care delivery reviews

Moving Beyond the Momentum: Innovative Approaches to Clinical Trial Implementation

Cathy Eng, MD[1]; Emerson Y. Chen, MD[2]; Jane Rogers, PharmD[3]; Mark Lewis, MD[4]; Jonathan Strosberg, MD[5]; Ramya Thota, MD[4]; Smitha Krishnamurthi, MD[6]; Paul Oberstein, MD[7]; Rang Govindarajan, MD[8]; Gary Buchschacher, MD[9]; Sandip Patel, MD[10]; Davendra Sohal, MD[11]; Taymeyah Al-Toubah, BS[5]; Philip Philip, MD[12]; Arvind Dasari, MD[13]; Hagan Kennecke, MD[14]; and Stacey Stein, MD[15]

abstract

Despite efforts to enhance enrollment and the merger of national cooperative groups, < 5% of patients with cancer will enroll into a clinical trial. Additionally, clinical trials are affected by a lack of diversity inclusive of minority patients, rural residents, or low-income individuals. COVID-19 further exacerbated known barriers of reduced physician-patient interaction, physician availability, trial activation and enrollment, financial resources, and capacity for conducting research. Based on the cumulative insight of academic and community clinical researchers, we have created a white paper identifying existing challenges in clinical trial conduct and have provided specific recommendations of sustainable modifications to improve efficiency in the activation and conduct of clinical trials with an overarching goal of providing improved access and care to our patients with cancer.

JCO Oncol Pract 17:607-614. © 2021 by American Society of Clinical Oncology

BACKGROUND

Cancer remains the 2nd leading cause of death in the United States.[1] It is estimated that in 2020 alone, 1.8 million individuals will be diagnosed with cancer, resulting in 606,520 deaths.[2,3] Historically, < 1 in 20 (< 5%) patients with cancer will participate in a clinical trial.[3–5] Review of the National Cancer Database (NCDB, 2004-2015) indicates that of > 12 million patients, only 0.1% participated in clinical trials.[5] In 2010, additional efforts to enhance clinical trial enrollment, as recommended by the Institute of Medicine, resulted in a merger of the National Cancer Institute (NCI) cooperative groups to reduce duplicative competing clinical trials and activation times and improve enrollment.[6] Despite these efforts, the percent of patients enrolled in cancer clinical trials, according to NCI analysis and a systematic review, has remained unchanged for over 10 years.[7,8] Furthermore, a lack of diversity remains. As per the US Federal Drug Administration (FDA) Global Clinical Trials Report (2015-2016), only 2.74% of patients with cancer enrolled are Black.[9] The Cancer Moonshot recognized the importance of reducing cancer disparities in rural and underserved patient populations.[10] A recent comparative analysis of SWOG trials involving nearly 37,000 patients demonstrated that uniform access to clinical trials could result in equivocal cancer outcomes regardless of rural or urban origin.[11]

Existing challenges to clinical trial enrollment remain multifactorial: patient perception, physician interest, socioeconomic barriers, and geographic access, among other barriers.[8] Multiple challenges arose following the onset of the COVID-19 pandemic, resulting in reduced physician-patient interaction, activation, and conduct of clinical trials. The impact is evident by the reduction of enrollment to the National Clinical Trials Network studies from approximately 300 to 150-200 patients per week at the height of the pandemic.[12] In the interim, clinics or hospitals adjusted their approach to cancer care to provide adequate treatment to patients. Based on the cumulative insight and experience of a group of community and academic clinical researchers, we perceive an unforeseen window of opportunity for innovation in the successful conduct of clinical trials. The purpose of this article is to provide recommendations to improve the efficiency and equity of patient participation in clinical trials by considering trial design, activation times, and conduct.

STANDARDIZING CLINICAL TRIAL ELECTRONIC HEALTH RECORD ORDER SETS

Traditionally, a multi-institutional clinical trial protocol contains intricate details regarding treatment and protocol-driven procedures or visits that can inundate a local research team. Although a generic informed

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on December 22, 2020 and published at ascopubs.org/journal/op on February 3, 2021: DOI https://doi.org/10.1200/OP.20.00701

consent (IC) document is often provided to each study site for their local institutional review board, there is no standard approach in converting the clinical trial schedule of events and orders as written in the protocol into practical implementation. A standard treatment order set template provided to all participating sites could be incorporated into the chemotherapy order sets.

Electronic health record (EHR) order sets have been now incorporated into many practices to ensure that the oncology team can provide the recommended therapy in a safe, efficient, and uniform manner. Given its complexities, an EHR order set requires detailed preparation and extensive validation. ASCO discussed the importance of establishing formal treatment plan templates and/or summaries to foster communication between multidisciplinary providers and trial sponsors.[13] The National Comprehensive Cancer Network has also recently collaborated with EPIC and Cerner PowerChart Oncology to provide templates,[14,15] which would be especially helpful for providers with limited experience in developing EHR research protocol order sets.[16] An EHR order set typically includes five basic components (Table 1). Figure 1 exemplifies the potential bottlenecks for the creation and validation of an EHR order set. A standard treatment template would reduce potential bottleneck delays in EHR order set development. The structure for these templates and specifics would vary based on the intricacy and phase of the trial. However, we believe that there are many ways to leverage existing information technology (IT) to design templates for all trials regardless of phase (ie, templates for dose escalation, templates for dose expansion, etc). Treatment templates could also be modified for subsequent protocol amendments.

