# Broadening Eligibility Criteria to Make Clinical Trials More Representative

Joint Recommendations of the
American Society of Clinical Oncology
and Friends of Cancer Research

October 2, 2017

# What is the goal?

- Challenge assumptions & past practice
- Create new culture – only exclude where safety warrants
  - Shape perception/attitudes/practice of clinical trial eligibility
  - Create and implement new criteria
  - Justify exclusions or differences between trial participants and overall patient population with the indicated disease
  - Active discussion during trial design and FDA pre-IND meetings
- Not just publication of recommendations, but implementation

# ASCO-Friends of Cancer Research Project Overview

- Prioritized assessment of specific eligibility criteria:
  - Brain Metastases, Minimum Age, HIV/AIDS, Organ Dysfunction, and Prior and Concurrent Malignancies
- Formed multi-stakeholder working groups
  - Patient advocates
  - Clinical investigators
  - FDA medical reviewers
  - Drug and biotech manufacturers
  - Biostatisticians
  - Pharmacologists

# ASCO-Friends Recommendations Development

- Working Groups developed consensus recommendations as four separate manuscripts.
  - Recommendations presented at November 2016 Friends' Annual Meeting and highlighted in Moonshot Task Force report.
- ASCO and Friends developed joint statement including summary recommendations and discussion of implementation.
  - ASCO Board of Directors and Friends' leadership approved the statement.
- Manuscripts published as *Journal of Clinical Oncology* Special Series.
  - October 2, 2017 at ascopubs.org/journal/jco

# Brain Metastases Recommendations

- Patients with treated and/or stable brain metastases:
  - Stable = no progression for at least 4 weeks after local therapy
  - Routinely include in all phases, except where compelling rationale
- Patients with active (untreated or progressive) brain metastases:
  - No automatic exclusion.
  - A one-size-fits-all approach is not appropriate. Factors such as history of the disease, trial phase and design, and the drug mechanism and potential for CNS interaction should determine eligibility.
- Patients with leptomeningeal disease:
  - In most trials, exclude, although there may be situations that warrant a cohort of such patients in early phase trials.

# Minimum Age Recommendations

- Initial dose-finding trials:
  - Pediatric-specific cohorts should be included when there is strong scientific rationale (based on molecular pathways or histology and preclinical data)
- Later-phase trials:
  - Trials in diseases and therapeutic targets that span adult and pediatric populations should include pediatric patients with the specific disease under study
  - Patients aged 12 years and above should be enrolled in such trials.
  - Patients under 12 years may also be appropriate.

# HIV+ Recommendations

- Cancer patients with HIV infection who are healthy and low-risk for AIDS-related outcomes should be included.
- HIV-related eligibility criteria should be straight-forward and focus on:
  - Current and past CD4 and T-cell counts
  - History (if any) of AIDS-defining conditions
  - Status of HIV treatment
- Treated using the same standards as other patients with co-morbidities, and anti-retroviral therapy should be considered a concomitant medication.

# Organ Dysfunction Recommendations

- Informed by an analysis of Kaiser dataset of 13,000 patients newly diagnosed in 2013-2014.
- Renal function should be based on creatinine clearance (calculated by Cockcroft-Gault or MDRD).
  - Liberal creatinine clearance (e.g., >30 mL/min) should be applied when renal excretion not significant
  - Follow established dose modification strategies.
- Hepatic Function
  - Current tests are inadequate, particularly drug metabolism capability
  - Employ standard clinical assessments relative to institutional normal ranges

# Prior and Concurrent Malignancies Recommendations and Cardiac Testing

- Prior Malignancy
  - Patients eligible if prior therapy at least 2 years prior and no evidence of disease
- Concurrent Malignancy
  - Patients eligible if clinically stable and not requiring tumor-directed therapy
- Cardiac testing
  - If no known cardiac risks, ejection fraction tests should not be exclusionary
  - Investigator assessment with a validated clinical classification system
  - If no cardiac risks, ECG should be eliminated in later phases

# Next Steps (as of October 2017)

- Initiate implementation projects
  - Education and awareness campaigns for sponsors, investigators, IRBs, patients, etc.
  - NCI and Cooperative Group endorsements
  - Tools for sponsors, investigators, and IRBs
- Consider new working groups to make recommendations for additional eligibility criteria
  - Project leadership emphasizes that concrete steps toward implementation of the existing recommendations must take priority