Biomarkers dramatically improve success rates of new cancer drugs

23 February 2021, by Mark Witten

Credit: National Cancer Institute via Unsplash

In recent decades there have been some big advances in developing new cancer medicines, such as Herceptin, the targeted drug to treat women diagnosed with HER2-positive breast cancer. Despite these successes, cancer remains the second leading cause of death after heart disease and nearly 90% of all cancer drugs entering clinical trial testing fail.

Given the millions of lives at stake and the enormous size of the US$200-billion global oncology drug market, University of Toronto Mississauga biology professor Jayson Parker asked a simple, but all-important question: "Is there a way to improve clinical trial failure risk?"

To find an answer, Parker launched a large-scale research project seven years ago to determine whether the use of predictive biomarkers—which help assess a patient's likely response to a particular treatment—improved the odds that a new cancer drug would be approved in clinical trials conducted over the past two decades. "We know the high failure rate isn't because the medicines being tested aren't working. We wanted to see if biomarkers improved success rates," says Parker, who is also associate director for the Master of Biotechnology Program at UTM.

Now, in a study published on Feb. 23, 2021 in the journal *Cancer Medicine*, Parker and his co-authors provide the first systematic statistical evidence that biomarkers dramatically improve oncology outcomes when it comes to testing new medicines.

The new research compared drug approval success rates in biomarker-based clinical trials to outcomes in trials without biomarkers for four types of cancer: breast cancer, melanoma, non-small cell lung cancer, and colorectal cancer. "Our overall analysis of these four cancers showed drugs tested in biomarker-based trials were almost five times more likely to receive regulatory approval. The evidence strongly supports using biomarkers to improve testing outcomes with new cancer medicines," says Parker.

The greatest benefit was seen in testing new drugs for breast cancer, where biomarker-based trials were 12 times more likely to succeed. There was an eightfold increase in success rates for melanoma drugs that used biomarkers, and a sevenfold increase for lung cancer medicines. While drugs for colorectal cancer showed no overall benefit, the researchers suggest this could change in the future as more biomarkers for colorectal cancer are introduced.

Parker evaluated the performance of both well-established and new, exploratory biomarkers. The study's second key finding revealed that using new biomarkers, before they had been properly validated, also improved success rates in oncology clinical trials. That is surprising and encouraging because some experts thought the use of new, unproven biomarkers could potentially increase failure risk.

"The data showed exploratory biomarkers still

conferred a fourfold benefit compared to no biomarkers. This suggests drug developers can take a chance on new biomarkers because the broad benefits of biomarkers are so strong," he explains.

Parker's paper started as a UTM Research Opportunity Program project in 2014. Seven students have been involved, including four from the MBiotech Program, and they collaborated with an oncologist, computer scientist and data scientist.

Data scientist Nicholas Mitsakakis applied an innovative machine-learning statistical method, known as multi-state Markov modeling, to analyze 20 years of multi-phase clinical trial data. "It was challenging, but exciting to use this method for the first time in an application for cancer drug testing. The data set was a gold mine," says Mitsakakis, who teaches data science in the MBiotech program and is an adjunct lecturer in biostatistics at U of T's Dalla Lana School of Public Health.

The study's robust statistical analysis supports early and aggressive adoption of biomarkers in the design of oncology clinical trials. These new findings matter because oncologists will be more likely to encourage their patients to participate in drug trials that use biomarkers. For the pharmaceutical industry, wider use of biomarkers could reduce drug development costs through better outcomes and the weight of the evidence could help overcome hesitancy or reluctance to use biomarkers because they target subpopulations of patients.

Precision medicine is about choosing the right drug for the right group of patients. Biomarkers are a critical tool in precision medicine with the potential to substantially improve success rates in cancer drug development and treatment.

"The goal is to get more new cancer medicines approved and medicines that work better in a field with a high risk of failure. Using biomarkers in designing clinical trials is a win-win for drug manufacturers, insurers, oncologists, and for patients. The only excuse now for conducting a clinical trial without a biomarker is if there is none available," says Parker.

More information: Jayson L. Parker et al. Does biomarker use in oncology improve clinical trial failure risk? A large?scale analysis, *Cancer Medicine* (2021). DOI: 10.1002/cam4.3732

Provided by University of Toronto Mississauga