Recommendation

The authors propose that all multi-institutional studies include standardized treatment order sets that are adaptable to different technology platforms as a means to communicate specific research treatment plans and to eliminate individual builds at each study site, thereby enhancing uniformity of care, workflow, patient safety, and reduced activation time while respecting flexibility for individual formularies.

TELEMEDICINE OR TELEONCOLOGY

Barriers to in-person contact during COVID-19 have significantly expanded the use of telemedicine in oncology,[17,18] illustrating that necessity is the mother of invention. As concerns arose about virus transmission, teleoncology came to fruition. Defined as "the delivery of clinical oncology services via audio and video communication technologies to patients at a distance,"[19] it has proven to be effective in providing remote consultations,[20] treatment supervision, and palliative care.[21] Regulatory restrictions have hampered widespread implementation of virtual visits. Despite oncologists taking the same national board exams, various regulations exist regarding physician authorization across state lines and insurance reimbursement.[22,23] To date, these regulatory impediments to telemedicine remain and vary state by state.[24]

Discussion of a clinical trial can be overwhelming for a patient[25] given the stringent guidelines of multiple visits at specified intervals, required laboratory tests, diagnostic imaging, and the investigational therapy to maintain the trial's integrity and quality. Virtual tumor boards would provide an opportunity for bidirectional information and serve as a venue for referring providers and patients (community and academic). Virtual visits could also promote clinical trial education and awareness to underserved and rural patient populations. It is estimated that the median distance from patients' homes to study sites is >25 miles, with disproportionately longer trips for lower-income and rural patients.[26] The benefits of allowing virtual clinical trials are readily identifiable: increased accessibility, improved retention and compliance, and reduced cost, which have been established in standard of care for both cancer and noncancer conditions.[27–29]

Clinical trial protocols should make allowances for telemedicine visits. Telemedicine visits can be used to review with patients' current symptoms and medication changes and confirm adherence to prescribed medications. Keeping in mind that in-person visits may not necessarily replace face-to-face physician-patient interaction, virtual visits may vary per patient and protocol. Increasing virtual visits will require significant IT support for troubleshooting any technical issues. Patient familiarity and ownership of digital technology (eg, smartphones) are an important factor. A smartphone application (app) supported by the sponsor (eg, hospital, pharma, NCI, etc) would improve communication, provide real-time documentation, and reduce travel and patient and caregiver burden.[30,31] The availability of telemedicine resources, and each patient's ability to use telemedicine, can vary widely, however.[32–34] It is imperative that this variability is considered carefully; otherwise, it can further increase disparity across cancer clinical trials.

Recommendation

Teleoncology offers an important means to increase access to clinical trials. Clinical trial participants should be offered the option of virtual visits, which would be defined in the study protocol.

IDENTIFICATION OF TRIALS AND NEXT-GENERATION SEQUENCING

Currently, there are general resources for accessing clinical trial information, including www.clincialtrials.gov, but often these websites are difficult to navigate for patients and caregivers. Advocacy groups have initiated clinical trial identification[35] to address this difficulty. Ultimately,

TABLE 1. Common Components of an EHR Research Treatment Order Set Required for Institutional Validation

Study Design Elements	Medication Elements	Administration Elements	Supportive Care Elements	Monitoring Elements
• Number of treatment arms • Blinding and use of placebo • Cycle length and days • Number of cycles • Infusion time appointments	• Route of administration (eg, oral, intravenous, etc) • Frequency of administration • Drug supply source • Allowance of biosimilar • Dose and modification guidelines • Provider communication orders • Dilution and/or mixture requirements	• Line requirements • Dose rounding allowances • Calculated weight requirements • Nursing communication orders • Administration times • Product-specific administration instructions (eg, vesicant, refrigerate, etc)	• Antiemetic orders • Premedication orders • Growth factor support orders • Supportive care prescriptions • PRN orders	• Treatment parameter • Vital sign requirements • Laboratory requirements • Biomarker and pharmacokinetic requirements • Hypersensitivity orders • Discharge instructions • Procedure and/or diagnostic test requirements

Abbreviations: EHR, electronic health record; PRN, *Pro re nata* or as needed.

physician engagement is an essential determinant of clinical trial enrollment,[36] and thus, there is a need for physician outreach to increase awareness.

Next-generation sequencing (NGS) is considered routine for patients with metastatic cancer as the number of treatable molecular alterations has increased and the cost and turnaround time of NGS results have decreased.[37] In 2017, > 75% of oncologists reported using NGS tests to guide treatment decisions to improve efficacy of therapy.[38] Examples include tissue-agnostic FDA approvals of pembrolizumab for tumors with high microsatellite instability[39] or high tumor mutational burden[40] and detection of the *BRAF* mutation as an actionable mutation in melanoma[41] and colorectal cancer,[42] providing rationale for NGS for patients with metastatic cancers. In 2018, the Centers for Medicare & Medicaid Services determined National Coverage Determination for FDA-approved NGS companion diagnostic testing for patients with cancer.[43]

The NCI-Molecular Analysis for Therapy Choice provided a single platform for tumor genotyping and matching of patients to clinical trials (ClinicalTrials.gov identifier: NCT02465060). The prevalence of actionable mutations ranged from 1% to 7% with many molecular alterations occurring in < 3% of patients.[44] The SWOG Lung-MAP study (ClinicalTrials.gov identifier: NCT03851445) is an example of a genotype-driven platform study that has enrolled > 2,000 patients into an umbrella protocol of multiple biomarker arms.

