Study exposes opportunities for strengthening cancer drugs trials in China

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Researchers expose opportunity for strengthening cancer drug trials between 2016 and 2021 in China. Credit: Etactics Inc, Unsplash (CC0, creativecommons.org/publicdomain/zero/1.0/)

More than one-eighth of the randomized trials of cancer drugs seeking

regulatory approval in China in recent years used inappropriate controls to test the effectiveness and safety of the drugs, according to a new study published December 12 in the open access journal *PLOS Medicine* by Professor Xiaodong Guan of Peking University, China, and colleagues.

In randomized trials, patients are assigned to either a control arm, in which they receive the current optimal treatment, or an experimental arm, in which they receive the new drug being tested. However, studies have previously found that control arms in cancer clinical trials (including in the United States) are not supported by relevant guidelines, instead using treatments other than the standard-of-care.

Adopting a suboptimal control group may bias a study's results in favor of the experimental arm, potentially exposing patients to substandard therapy and producing unreliable results of clinical efficacy.

In the new study, researchers analyzed the control arms of 453 Phase II/III and Phase III randomized oncology trials authorized by Chinese institutional review boards between 2016 and 2021, supporting investigational new drug applications of these drugs in China.

Overall, 60 trials (13.2%) used suboptimal control arms. Of those suboptimal trials, 35 (58.3%) used comparators that were not recommended by a prior guideline. In total, 18,610 people enrolled in clinical trials (15.1% of the total number in all samples trials) were exposed to suboptimal treatments due to the control arms.

Trials using suboptimal controls were more likely to report a positive result for the experimental arm. In addition, the researchers found an overall upward trend in the number of trials using inappropriate control arms.

"Trial sponsors, ethical review boards, and oncologists should make

collaborative efforts to protect patients from unnecessary harm and drugs with uncertain clinical benefits over the existing standard of care," the authors say. "Regulatory agencies should be cautious when reviewing investigational new drug applications whose supporting trial used a suboptimal control."

The authors add, "This research highlights the necessity to refine the design of randomized trials to generate optimal clinical evidence for new cancer therapies. In November 2021, China issued the 'Guidance on Clinical Value-Oriented Oncology Drug Research and Development,' aiming to promote a better generation of clinically relevant novel oncology drugs in China."

"We hope our research findings can provide empirical evidence to the stakeholders and draw regulators' attention to this matter so that the guideline can be delivered in the manner that it set out to be."

More information: Zhang Y, Chen D, Cheng S, Liang Z, Yang L, Li Q, et al. (2023) Use of suboptimal control arms in randomized clinical trials of investigational cancer drugs in China, 2016–2021: An observational study. *PLoS Medicine* (2023). DOI: 10.1371/journal.pmed.1004319

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