OXFORD

JNCI J Natl Cancer Inst (2021) 113(11): djab070

doi: 10.1093/jnci/djab070
First published online April 21, 2021
Commentary

Age Is Just a Number: Considerations for Older Adults in Cancer Clinical Trials

Dany Habr, MD,* Lynn McRoy, MD, Vassiliki A. Papadimitrakopoulou, MD

Pfizer Oncology, New York, NY, USA

*Correspondence to: Dany Habr, MD, Chief Medical Officer, Pfizer Oncology, Pfizer Inc, 235 East 42nd Street, New York, NY 10011, USA (e-mail: dany.habr@pfizer.com).

COMMENTARY

Abstract

Older adults continue to be underrepresented in cancer clinical trials, despite most cancer occurrence peaking in the later decades of life. Consequently, diagnostic and management strategies are commonly extrapolated from data on younger patients, thus challenging the delivery of informed cancer care in this patient population. Several recommendations and calls to action have been released by cancer societies, advocacy organizations, and regulatory agencies to guide inclusion of older adults in clinical trials. Effective implementation, however, requires awareness and close collaboration between all stakeholders involved in the clinical trial journey. We herein provide insights and experience from a drug developer on key considerations to optimize participation and retention of older adults in cancer clinical trials and discuss those under 4 key domains: trial eligibility and design, assessments and endpoints, patients and oncologists, and data reporting.

There is no doubt that cancer incidence increases with age (1). Although this has been putatively attributed to a constellation of changes due to ageing including accumulation of mutations over time, carcinogen exposure-dependent changes in bodily tissues, and decreased efficiency of immune surveillance, the precise explanations remain largely unknown (1). In the United States, it is estimated that by 2030, around 70% of all new cancer cases will be in patients 65 years and older (2). Notable improvements in cancer survival remain limited in older adults despite the impact of targeted therapies and immunotherapies in cancer care, as evident from a pooled analysis of population-based cancer registries (1995-2014) of around 4 million patients from 7 high-income countries (3). One reason for this is suboptimal or undertreatment of older patients with cancer. In a Surveillance, Epidemiology, and End Results (SEER)–Medicare retrospective review of patients with stage IV non-small cell lung cancer diagnosed after 66 years of age between 2012 and 2015, age was a statistically significant risk factor for underutilization of both first- and second-line therapy (4). Similar findings were also noted in older patients with earlier stages of the disease (5). There are surely demographic, socioeconomic, comorbidity, and regional variations influencing management decisions in older patients (6); however, one shared challenge is lack of evidence to inform delivery of personalized cancer care to elderly patients. Diagnostic and management strategies need to be extrapolated from data on younger patients, which is problematic because these would be empirically applied in a patient subgroup with different comorbidity profiles and, hence, unclear dosage requirements, drug response, and toxicity tolerance (7,8). The primary contributor to this lack of data is underrepresentation or exclusion of older adults in cancer clinical trials despite most cancer occurrence peaking in the later decades of life (9). This evidence gap limits the potential benefits of new treatments for older patients and relegates treatment decisions to informed guesswork.

A seminal paper that alerted the medical community to underrepresentation of older patients (older than 65 years) in cancer clinical trials was based on cross-sectional population-based analysis of all participants in therapeutic trials funded by the National Cancer Institute (NCI) Clinical Trial Cooperative Group between 2000 and 2002 (10). Findings were also echoed by various studies from other groups (8). The gap is even wider for the "oldest" of the old, with only 4% of patients 80 years or older included in US Food and Drug Administration (FDA) registration clinical trials, despite representing 16% of all cancer patients (11). There is some variability in data according to tumor type. In one review of data sources from 2010 through 2014, a higher proportion of older adults (older than 65 years) were enrolled in prostate cancer clinical trials than actually seen in clinical practice (58% vs 45%), whereas underrepresentation was observed in breast and colorectal cancers (12). Nonetheless, age disparities between cancer clinical trial participation and the incident

