The global imperative to make cancer medications affordable

The value of any medication is determined by the magnitude of the clinical benefit (improved survival and quality of life of patients) and the cost of the medication. Recent studies\(^1\)\(^2\) have suggested that, in the USA, there is no correlation between value and list prices for new cancer medicines. Assuming that this disparity is an aberration caused by the suspension of market forces in cancer medication pricing in the USA, it seemed reasonable to hypothesise that the situation might be different in countries with robust processes for health technology assessment and managed market entry with price negotiation.

On the basis of their analysis of medication prices in England, Germany, France, and Switzerland, all of which have strong health technology assessment processes and price negotiation, Kerstin Vokinger and colleagues\(^3\) conclude that this hypothesis is not correct. Findings from Vokinger and colleagues’ study showed that although drug prices in these European countries are lower than in the USA, prices are high, and the disconnect between value and pricing persists, which is consistent with findings previously reported from Italy.\(^4\)

In a combination of circumstances, the era of targeted and biological cancer therapies coincided with a deliberate suspension of market forces in the pricing of cancer medicines in the USA with the enactment of the US Medicare Modernization Act of 2003. This legislation included a non-interference clause, compelling Medicare Part D, which is a major federal programme to facilitate medication access to older citizens and citizens on low-incomes, and its providers to provide all cancer medications approved by the US Food and Drug Administration at the manufacturers’ list price without price negotiation.\(^5\) At the time of massive innovation in cancer care, this policy of unrestrained market access facilitated spiralling prices and profits and a disconnect between value and cost.\(^5\)\(^6\) In the global economy of cancer therapeutics, there is a bidirectional relation between pricing in the USA and the rest of the world, including Europe. These circumstances incentivised pharmaceutical manufacturers to price new medications as high as the US market would bear.\(^1\)\(^4\) These high prices served not only to maximise local profit from the US market, but also to peg future negotiations with other countries, thereby buffering the effect of the downward pressure of international reference pricing and price negotiation for managed market entry.\(^7\)

Furthermore, in countries with price negotiation and managed market entry for cancer medicines, the terms of the agreements and the true net purchase prices are generally concealed in non-disclosure contracts. This concealment effectively precludes truly informed international reference pricing.\(^7\)

A 2018 report by WHO highlighted that these spiralling medication prices and the disconnect between price and value adversely affect the health and financial wellbeing of many individual patients and their families, equitable access to care, and the sustainability of health-care systems.\(^8\)

Confronting the factors that have contributed to these pricing conditions is a global problem. The dual aim of improving affordability and value, while also preserving and promoting adequate incentives to capital investment, research, and development for oncology treatments, is intrinsically challenging. This challenge is reflected in the conclusions of the 2019 WHO Fair Pricing Forum,\(^9\) which acknowledged the difficulties in defining fair pricing and which established a working group to address this issue.

Other important developments are emerging. In May, 2019, the World Health Assembly approved a resolution to improve the transparency of markets for medicines, vaccines, and other health products, aiming to gather evidence on whether transparency can reduce costs and expand access. Promoting price setting that is linked to performance can be facilitated by coordinated health technology assessment processes and managed market entry in all markets, including that of the USA. Such processes are increasingly assisted by the use of well validated scales for the evaluation of clinical benefit, such as the European Society for Medical Oncology Magnitude of Clinical Benefit Scale.\(^10\) In the USA, there is a growing bipartisan appreciation that the rapidly rising cost
FGFR inhibitors for advanced cholangiocarcinoma

The prognosis of advanced or metastatic cholangiocarcinoma is extremely unsatisfactory, mainly owing to few treatment options and poor responses to conventional chemotherapy regimens. Since 2007, advances in next-generation sequencing have substantially improved the ability to understand the complex molecular mechanisms underlying the progression of cholangiocarcinoma. The most promising target for cholangiocarcinoma identified in recent years is the fibroblast growth factor (FGF) signalling pathway, which consists of 22 human FGFs and four transmembrane receptor tyrosine kinases (FGF receptors [FGFRs] 1–4). Fusions, rearrangements, translocations, and amplifications of FGFR genes are closely related to the initiation and progression of some cancers. FGFR2 mutations have been identified in nearly 20% of all cholangiocarcinomas and targeting this kinase presents a novel and exciting therapeutic strategy against cholangiocarcinomas. Several FGFR-specific inhibitors are being assessed in clinical trials for FGFR-mutant cholangiocarcinomas, including non-selective and selective FGFR inhibitors.

Non-selective FGFR inhibitors bind to the conserved ATP-binding domain in receptor tyrosine kinases such as platelet-derived growth factor receptors (PDGFRs) and vascular endothelial growth factor receptors (VEGFRs). These agents are less potent against the FGF signalling pathways than selective FGFR inhibitors and have some toxic side-effects, which limit their clinical use even when administered at the required