Purpose: Patients with organ dysfunction, prior or concurrent malignancies, and comorbidities are often excluded from clinical trials. Excluding patients on the basis of these factors results in clinical trial participants who are healthier and younger than the overall population of patients with cancer.

Methods: ASCO and Friends of Cancer Research established a multidisciplinary working group that included experts in trial design and conduct to examine how eligibility criteria could be more inclusive. The group analyzed current eligibility criteria; conducted original data analysis; considered safety concerns, potential benefits, research, and potential hurdles of this approach through discussion; and reached consensus on recommendations regarding updated eligibility criteria that prioritize inclusiveness without compromising patient safety.

Results: If renal toxicity and clearance are not of direct treatment-related concern, then patients with lower creatinine clearance values of > 30 mL/min should be included in trials. Inclusion of patients with mild to moderate hepatic dysfunction may be possible when the totality of the available nonclinical and clinical data indicates that inclusion is safe. Ejection fraction values should be used with investigator assessment of a patient’s risk for heart failure to determine eligibility. Patients with laboratory parameters out of normal range as a result of hematologic disease should be included in trials. Measures of patient functional status should be included in trials to better assess fit versus frail patients.

Conclusion: Expanding inclusion of these patients will increase the number and diversity of patients in clinical trials and result in a more appropriate population of patients.
Key points

- Patients with organ dysfunction are often excluded from clinical trials, regardless of specific drug metabolism or relative function of the organ.

- The general population is aging and thus includes increasing numbers of patients with renal disease, hepatic dysfunction, cardiac disease, prior history of cancer, and other comorbidities.

- In the absence of understanding nonclinical pharmacokinetics (PK) and major routes of elimination in humans, it is reasonable to enroll patients with normal organ function, primarily renal and hepatic.

- Dosing for patients with organ dysfunction is often excluded from clinical trials, regardless of specific drug metabolism or relative function of the organ. For instance, the physiologic decline in renal function may make a patient ineligible even when the drug under study does not have significant renal excretion. The general population is aging and thus includes increasing numbers of patients with renal disease, hepatic dysfunction, cardiac disease, prior history of cancer, and other comorbidities. Once a drug enters the marketplace, it may be prescribed to patients with these conditions for whom clinical trial safety and efficacy data have not been evaluated.

- In the absence of understanding nonclinical pharmacokinetics (PK) and major routes of elimination in humans, it is reasonable to enroll patients with normal organ function, primarily renal and hepatic. However, as data on toxicity, PK, and pharmacodynamics (PD) become available during drug development, protocols are rarely revised to include patients with compromised organ function where safe parameters have been determined.

- Standard criteria for normal organ function are included in most trial protocols. These criteria typically include the following: adequate renal function characterized as calculated creatinine clearance (CrCl; commonly set at > 60 mL/min); adequate hepatic function characterized as total bilirubin (commonly set at < 1.5 mg/dL) and/or ALT and AST (commonly set at < 2 to 3 × upper limit of normal [ULN]); and parameters for left ventricular ejection fraction (commonly set at > 50%). Although these criteria are often included in trial protocols, the degree to which deviation from normal organ function affects the overall trial objective and primary end point needs to be assessed. For instance, trials in which the PK of an investigational agent are being determined frequently exclude patients with any deviation from normal organ function. Sometimes, dosing for patients with organ dysfunction is determined through a dedicated phase I trial that evaluates PK exposure differences between patients with organ dysfunction versus normal organ function.

Herein, we address the safety and efficacy concerns of including patients with organ dysfunction, prior or concurrent malignancies, and comorbidities in clinical trials and provide recommendations where inclusion of such patients is appropriate.

Process

ASCO and Friends of Cancer Research established a working group that included a multidisciplinary team of experts in oncology practice and clinical trial design and conduct to examine how eligibility criteria could be more inclusive for patients with organ dysfunction, prior or concurrent malignancies, and comorbidities. The group analyzed current eligibility criteria and considered safety concerns, potential benefits, research impact, and potential hurdles of enrolling greater numbers of trial participants. Recommendations regarding updated eligibility criteria that prioritize inclusiveness without compromising patient safety were reached through discussion until group consensus was met.

The organ dysfunction, prior or concurrent malignancy, and comorbidities group included clinical investigators, clinical pharmacologists, patient advocates, and industry and regulatory representatives. The recommendations stated here were drafted on the basis of analysis of clinical data and review of relevant literature and refined after discussion among similar groups assigned to consider other criteria and additional patient advocate, industry, and regulatory representatives.
The group reviewed clinical data from Kaiser Permanente Northern California (KPNC). The goal of this analysis was to explore whether changes in standard eligibility criteria would enable greater numbers of patients with commonly diagnosed cancers to participate in clinical trials.