Received: January 16, 2021; **Revised:** March 23, 2021; **Accepted:** April 5, 2021

disease population appear to be increasing over time (13). This disparity seems to even be higher in industry-sponsored clinical trials, as evident in a recent (2018) analysis of 302 randomized clinical trials enrolling 262 354 participants. The trials median age of participants was around 6.5 years younger than the population disease-site–specific median age and was statistically significantly lower in industry-funded trials (82.5% of trials) compared with non-industry–funded trials (13). These findings should prompt drug developers from the pharmaceutical and biotech industry to pause and reflect on why this is happening and how they can bring about effective change. Efforts to understand and address age disparities are necessary to ensure generalizability of trial results as well as equity in trial access (13). The task is challenging considering the paucity of information on associated barriers and solutions (14), but this should not deter the research community from attempting to bring about change based on insights and recommendations from available expertise.

Through this commentary, we hope to spur action from our colleagues in the industry to include representative age groups reflecting the epidemiology of the tumor to be studied and design trials to facilitate enrollment and decrease the burden of participation for elderly patients across the cancer spectrum. We summarize recommendations from the FDA, American Society of Clinical Oncology (ASCO), and advocacy organizations that we believe should be enacted without delay while also sharing relevant experience and examples from our programs.

Trial Eligibility and Design

The use of eligibility criteria that explicitly exclude patients on the basis of age appears to be declining. In a recent study, upper age restriction criteria were identified in as low as 10.1% of 742 phase 3 randomized clinical trials (combined total enrollment of 449 720 patients), with a median age cutoff of 72 years (15). Thus, although enrollment criteria restrictions based on age cutoffs could be a prime cause of age disparities, they cannot fully explain the persistent underrepresentation of older adults in cancer clinical trials.

There is now increased understanding that reliance on age alone to determine clinical trial eligibility should be avoided. Alternate eligibility criteria that exclude patients on the basis of functional status, organ function, comorbidity or co-medication profile, and previous malignancy may also contribute to underrepresentation of older patients, especially when uniformly applied. These criteria are aimed to homogenize the study population and mitigate the risk of potential adverse reactions from experimental drugs; however, they are often included from one study protocol to the next with little scientific basis (8,16,17). Ideally, protocol design should begin with zero exclusions, and criteria added only based on specific compelling scientific or ethical rationale (8). Suggestions and recommendations to revise criteria such as creatinine clearance, previous malignancy, performance status, and frailty to maximize participation have already been made through joint statements by ASCO, Friends of Cancer Research, and the FDA (8,18). Seeking input from geriatric oncology specialists when such exclusion criteria are considered can help mitigate overuse (19). Moreover, when exclusions are necessary because participants with impaired organ function would be at higher toxicity risk, an appropriately specific measure of organ dysfunction should be used that does not lead to the unnecessary exclusion of older participants with milder dysfunction (17).

The inclusion of older patients in early phase studies would establish drug metabolism and clearance, drug-drug or drug-disease interactions, and concerns regarding vulnerability to a particular toxicity in older adults (17,20). Decisions on pivotal trial eligibility criteria and design could then stem from translational research and early phase trials to inform the impact of specific parameters on efficacy, safety, and dosing and should begin with zero exclusion assumptions (17). For example, in a retrospective analysis of patients enrolled in phase 1 clinical trials for gynecologic malignancies from 2010 to 2016, older patients (70 years and older) had similar toxicity profiles compared with younger patients, suggesting they do not need to be categorically excluded from further randomized trials (21). Specific dose evaluation in older patients could prove noninferior in terms of overall treatment benefit and produce less toxicity in elderly, frail patients (8). A considerable gap persists in such “early” knowledge, and inclusion of older patients in early phase trials remains rare. Real-world evidence can provide valuable insights to inform trial designs by evaluating effectiveness and safety in older and diverse patients not represented in clinical trials (14,22).

