American Society of Clinical Oncology Position Statement: Reaffirming the Critical Role of Phase I Trials in Cancer Research and Treatment

Approved by the ASCO Board of Directors November 13, 2025

INTRODUCTION

In 1997, the American Society of Clinical Oncology (ASCO) published a pivotal policy statement on the importance of phase I clinical trials in cancer research and treatment.[1] As a national organization representing over 50,000 physicians and other health care professionals specializing in cancer treatment, diagnosis, and prevention, ASCO has long expressed strong support for patient participation in these early-stage trials.

In 2014, ASCO updated its policy statement, reaffirming the critical importance of phase I cancer research and treatment.[2] For more than a decade, dose finding trials in oncology have been undergoing a profound transformation evolving from studies that primarily evaluated toxicity in broad populations to studies dominated by adaptive designs and biomarker-driven evaluations in selected patient subsets.[3] While these trials do still evaluate safety, this change redefines the purpose of phase I trials from simply finding a maximum tolerated dose in general populations to identifying an optimal biological dose that targets the selected patient population with an acceptable safety profile. ASCO worked closely with FDA specifically to encourage researchers and trial sponsors to use phase I trial designs that minimize the number of patients exposed to potentially subtherapeutic doses of the agent being tested. The shift towards precision medicine from the earliest stages of drug development reflects the opportunity to identify efficacy signals earlier in the process and to gain a deeper understanding of cancer biology.[4]

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[1] Critical role of phase I clinical trials in cancer treatment. American Society of Clinical Oncology. *J Clin Oncol* **15**, 853-9(1997).

[2] Weber JS, Levit LA, et al. American Society of Clinical Oncology policy statement update: the critical role of phase I trials in cancer research and treatment. J Clin Oncol. 2015 Jan 20;33(3):278-84. doi: 10.1200/JCO.2014.58.2635. Epub 2014 Dec 15. Erratum in: J Clin Oncol. 2019 Feb 1;37(4):353. doi: 10.1200/JCO.18.02274. PMID: 25512456; PMCID: PMC4516884.

[3] Saxena A, Rubens M, Ramamoorthy V, Zhang Z, Ahmed MA, McGranaghan P, Das S, Veledar E. A Brief Overview of Adaptive Designs for Phase I Cancer Trials. Cancers (Basel). 2022 Mar 18;14(6):1566.

[4] https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCDId=1

While the landscape of cancer care, research, and health care delivery has changed, many of the challenges surrounding phase I trials, such as patient access, education, and financial barriers, persist. This position statement addresses the persistent challenges that continue to hinder patient enrollment and provides recommendations to support phase I trials in oncology clinical research.

BACKGROUND

The development of new drugs is a complex and multistage process with a series of clinical trial phases, each with a distinct purpose crucial for modern medicine. It is the primary mechanism for developing and bringing more effective treatments to patients with cancer. Phase I clinical trials in oncology are the foundation of a successful clinical drug development program and help advance the standard of care.[5] These studies are important because they help researchers define the drug dose and schedule to be further evaluated in subsequent trials.[6]

For many years there has been a debate about the therapeutic intent of phase I trials. While the primary goal is to identify a safe dose (or doses) to take forward for further study, these trials are also designed to advance scientific knowledge and can provide an opportunity for improved health outcomes for trial participants. ASCO has long maintained that phase I trials can and often do provide direct clinical benefit to patients.[7]

Today's modern phase I trials are more sophisticated, leveraging innovative adaptive designs and cutting-edge technologies such as artificial intelligence to accelerate the development of personalized medicine.[8] Despite methodologic advancements, there are significant barriers to patient participation in phase I clinical trials, including reluctance by many payers to cover routine care costs in the context of a phase I study. For example, Medicare's national clinical trials coverage policy requires researchers to prove "therapeutic intent," requiring that benefit to patients be a central aim and question of any clinical trial.[9] This requirement has been used to deny coverage for patient participation in phase I trials. Medicare Advantage, in particular, can potentially raise obstacles to participation via to prior authorization or requirements to convert coverage for routine care costs to Fee-for-Service Medicare, a confusing process for patients that ASCO has

