New Zealand

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ABSTRACT

Publicly funded cancer medicines listed on the New Zealand Pharmaceutical Schedule were compared with those listed on the Australian Pharmaceutical Benefits Scheme. To quantify the health gains offered by the cancer medicines funded in Australia but not in New Zealand, clinical trial data reporting median progression-free survival (PFS) and overall survival (OS) were sought. The differences in the median PFS and OS for the unfunded medicines, relative to the comparator medicine funded in NZ, were then assessed against the American Society of Clinical Oncology Cancer Research Committee (ASCO-CRC) recommended targets for clinically meaningful health gains. Our analysis confirms that, whilst New Zealand funds fewer cancer medicines than Australia, most of the additional medicines funded in Australia do not deliver clinically meaningful health gains as defined by the ASCO-CRC guidance. This suggests that New Zealand is not missing substantive opportunities for improvements to New Zealand's cancer survival rates through additional medicines funding. A policy of funding more new cancer medicines in order to achieve numerical parity with Australia or other countries would not result in substantive health improvement and would cost significantly more, and investing the millions of dollars needed to achieve funding parity with other countries would not represent good value for money in terms of delivering the best health outcomes for all New Zealanders, rather selective funding of new medicines that demonstrate clear clinical benefit and that are cost-effective and affordable is the sensible approach.

1. Introduction

The Pharmaceutical Management Agency, or PHARMAC, is the government agency that decides which medicines are publicly funded in New Zealand. PHARMAC is charged with ensuring that New Zealand obtains the best health outcomes from funded pharmaceuticals from within the amount of funding provided [1]. It is therefore interested in understanding whether its funding decisions enable access to the right mix of medicines to achieve that goal.

Pharmaceutical industry–funded reports frequently provide comparisons of medicines funded by various countries national healthcare systems [2–5], with some painting a picture of funded medicines access in New Zealand being low and slow. The authors of such reports usually draw their conclusions by counting the number of medicines funded in each country, or the time taken to fund them from regulatory approval, but rarely do they explore the value of the unfunded medicines in terms of their health benefits, risks, affordability, and likely impact on population health outcomes, including consideration of opportunity cost (alternative medicines or health services that the same funding could purchase). Some reports suggest that access to fewer cancer medicines in New Zealand results in worse population health outcomes. A recent example written by Medicines New Zealand [6], the New Zealand Pharmaceutical Industry association, argued that the observed lower cancer survival rate in New Zealand compared

A preliminary analysis comparing Australian and NZ cancer medicine funding at the cut-off date of 25 March 2015 was presented at the New Zealand Society of Oncology (NZSO) Meeting in October 2015, a report of these finding was also published on PHARMACs website http://www.pharmac.govt.nz/assets/cancer-comparisons-summary-2015-10-03.pdf. A short presentation of some of the analyses contained in this paper, cut-off date of 30 April 2016, was presented at the NZSO Meeting in October 2016.

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with Australia [7] was likely the result of differences in funding of cancer medicines between the two countries. We were interested in exploring this further by asking the question whether achieving numerical parity with Australia for funded cancer medicines would make a clinically meaningful impact on cancer outcomes for New Zealand.

Health benefits offered by new cancer medicines may range from marginal (progression-free survival [PFS] improvement of only a few weeks or less, with no effects on overall survival [OS]) to substantial and clinically meaningful (improved long-term OS of several months or more).

Most new cancer medicines are developed and marketed on the basis of clinical trial data showing *statistically* significant improvements in length of life or time to disease progression over placebo or a comparator treatment. However, in many cases, the *absolute* health gains for patients from these medicines are small, coupled with prices that are increasingly disproportionate to the small benefits provided [8–10]. A recent analysis by Howard and colleagues showed that the average launch price of new cancer medicines, adjusted for inflation and survival benefits, had increased 10% annually over the last decade, up US $8,500 each year [11]. This price inflation far outweighs the survival benefits offered by these new medicines with the estimated price per year of life in 1995 being $54,100, rising to $139,100 in 2005 and $207,000 by 2013. One example of disproportional pricing is in colorectal cancer; although new medicines have indeed improved outcomes for patients with metastatic disease, nearly doubling the median survival time from 12 to 21 months, this gain has come at a 340-fold increase in cost [12].