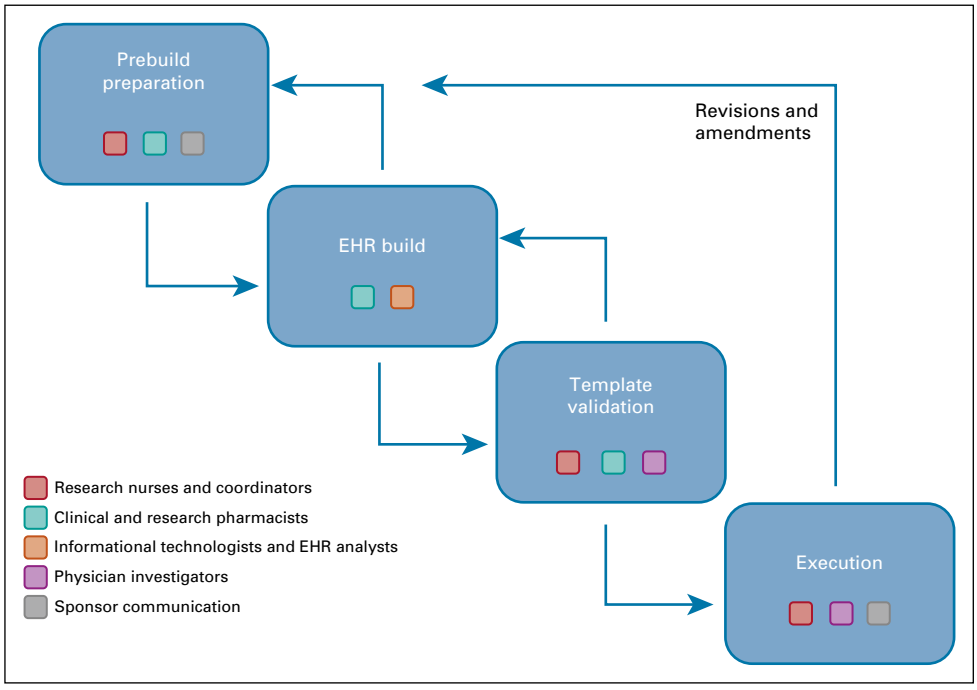

FIG 1. Example of an EHR research protocol order set validation. EHR, electronic health record.

The NGS results could be used to direct patients to specific clinical trials. Companies performing NGS have developed platforms and/or partnerships for genomic-driven clinical trials. Given the rarity of targetable alterations, it can be prohibitively expensive for most sites because of massive screening efforts, such as pancreatic cancer with a *BRCA* mutation and cholangiocarcinoma with *FGFR2* fusions and rearrangements.[45,46] For instance, for a biomarker-driven trial, a site may enroll a handful of patients, which is not cost-effective. Caris Life Sciences,[47] Foundation Medicine,[48] and Tempus[49] use a master confidentiality research agreement. When a potential patient is identified, the physician is notified about the closest participating site. With further integration, physicians could be contacted by the NGS laboratory when their patients match. Foundation Medicine has partnered with Science37 to offer a virtual clinical trial platform where investigators connect with clinical trial patients, bypassing institutional study activation. In this decentralized model, brick and mortar sites are not required. Study visits are conducted by telemedicine, and an app is used for participants to remain connected to the study team.

Another approach would be to notify patients directly. Ciitizen is a consumer health company in partnership with The Cholangiocarcinoma Foundation, giving access to patients and enabling them to gather their medical records and NGS data and consolidate them into a profile sharable with their doctor, family, and researchers.[50] Currently, none of the major NGS vendors send results directly to patients.

Recommendation

NGS platforms are widely used to guide treatment. Resources should be shared between NGS vendors, providers, and patients to help identify clinical trials and enhance enrollment.

REMOTE CLINICAL TRIAL EDUCATION AND PRESCREENING

Clinical trial enrollment is a multistep process. After initial discussion in the physician's office, the patient is given the IC for consideration of the risks, benefits, and required pretreatment testing, which can be burdensome and a deterrent to enrollment.[51,52] Telemedicine would allow this initial step to be conducted remotely. Additionally, opportunities to begin prescreening remotely by reviewing locally completed blood work, vital signs, and electrocardiograms would reduce delays and unnecessary travel especially for patients in remote areas. Obtaining consent via telemedicine can be used productively without compromising patient comprehension.[53] Furthermore, the use of secured electronic signatures or smartphone apps that allow faxing or scanning could replace wet signature originals.

To encourage patients to participate in a trial, a partnership with a local oncologist or a hybrid and/or co-site enrollment model for phase II and/or III trials would be of immense benefit. The clinical research assistant (CRA) and/or research nurse would provide a copy of the protocol, study schema, and the study calendar to the local oncologist. The CRA and/or research nurse would follow up with all necessary labs, scans, and other required components of the clinical trial. Although the patient is under the care of their local oncologist, a telemedicine visit with the study site PI and/or collaborator conducted every 4-8 weeks may reduce the risk of protocol violations.

Recommendation

Partnership between advocacy groups, trial sponsors, and research teams using innovative strategies can expand clinical trial awareness and availability for patients with cancer and expedite accrual to studies.