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[5] Weber, J. S., et al. (2015). American Society of Clinical Oncology Policy Statement Update: The Critical Role of Phase I Trials in Cancer Research and Treatment. *Journal of Clinical Oncology*, 33(3), 226–231.
[6] Early phase clinical trials in oncology: Realising the potential of seamless designs. Jaki, Thomas et al. European Journal of Cancer, Volume 189, 112916.
[7] Weber, J. S., et al. (2015). American Society of Clinical Oncology Policy Statement Update: The Critical Role of Phase I Trials in Cancer Research and Treatment. Journal of Clinical Oncology, 33(3), 226–231.
[8] Harrer, S., et al. (2019). Artificial intelligence for clinical trial design. Trends in Pharmacological Sciences, 40(8), 577–591.
[9] https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCDId=1

previously recommended abolishing.[10] Ethical considerations regarding informed consent, equitable patient access, the continuing presence of restrictive eligibility criteria, and geographic barriers all remain critical areas for improvement.[11] These challenges, combined with the misperception that phase I trials lack patient benefit, must be addressed to ensure patients have the opportunity to participate in this stage of cancer drug development research.

CHALLENGES AND CONSIDERATIONS IN CLINICAL CANCER TRIALS

Patient participation in clinical trials is critical for developing new oncology treatments, but recruiting and retaining participants remains a significant challenge - especially for phase I clinical trials. Only about 7 percent of adult patients with cancer participate in clinical trials overall.[12] Often, narrow inclusion and exclusion criteria complicate recruitment efforts. In 2016, ASCO and Friends of Cancer Research (Friends) launched a major initiative to modernize clinical trial eligibility criteria, aiming to make cancer trials more inclusive, representative of real-world patient populations, and efficient.[13] The recommendations from the joint manuscript are slowly being implemented in federally sponsored trials (primarily those run by the National Cancer Institute's (NCI) Cancer Therapy Evaluation Program (CTEP) and have led to new guidance from the Food and Drug Administration (FDA).

Geographic disparities also significantly lower the likelihood of having cancer clinical trials available. Rural and lower-income counties have fewer medical oncologists in practice which creates a critical barrier for patients in rural, nonmetropolitan and socioeconomically disadvantaged communities.[14] This leads to fewer referrals and limited awareness of available clinical trials, resulting in a significantly lower likelihood of having a phase I cancer clinical trial available in those areas.[15] Logistic barriers also play a role. Access to urban, academic, and major medical centers requires patients to travel significant distances to the nearest trial site.[16] This creates financial difficulties, and time

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[10] Karen M. Winkfield et al. Addressing Financial Barriers to Patient Participation in Clinical Trials: ASCO Policy Statement. *J Clin Oncol* 36, 3331-3339(2018). DOI:10.1200/JCO.18.01132.

[11] Chen J, Lu Y, Kummar S. Increasing patient participation in oncology clinical trials. Cancer Med. 2023 Feb;12(3):2219-2226.

[12] Joseph M. Unger et al. National Estimates of the Participation of Patients With Cancer in Clinical Research Studies Based on Commission on Cancer Accreditation Data. J Clin Oncol 42, 2139-2148(2024).

[13] Kim, E. S., et al. (2017). Broadening Eligibility Criteria to Make Clinical Trials More Representative: American Society of Clinical Oncology and Friends of Cancer Research Joint Research Statement. Journal of Clinical Oncology, 35(34), 3737–3746.

[14] Unger, J. M., et al. (2020). Closing the Rural Cancer Care Gap: Three Institutional Approaches. *JCO Oncology Practice, 16*(7), 405–412.

[15] Chen, S., et al. (2024). Geographic disparity in the distribution of cancer clinical trials in the United States and the associated factors. *Journal of Managed Care & Specialty Pharmacy, 30*(4), 376–383.