KPNC is a fully integrated prepaid health care delivery system established in 1948. It has nearly four million members and serves approximately 20,000 new analytic patients annually. The median age of members is approximately the same as that of the SEER Program database.

Data for all KPNC patients who were diagnosed with breast, colon, lung, and bladder cancer between 2013 and 2014 (n = 12,881) were analyzed against organ function, comorbidity, and prior malignancy parameters commonly found in clinical trial eligibility criteria (Table 1). The specific parameters analyzed were as follows: diagnosis of prior malignancy in the past 5 years, history of congestive heart failure and/or cardiomyopathy, prior myocardial infarction, liver chemistries, glomerular filtration rate (GFR), and age. Total ineligibility score (TIS) is an empirically derived number that conveys the potential magnitude of ineligibility by summing the preceding columns (Table 1). In this model, TIS aided in determining what the potential effect of changing eligibility parameters would be on the number of eligible patients.

The KPNC analysis demonstrates the significant affect of renal function on patient eligibility. Results demonstrate a marked difference in renal function by diagnoses. Patients with breast cancer, many of them otherwise healthy and receiving adjuvant treatment, had a 15% incidence of GFR < 60 mL/min, whereas the incidence in patients with bladder cancer was 34%. This also correlated with patients with bladder cancer being much older (45% > 75 years old vs. 16% of patients with breast cancer) and having more comorbidities (Table 1).
Additional analysis by degrees of renal dysfunction (Table 2) demonstrates how standardized inclusion and exclusion criteria affects patient eligibility across common cancer types and suggests that renal function criteria should be specific to the patient population under study (eg, adjusted for diagnosis, age, comorbidity, etc).

Exclusion of patients with CrCl < 60 mL/min would preclude between 20.3% and 45.9% of patients from participating in cancer clinical trials. This result is likely conservative because the patients were measured at diagnosis and not heavily pretreated or phase I trial candidates.

The KPNC analysis indicates that newly diagnosed patients across all four disease types rarely (< 1%) have significant hepatic dysfunction, defined as ALT > 2 × the ULN. Congestive heart failure and myocardial infarction were present in greater percentages of patients with lung and bladder cancers (congestive heart failure: 11% in both lung and bladder cancer vs. 5% in breast cancer and 8% in colorectal cancer).

Our analysis reveals how changing the standard criteria may increase the number of patients eligible for clinical trials.

Risks and benefits associated with including patients with organ dysfunction and prior or concurrent malignancies in trials are outlined in the following sections.

Clinical trials have often mandated a calculated CrCl of > 60 mL/min for inclusion.

### Risks and benefits to inclusion

Standard organ function measurements and cutoff points may exclude patients without adequately assessing the function of the organ. In addition, the organ may not be clinically relevant to the therapy under investigation or raise any concerns about patient safety. Risks and benefits associated with including patients with organ dysfunction and prior or concurrent malignancies in trials are outlined in the following sections.

#### Renal dysfunction

In a diagnosis that predominantly affects older patients, such as bladder cancer, the KPNC analysis demonstrated that rigid CrCl limits will exclude a significant number of patients (Table 1). The rationale to exclude patients with renal dysfunction from studies, particularly in early-phase trials, is to avoid adverse events as a result of renal insufficiency and potential renal toxicities associated with drugs that have renal clearance. Clinical trials have often mandated a calculated CrCl of > 60 mL/min for inclusion. Serum creatinine values have also been used, but serum creatinine does not accurately reflect renal function and CrCl should be the standard. Studies of patients with normal serum creatinine values demonstrate varying degrees of renal insufficiency, emphasizing the need for calculating CrCl. Although ideally a measured CrCl is preferable, it is not a practical solution. Twenty-four-hour urine collections for measured CrCl are often not accurately performed, particularly when collection takes place at home, and radionuclide assessment of CrCl is costly and unnecessary in the majority of patients.
There are various formulae available for CrCl calculation, but the two most common estimates are the Cockcroft-Gault equation and the Modification of Diet in Renal Disease (MDRD) equation. The National Kidney Foundation generally recommends the use of MDRD over Cockcroft-Gault as a result of improved agreement with directly measured GFR values, particularly in the elderly and obese populations. However, when each equation is used and compared with GFR and PK is considered, the actual difference in drug dosing is clinically insignificant in the majority of patients. Both the Cockcroft-Gault and MDRD equations are readily calculated from common clinical values and are incorporated in many electronic health record systems.