Additional opportunities to address the evidence gap may include the use of adaptive clinical trial designs, starting with a narrower population with further cohort expansion to a broader diverse and older population, using lower or stepwise dose interventions in older patients if suggested by interim safety data (17,23). Stratification in randomized trials and assignment of parallel arms with older patients in open-label trials may also be used to evaluate efficacy and safety. Hierarchical testing could be used to evaluate the primary endpoint in a modified intent-to-treat population of younger patients for example, and secondary endpoints can be assessed in the overall intent-to-treat population including all age groups (20). Several innovative and contemporary trial design approaches have also been proposed (23,24). Pragmatic clinical trials conducted in the context of standard care are also an option to enroll older and more vulnerable patients with more flexible eligibility criteria (25).

At Pfizer, we have established the Diversity in Clinical Trials Center of Excellence to support our clinical trial teams and promote considerations of diversity from the earliest stages of study design. The center provides demographic data on epidemiology of the disease we are targeting to help drive diverse and representative enrollment as well as support appropriate trial site identification based on population distribution. We have also designed technology platforms that allow real-time patient recruitment and retention data and provide early signals on where we should deploy additional recruitment tactics. Thus, our general approach entails consideration of the epidemiology of the disease and design of studies that reflect the age distribution, beginning with no age exclusion. For example, in some of our recent trials recruiting heavily pretreated men with metastatic castration-resistant prostate cancer, which naturally implies an advanced age group, removal of upper age cutoffs from eligibly criteria and reliance on functional measures that have a scientific rationale allowed recruitment of a trial sample with a median age of 69 years and up to 84 years (TALAPRO-1, NCT03148795) (26). Beyond data from clinical trials, we also rely on real-world evidence studies to further our understanding of treatment patterns and functional and quality-of-life outcomes in older patients; for instance, the PalomAGE study (EUPAS23012) is a prospective observational study that we recently initiated specifically to understand experience of women aged 70 years and older with locally advanced or metastatic breast cancer (27).

Assessments and Endpoints

Optimized inclusion of older adults in cancer clinical trials should be accompanied by the addition of appropriate endpoints for this patient subgroup. In a review of endpoints of all phase 1-3 trials reporting data from elderly patients in 2001-2004 and 2011-2014, overall survival was the most common primary endpoint, and a shift was noted in the reporting of tumor-centered endpoints to composite endpoints. Disease-specific survival was very infrequently reported despite its importance in distinguishing deaths from cancer-unrelated causes. The use of functional endpoints and patient-reported outcomes was notably rare across both time periods (28). This surely needs to be revisited considering the value and weight of quality of life and functional independence in older patients compared with prolongation of life (8,23).

Collection of typical geriatric assessment data including functional status, cognitive function, frailty measures, nutritional status, and comorbidities during the trial would help further establish the benefits and risks of interventions in older patients and identify independent predictors of morbidity and mortality (19,23,29). Sponsors could work closely with patient relatives and caregivers, social and behavioral scientists, patient advocates and advocacy groups, geriatricians, and geriatric oncologists to consider the relevance and feasibility of clinical trial assessments and endpoints in older adults, which could also help materialize treatment value during drug approval and reimbursement discussions (20,22). Developing appropriate strategies to capture and manage adverse events in older patients may also facilitate retention and completion of clinical trials (20).

We have had successful experience in using geriatric assessment tools in studies targeting older patients with cancer. For example, in a real-world observational study analyzing outcomes in advanced or metastatic breast cancer [POLARIS, NCT03280303 (30)], assessment of functional status and degree of dependence using the Activities of Daily Living (31) and of frailty using the Geriatric 8 (32) screening tools in women aged 70 years and older provided us with further insights on the role of therapy in this age group beyond what we could have realized using conventional assessment of Eastern Cooperative Oncology Group performance status alone. In the aforementioned PalomAGE study (27), we are also using the DIALOG Geriatric Core Dataset (G-CODE) as a standardized, validated, and reproducible set of tools for geriatric evaluation across 7 domains: social environment, autonomy, mobility, nutritional status, cognitive status, mood, and comorbidities (33). This would be the first prospective study to incorporate the DIALOG G-CODE questionnaire in a population of patients with advanced breast cancer.

