Inclusion of Older Adults in Cancer Clinical Trials

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Background

- Inadequate representation of older adults patients in clinical trials
  - ✓ In majority of clinical trials adults > 18 years are included in the eligibility criteria
- Why older adult patients are not enrolled?
  - ✓ In majority of clinical trials exclusion criteria includes some comorbid conditions
  - o Are there other reasons for low enrollment of older adults patients?
  - o What can be done to increase enrollment of older adults patients?
    - o Design of Clinical Trials

Increasing Participation of Older Adults in Clinical Trials

- Without compromising safety
- Expand eligibility to include patients with some comorbid conditions

- What are the design options for such a trial and how to interpret the data from such a clinical trial?

- Address other road blocks such as accessibility/feasibility for elderly patients to participate; educating patients and investigators, etc. Tele-health may help in enrolling older patients

➢ *Among the total US population[1] 16.5% are estimated to be 65 years or older; Proportion of older adult population varies with disease*

Points to consider to increase participation of older adult patients

- Prevalence of disease in the elderly population
- Access to care facility
- Frequency of outcome assessment; invasive or non-invasive outcome assessments
- Thoughtful consideration for exclusion criteria
  - Toxicity of the drug, any drug-drug interaction

Clinical Trial Designs

- During early phase of drug development consider adding a small cohort of elderly patients to:
  - Better understand the safety and tolerability of the treatment
  - Dose selection and potential dose modifications
  - To study drug-drug interactions
  - Feasibility of outcome assessments
- During late phase of drug development in confirmatory studies different trial designs can be considered without compromising safety
- Post-marketing studies (clinical trial, registry, or RWD)

Confirmatory Trial Design Options

- Randomized Clinical Trial
  - Population: for example, ≤ 75 years age + expanded older age high risk population > 75 years
  - Stratification factors: restricted population and high risk population
  - Primary analysis based on modified ITT population with only restricted population (modified ITT population, MITT)
  - Hierarchical testing: ITT after MITT; high risk population can be tested separately if it is hypothesis driven and sample size is adequate
  - Can add adaptive feature to stop enrolling older patients based on interim analysis if safety concerns arise
- Simultaneous RCT in restricted population and single arm cohort in the high-risk population
  - RCT and single arm cohort analyzed separately
  - Single arm high risk cohort – descriptive statistics

Key Considerations

- Who should be in the expanded, older age high risk population
  - What co-morbidities, drug-drug interactions, level of toxicity are acceptable?
- Randomized Control Trial
  - Proportion of patients in older age high risk group; limit number of patients in high risk stratum?
  - Primary hypothesis, Type I and Type II errors, number of events for the final analysis, benefit:risk assessment based on restricted population
  - Hierarchical testing feasible? – what if more events occur in the high risk stratum?
  - Consideration of safety assessment in the high risk population
- Single arm cohort of older age, high risk population
  - Could consider enrolling patients only in certain sites
  - Difficult to interpret toxic events, in particular deaths without a control arm in a single arm study
- Post-market studies
  - Reproducible outcome definition and assessment
  - Measures for safety evaluation, consistency in recording data

References

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