Because a large proportion of potential patients with cancer are older than age 65 years, the issue of aging physiology is significant. Normal aging is associated with a decline in CrCl of approximately 0.8 mL/min per year after the age of 40. Decline in renal function is often exacerbated by comorbidity, contrast dyes, or medication. Studies of patients with normal serum creatinine values demonstrate varying degrees of renal insufficiency, emphasizing the need for calculating CrCl.

The need for a specific CrCl eligibility criterion is dependent on the type of study contemplated and the agent(s) used. For a phase I trial in which PK data are required and the human renal toxicity and clearance may not be fully known, a normal CrCl of ≥ 60 mL/min is reasonable. When PK and PD data and renal safety have been explored, lower values are reasonable to prevent unnecessary patient exclusion.

A study by the Alliance for Clinical Trials in Oncology analyzed the effect of renal function on various outcomes in an adjuvant breast cancer trial in women older than age 65 years. This prospective randomized study analyzed physician-selected multiagent regimens of capecitabine versus either cyclophosphamide plus doxorubicin or cyclophosphamide, methotrexate, and fluorouracil. Patients were required to have a CrCl > 30 mL/min, and doses of capecitabine and methotrexate were adjusted per on-study renal function. The authors concluded that there was no relationship between pretreatment renal function and the five end points (toxicity, dose modification, therapy completion, relapse-free survival, and overall survival) for any regimen. Patients with renal insufficiency who received a modified dose were not at increased risk for complications compared with those who did not have renal insufficiency and received a full dose. The investigators concluded that the risk of excessive hematologic toxicity or poor outcomes in patients with renal insufficiency but good performance status may be mitigated with appropriate dosing modifications.

After a retrospective analysis, authors of the Gynecologic Oncology Group 182 trial concluded that their data do not support excluding patients with CrCl < 60 mL/min from clinical trials. Patients were randomly assigned among five arms that incorporated gemcitabine, methoxypolyethylene glycosylated liposomal doxorubicin, or topotecan as a triplet compared with carboplatin and paclitaxel as doublet therapy. Eligibility criteria required a patient’s creatinine to be ≤ 1.5 × the institutional ULN using the Jelliffe formula. The trial accrued 3,830 evaluable patients with a mean age of 58.7 years and a mean baseline CrCl of 81.9 mL/min (range, 23.4 to 239 mL/min). A cutoff value of CrCl < 60 mL/min would have deemed 15% of patients treated on the Gynecologic Oncology Group 182 trial ineligible.

Finally, the National Cancer Institute analyzed extramural phase I studies from 1979 to 2010. Approximately 36% of patients enrolled onto phase I trials had mild renal dysfunction (CrCl, 50 to 80 mL/min). In a comparison with patients with normal function, mild renal dysfunction was associated with a statistically significant but small increase in grade 3 or 4 nonhematologic toxicity. The authors concluded that patients with mild renal dysfunction can be dosed appropriately.

**Key points**

- Normal aging is associated with a decline in CrCl of approximately 0.8 mL/min per year after the age of 40. Decline in renal function is often exacerbated by comorbidity, contrast dyes, or medication.
- Studies of patients with normal serum creatinine values demonstrate varying degrees of renal insufficiency, emphasizing the need for calculating CrCl.
- The investigators concluded that there was no relationship between pretreatment renal function and the five end points (toxicity, dose modification, therapy completion, relapse-free survival, and overall survival) for any regimen.
- Patients with renal insufficiency who received a modified dose were not at increased risk for complications compared with those who did not have renal insufficiency and received a full dose.
- The investigators concluded that the risk of excessive hematologic toxicity or poor outcomes in patients with renal insufficiency but good performance status may be mitigated with appropriate dosing modifications.
- Patients were randomly assigned among five arms that incorporated gemcitabine, methoxypolyethylene glycosylated liposomal doxorubicin, or topotecan as a triplet compared with carboplatin and paclitaxel as doublet therapy.
be enrolled without clinically meaningful increase in the risk of toxicity and without altering the maximum-tolerated dose determination.

