SESSION I
OVERVIEW OF BARRIERS, SOLUTIONS

Issues

- Trials are not designed to enroll older adults
- Sponsors are not incentivized to enroll representative older adults
- Older adults are not routinely engaged in trial design and education
- Education regarding the value of trials for older adults is lacking
- Access to trials is a barrier (geographic, community settings, rural/urban, cost, transportation)
- Eligibility criteria limit enrollment
- Vulnerable/frail older adults are not studied yet are treated in practice
- Providers are reluctant to enroll older adults on trials
- Geriatric measures are not routinely captured in clinical trials

Solutions

- Require early collaboration in trial design with older adult patients/advocates
- Develop and disseminate education tools in collaboration with senior advocates
- Enhance reporting requirements from clinical trials
- Require implementation of modernized eligibility criteria as standard including new PS recommendations* (i.e. NCI protocols, FDA review)
- Conduct older adult specific trials with emphasis on minimum effective dosing, treatment tolerance, and geriatric focused endpoints
- Utilize inclusion across the lifespan principle (i.e. study population matches disease population) to inform requirement for expansion cohort or post-marketing commitment.

* Require data driven scientific justification to restrict

Solutions, continued

- Identify "geriatric" endpoints (i.e. overall treatment utility) that can be used to support new drug indications or labelling.
- Utilize standardized GA measures to design trials for vulnerable/frail older adults.
- Incorporate GA into all older adult specific trials
- Incorporate a standardized set of core GA measures (minimum data set) into all treatment trials enrolling older adults (i.e. Table 1 Initiative)
- Include geriatric experts and patient advocates in design and review of trials
- Develop guidance, create incentive, build infrastructure to expand access to community sites (decentralized trials, telemedicine)
- Utilize labelling to incentivize enrollment of older adults and collection of data to describe the population (carrot/stick).

SESSION 2
EARLY PHASE DRUG DEVELOPMENT

Issues

- Lack of preclinical studies conducted to assess impact of age on pharmacology/toxicology of anticancer agents
- Phase I trial designs are not inherently amenable to older adult enrollment
  - Frequent visits, long days, limited sites – travel out of town, cost, pre-trial screening procedures (biopsies, etc.)
- Endpoints that matter to older adults for dose derivation in early phase trials
  - Grade I/II chronic adverse events vs acute Grade III/IV toxicities
  - QoL and functional impact
- Eligibility restriction in phase I trials may miss safety signals that can be managed, exclude relevant populations, and safety data derived not incorporated into next trial(s)
- Lack of wider adoption of novel phase I study design

Solutions

- Extend geroscience to the nonclinical investigation of anticancer agent efficacy and toxicity
- Leverage local trial/practice sites and laboratories collaboratively, use web- and app-based tools for symptom assessment, and minimize PK/PD collection
- Use dose derivation trial designs that incorporate differing baskets of populations based on frailty, comorbidities, and concomitant medications
  - Perpetual design platforms
  - Continuous toxicity monitoring to assess longer term tolerability
  - Output = Differing doses for differing populations as defined above
- More extensive use of Bayesian designs and borrowing of data across subgroups in development
- Establish overnight accommodations and provide travel and expense monies in budgets for volunteers

Solutions, continued

- Update eligibility criteria as early as possible in development based on real-time safety data obtained
  - Comorbidity allowances
  - Organ function liberalization
  - Concomitant medications
- Design proper learning trials as platforms in early phase trials and incentivize their enrollment and outcome adoption when appropriate
- Incentivize physicians to refer older adults to trials and empower older adults to inquire and advocate
- Simplify, simplify, simplify
  - Visits
  - Informed consent
  - Correlative studies

SESSION 3: STUDIES DESIGNED WITH REGISTRATIONAL INTENT AND POLICY OPPORTUNITIES TO IMPROVE THE EVIDENCE BASE

Issues

- Lack of evidence to guide treatment for older adults represents an ethical issue of importance to our society
- Study designs that do not specifically address the needs of older adults are unlikely to achieve sufficient representation from older patients and may not involve endpoints that are most meaningful for older adults
- For most diseases in oncology, there is limited incentive for pharmaceutical companies to obtain data relevant to patients who are older or more frail
- Studies that specifically address treatment of older adults are of relatively low priority once a drug is approved without an age restriction in the label
- FDA has limited authority to require data on treatment of elderly patients, even when these patients represent a significant proportion of patients with the target disease

Solutions

- Trials that target older or frail populations are feasible and well received by both patients and treating clinicians, and should be prioritized whenever disease prevalence is high in older adults
- Keys to success include:
  - Obtain safety and dose data in early-phase clinical studies to support inclusion of older patients in phase 3 studies
  - Include geriatric oncology experts on therapeutic development and study design teams
  - When possible, conduct separate, adequately powered studies with eligibility limited to older or frail adults
  - For diseases with a wide age distribution, include expansion cohorts as necessary to test therapy in older adults
  - Studies should include community sites whenever possible and support access to trial participation by less fit individuals (e.g. participant travel, pragmatic study designs)

Solutions, continued

- Bring geriatric oncology into the mainstream of clinical research by disseminating tools and best practices that enable enrollment of older or frail adults
- Develop and validate new endpoints, such as composite endpoints, that better define clinical benefit in older or more frail adults
- Expand FDA authority to require submission of data to address agent use in older or less fit adults when these individuals make up a significant percentage of those with the target disease

SESSION 4
POST-MARKETING STRATEGIES

Issues

- Are we framing the problem correctly? Should we be focused on age or on fitness/organ function/co-morbidity, regardless of age?
- FDA has limited authority to enforce post-marketing commitments.
- All data sources (trials, claims, EHRs, prior auth, etc.) have strengths/limitations. Need to pre-specify objectives/analyses and use data that are "fit for purpose".
- Post-market data sources may not represent the patient experience well or include endpoints important to older individuals, e.g., physical and cognitive function, chronic low-grade AEs.
- Unclear what level of evidence derived from post-marketing studies is sufficient to change practice guidelines; drug labels; payer policies.

Solutions

- Create infrastructure and motivation (carrots and sticks) to do post-market research
- Expand FDA authority to enforce post-marketing commitments for studies of older individuals, even in the absence of a risk signal
- At the outset, sponsors and FDA should agree on post-marketing studies to acquire missing data related to older individuals or those with frailty/organ dysfunction and how that will inform the product label
- Enhance data utility through data linkages:
  - SEER-Medicare
  - SEER-commercial claims
  - RCT data-claims
  - RCT data-RWD
  - RWD-claims

Solutions, continued

- Expand cadre of qualified investigators through training programs and funding opportunities
- Adopt universal data standards, e.g., mCODE, to facilitate data entry and improve data quality
- Develop validated endpoints that assess outcomes important to older people and capture those routinely in EHRs
- Define the level of evidence derived from post-marketing studies that is sufficient to change practice guidelines; drug labels; payer policies.