Patients and Oncologists

Elderly patients are usually willing to consider participation in cancer clinical trials but cite lack of information on opportunities being readily available to them as a barrier to participation (23,34,35). Oncologists may not consider older adults for participation in clinical trials, with bias, toxicity concerns, and insufficient time or support being recognized as key factors in failing to offer clinical trials for their older patients (23,36). Community oncologists additionally report that patient attitudes, beliefs, and understanding are among the main barriers for inclusion of their older patients in clinical trials (36). A large proportion of older adults receive their cancer care in the community, with limited access to clinical trials conducted at large urban centers (36).

The accelerated adoption of digital tools for data capture, passive collection of patient information, and decentralized study design brought about by the COVID-19 pandemic should be further leveraged to improve diversity of clinical trial participants including those in rural areas as well as patients with limited mobility or lacking access to research institutions, including older adults (17). More trials can be open in the community setting by reducing the institutional burden on participation through improved technology (22), coupled with improving awareness and education about clinical trials through adapted materials and collaboration with community health educators to better reach older patients (19). Offering caregiver support and mitigating the challenges of trial logistics through alternative approaches to site visits and support when they are necessary will encourage participation (20). Recruitment challenges can be addressed during study design by placing the patient experience at the center of the process with a focus on reduced burden of participation and ease of monitoring via alternative approaches such as local imaging and home visits so that we can meet older and frail patients where they are (14,17). Routine patient care costs during clinical trials may not always be covered, especially for underrepresented groups, and add to the disparity in clinical trial inclusion. Efforts to reduce such cost and coverage barriers are necessary to optimize participation (37,38).

At Pfizer, we have adopted several initiatives to optimize awareness and access to clinical trials in underserved and underrepresented populations, especially in the community setting. In some programs, we are offering study sites augmented staffing with a clinical recruitment coordinator to facilitate community reach. Moreover, the Patient Centricity Initiative launched by Pfizer Oncology in 2019 utilizes partnerships with various cancer patient and professional advocacy organizations to prioritize health equity and health literacy and involve underrepresented patients in clinical research. The Blue Button Program at Pfizer was also first of its kind to give patients participating in our trials their clinical data, with the hope that this can build trust in the clinical trial process and study sponsor and mitigate any concerns an elderly patient may have with regards to experimentation. We have also joined other industry partners in the Center for Information and Study on Clinical Research Participation (www.ciscrp.com), a first-of-its-kind cross sponsor collaborative dedicated to educating and informing the public, patients, medical and research communities, the media, and policy makers about clinical research and the role each party plays in the process. The initiative provides an opportunity to share best practices, identify barriers to recruitment in clinical trials, and co-create actionable solutions. Although the use of telemedicine in clinical care and research has considerably evolved over the past 2 decades, the COVID-19 outbreak forced us to implement these changes more quickly and on a larger scale. We have shared our experience and best practices in a recent industry report (39) and echo the recent call from ASCO to utilize learnings from this experience to improve clinical research especially as this pertains to optimizing access for older patients (40). We already had positive experience with the use of novel mobile applications to capture patient-reported functioning and quality of life in metastatic breast cancer studies recruiting patients aged 84 years and younger (41), further highlighting feasibility of using digital technology even in the oldest patients. In addition to these design and planning elements, proactive discussions with

