Ravidasvir: equitable access through an alternative drug development pathway

The development of highly effective direct-acting antivirals has made it possible to imagine the global elimination of hepatitis C, which afflicts an estimated 58 million people and causes 290 000 deaths globally each year.[1] Inspired by this possibility, in 2016, WHO established the goal of eliminating viral hepatitis globally by 2030.[2]

However, there are several challenges that stand in the way. For instance, direct-acting antivirals are prohibitively expensive, especially in countries that cannot procure generic versions. Middle-income countries also struggle to procure generic direct-acting antivirals as they are excluded from voluntary licensing agreements, which allow only specific countries to procure generic direct-acting antivirals from manufacturers licensed by the patent holders. Many patients, especially those from marginalised populations, also face difficulties in accessing testing and treatment services for hepatitis C.[3]

To resolve these challenges, the Drugs for Neglected Diseases initiative (DNDi) set a goal in 2016 to develop a safe and effective direct-acting antiviral that would be made accessible and affordable to all. To meet this goal, DNDi pursued an alternative drug research and development pathway: one with affordability at its core and founded on collaborations with low-income and middle-income countries (LMICs). This alternative pathway is in direct contrast to the traditional pharmaceutical research and development model, which focuses on profit maximisation and collaborations in high-income countries.

In 2016, DNDi established an innovative partnership between the Ministry of Health in Malaysia, the Ministry of Public Health in Thailand, Pharco Pharmaceuticals in Egypt, and Pharmaniaga in Malaysia to jointly develop ravidasvir using this alternative pathway. Pharco agreed to collaborate on the development of ravidasvir and to supply generic sofosbuvir for the clinical trials of the ravidasvir–sofosbuvir combination. The clinical trials were largely funded by the Malaysian and Thai ministries, and the Transformative Investment Capacity of Médecins Sans Frontières (Doctors Without Borders). Once successfully developed, Pharmaniaga would manufacture and hold the license for ravidasvir in Malaysia. Legal agreements were signed with all parties to ensure that ravidasvir would be widely affordable and accessible, and that other pharmaceutical manufacturers would be allowed to make generic versions.

Clinical trials (STORM-C) for ravidasvir were done in Malaysia and Thailand between July, 2016, and September, 2017. The results of the STORM-C trials showed that the ravidasvir–sofosbuvir combination was safe and effective in curing hepatitis C for 97% of enrolled participants, including those with genotype 3 infection, the hardest to treat genotype.[4]

Following the success of the STORM-C trials, Pharmaniaga successfully registered ravidasvir as a treatment for hepatitis C with the Malaysian National Pharmaceutical Regulatory Agency in June, 2021. This decision was a first in two respects. It was the first time that either DNDi, Pharco, or Pharmaniaga had ever applied to register a new chemical entity without partnering with a major pharmaceutical company. It was also the first time that the National Pharmaceutical Regulatory Agency evaluated a new chemical entity that had not already been approved by one of the WHO-designated Stringent Regulatory Authorities.[5]

The successful development of ravidasvir has a few lessons to offer. First, country leadership is crucial to tackle public health challenges such as hepatitis C. The leadership of the Ministry of Health and the Malaysian Government helped the partners navigate the complex obstacles of the drug development process. The Ministry of Health also expanded hepatitis C testing and treatment services in the Malaysian public health-care system, while using compulsory licensing to secure affordable supplies of sofosbuvir from Pharco, despite the intense global political pressure against it.[6,7] Similarly, the Thai Ministry of Public Health invested heavily in the STORM-C trials, despite the possible risk of failure.

Second, successful drug development can be done through collaborations based in LMICs. It is often assumed that novel drug development can only be done in high-income countries and dispelling this myth is an important step towards addressing the need

for accessible treatments in LMICs.[8–10] This is crucial especially because LMIC-based collaborations provide opportunities for learning, technology transfers, and self-reliance.

Third, it is possible to place affordability and public health priorities at the heart of drug development. DNDi's goal to develop an affordable direct-acting antiviral largely succeeded due to industrial partners who chose to maximise societal impact rather than profit, and government partners who chose to invest in clinical trials despite the risk of failure. In other words, this successful alternative model brought public duty principles to private companies and private risk-taking principles to public organisations.

Ravidasvir will help cure hepatitis C in many people who would not otherwise receive direct-acting antivirals. The innovative partnership built by DNDi shows that LMIC-based collaborations in novel drug development are both possible and desirable, and perhaps a signal even to high-income countries that the traditional reliance on major pharmaceutical companies for drug development might change with time. Alternative models of drug development, including this one, will support our shared aim for health equity worldwide.

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