MODIFICATIONS OF TRIALS WITH ORAL AGENTS

Following COVID-19, many centers had to rapidly establish new procedures for oncology clinical trials. For some studies, shipping oral study medications directly to patients was facilitated. Some trials lend themselves to being partially or exclusively conducted via telemedicine, thereby making shipping of oral study medications a tenable option.

To guarantee high-quality and reliable processes for delivery of oral investigational agents, clear and concise standard operating procedures (SOPs) are essential. The most obvious of these is to ensure that the integrity of the shipment is guaranteed. Establishing standards for overnight temperature-controlled shipping with tracking and temperature monitoring would be required. Telemedicine visits and direct shipment of drugs must involve compliance with state and federal regulations, which might be complicated when crossing state lines. For interstate shipping, state-specific regulatory requirements must be met. SOPs should include critical logistics: contact with the patient before shipment to ensure proper handling upon arrival, protocols for communication between patient and research staff for postdelivery confirmation of arrival and investigational agent integrity, telemedicine evaluation of the patient and review of instructions, short-term follow-up after starting the medication to confirm patient understanding and compliance, and prepaid return shipping materials for empty bottles and unused medication. These issues should be analyzed before implementation but would substantially ease the burden on patients with cancer.

Recommendation

Trials of oral cancer therapies could make greater use of telemedicine, and a framework for direct patient shipping of experimental therapeutics should be established.

CAPTURE OF ADVERSE EVENTS OR PATIENT-REPORTED OUTCOMES

It is now widely accepted that patient-reported outcomes (PROs) are important assessments that accurately capture a patient's quality of life, adverse events, or other symptoms from their cancer.[54–56] The US FDA defines a PRO as "any report of the status of a patient's health condition that

comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else."[57] Data can include information about health-related quality of life, symptoms, function, satisfaction with care or symptoms, adherence to prescribed medications or other therapy, and perceived value of treatment.[58]

Although PROs can be the primary or secondary end point of a study, they are often used to measure the adverse effects independent of effectiveness. There are several guidelines for how to incorporate PRO data into clinical trials.[59–61] The SPIRIT-PRO extension offers recommended items to include in clinical trials.[62] The NCI PRO-CTCAE (Common Terminology Adverse Events) is a patient-reported outcomes version of the CTCAE that has been validated in large patient populations.[63]

Capturing PROs via a smartphone or tablet app[64] would be advantageous and would reduce recall bias. Other valuable data, including nutrition diaries and device information (eg, fitness tracker), could be captured providing valuable patient-generated health data (PGHD) information.

The PROs and PGHD data can be collected and used to help manage patient care. In one clinical trial, 766 patients were assigned to either standard care or a PRO, in which NCI-CTCAEs were self-reported by patients.[65] If a PRO of concern was reported, the research nurse received an immediate e-mail alert. The primary end point, improvement of health-related quality of life at 6 months, was met, as well as an increase in overall survival by 5 months.[66]

Recommendation

PROs are commonly integrated into clinical trials. A smartphone app would be advantageous in improved symptom management, expedited adverse event reporting, PGHD, and improved compliance.

REGULATORY

Site initiation visits (SIVs) are conducted before trial activation and are commonly conducted on-site where sponsor-assigned monitors review the protocol with the study team and inspect the facility to ensure that the site can successfully conduct the trial. Data suggest that on-site SIV may not make a difference in patient recruitment.[67] In addition, SIVs are expensive, time-consuming, and difficult to coordinate because of scheduling conflicts. Remote SIVs could reduce cost, allow flexible scheduling, and reduce travel. Outside of the on-site facility inspection, a fair share of SIVs can be remote. Teleconferencing platforms can reduce the administrative burden on research sites and sponsors while still providing necessary training to all study team members.

Auditing of clinical trials is a critical component of ensuring high-quality research and data integrity and requires extensive resources. The traditional model includes in-person visits by nurses, pharmacists, physicians, etc, which are either at a priori set points (eg, enrollment of a certain number of patients and a preplanned interim analysis) or triggered by major protocol deviations and/or serious AEs.

These audits usually require site visits and reviews of all items related to the conduct of clinical trials: medical information, SOPs, delegation of authority logs, pharmacy and biological sample documentation, review board procedures, and physical infrastructure. Given advances in technology, most of this information can now be audited remotely. If most data queries and monitoring could be conducted remotely, this would reduce financial cost and time. Scaled over the entire clinical trial landscape, the time and resources saved by the sponsor and institutions could be beneficial. In addition, small, efficient web-based audits could be conducted more frequently, leading to earlier identification and resolution of problems.

Recommendation

The majority of SIVs and monitoring can be conducted remotely and should be incorporated into standard practice.