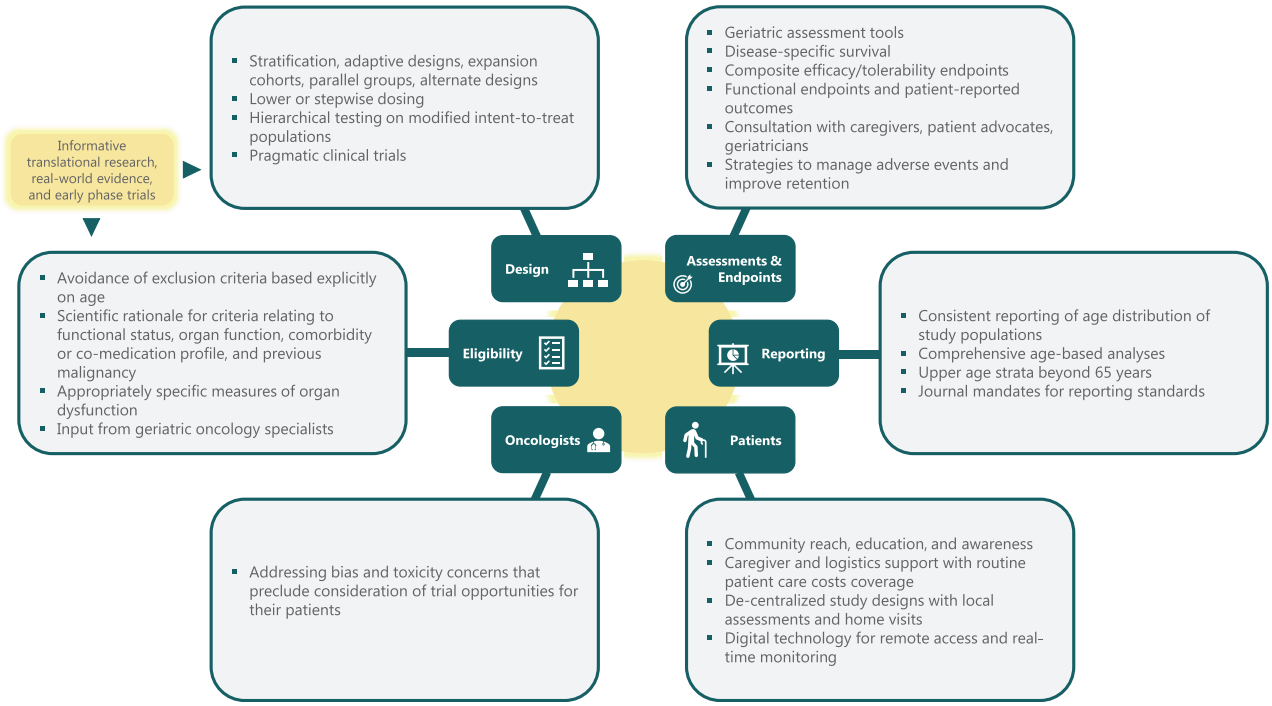

Figure 1. Strategies to optimize participation of older adults in cancer clinical trials

investigators addressing our intention to include representative populations and specifically encouraging enrollment of older adults avoid hesitancy on the part of investigators to approach older patients.

Reporting

There is great room for improvement in clinical trial data reporting that should help shed more light on outcomes specific to older patients. Although there is a trend for improved reporting of elderly subgroups in phase 3 trials, especially in industry-funded studies, international trials with large sample size, and trials published in high impact factor journals (42), requiring authors to submit detailed age distribution of study populations and age-based analysis and adding geriatric oncology experts to journal reviewers would further the quality of evidence for older patients (19). Among patients older than 65 years of age, stratification of data for incremental age groups can further differentiate outcomes for subpopulations in the elderly (20).

Even when subgroup or stratified analysis in elderly patients is not feasible or done in individual trials, one approach we have previously taken in our breast cancer studies is the use of pooled analysis from several trials to generate and report efficacy and safety findings in larger sets of older adults, which also allowed further stratification of outcomes by incremental age groups among the elderly (43).

