Journal of Population Therapeutics & Clinical Pharmacology

Editorial

Joel Lexchin, MSc, MD
Professor Emeritus, School of Health Policy and Management, York University
Emergency Physician, University Health Network
Associate Professor, Department of Family and Community Medicine, University of Toronto

Correspondence: jlexchin@yorku.ca

Submitted: May 7, 2018. Accepted: July 23, 2018. Published: September X, 2018.

The article by Rawson and Chhabra in this issue of the *Journal of Population Therapeutics and Clinical Pharmacology* argues that the Ontario Drug Benefit Formulary should not use cost savings as a rationale for funding drugs for off-label use unless there are no other products available to treat a serious condition.[1] In this particular instance, the authors are warning against using bevacizumab as opposed to ranibizumab for retinal conditions. The basis for their warning is the apparent safety difference between the two drugs and the fact that the former has not been approved by Health Canada for treating retinal problems.

However, the first reason is contested ground. A 2014 Cochrane review of non-industry funded randomized controlled trials concluded there was no difference between intravitreal bevacizumab and ranibizumab for deaths, all serious system adverse events (SSAEs), or specific subsets of SSAEs in the first two years of treatment, with the exception of gastrointestinal disorders.[2] If the results of the Cochrane review are valid, then any additional risk of an adverse event from using bevacizumab may be minimal to nonexistent. When there is strong evidence for off-label use as there is for bevacizumab and retinal conditions then the risk of an adverse drug event is the same as for on-label use.[3]

The latter rational introduces the issue of how drugs reach the Canadian market. In this respect, Health Canada, as with all other national drug authorities, is a passive agent, in the sense that it waits until a company submits a drug for approval. Without the application from a company there is no drug to evaluate or to approve. In the case of bevacizumab and ranibizumab, both drugs are owned by Genentech; the one-year cost of the former is $580 per patient, while the one-year cost of the latter is $6,720 per patient.[4] Drug companies sponsor virtually 100% of the trials for new drugs and new indications for existing drugs. It makes no economic sense for Genentech to run a trial to look at the safety and efficacy of bevacizumab for retinal conditions. If the trial was successful Genentech would be cannibalizing its market for ranibizumab, a drug that earns it almost 12 times as much revenue.

Finally, the sponsorship of clinical trials raises the point that not all "evidence" arising from these trials is equal. A Cochrane review, of which I was one of the authors, looked at the results and conclusions of clinical trials sponsored by drug and device companies versus all other sponsors.[5] Industry sponsored studies more often had favourable efficacy results and conclusions compared to studies with any other type of sponsorship.

Companies control what indications are considered by regulatory authorities and what evidence is available to those authorities. Indications chosen by companies and validated by trials that companies control should not be the basis for deciding how public money is spent.

DOI: 10.22374/1710-6222.25.2.4
J Popul Ther Clin Pharmacol Vol 25(2):e31-e32; September 24, 2018.
This article is distributed under the terms of the Creative Commons Attribution-Non Commercial 4.0 International License. ©2018 Lexchin.

CONFLICT OF INTEREST

In 2015–2018, Joel Lexchin was a paid consultant on three projects: one looking at indication-based prescribing (United States Agency for Healthcare Research and Quality), a second to develop principles for conservative diagnosis (Gordon and Betty Moore Foundation) and a third deciding what drugs should be provided free of charge by general practitioners (Government of Canada, Ontario Supporting Patient Oriented Research Support Unit and the St Michael's Hospital Foundation). He also received payment for being on a panel that discussed a pharmacare plan for Canada (Canadian Institute, a for-profit organization) and for writing a brief for a law firm. He is currently a member of research groups that are receiving money from the Canadian Institutes of Health Research and the Australian National Health and Medical Research Council. He is member of the Foundation Board of Health Action International and the Board of Canadian Doctors for Medicare.

REFERENCES

1. Rawson N, Chhabra A. Public reimbursement of prescription drugs used for off-label indications in Ontario. J Pop Ther Clin Pharmacol 2018;25(2).
2. Moja L, Lucenteforte E, Kwag KH, Bertele V, Campomori A, Chakravarthy U, et al. Systemic safety of bevacizumab versus ranibizumab for neovascular age- related macular degeneration. Cochrane Database System Rev 2014;9: CD011230.
3. Eguale T, Buckeridge D, Verma A, et al. Association of off-label dur use and adverse drug events in an adult population. JAMA Int Med 2016;176:55–63.
4. CADTH. Anti-vascular endothelial growth factor drugs for the treatment of retinal conditions - recommendations report. Ottawa; 2016. Available at: https://www.cadth.ca/anti-vascular-endothelial-growth-factor-drugs-retinal-conditions
5. Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. Cochrane Data Syst Rev 2017;2: MR000033.

This article is distributed under the terms of the Creative Commons Attribution-Non Commercial 4.0 International License. ©2018 Lexchin.