### Hepatic dysfunction

**Eligibility criteria for hepatic function**

Include liver function tests (LFTs), such as serum aminotransferases (ALT and AST), bilirubin, and, less frequently, alkaline phosphatase, γ-glutamyl transpeptidase, albumin, lactate dehydrogenase, and coagulation tests. Categorization of function is considered as synthetic (eg, albumin), cellular injury (eg, AST, ALT), and cholestatic and ductal function (eg, bilirubin). Concentrations of these enzymes are used to classify patients into groups for trial purposes (ie, normal function or mild, moderate, or severe dysfunction). The more conservative approach of excluding patients with values greater than the ULN is routinely done to ensure safety and is historically done on the assumption that elevated enzymes are surrogates for impaired drug metabolism. As an exception to this, patients with hepatic metastases are often allowed on trial with higher values, up to 5 × ULN, under the assumption that abnormal LFT values are a result of cancer and do not reflect intrinsic hepatic or metabolic function. This exception highlights the need to discern etiology of elevated LFT values in patients before initiating treatment, because some cancers (eg, colorectal) may be causative and, therefore, effective treatment may lead to a return to normal values.

Patients with hepatic impairment are often excluded from clinical trials where safety or efficacy is the primary objective. Dosing guidance for patients with hepatic impairment is on the basis of smaller trials specifically designed to evaluate exposure differences between patients with and without liver dysfunction. Current clinically available hepatic function testing does not fully describe liver function, particularly drug metabolism capability (ie, there is no reliable comparator to the relationship between creatinine and renal drug clearance).

Hepatic metabolism may also be influenced by cancer and inflammation, even in the setting of normal test results.

**Estimates of hepatic function that incorporate clinical variables as well as functional and laboratory values, such as the Child-Pugh and Model for End-Stage Liver Disease scoring systems, may more closely align with hepatic metabolism.**

### Cardiac dysfunction

Oncology clinical trials often exclude patients with a previous cardiovascular history, including coronary artery disease, symptomatic heart failure, and other cardiac events within specified time frames. Exclusions on the basis of cardiac disease may decrease enrollment of older patients by approximately 5%. Ejection fraction (EF) as a marker of current cardiac function is considered as synthetic (eg, albumin), cellular injury (eg, AST, ALT), and cholestatic and ductal function (eg, bilirubin). Concentrations of these enzymes are used to classify patients into groups for trial purposes (ie, normal function or mild, moderate, or severe dysfunction). The more conservative approach of excluding patients with values greater than the ULN is routinely done to ensure safety and is historically done on the assumption that elevated enzymes are surrogates for impaired drug metabolism. As an exception to this, patients with hepatic metastases are often allowed on trial with higher values, up to 5 × ULN, under the assumption that abnormal LFT values are a result of cancer and do not reflect intrinsic hepatic or metabolic function. This exception highlights the need to discern etiology of elevated LFT values in patients before initiating treatment, because some cancers (eg, colorectal) may be causative and, therefore, effective treatment may lead to a return to normal values.

Patients with hepatic impairment are often excluded from clinical trials where safety or efficacy is the primary objective. Dosing guidance for patients with hepatic impairment is on the basis of smaller trials specifically designed to evaluate exposure differences between patients with and without liver dysfunction. For drugs extensively metabolized by liver enzymes, it has been shown repeatedly that LFT values in patients with mild and moderate hepatic impairment do not reliably predict systemic exposure of anticancer agents. Patients with mild and moderate impairment, as well as those with AST or ALT elevations defined as grade 3 by the National Cancer Institute Common Terminology Criteria for Adverse Events (> 5 to 20 × ULN), may be asymptomatic and able to take doses equivalent to patients with normal hepatic function. However, patients with severe hepatic impairment often do not tolerate approved doses. This intolerance, however, is often a result of poor performance status rather than an alteration in systemic PK measures. Another complicating factor in patients with liver dysfunction is that an investigational agent may cause liver toxicity and therefore may exacerbate underlying liver dysfunction.
contractility is also commonly determined at study entry. Typically, patients must have an EF of 45% to 50% or higher by echocardiography or multigated acquisition scan. Accuracy of each method is reasonable; however, when continued EF measures are needed during the clinical trial, a consistent approach should be used for comparability to screening values. The ability of a specific EF to predict anticancer agent cardiotoxicity tolerability is unclear, and entry criteria percentages have largely been chosen because of historical precedent.