A multitiered strategy needs to be adopted with collaboration between various stakeholders to ensure appropriate representation of older adults in cancer clinical trials (Figure 1). Over the past 10 years, several recommendations have become available through a dedicated Institute of Medicine report; ASCO statements; action items from an ASCO-FDA Workshop; proceedings of a U13 conference held by the Cancer and Aging Research Group in collaboration with the NCI, the National Institute on Aging, and the Alliance for Clinical Trials in Oncology; and FDA guidance documents to the industry—all summarized in this commentary (8,17,19,20,22,23,29,44). These resources provide valuable advice on considerations for trial design but require active and serious adoption by study sponsors and clinical trial teams. Continued amplification of such recommendations and potentially using them as regulatory or funding incentives may further encourage inclusion of older patients in oncology research. Similar to directions under the Pediatric Research Equity Act and Best Pharmaceuticals for Children Act, a call has been made in a recent FDA-ASCO workshop for the FDA to highlight incentives for companies to enroll older adults in registration trials during pre-Investigational New Drug and end of phase 2 meetings (22). Similarly, pharmaceutical companies can require applicants for research grants to outline how the study design and execution promotes inclusion of older adults. Grant programs dedicated to cancer research in older adults can also be established. Collaborations between several pharmaceutical companies, including Pfizer, and cancer societies on grant programs that intend to promote diversity and representation in cancer research are already underway (45,46), and the same channels may be used to optimize representation of older adults in cancer clinical trials. All stakeholders in cancer care have a responsibility to improve representation of older adults in oncology research and thus improve applicability of evidence and quality of care for the older oncology patient.

Funding

None.

Notes

Role of the funder: Not applicable.

Author disclosures: DH, LM, and VAP are employees of and own stock in Pfizer Inc.

Author contributions: All authors have contributed to conceptualization, critical review, and final approval of the manuscript for submission.

Acknowledgments: Medical writing support was provided by Khaled Musallam, MD, PhD, at Evida Medical DMCC and was funded by Pfizer.

