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Epidemiology

Beyond borders: advancing oncology trials

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A recent British Journal of Cancer study by Anderson et al. comparing real-world NHS England outcomes for abemaciclib plus fulvestrant against the pivotal MONARCH-2 trial found a median overall survival gap of nearly 21 months that could not be explained by differences in age, gender, or performance status, a reminder that pivotal trial evidence sometimes fails to generalise to real-world populations [1]. This intersects with broader concerns about the evidentiary foundations of oncology drug approvals globally, motivating us to combine perspectives from China, Switzerland, and the United States to encourage enhanced international collaboration in cancer research. A recent study highlights that a substantial portion of pivotal studies supporting cancer drug approvals in China from 2017 to 2021 involved single-arm trials or randomised controlled trials (RCTs) with potential biases [2]. These findings reflect a shared global challenge in oncology: balancing the urgent need for rapid access to innovative therapies with the need to generate robust evidence to ensure patient safety and treatment efficacy.

China's regulatory reforms since 2015 have successfully accelerated approvals, bringing vital therapies to patients faster while aligning with international trends toward flexibility in evidence requirements. Similarly, the European Medicines Agency (EMA) has employed conditional marketing authorisations (CMAs) to expedite access to oncology therapies, though studies have shown that EMA review times remain longer than those of the FDA, with median review times of 337–426 days compared to 136–200 days in the United States [3]. However, as Zhang et al. demonstrate, reliance on single-arm trials (30% of indications) and RCTs with a high risk of bias (38%) can introduce uncertainty in estimating true treatment effects [2]. This pattern is not unique to any single region; similar challenges appear in approvals by agencies like the US Food and Drug Administration and the European Medicines Agency, where expedited pathways often prioritise speed amid unmet medical needs. For instance, between 2000 and 2020, 49% of US FDA approvals for novel cancer therapies lacked supporting evidence from RCTs, with 81% based on a single trial and overall survival as the primary endpoint in only 14% of trials [4]. Moreover, in an analysis of 791 US phase 3 oncology trials from 2002 to 2024, 63% utilised alternative primary endpoints, with overall survival superiority demonstrated in just 28% [5]. We acknowledge, however, that regulatory evaluation must continually balance evidentiary rigour with the ethical and clinical imperative to expedite access to therapies that may meaningfully improve patient outcomes, particularly in settings of substantial unmet medical need.

To strengthen the quality of evidence globally, we advocate for collaborative frameworks that build on existing strengths and foster mutual learning across regions. First, incentives such as priority review vouchers or extended data exclusivity, which reward sponsors for providing submissions supported by randomised trials with a lower risk of bias, could encourage the adoption of rigorous methodologies without delaying innovation. Second, for single-arm trials, standardised guidelines for external validation, including the use of adjusted historical controls and prespecified protocols, could enhance reliability by drawing on shared best practices across regulatory authorities. Third, expanding international partnerships, such as integrating China into initiatives like Project Orbis [6], would promote harmonised standards, joint bias assessments using tools like Cochrane's RoB 2 [7], and transparent data sharing.

Furthermore, we emphasise the importance of addressing issues of representativeness and inclusivity in oncology trials. The Anderson et al. analysis underscores this concern empirically: even within a high-resource health system, real-world patients receiving an approved therapy experienced substantially worse outcomes than the registrational cohort suggested [1]. Ensuring diverse patient populations in and broad access to trial enrolment may not only enhance the generalisability of findings but also aligns with the global research community's commitment to equitable cancer care and outcomes [8].

We believe collaborative research, through joint trials, cross-border and multidisciplinary expertise, inclusive authorship (ensuring equitable representation of investigators from diverse regions, disciplines and institutions, including those from low- and middle-income countries), and patient advocacy input, can overcome geopolitical challenges and systemic limitations. By uniting efforts across continents, we can advance the generation of high-quality evidence that benefits patients worldwide, transforming potential vulnerabilities into opportunities for collective progress.

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AUTHOR CONTRIBUTIONS

MSP and ECD conceptualised the commentary and drafted the initial manuscript. JSKC, NNS, JW and PI provided critical regional and disciplinary perspectives and contributed to manuscript revision. All authors reviewed the literature, contributed to interpretation of the evidence, critically revised the manuscript for important intellectual content, and approved the final version for submission.

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COMPETING INTERESTS

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ADDITIONAL INFORMATION

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