ECG eligibility criteria focus on QTc interval, frequently with a baseline interval of 450 milliseconds. For some agents that have preclinical risk of QTc prolongation, frequent serial ECGs are required during early-phase trials to determine a concentration–QTc prolongation relationship. However, an analysis of 8,518 ECGs in phase I anticancer studies found that none of the ECGs performed predicted a cardiac event and that prolonged QTc intervals did not lead to arrhythmic events. The study authors emphasize the importance of clinical evaluation and recommend more modest use of ECG monitoring in early-phase studies. This should be in coordination with regulatory agencies, especially in early-phase studies.

■ Prior or concurrent malignancy
Diagnoses of more than one malignancy are not unusual, occurring in approximately 15% of patients. By excluding individuals with previous cancers, as most trials traditionally do, trial recruitment favors younger patients. Many patients with prior malignancies could be appropriate clinical trial participants for interventions related to subsequent malignancies. Diagnosis and treatment may have occurred many years prior and may be clinically insignificant, particularly in situations with few indicators of relapse. In the case of concurrent malignancies that do not require treatment and are clinically stable, there would be no interference with protocol therapy. Evidence is insufficient to determine the affect of previous, nonactive cancers on study-related outcomes.

Explicitly including patients with prior malignancies rather than removing prior malignancy as an exclusion may have a positive effect on accrual. For example, trials that explicitly include older patients with impaired functional status were found to enroll higher numbers of older adults overall than trials that did not specify functional status exclusion. To exclude a patient from intervention on current malignancy solely on the basis of a prior or clinically stable concurrent malignancy is inappropriate.

■ Hematologic malignancies
Although group discussion and recommendations focused on solid tumors, issues for eligibility criteria are similar in hematologic malignancies. A 2016 analysis of randomized controlled trials in hematologic malignancies found that standard eligibility criteria include restrictions that may be overly conservative on the basis of the known toxicity profiles of the interventions being studied. Exclusions on the basis of hematologic function abnormality may decrease enrollment of older patients by approximately 14%.

Patients may be excluded from hematologic studies on the basis of non–drug-relevant organ dysfunction or performance status (PS) of ≥ 2. Some studies have allowed expanded PS if the worsened PS is from disease (eg, PS > 2 if secondary to neuropathy or acute bone event; S. Kumar, personal communication, January 2017). The Eastern Cooperative Oncology Group–American College of Radiology Imaging Network E1912 study is notable for the following more inclusive criteria: PS (0 to 2 allowed); liver function (eligible if value is higher as a result of hepatic involvement by chronic lymphocytic leukemia); GFR > 40 mL/min; and prior malignancy (the provision that “if there is a history of prior malignancy, [patients] must not be receiving other specific treatment [other

Key points

- Accuracy of each method is reasonable; however, when continued EF measures are needed during the clinical trial, a consistent approach should be used for comparability to screening values.
- The ability of a specific EF to predict anticancer agent cardiotoxicity tolerability is unclear, and entry criteria percentages have largely been chosen because of historical precedent.
- ECG eligibility criteria focus on QTc interval, frequently with a baseline interval of 450 milliseconds.
- Diagnosis and treatment may have occurred many years prior and may be clinically insignificant, particularly in situations with few indicators of relapse.
- In the case of concurrent malignancies that do not require treatment and are clinically stable, there would be no interference with protocol therapy.
- A 2016 analysis of randomized controlled trials in hematologic malignancies found that standard eligibility criteria include restrictions that may be overly conservative on the basis of the known toxicity profiles of the interventions being studied.
- Exclusions on the basis of hematologic function abnormality may decrease enrollment of older patients by approximately 14%.
Key points

- Clinical trials do not usually include older patients, and when they do, geriatric-specific baseline data are almost never obtained.
- The inclusion of baseline data on patients’ comorbidities and function will make study results more applicable to a broader oncology population.
- On the basis of a literature review, the KPNC analysis, and expert opinion, the working group makes the following recommendations for increased inclusiveness of patients with organ dysfunction, prior or concurrent malignancies, and comorbidities in clinical trials.
- Eligibility criteria should include assessment of CrCl rather than serum creatinine concentrations.
- The Cockcroft-Gault and MDRD equations are reasonable standards for calculating kidney function and are accepted in practice.
- Inclusion of patients with mild to moderate hepatic dysfunction may be acceptable when the totality of the available nonclinical and clinical data, including PK and PD data, indicates that inclusion of these patients is safe.
- New measures that adequately reflect hepatic function should be developed to improve the accuracy of identifying patients with true hepatic dysfunction.

