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Patent expiry and costs for anti-cancer medicines for clinical use

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Venkatesan S et al. have researched patent rights and pricing for (non-)tyrosine kinase inhibitors. It is not clear why the patent rights are so long and why prices of (non-)tyrosine kinase inhibitors can be high. These issues are discussed.

Keywords: Cancer medicines, generics, health gain, prices, tyrosine kinase inhibitors

Drs Brian Godman, Claudia Wild and Alan Haycox review the paper by Venkatesan S et al. on the patent expiry of (non-)tyrosine kinase inhibitors (TKIs) [1].

Venkatesan S et al. are to be congratulated on publishing their interesting paper providing general insight into exclusivity and patent rights for the non-TKIs [1] used in the treatment of patients with cancer. The authors point out that the TKIs and some of the non-TKIs have long exclusive rights, which is a concern especially given some of their marginal or small health gains versus current standards. It is not clear why the patent lives are so long, and why there are such differences between Europe and the US. This may well be because of orphan status and other considerations; however, this information is not provided in their paper. The authors suggest that the long patent life may be due to the limited development time for these compounds; but this may also not necessarily be the case. In any event, as Venkatesan S et al. point out, there is increasing concern with the growing cost of new medicines [2], which would be enhanced by granting premium prices and long patent lives for new medicines. Countries, even high-income countries, are now struggling to fund all new valued medicines, which is not in the interest of any key stakeholder group [2, 3].

There has been a rise in the clinical approvals of kinase inhibitors. Consequently, this is one of the reasons why TKIs were singled out for special attention in this paper. However, the review suggests that all TKIs are equally beneficial, which is not the case. Having said this, imatinib is a concern to payers with sales

enhanced by off-label use with initially high prices granted on the basis of orphan status [4]. Global sales were estimated at US\$4.75 billion in 2014, making imatinib the 14th highest selling product worldwide that year [5]. The rationale for choosing the non-TKIs is also not fully explained. Nevertheless, the paper gives very good insight into their likely generic drug availability, which is crucial for health authorities given the low prices that could be achieved for some of these cancer medicines [6].

In the discussion, the authors make a number of good points regarding high prices for new cancer medicines. This is a key concern across countries, with prices of new cancer medicines rising up to tenfold during the past decade [7, 8]. Prices for new cancer medicines now average US\$150,000 or more per year of life gained [9], often with marginal health gain versus current standards [10]. In their recent review, Grössmann and Wild [11] documented that out of 134 new indications approved for cancer medicines since 2009, no data was available for progression-free survival or overall survival in 27%. A positive impact was seen for median overall survival in 55.5%; however, only 16% showed a difference of more than three months [11], which is increasingly seen as a minimum for a new cancer medicine to be seen as an advance [2, 10]. These concerns with ever increasing prices led to calls by US oncologists to pharmaceutical companies to moderate their growth in the future [12, 13]. High prices are also a major concern to lower- and middle-income countries, which currently account for more than 70% of cancer mortality [14]. Increasing prices of new cancer medicines are also threatening the sustainability of universal health care



in those countries that provide this given ever-growing prevalence rates for cancer [7, 15]. This is leading to calls that cancer should no longer be singled out for special attention as this has been exploited [16].

It is estimated by some authors that the cost of bringing a new cancer medicine to the market is lower than US\$100 million [13], and that prices of generic bortezomib, dasatinib, everolimus and gefitinib could potentially be as low as 1% of the current selling price [6]. This justifies calls for price moderation for new cancer medicines, as well as initiatives to make generics of valued cancer medicines available as early as possible with the cost of cancer medicines now accounting for an ever increasing proportion of the total costs of cancer care [7]. In the meantime, health authorities need to critically rethink how new cancer medicines should be valued, especially given concerns with surrogate markers [2, 10, 17]. Payers and providers also need to increasingly collaborate before product launch to agree on the likely patient populations that will receive the most benefits from the new cancer medicines in order to limit their budget impact [18], and keep to this, as well as seek extensive discounts through risk-sharing arrangements [2, 19].

Overall, the paper by Venkatesan S et al. gives good insight into likely generic drug availability of key cancer medicines, which is crucial for health authorities given the potentially low prices that could be achieved [6]. The paper also highlights the need for increased transparency in relation to development times and patent periods, the need for new cancer medicines to be appraised similarly to all other medicines

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for pricing and reimbursement evaluations, and not singled out for special status, as well as greater transparency in pricing and reimbursement evaluations. The latter gives increasing concerns with high prices for new cancer medicines coupled with the low cost of goods of some [6, 13]. Finally, the observation that the development time for these (non-)TKIs is rather short should be investigated further through researching the actual timescales for phases I to III trials and earlier of the TKIs.

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