Data Availability

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

References

1. Laconi E, Marongiu F, DeGregori J. Cancer as a disease of old age: changing mutational and microenvironmental landscapes. *Br J Cancer*. 2020;122(7):943–952.
2. Smith BD, Smith GL, Hurria A, et al. Future of cancer incidence in the United States: burdens upon an aging, changing nation. *J Clin Oncol*. 2009;27(17):2758–2765.
3. Arnold M, Rutherford MJ, Bardot A, et al. Progress in cancer survival, mortality, and incidence in seven high-income countries 1995-2014 (ICBP SURVMARK-2): a population-based study. *Lancet Oncol*. 2019;20(11):1493–1505.
4. Kehl KL, Hassett MJ, Schrag D. Patterns of care for older patients with stage IV non-small cell lung cancer in the immunotherapy era. *Cancer Med*. 2020;9(6):2019–2029.
5. Wong ML, McMurry TL, Stukenborg GJ, et al. Impact of age and comorbidity on treatment of non-small cell lung cancer recurrence following complete resection: a nationally representative cohort study. *Lung Cancer*. 2016;102:108–117.
6. Moreno AC, Verma V, Hofstetter WL, et al. Patterns of care and treatment outcomes of elderly patients with stage I esophageal cancer: analysis of the National Cancer Data Base. *J Thorac Oncol*. 2017;12(7):1152–1160.
7. Gosain R, Pollock Y, Jain D. Age-related disparity: breast cancer in the elderly. *Curr Oncol Rep*. 2016;18(11):69.
8. Abbasi J. Older patients (still) left out of cancer clinical trials. *JAMA*. 2019;322(18):1751–1753.
9. Aapro MS, Kohne CH, Cohen HJ, et al. Never too old? Age should not be a barrier to enrollment in cancer clinical trials. *Oncologist*. 2005;10(3):198–204.
10. Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials: race-, sex-, and age-based disparities. *JAMA*. 2004;291(22):2720–2726.
11. Singh H, Kanapuru B, Smith C, et al. FDA analysis of enrollment of older adults in clinical trials for cancer drug registration: a 10-year experience by the U.S. Food and Drug Administration. *J Clin Oncol*. 2017;35(15_suppl):10009.
12. Borno HT, Small EJ, Zhang L, et al. How current reporting practices may mask differences: a call for examining cancer-specific demographic enrollment patterns in cancer treatment clinical trials. *Contemp Clin Trials Commun*. 2019;16:100476.
13. Ludmir EB, Mainwaring W, Lin TA, et al. Factors associated with age disparities among cancer clinical trial participants. *JAMA Oncol*. 2019;5(12):1769–1773.
14. Sedrak MS, Freedman RA, Cohen HJ, et al.; Cancer and Aging Research Group (CARG). Older adult participation in cancer clinical trials: a systematic review of barriers and interventions. *CA Cancer J Clin*. 2021;71(1):78–92.
15. Ludmir EB, Subbiah IM, Mainwaring W, et al. Decreasing incidence of upper age restriction enrollment criteria among cancer clinical trials. *J Geriatr Oncol*. 2020;11(3):451–454.
16. Jin S, Pazdur R, Sridhara R. Re-evaluating eligibility criteria for oncology clinical trials: analysis of investigational new drug applications in 2015. *J Clin Oncol*. 2017;35(33):3745–3752.
17. US Food and Drug Administration. *Enhancing the Diversity of Clinical Trial Populations— Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry*; 2020. https://www.fda.gov/media/127712/download. Accessed November 22, 2020.
18. Kim ES, Bruinooge SS, Roberts S, et al. Broadening eligibility criteria to make clinical trials more representative: American Society of Clinical Oncology and Friends of Cancer Research Joint Research Statement. *J Clin Oncol*. 2017;35(33):3737–3744.
19. Hurria A, Levit LA, Dale W, et al.; American Society of Clinical Oncology. Improving the evidence base for treating older adults with cancer: American Society of Clinical Oncology Statement. *J Clin Oncol*. 2015;33(32):3826–3833.
20. US Food and Drug Administration. *Inclusion of Older Adults in Cancer Clinical Trials Guidance for Industry*. Updated March 2020. https://www.fda.gov/media/135804/download. Accessed November 22, 2020.
21. Buechel M, McGinnis A, Vesely SK, et al. Consideration of older patients for enrollment in phase 1 clinical trials: exploring treatment related toxicities and outcomes. *Gynecol Oncol*. 2018;149(1):28–32.
22. Levit LA, Singh H, Klepin HD, et al. Expanding the evidence base in geriatric oncology: action items from an FDA-ASCO Workshop. *J Natl Cancer Inst*. 2018;110(11):1163–1170.
23. Hurria A, Dale W, Mooney M, et al.; Cancer and Aging Research Group. Designing therapeutic clinical trials for older and frail adults with cancer: U13 conference recommendations. *J Clin Oncol*. 2014;32(24):2587–2594.
24. Whelehan S, Lynch O, Treacy N, et al. Optimising clinical trial design in older cancer patients. *Geriatrics (Basel)*. 2018;3(3):34.
25. Soto-Perez-De-Celis E, Lichtman SM. Considerations for clinical trial design in older adults with cancer. *Expert Opin Investig Drugs*. 2017;26(10):1099–1102.