In conclusion, challenges in providing efficient and economically productive enrollment to clinical trials have been

TABLE 2. Summary of Recommendations

EHR order sets: Standardized order sets of the study protocol treatments should be developed in adaptable technology platforms to eliminate the need for treatment builds at individual study sites
Telemedicine: Teleoncology offers an important means to increase clinical trial awareness and access. Clinical trial participants should be offered the option of virtual visits, and these may be defined in the study protocol
NGS platforms: Resources should be shared between NGS vendors, providers, and patients, to help identify clinical trials and enhance enrollment
Education and accrual support: Partnerships between advocacy groups, clinical trial sponsors, and research teams should be expanded to help expedite accrual to studies
Oral therapies: Trials of oral cancer therapies could make greater use of telemedicine, and a framework for direct-to-patient shipping of experimental therapeutics should be established
Adverse event reporting: Greater use should be made of technology solutions including smartphone apps to collect PROs, adverse events, PGHD data, and medication adherence information
Regulatory: Site initiation and monitoring can efficiently be done remotely and should be incorporated into standard practice

Abbreviations: NGS, next-generation sequencing; PGHD, patient-generated health data.

emerging topics of discussion for years. Prolonged trial activation times, reduced patient participation, duplication of efforts, and subsequent costs are long-standing barriers associated with the successful conduct of clinical trials.[68–71] As a consequence of the COVID-19 pandemic, many clinicians were forced to provide temporary innovative solutions to maintain the continuum of care for their patients. We propose expanding these temporary measures into enduring options to dismantle barriers to trial accrual while maintaining data integrity and preserving patient safety. Examples include standardizing treatment order sets; optimizing telemedicine to provide clinical trial awareness and education, as well as outreach to underserved patient populations; and the use of commonly available IT to allow for clinical trial matching based on molecular data (Table 2). Ideally, some of the financial resources could then be shifted to other resources needed for advances in cancer. Metrics and cost-benefit analyses would need to be supported to demonstrate benefit.

We strongly believe that these challenges can be overcome over time, with a focus on the common interest of providing improved access and care to our patients with cancer. We understand that these are not all the potential aspects of change required to improve the conduct of clinical trials, but we believe that these recommendations are feasible and transformative and can be accomplished with the support of all stakeholders: patients, patient advocates, healthcare providers, research organizations, the pharmaceutical industry, NCI, and the FDA.

AFFILIATIONS

[1]Vanderbilt-Ingram Cancer Center, Nashville, TN
[2]Division of Hematology and Oncology, Oregon Health and Science University, Knight Cancer Institute, Portland, OR
[3]University of Texas MD Anderson Cancer Center Pharmacy Clinical Programs, Houston, TX
[4]Intermountain Healthcare, Salt Lake, UT
[5]Moffitt Cancer Center, Tampa, FL
[6]Cleveland Clinic Taussig Cancer Center, Cleveland, OH
[7]New York University Langone Health, New York, NY
[8]Winthrop P. Rockefeller Cancer Institute, University of Arkansas, Little Rock, AR
[9]Kaiser Permanente, Los Angeles Cancer Clinic, Los Angeles, CA
[10]Moores Cancer Center, UC San Diego Health, La Jolla, CA
[11]University of Cincinnati Health Barrett Cancer Center, Cincinnati, OH
[12]Karmanos Cancer Center, Detroit, MI
[13]University of Texas MD Anderson Cancer Center, Houston, TX
[14]Virginia Mason Cancer Center, Seattle, WA
[15]Smilow Cancer Center, Yale School of Medicine, New Haven, CT

CORRESPONDING AUTHOR

Cathy Eng, MD, Vanderbilt-Ingram Cancer Center, Gastrointestinal Cancer Research Program, 2220 Pierce Avenue, 777 Preston Research Building, Nashville, TN 37232; e-mail: cathy.eng@vumc.org.

SUPPORT

Supported [in part] by the National Cancer Institute of the National Institutes of Health under Award Number U10CA180888 (CD Blanke, PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/OP.20.00701.

AUTHOR CONTRIBUTIONS

Conception and design: Cathy Eng, Jane Rogers, Paul Oberstein, Mark Lewis, Smitha Krishnamurthi, Gary Buchschacher, Emerson Chen, Stacey Stein
Administrative support: Cathy Eng, Emerson Chen, Gary Buchschacher
Provision of study materials or patients: Cathy Eng, Emerson Y. Chen, Jane Rogers, Ramya Thota, Smitha Krishnamurthi, Paul Oberstein, Rang Govindarajan, Gary Buchschacher, Sandip Patel, Davendra Sohal, Taymeyah Al-Toubah, Arvind Dasari, Hagan Kennecke, Stacey Stein
Collection and assembly of data: Cathy Eng, Emerson Y. Chen, Jane Rogers, Ramya Thota, Smitha Krishnamurthi, Paul Oberstein, Rang Govindarajan, Gary Buchschacher, Sandip Patel, Davendra Sohal, Taymeyah Al-Toubah, Arvind Dasari, Hagan Kennecke, Stacey Stein
Data analysis and interpretation: Cathy Eng, Emerson Y. Chen, Jane Rogers, Mark Lewis, Jonathan Strosberg, Smitha Krishnamurthi, Rang Govindarajan, Gary Buchschacher, Sandip Patel, Davendra Sohal, Taymeyah Al-Toubah, Philip Philip, Arvind Dasari, Hagan Kennecke, Stacey Stein
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

REFERENCES

1. Centers for Disease Control and Prevention: Leading Causes of Death. https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm
2. NCI: The Surveillance, Epidemiology, and End Results (SEER): Cancer Stat Facts: Common Cancer Sites. https://seer.cancer.gov/statfacts/html/common.html#:~:text=How%20Many%20People%20Are%20Diagnosed,the%20most%20common%20cancer%20diagnosis
3. Unger JM, Cook E, Tai E, et al: The role of clinical trial participation in cancer research: Barriers, evidence, and strategies. Am Soc Clin Oncol Ed Book 35: 185-198, 2016
4. Murthy VH, Krumholz HM, Gross CP: Participation in cancer clinical trials: Race-, sex-, and age-based disparities. JAMA 291:2720-2726, 2004
5. Zaorsky NG, Zhang Y, Walter V, et al: Clinical trial accrual at initial course of therapy for cancer and its impact on survival. J Natl Compr Canc Netw 17: 1309-1316, 2019
6. Giffin RB, Lebovitz Y, English RA: Transforming Clinical Research in the United States: Challenges and Opportunities: Workshop Summary. Washington, DC, National Academies Press, 2010
7. Pang HH, Wang X, Stinchcombe TE, et al: Enrollment trends and disparity among patients with lung cancer in national clinical trials, 1990 to 2012. J Clin Oncol 34:3992-3999, 2016