Renal function
- Eligibility criteria should include assessment of CrCl rather than serum creatinine concentrations.
- The Cockcroft-Gault and MDRD equations are reasonable standards for calculating kidney function and are accepted in practice. A consistent measure should be applied throughout the drug development process. Inclusion of patients with renal dysfunction could be liberalized in the following specific settings: if renal toxicity and clearance are not of concern, then lower CrCl values of > 30 mL/min should be used for inclusion; when published dose modifications allow for safe and effective administration of the drug and are not likely to change outcomes (eg, carboplatin, methotrexate, capecitabine); and when the totality of the available nonclinical and clinical data, including PK and PD data, indicates that inclusion of patients with renal dysfunction is safe.

Hepatic function
- Inclusion of patients with mild to moderate hepatic dysfunction may be acceptable when the totality of the available nonclinical and clinical data, including PK and PD data, indicates that inclusion of these patients is safe.
- New measures that adequately reflect hepatic function should be developed to improve the accuracy of identifying patients with true hepatic dysfunction.

Cardiac function
- Treatment-emergent cardiac adverse events may be difficult to predict. Eligibility criteria should reflect a conservative approach to cardiac safety measures, so that patients with significant cardiac abnormalities or EF < 35% are excluded, especially in early-phase studies. Inclusion of patients with cardiovascular dysfunction may be possible when the totality of the available nonclinical and clinical data, including PK and PD data, indicates that inclusion of these patients is safe.
- EF values should not be used in isolation to exclude patients from trials. Trials should recommend investigator assessment of a potential participant’s risk for heart failure with a validated clinical classification system (eg, the New York Heart Association functional classification).
- If QTc prolongation is not identified as a concern in first-in-human studies, QTc interval eligibility criteria in phase IB and later trials should be re-evaluated.

Comorbidities

Clinical trials do not usually include older patients, and when they do, geriatric-specific baseline data are almost never obtained. The inclusion of baseline data on patients’ comorbidities and function will make study results more applicable to a broader oncology population. When included in the final study analysis, these data will help guide clinicians to treat older patients with more precision.

Recommendations

On the basis of a literature review, the KPNC analysis, and expert opinion, the working group makes the following recommendations for increased inclusiveness of patients with organ dysfunction, prior or concurrent malignancies, and comorbidities in clinical trials.
and ongoing ECG monitoring may not be required.

- Cardiovascular safety measures and close collaboration with cardiology should be considered, particularly when investigating compounds or regimens where trial-emergent cardiac contractility toxicity is a factor (eg, trastuzumab or sunitinib).

Prior or concurrent malignancy

- Inclusion of patients with prior malignancies is recommended, especially when the risk of the prior malignancy interfering with either safety or efficacy end points is very low.
- Patients with a previously treated malignancy should be eligible to participate if all treatment of that malignancy was completed at least 2 years before registration and the patient has no evidence of disease.
- Patients who have a concurrent malignancy that is clinically stable and does not require tumor-directed treatment should be allowed to participate on a trial for another cancer that requires treatment.

Hematologic malignancies

- Inclusion of patients with laboratory parameters that are out of normal range as a result of disease may be appropriate (eg, cytopenias from bone marrow infiltration, LFT abnormalities from disease involvement in lymphoma).
- Inclusion of patients with disease-specific comorbidities (eg, peripheral neuropathy or bone symptoms in multiple myeloma) that are thought to be unaffected by the study agents and would otherwise be treated in practice is recommended.

Comorbidities

- Inclusion of measures of function other than PS into trial design to better assess the safety and efficacy of an investigational agent in fit versus frail patients is recommended.

Conclusion

The working group has outlined a number of areas in which modifying current clinical trial eligibility can enhance trial participation. Implementation of these changes will take the cooperation of multiple stakeholders including individual clinicians, institutions, and their investigational review boards, cooperative oncology groups, the pharmaceutical industry, and patients. Increasing the numbers of patients and including a broader array of patients in clinical trials will ultimately help all of these groups and enhance cancer treatment overall.

Key points

- Patients with a previously treated malignancy should be eligible to participate if all treatment of that malignancy was completed at least 2 years before registration and the patient has no evidence of disease.
- Inclusion of measures of function other than PS into trial design to better assess the safety and efficacy of an investigational agent in fit versus frail patients is recommended.
- The working group has outlined a number of areas in which modifying current clinical trial eligibility can enhance trial participation.
- Implementation of these changes will take the cooperation of multiple stakeholders including individual clinicians, institutions, and their investigational review boards, cooperative oncology groups, the pharmaceutical industry, and patients.

References