26. de Bono JS, Mehra N, Higano CS, et al. TALAPRO-1: phase 2 study of talazoparib in patients with DNA damage repair alterations and metastatic castration-resistant prostate cancer. Presented at the 2021 ASCO GU Cancers Symposium: Poster 93; February 11–13, 2021; Virtual meeting, Online, USA.
27. Brain E, Grosjean J, Pulido M, et al. Real-world analysis of patients' clinical and geriatric characteristics aged ≥70 years with advanced breast cancer receiving palbociclib with endocrine therapy in the French cohort PalomAGE. *Eur J Cancer*. 2020;138(1):S20.
28. Le Saux O, Falandry C, Gan HK, et al. Changes in the use of end points in clinical trials for elderly cancer patients over time. *Ann Oncol*. 2017;28(10):2606–2611.
29. Singh H, Beaver JA, Kim G, et al. Enrollment of older adults on oncology trials: an FDA perspective. *J Geriatr Oncol*. 2017;8(3):149–150.
30. Karuturi MS, Blum JL, Wallmark J, et al. Measures of functional status in adults aged ≥70 years with advanced breast cancer (ABC) receiving palbociclib (PAL) combination therapy in POLARIS. *Ann Oncol*. 2019;30(suppl 5):V133.
31. Shelkey M, Wallace M. Katz Index of independence in activities of daily living. *J Gerontol Nurs*. 1999;25(3):8–9.
32. Takahashi M, Takahashi M, Komine K, et al. The G8 screening tool enhances prognostic value to ECOG performance status in elderly cancer patients: a retrospective, single institutional study. *PLoS One*. 2017;12(6):e0179694.
33. Paillaud E, Soubeyran P, Caillet P, et al.; G-CODE orators. Multidisciplinary development of the Geriatric Core Dataset for clinical research in older patients with cancer: a French initiative with international survey. *Eur J Cancer*. 2018;103:61–68.
34. Townsley CA, Chan KK, Pond GR, et al. Understanding the attitudes of the elderly towards enrolment into cancer clinical trials. *BMC Cancer*. 2006;6:34.
35. Townsley CA, Selby R, Siu LL. Systematic review of barriers to the recruitment of older patients with cancer onto clinical trials. *J Clin Oncol*. 2005;23(13):3112–3124.
36. Sedrak MS, Mohile SG, Sun V, et al. Barriers to clinical trial enrollment of older adults with cancer: a qualitative study of the perceptions of community and academic oncologists. *J Geriatr Oncol*. 2020;11(2):327–334.
37. Polite BN, Adams-Campbell LL, Brawley OW, et al. Charting the future of cancer health disparities research: a position statement from the American Association for Cancer Research, the American Cancer Society, the American Society of Clinical Oncology, and the National Cancer Institute. *J Clin Oncol*. 2017;35(26):3075–3082.
38. Herrera AP, Snipes SA, King DW, et al. Disparate inclusion of older adults in clinical trials: priorities and opportunities for policy and practice change. *Am J Public Health*. 2010;100(suppl 1):S105–12.
39. TransCelerate BioPharma Inc. Beyond COVID-19: Modernizing Clinical Trial Conduct. 2020. http://transceleratebiopharmainc.com/wp-content/uploads/2020/07/TransCelerate_Beyond-COVID19_Modernizing-Clinical-Trial-Conduct_July-2020.pdf . Accessed February 19, 2021.
40. Pennell NA, Dillmon M, Levit LA, et al. American Society of Clinical Oncology road to recovery report: learning from the COVID-19 experience to improve clinical research and cancer care. *J Clin Oncol*. 2021;39(2):155–169.
41. Richardson D, Zhan L, Mahtani R, et al. A prospective observational study of patient-reported functioning and quality of life in advanced and metastatic breast cancer utilizing a novel mobile application. *Breast Cancer Res Treat*. 2021;187(1):113–124. doi: 10.1007/s10549-020-06082-7.
42. Le Saux O, Falandry C, Gan HK, et al. Inclusion of elderly patients in oncology clinical trials. *Ann Oncol*. 2016;27(9):1799–1804.
43. Rugo HS, Turner NC, Finn RS, et al. Palbociclib plus endocrine therapy in older women with HR+/HER2- advanced breast cancer: a pooled analysis of randomised PALOMA clinical studies. *Eur J Cancer*. 2018;101:123–133.
44. Institute of Medicine. *Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis*. Washington, DC: National Academies Press; 2013.
45. American Cancer Society. The American Cancer Society and Pfizer launch community grants focused on addressing systemic race-related barriers that contribute to disparities in care among Black men and women with cancer; 2020. http://pressroom.cancer.org/2020-11-17-The-American-Cancer-Society-and-Pfizer-Launch-Community-Grants-Focused-on-Addressing-Systemic-Race-Related-Barriers-that-Contribute-to-Disparities-in-care-Among-Black-Men-and-Women-with-Cancer. Accessed February 19, 2021.
46. Bristol Myers Squibb. The Bristol Myers Squibb Foundation and National Medical Fellowships launch $100 million program to help increase diversity and inclusion in clinical trials; November 17, 2020. https://news.bms.com/news/details/2020/The-Bristol-Myers-Squibb-Foundation-and-National-Medical-Fellowships-Launch-100-Million-Program-to-Help-Increase-Diversity-and-Inclusion-in-Clinical-Trials/default.aspx. Accessed February 19, 2021.