8. Unger JM, Vaidya R, Hershman DL, et al: Systematic review and meta-analysis of the magnitude of structural, clinical, and physician and patient barriers to cancer clinical trial participation. J Natl Cancer Inst 111:245-255, 2019
9. American Cancer Society: Cancer Facts & Figures for African Americans 2019-2021. Atlanta, GA, American Cancer Society, 2019
10. Martinez ME, Paskett ED: Using the Cancer Moonshot to conquer cancer disparities: A model for action. JAMA Oncol 4:624-625, 2018
11. Al-Shamsi HO, Alhazzani W, Alhuraiji A, et al: A practical approach to the management of cancer patients during the novel coronavirus disease 2019 (COVID-19) pandemic: An international collaborative group. Oncologist 25:e936-e945, 2020
12. Sharpless NE: Ensuring cancer research progress during a global pandemic [Video presentation], https://meetinglibrary.asco.org/record/191996/video
13. Mulvey TM: Treatment plan and summary templates: The experience of one practice. J Oncol Pract 5:106-107, 2009
14. The ASCO Post Staff: CureMD Oncology Integrates NCCN Templates, 2019. https://www.ascopost.com/issues/september-10-2019/curemd-oncology-integrates-nccn-templates/
15. National Comprehensive Cancer Network: NCCN Guidelines® & Clinical Resources: Electronic Health Record (EHR) Integration. https://www.nccn.org/professionals/OrderTemplates/EHRintegration.aspx
16. National Comprehensive Cancer Network: Guidelines® & Clinical Resources: NCCN Chemotherapy Order Templates (NCCN Templates®). https://www.nccn.org/professionals/OrderTemplates/Default.aspx
17. Marcum M, Kurtzweil N, Vollmer C, et al: COVID-19 pandemic and impact on cancer clinical trials: An academic medical center perspective. Cancer Med 9:6141-6146, 2020
18. Leung MST, Lin SG, Chow J, et al: COVID-19 and oncology: Service transformation during pandemic. Cancer Med 9:7161-7171, 2020
19. Harky A, Chiu CM, Yau THL, et al: Cancer patient care during COVID-19. Cancer Cell 37:749-750, 2020
20. Thota R, Gill DM, Brant JL, et al: Telehealth is a sustainable population health strategy to lower costs and increase quality of health care in rural Utah. JCO Oncol Pract 16:e557-e562, 2020
21. Shirke MM, Shaikh SA, Harky A: Tele-oncology in the COVID-19 era: The way forward? Trends Cancer 6:547-549, 2020
22. Slomski A: Telehealth success spurs a call for greater post–COVID-19 license portability. JAMA 324:1021-1022, 2020
23. US Department of Health and Human Services Press Office: HHS Awards $20 Million to Combat COVID-19 Pandemic Through Telehealth. https://www.hhs.gov/about/news/2020/04/30/hhs-awards-20-million-to-combat-covid19-pandemic-through-telehealth.html
24. American Federation of State Medical Boards: US States and Territories Modifying Requirements for Telehealth in Response to COVID-19. https://www.fsmb.org/siteassets/advocacy/pdf/states-waiving-licensure-requirements-for-telehealth-in-response-to-covid-19.pdf
25. Buss MK, DuBenske LL, Dinauer S, et al: Patient/caregiver influences for declining participation in supportive oncology trials. J Support Oncol 6:168-174, 2008
26. Borno HT, Zhang L, Siegel A, et al: At what cost to clinical trial enrollment? A retrospective study of patient travel burden in cancer clinical trials. Oncologist 23:1242, 2018
27. Ream E, Hughes AE, Cox A, et al: Telephone interventions for symptom management in adults with cancer. Cochrane Database Syst Rev 6:CD007568, 2020
28. Inglis SC, Clark RA, Dierckx R, et al: Structured telephone support or non-invasive telemonitoring for patients with heart failure. Cochrane Database Syst Rev 10:CD007228, 2015
29. Beck CA, Beran DB, Biglan KM, et al: National randomized controlled trial of virtual house calls for Parkinson disease. Neurology 89:1152-1161, 2017
30. Cheong IY, An SY, Cha WC, et al: Efficacy of mobile health care application and wearable device in improvement of physical performance in colorectal cancer patients undergoing chemotherapy. Clin Colorectal Cancer 17:e353-e362, 2018
31. Osborn J, Ajakaiye A, Cooksley T, et al: Do mHealth applications improve clinical outcomes of patients with cancer? A critical appraisal of the peer-reviewed literature. Support Care Cancer 28:1469-1479, 2020
32. Kichloo A, Albosta M, Dettloff K, et al: Telemedicine, the current COVID-19 pandemic and the future: A narrative review and perspectives moving forward in the USA. Fam Med Community Health 8:e000530, 2020
33. Dawson AZ, Walker RJ, Campbell JA, et al: Telehealth and indigenous populations around the world: A systematic review on current modalities for physical and mental health. Mhealth 6:30, 2020
34. Heath S: Patient Education, Support Key for Senior Telehealth Care Access. https://patientengagementhit.com/news/patient-education-support-key-for-senior-telehealth-care-access
35. Kim P, Fleshman J, Muething M, et al: PanCAN PALS—Patient And Liaison Services: An innovative model for informed patient decision-making, including patient information and clinical trials. Oncology (Williston Park) 17:16-17, 2003
36. Comis RL, Miller JD, Colaizzi DD, et al: Physician-related factors involved in patient decisions to enroll onto cancer clinical trials. J Oncol Pract 5:50-56, 2009
37. Mosele F, Remon J, Mateo J, et al: Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: A report from the ESMO Precision Medicine Working Group. Ann Oncol 31:1491-1505, 2020
38. Freedman AN, Klabunde CN, Wiant K, et al: Use of next-generation sequencing tests to guide cancer treatment: Results from a nationally representative survey of oncologists in the United States. JCO Precision Oncol 2:1-13, 2018
39. Marabelle A, Le DT, Ascierto PA, et al: Efficacy of pembrolizumab in patients with noncolorectal high microsatellite instability/mismatch repair–deficient cancer: Results from the phase II KEYNOTE-158 study. J Clin Oncol 38:1-10, 2020
40. Marabelle A, Fakih M, Lopez J, et al: Association of tumour mutational burden with outcomes in patients with advanced solid tumours treated with pembrolizumab: Prospective biomarker analysis of the multicohort, open-label, phase 2 KEYNOTE-158 study. Lancet Oncol 21:1353-1365, 2020
41. Kim G, McKee AE, Ning YM, et al: FDA approval summary: Vemurafenib for treatment of unresectable or metastatic melanoma with the BRAFV600E mutation. Clin Cancer Res 20:4994-5000, 2014
42. Kopetz S, Grothey A, Van Cutsem E, et al: Encorafenib plus cetuximab with or without binimetinib for BRAF V600E-mutant metastatic colorectal cancer: Quality-of-life results from a randomized, three-arm, phase III study versus the choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC). J Clin Oncol 37:1460-1469, 2020
43. Centers for Medicare & Medicaid Services: CMS Finalizes Coverage of Next Generation Sequencing Tests, Ensuring Enhanced Access for Cancer Patients. https://www.cms.gov/newsroom/press-releases/cms-finalizes-coverage-next-generation-sequencing-tests-ensuring-enhanced-access-cancer-patients
44. Flaherty KT, Gray R, Chen A, et al: The Molecular Analysis For Therapy Choice (NCI-MATCH) trial: Lessons for genomic trial design. J Natl Cancer Inst 112:1021-1029, 2020
45. Abou-Alfa GK, Sahai V, Hollebecque A, et al: Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: A multicentre, open-label, phase 2 study. Lancet Oncol 21:671-684, 2020
46. Golan T, Hammel P, Reni M, et al: Maintenance olaparib for germline BRCA-mutated metastatic pancreatic cancer. N Engl J Med 381:317-327, 2019
47. Caris Life Sciences: https://www.carislifesciences.com/clinical-trials/

