Delayed access

THE IMPACT OF BOTTLENECKS IN REGULATORY PROCESSES

Moira Rushton-Marovac, MD FRCPC, PGY5 Medical Oncology, University of Ottawa

TRIAL SUMMARY: The human cost of regulatory delays

Gotfrit J, Shin J, Mallick R, et al. Potential life-years lost: the impact of the cancer drug regulatory process in Canada. Canadian Association of Medical Oncology Annual Meeting. April 26, 2018, Toronto. Abstract 47.

The authors describe the complexities of the Canadian cancer drug approval and funding process, and calculate the life-years lost before assessment by regulatory bodies responsible for technology assessment is complete.

After a positive trial is reported, the drug in question is submitted for Health Technology Assessment (HTA), and the pan-Canadian Oncology Drug Review (pCODR) issues a recommendation that informs subsequent decisions in each province about public coverage of the drug. This study quantified potential life-years lost between the proof of efficacy (POE) presented in either a publication or conference, and completion of the HTA process.

The analysis looked at all drugs for advanced lung, breast and colorectal cancer that underwent a pCODR HTA between 2011 and 2017. Life-years lost were calculated by multiplying the documented improvement for both progression-free survival (PFS) and overall survival (OS) by the number of patients who would have been eligible to receive the drug. This was then multiplied by the time interval from POE to HTA completion, as well as the time from HTA start to completion.

Results: For the 21 drugs included in the analysis, time from POE to HTA decision ranged from 5.4–74.3 months (median 23.9). The HTA assessment itself took 5.6–33.9 months (median 8.8). The remaining time represents the delay between POE and the start of the HTA.

Between POE and HTA decision, 50,881 progression-free life-years were lost (8,523 years in patients with lung cancer; 12,385 years in patients with breast cancer; and 29,972 years in patients with colorectal cancer). The delay between POE and the start of the HTA accounted for

35,199 of those lost years, while the HTA process itself resulted in 15,681 progression-free life-years lost.

Looking at the years lost in OS, life-years lost during the interval between POE and HTA decision were 44,332 (lung cancer 22,940 years; breast cancer 4,509 years; and colorectal cancer 17,333 years). Of these, 23,586 life-years were lost between POE and the start of HTA, while the HTA process itself resulted in 20,746 overall life-years lost.

The study found that a substantial number of potential life-years are lost during the drug regulatory process. Even if one considers that eligible patients may not all receive a given drug, the impact of delays remains substantive. The analysis does not report the substantial additional delays between the HTA decision and the actual provision of provincial funding for a drug. The authors conclude that collaborative national and provincial initiatives are required to address this major barrier to access to treatment.

COMMENTARY: Oncology drug review is an ongoing concern for both patients and providers in Canada and around the world. Not only are new therapeutics required to demonstrate efficacy and safety to Health Canada, but drugs then have to go through various approvals from other organizations, such as pCODR, the pan-Canadian Pharmaceutical Alliance, and provincial cancer agencies, before they are fully accessible to patients.[1] pCODR came into existence in 2011 to increase consistency and clarity in oncology drug assessment, approval and funding across all provinces and territories except Quebec.[2,3]

Recent review of the oncology drug approval process before and after pCODR came into existence found that there has been a significant decrease in the number of days, from 522 days, to 393 days, $p<0.001$.[3] While this may represent an improvement, we are still looking at over a year, on average, in delay from the time a novel therapy is approved by Health Canada to the time a decision is made by pCODR. The work by Gotfrit et al attempted to quantify, in terms of human life-years lost, the effect of regulatory delays on cancer patients in Canada at the pCODR level. This is a compelling approach to an often-lamented problem.

To read that 44,332 OS life-years were lost in 6 years due to regulatory delays is shocking. By looking at the time from proof of efficacy to pCODR decision, the authors provide a real-world estimate of the time it takes oncology drugs to reach Canadian patients—a median 23.9 months. The Health Canada oncology drug approval process has been compared to the US Food and Drug Administration (FDA), showing significantly faster approvals granted by the FDA (8.9 months interquartile range [IQR] 6.0–14.5 vs 12.2 months IQR 10.0–21.1; $p=0.0006$) compared to Health Canada.[4] Unlike in Canada, the FDA has several means to expedite oncology drug review, including the breakthrough therapy program. While this program does get drugs to market faster, it has been criticized as not increasing efficacy or safety of approved therapeutics[5] and often accepts phase 1 and 2 trial data, as opposed to waiting for more rigorous phase 3 data.[6]

Each day an effective oncology drug is delayed in reaching patients who might benefit will result in lives lost. The urgent need to get treatments to patients must be balanced with ensuring that rigor is maintained in the approval process. In Canada, further collaboration between levels of government and the various organizations involved is needed to improve on the successes of the pCODR program. We should advocate for a system that minimizes the number of regulatory organizations that each need time to render their own decisions, in hopes of reducing the red tape involved in getting effective treatments into the hands of patients as safely and quickly as possible.

IN BRIEF

Already known

- Canada has a multi-pronged process for approving new oncology drugs and recommending that they be publicly funded.

What this study showed

- Delays between proof of efficacy of an oncology drug and the start of assessment were a median 23.9 months, with assessment itself taking a further median 8.8 months.
- Over a 6-year period (2011–2017), 50,881 progression-free life-years were lost in patients with breast, colorectal and lung cancer due to these delays.

Next steps

- Collaborative initiatives at federal and provincial levels are required to overcome barriers to access to treatment.

References

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