July 7, 2011

To The Editor, Journal of the American Medical Association:

Response to: Kesselheim, Meyers and Avorn, *Characteristics of Clinical Trials to Support Approval of Orphan versus Non-orphan Drugs for Cancer, JAMA Vol. 305, p2320-2326.*

Word Count: 412

Kesselheim et al have impugned the critical value of the Orphan Drug Act and Accelerated Approval regulations which have been extremely successful at bringing live saving treatments to patients. The authors attempted a statistically driven comparison of two different disease treatment classes as if this were a randomized controlled comparison. Although they are prone to complain about design flaws in orphan drug trials, they should have spent more time developing their own study design, and used proper controls and analyses to avoid making sweeping and inaccurate conclusions by comparing different groups of diseases and drugs. Regardless of the analysis used, Kesselheim failed to effectively dispute that approved orphan drugs are improving cancer care, or that Accelerated Approval has resulted in more than 70 effective drugs being available in its first 16 years.

The authors consistently confuse two aspects of regulatory law as if they are the same thing: the Orphan Drug Act and Accelerated Approval Regulations. Being an orphan does not guarantee access to Accelerated Approval, and Accelerated Approval can be granted for non-orphan drugs. The Accelerated Approval regulations promulgated during the AIDS crisis have dramatically increased the number of approved cancer and HIV drugs which have transformed care and increased survival. The

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addition of new agents in combination with current treatment is moving us forward in treating cancer, both orphan and non-orphan.

The FDA has done an excellent job using Accelerated Approval to enable cancer drugs to reach the market sooner, which has led to a surge in investment and development of novel and effective cancer treatments. The recent turn away from Accelerated Approval for cancer drugs at an Oncologic Drug Advisory Committee (ODAC), and other misguided analyses, are a threat to the successful transformation of care for rare cancers from one of wishing and waiting, to finally receiving and surviving. The FDA's application of Accelerated Approval is an enormous success with few products being removed from the market. Given that "reasonably likely to predict benefit" is the legal standard, removal of some products from the market was anticipated. The infrequent removal of orphan cancer drugs from the market is testament to the effective use of Accelerated Approval.

The FDA should further improve access to the Accelerated Approval pathway for other orphan products targeting the many rare disease indications that lack treatment today outside of cancer and HIV, which are just as serious and life-threatening but are hampered by far less science and experience and far less development interest and investment.

Regards,

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