The rising cost of cancer medicines, and the impact on healthcare systems and patients, has been debated in many countries including the United States. Some US hematologists and oncologists have strongly asserted that the health gains offered for some new cancer medicines do not justify their premium costs, leading to decisions not to prescribe them [13–16] and recommendations to consider the so-called “financial toxicity” new medicines place on patients [17]. In countries with universal publicly funded healthcare the rising cost of medicines threatens the sustainability of these systems, risking budget overspend and diversion of funding away from other, more cost-effective health interventions [18,19].

In response to this increasing trend of higher pricing and more marginal health gains, the American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology (ESMO) have developed tools to help prescribers determine the value of the health benefits offered by new medicines [20,21]. The ASCO Cancer Research Committee (ASCO-CRC) also recently published recommended targets for clinically meaningful PFS and OS gains for new cancer treatments [22]. These targets were developed with broad input and diverse points of view by working groups comprising pancreas, breast, lung, and colon cancer experts including clinical investigators, biostatisticians, patient advocates, US Food and Drug Administration (FDA) oncologists, and industry oncologists.

PHARMAC uses its Factors for Consideration [23], previously Decision Criteria [24], which include, amongst other things, consideration of health need, benefits and risks, value for money and affordability to determine the relative importance (rank) of its various funding options and inform its funding decisions. Like many other public medicines funding bodies internationally, PHARMAC uses cost utility analyses (CUAs) to estimate the value-for-money, or cost effectiveness, of new medicines in terms of cost per quality-adjusted life-year (QALY). However, such analyses are complex to perform and can be highly imprecise, or biased, where the evidence base from clinical trials is limited or confounded, for example by cross-over of patients from the comparator arm to the intervention arm. Thus, relying on cost-effectiveness analyses alone to drive funding decisions through use of explicit cost-effectiveness thresholds as some public funding bodies do, is problematic. PHARMAC uses cost-effectiveness analyses to provide information on the relative value of one medicine funding choice compared with other funding choices. When used this way to deliver information regarding relative value, or rank, rather than trying to derive an absolute value, the impact of poor quality or biased clinical trial evidence is less critical. Using cost-effectiveness this way is also less resource intensive, in many cases simple models can be used with the impact of various inputs tested through sensitivity analyses, thus resource can be focussed on the few key inputs that impact the model outputs, and other inputs that don’t substantially change the output can be largely ignored.

However, when used in isolation cost-effectiveness analyses, whichever way they are used, do not address the issue of opportunity cost and affordability of new medicines. PHARMAC’s national fixed budget for medicines ensures that it fully considers the opportunity cost and affordability of new medicines when making its funding decisions. PHARMAC ranks new medicines as options for investment taking into account its Factors for Consideration, a process that ensures that funding for the most valuable and affordable medicines is progressed. However, having a fixed budget means that not all new medicines can be funded as health demands exceed ability to pay. Health gains may need to be foregone in some disease settings in order for PHARMAC to deliver on its objective of providing the best health outcomes from medicines for all New Zealanders from the available funding.

To describe the population health gains foregone from unfunded cancer medicines, PHARMAC commissioned research comparing funded cancer medicines in New Zealand and Australia. To understand whether any funding gap would likely be substantively contributing to New Zealanders’ poorer cancer outcomes compared with Australia, we considered whether the non-funded cancer medicines would deliver clinically meaningful health gains for patients or not. Australia was selected as the comparator because of cultural proximity, readily available medicines funding information, and its reportedly superior cancer survival rates compared with New Zealand [7]. For reasons of geographic proximity, along with population ties between the two countries, it is also often quoted in New Zealand as the most obvious comparator country.

2. Method

The Australian Pharmaceutical Benefits Scheme (PBS) [25] and the New Zealand Pharmaceutical Schedule [26] were queried to identify publicly funded cancer medicines as of April 30, 2016. Analyses were performed to identify the medicines and their funded indications in cancer that were the same in both countries as well as those funded in one country and not the other.

To describe the health gain expected from the medicines funded only in Australia and not in New Zealand, we sourced clinical trial data reporting PFS and OS for each of the Australian funded indications for these medicines from the Australian Product Information (PI) document. We selected PFS and OS as the most appropriate measure of health gain as these are standard, internationally recognised cancer endpoints widely used in comparative clinical trials to quantify health benefits.

PFS is defined as the time from randomisation (ie, when a patient is enrolled into a clinical trial) until cancer disease progression or death. OS is defined as the time from randomisation until death from any cause [27]. The Australian PI document was chosen as the primary source document for PFS and OS data.