INFLUENCE OF PHARMACEUTICAL INDUSTRY ON PUBLISHED CLINICAL TRIAL RESULTS

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ABSTRACT/BACKGROUND

- There have been instances where the drug development process faced challenges and issues related to the accuracy of the data. In many instances the drugs were approved by the FDA only to find out later on that there were gaps in the development process of the drug. Such incidences in the past have created major safety problems. We looked at some of the published data on some of these incidences to make all of us aware that safety and honesty are the best recourse for the development of the drug.

OBJECTIVES

We reviewed three reported cases where there were concerns about the accuracy of the data. The instances to be analyzed in this presentation include the Record 4 Trial, the BMJ Report, and the story of Rezulin.

RECORD 4 TRIAL

- The FDA approved rivaroxaban in July 2011
- The results of the four RECORD trials revealed data integrity problems in the RECORD4 trial.
- An investigation was initiated after concerns were reported by the BMJ and JAMA viewpoints.
- The Lancet published the study in 2009 without mentioning data integrity problems.
- This indicates an incidence where there were some glitches in the clinical development of rivaroxaban.

RECORD 4 TRIAL, contd.

- The Lancet issued a formal correction and apology in December 2022, acknowledging inaccuracies in the original paper.
- Janssen, the drug's marketer, acknowledged the FDA's concerns but stated that the study's safety and efficacy conclusions remain unchanged.

THE BMJ REPORT

- ·Brook Jackson filed a complaint with the FDA regarding issues in Pfizer's COVID-19 mRNA vaccine clinical trials, and reported manipulated data, lack of blinding, and inadequate follow-up on adverse events at three trial sites.

THE LANCET CHALLENGE

- The Lancet Challenge was introduced in 2003 by the editors of The Lancet, Dr. Richard Horton and Dr. Sabine Kleinert.
- This initiative called for pharmaceutical companies to provide the raw data of their clinical trials for independent review to promote openness in reporting clinical trials and to ensure that published projects were accurate and unbiased.
- GlaxoSmithKline and Pfizer responded, providing free access to the raw data of their clinical trials.
- This was a huge step towards promoting honesty in the reporting of clinical trials opened the way for other efforts aimed to improve the reporting of clinical trial results, such as the International Committee of Medical Journal Editors (ICMJE) conditions for clinical trial registration and reporting, and the AllTrials campaign.

THE REZULIN STORY

- Troglitazone was developed by Parke-Davis as the first anti-diabetic drug for patients with insulin resistance.
- The FDA's medical officer cited Rezulin's potential to harm the liver and the heart and recommended against the drug's approval.
- Parke-Davis maintained that the risk of liver toxicity was comparable to placebo.
- Parke-Davis complained to the FDA, and the medical officer was removed from his post.
- Approved on January 29, 1997.
- May 17, 1998: a 55-year-old patient died of acute liver failure after taking troglitazone.
- June 4, 1988: The NIH dropped troglitazone from the study.
- Dr. David J. Graham, an FDA epidemiologist, concluded that patient monitoring was not effective in protecting against liver failure.
- Dr. Janet B. McGill, an endocrinologist wrote in a March 1, 2000 letter to Sen. Edward M. Kennedy: "I believe that the company... deliberately omitted reports of liver toxicity and misrepresented serious adverse events experienced by patients in their clinical studies."
- March 21, 2000, the FDA withdrew the drug from the market.

CONCLUSIONS

- Industry involvement in data analysis and financial interest may lead to biased reports.
- Being honest, revealing financial relations to the industry, and the process of professional peer review are recommended.
- Our message is that honesty is the best policy, asking, "What if my physician gives me this drug? Will I take it?".

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