Editorial

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Are Chinese Oncology Trials Generalizable to Non-Chinese Patients? A Call for Systematic Evidence

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To the Editor:

China has emerged as a major producer of oncology randomized controlled trials (RCTs). Between 2008 and 2019, 751 phase II/III oncology new drug trials were conducted in China.[1] Yet a fundamental question remains unanswered: are results from trials conducted exclusively in Chinese patients generalizable to non-Chinese populations? This question has direct implications for regulatory decisions, clinical guidelines, and patient safety worldwide.

Several factors may limit generalizability. Biologically, EGFR-activating mutations occur in approximately 30% of East Asian patients with non-small cell lung cancer (NSCLC) versus only 8% of Europeans, partly explaining superior TKI outcomes in initially non-selected EGFR-mutant[2] East Asian cohorts. Pharmacogenomic differences in drug metabolism and immune microenvironment profiles may further modulate response across populations.[2,3] Methodologically, a 2023 PLOS Medicine analysis found that 13.2% of Chinese oncology RCTs used suboptimal control arms — 58.3% of which employed comparators not recommended by any prior guideline — potentially inflating apparent treatment benefits.[4]

The regulatory stakes became explicit in 2022, when the FDA Oncologic Drugs Advisory Committee voted 14-to-1 against approving sintilimab, a Chinese-developed PD-1 inhibitor, based solely on the China-only ORIENT-11 trial.[5,6] Regulators concluded that the data were not applicable to the US population and required a new international RCT—a precedent with broad implications for the growing number of Chinese oncology agents seeking global approval.

Preliminary data suggest partial generalizability. In the global RATIONALE-302 trial,[7] tislelizumab (a Chinese-developed PD-1 inhibitor) showed consistent benefit in 21% of patients from Europe and North America: median OS 11.2 vs. 6.3 months (HR 0.55), mirroring the overall population result. Conversely, FLAURA subgroup analyses of osimertinib in EGFR-mutant NSCLC revealed ethnic effect modification: OS benefit was substantial in non-Asian patients (HR 0.54) but absent in Asian patients (HR 1.0), despite comparable PFS benefit across groups.[3] These data confirm that ethnicity can materially alter the magnitude — and even the direction — of treatment benefit.

No systematic review or meta-epidemiological study has formally quantified the concordance of effect sizes between Chinese and non-Chinese oncology RCTs. We propose a pre-registered meta-epidemiological analysis identifying matched RCT pairs — trials testing the same intervention in the same indication, one in a Chinese and one in a non-Chinese population — and formally comparing hazard ratios, odds ratios, and absolute risk differences. Secondary analyses would explore sources of heterogeneity, including driver mutation prevalence, PD-L1 thresholds, performance status distribution, and comparator-arm quality. To conduct such studies, researchers may need access to a data repository of individual patient data. Therefore, given the accelerating global development of Chinese-origin oncology agents, we will need systematic reviews to inform regulatory standards, trial design, and international treatment guidelines.

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