[16] Gupta, A., & Eisenhauer, E. A. (2022). The Time Toxicity of Cancer Treatment. *Journal of Clinical Oncology, 40*(14), 1611–1615.

burdens associated with this travel and can be prohibitive for patients in rural and lower-income counties.

Coupled with geographic and logistical barriers is a lack of ancillary infrastructure. Many local community hospitals and clinicals in rural counties lack advanced diagnostic equipment, specialized staff training needed to support phase I clinical trials.[17] In 2024, ASCO authored a research statement aimed at improving access and bringing clinical trials closer to patients via decentralized clinical trials.[18] The paper highlighted how regulatory burdens such as FDA's 1572 form create barriers for community research sites.

Lastly, patient financial risk presents a significant barrier to enrollment, as routine care costs incurred during a clinical trial - such as physician visits, lab work, and scans are often not reliably reimbursed by insurance, leaving patients with unexpected and substantial out-of-pocket expenses. Clinical trials require patients to undergo evaluations, and specialized laboratory testing outside of standard of care cancer treatment. While the location of the laboratory facilities may also present a challenge, reimbursement for research related tests may limit patients' ability to obtain testing at sites other than those pre-certified in research contracts.[19]

ASCO POLICY RECOMMENDATIONS

ASCO makes the following recommendations related to phase I clinical trials:

- Professional societies and patient advocacy organizations should continue to develop enhanced educational materials for patients to explain the goals of phase I trials in cancer and what it means for patient involvement.
- Professional societies should enhance educational materials for clinicians and researchers to help overcome challenges to phase I trial enrollment, such as incomplete understanding of insurance coverage, reimbursement and perceptions that phase I trials should be considered only after other treatment options fail.
- CMS should revise its National Coverage Determination (NCD) for clinical trials to eliminate the requirement that researchers must explicitly prove "therapeutic intent". The current policy's reliance on therapeutic intent is an outdated standard that has been inappropriately used to deny coverage for routine patient care costs

[17] Unger, J. M., et al. (2024). Barriers to Clinical Trial Implementation Among Community Care Centers. *JAMA Oncology, 10*(5), 682–689.
[18] Ramya Thota et al. Improving Access to Patient-Focused, Decentralized Clinical Trials Requires Streamlined Regulatory Requirements: An ASCO Research Statement. *J Clin Oncol* 42, 3986-3995(2024).
[19] Chen J, Lu Y, Kummar S. Increasing patient participation in oncology clinical trials. Cancer Med. 2023 Feb;12(3):2219-2226. doi: 10.1002/cam4.5150.

(e.g., standard blood work, imaging, and hospital visits) associated with Phase I trial participation.

- Medicare Advantage plans should not impose prior authorization, network, or benefit design restrictions that make trial participation more difficult, despite trial coverage being required under Medicare. CMS should revise current policy that requires Medicare Advantage beneficiaries to revert to fee-for-service coverage during clinical trials.
- Policymakers should mandate that private payers implement comprehensive coverage for routine patient care costs associated with participation in Phase I clinical trials.
- ASCO expresses continued support for the NCI's Community Oncology Research Program (NCORP) sponsored clinical trials which focuses on conducting research in community hospitals and oncology practices where the majority of cancer patients receive their care.

CONCLUSION

Phase I clinical trials remain a critical part of cancer drug development, serving as the gateway for novel therapeutic approaches and for identifying safe and optimal dosages of cancer drugs. These trials are essential for accelerating the delivery of new and effective cancer drugs and therapies. The promise of these trials lies in their ability to accelerate the development of precision cancer treatment, ultimately leading to improved patient outcomes. The transformation in oncology research since ASCO's initial policy statements has reiterated the critical importance of these trials. ASCO remains committed to highlighting the importance of phase I clinical trials in oncology and helping increase participation.

Questions? Contact policy@asco.org