48. Foundation Medicine: https://www.foundationmedicine.com/service/clinical-trial-solutions
49. Tempus: https://www.tempus.com/clinical-trial-matching/
50. Ciitizen: https://www.ciitizen.com/
51. Coyle M, Gillies K: A systematic review of risk communication in clinical trials: How does it influence decisions to participate and what are the best methods to improve understanding in a trial context? PLoS One 15:e0242239, 2020
52. Holdsworth LM, Zionts D, Asch SM, et al: "Along for the Ride": A qualitative study exploring patient and caregiver perceptions of decision making in cancer care. MDM Policy Pract 5:2381468320933576, 2020
53. Welch BM, Marshall E, Qanungo S, et al: Teleconsent: A novel approach to obtain informed consent for research. Contemp Clin Trials Commun 3:74-79, 2016
54. Reeve BB, Mitchell SA, Dueck AC, et al: Recommended patient-reported core set of symptoms to measure in adult cancer treatment trials. J Natl Cancer Inst 106:dju129, 2014
55. Warsame R, D'Souza A: Patient reported outcomes have arrived: A practical overview for clinicians in using patient reported outcomes in oncology. Mayo Clin Proc 94:2291-2301, 2019
56. Basch E, Geoghegan C, Coons SJ, et al: Patient-reported outcomes in cancer drug development and US regulatory review: Perspectives from industry, the Food and Drug Administration, and the patient. JAMA Oncol 1:375-379, 2015
57. FDA Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims, 2009. http://www.fda.gov/downloads/Drugs/Guidances/UCM193282.pdf
58. LeBlanc TW, Abernethy AP: Patient-reported outcomes in cancer care: Hearing the patient voice at greater volume. Nat Rev Clin Oncol 14:763-772, 2017
59. Crossnohere NL, Brundage M, Calvert MJ, et al: International guidance on the selection of patient-reported outcome measures in clinical trials: A review. Qual Life Res 30:21-40, 2021
60. Wehrlen L, Krumlauf M, Ness E, et al: Systematic collection of patient reported outcome research data: A checklist for clinical research professionals. Contemp Clin Trials 48:21-29, 2016
61. Cella D, Rosenbloom SK, Beaumont JL, et al: Development and validation of 11 symptom indexes to evaluate response to chemotherapy for advanced cancer. J Natl Compr Canc Netw 9:268-278, 2011
62. Calvert M, Kyte D, Mercieca-Bebber R, et al: Guidelines for inclusion of patient-reported outcomes in clinical trial protocols: The SPIRIT-PRO extension. JAMA 319:483-494, 2018
63. Dueck AC, Mendoza TR, Mitchell SA, et al: Validity and reliability of the US National Cancer Institute's Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). JAMA Oncol 1:1051-1059, 2015
64. The United States Food and Drug Administration: Collection of Patient-Provided Information Through a Mobile Device Application for Use in Comparative Effectiveness and Drug Safety Research. https://www.fda.gov/media/119835/download
65. Basch E, Deal AM, Kris MG, et al: Symptom monitoring with patient-reported outcomes during routine cancer treatment: A randomized controlled trial. J Clin Oncol 34:557-565, 2016
66. Basch E, Deal AM, Dueck AC, et al: Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. JAMA 318:197-198, 2017
67. Lienard JL, Quinaux E, Fabre-Guillevin E, et al: Impact of on-site initiation visits on patient recruitment and data quality in a randomized trial of adjuvant chemotherapy for breast cancer. Clin Trials 3:486-492, 2006
68. Mendelsohn J, Moses HL, Nass SJ: A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program. Washington, DC, National Academies Press, 2010
69. Williams E, Brown TJ, Griffith P, et al: Improving the time to activation of new clinical trials at a National Cancer Institute–designated comprehensive cancer center. JCO Oncol Pract 16:e324-e332, 2020
70. Lai J, Forney L, Brinton DL, et al: Drivers of start-up delays in global randomized clinical trials. Ther Innov Regul Sci 55:212–227, 2021
71. Tang C, Hess KR, Sanders D, et al: Modifying the clinical research infrastructure at a dedicated clinical trials unit: Assessment of trial development, activation, and participant accrual. Clin Cancer Res 23:1407-1413, 2017

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Moving Beyond the Momentum: Innovative Approaches to Clinical Trial Implementation

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/op/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Cathy Eng
Consulting or Advisory Role: Bayer Schering Pharma, Foundation Medicine, Array BioPharma, Natera

Emerson Y. Chen
Other Relationship: Horizon CME, Taiho Pharmaceutical

Mark Lewis
Consulting or Advisory Role: Boehringer Ingelheim
Other Relationship: Medscape

Jonathan Strosberg
Consulting or Advisory Role: Novartis
Speakers' Bureau: Ipsen, Lexicon
Research Funding: Novartis

Ramya Thota
Consulting or Advisory Role: Array BioPharma
Research Funding: Abbvie, Bristol-Myers Squibb

Paul Oberstein
Consulting or Advisory Role: Merck, BTG, Tyme, Ipsen
Research Funding: Merck, Roche/Genentech
Travel, Accommodations, Expenses: Merck

Gary Buchschacher
Research Funding: Roche/Genentech, AstraZeneca, Merck
Travel, Accommodations, Expenses: Roche/Genentech, AstraZeneca

Sandip Patel
Consulting or Advisory Role: Bristol-Myers Squibb, AstraZeneca/MedImmune, Nektar, Compugen, Illumina
Speakers' Bureau: Merck, Boehringer Ingelheim
Research Funding: Bristol-Myers Squibb, Pfizer, Roche/Genentech, Amgen, AstraZeneca/MedImmune, Fate Therapeutics, Merck

Davendra Sohal
Consulting or Advisory Role: Perthera, Ability Pharma
Speakers' Bureau: Incyte
Research Funding: Celgene, Genentech, Bristol-Myers Squibb, Rafael Pharmaceuticals, Apexigen, Amgen

Philip Philip
Honoraria: Celgene, Bayer, Ipsen, Merck, AstraZeneca, TriSalus Life Sciences, Blueprint Medicines, Syncore, Array BioPharma
Consulting or Advisory Role: Celgene, Ipsen, Merck, TriSalus Life Sciences, Daiichi Sankyo, Syncore, Taiho Pharmaceutical
Speakers' Bureau: Celgene, Bayer, Ipsen, Novartis, Incyte
Research Funding: Bayer, Incyte, Karyopharm Therapeutics, Merck, Taiho Pharmaceutical, Momenta Pharmaceuticals, Novartis, Plexxikon, Immunomedics, Regeneron, Genentech, Tyme, Caris Life Sciences, ASLAN Pharmaceuticals, QED Therapeutics, Halozyme, Boston Biomedical, Advanced Accelerator Applications, Lilly, Merus, QED Therapeutics, Incyte, Caris Life Sciences
Travel, Accommodations, Expenses: Rafael Pharmaceuticals, Celgene, AbbVie

Arvind Dasari
Consulting or Advisory Role: Ipsen, Novartis, Voluntis, Lexicon
Research Funding: Novartis, Eisai, Hutchison MediPharma, Merck, Guardant Health, Ipsen

Hagan Kennecke
Honoraria: Ipsen
Research Funding: Taiho Pharmaceutical

Stacey Stein
Consulting or Advisory Role: Genentech/Roche, Eisai, QED Therapeutics, Exelixis

No other potential conflicts of interest were reported.