# The older patient in cancer clinical trials

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# Notice

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# Enrollment of older patients in industry sponsored cancer trials

- Despite knowledge of under representation of older patients in clinical trials for almost 20 years the downward trend has continued
- Over 60% of cancers are in people over 65
- 32% of participants in phase 2 and 3 studies from this older group and there is a downward trend as patients age
  - 3% of pts between 30-64 enroll in studies
  - 1.3% 65-74
  - 0.5% greater than 75

Murphy, V.H. et.al. JAMA (2004) 291:2720

Lewis, JH et.al., JCO (2003) 21:1383

# Trend to younger patients even in hematologic malignancies that focused on older patients

- Review of 20 trials enrolling 6033 patients
- No age limits in 92% of the studies
- 22 heme malignancies were included over the 20 trials
  - Median age in trial was 3.8 years younger that disease specific median age
  - DLBCL average age was 7 years younger for a trial
  - AML 7.8 years younger

Gajra, A, et.al. Blood (2020) 136suppl:21

# Focusing on the Inclusion/Exclusion criteria

- Review of 283 randomized clinical trials demonstrated
  - 37% had multiple inclusion or exclusion criteria who were not justified
  - 84% had at least one that was not justified
- Restriction in early trials may miss safety signals that can be managed
  - May limit use in patients included older patients where the drug is active
- Tension between a homogenous population and a clear signal


- FDA Public Workshop on Inclusion/Exclusion Criteria in Clinical Trials 4/10/2018
- J. Comp Eff. Res (2015)4:289.

# Prior history of cancer restricts enrollment

- Concerns about affecting survival endpoints
- In trials with non-survival endpoints 70% of patients are excluded
- Years from diagnosis from prior cancer and treatment to restrict entry
  - 16% excluded with any cancer
  - 39% 5 years from cancer
  - 7% 2-3 years
- In review on lung cancer studies 75% excluded based on 5 years or no history
  - Prior cancer did not convey an adverse effect on lung cancer-specific survival

J. Comp Eff. Res (2015)4:289

# Key areas that could impact enrollment in older patients

- Restrictions based on medications present in 54% of trials
- Co-morbidities are a key issue in older patients
  - Lose evaluation in a patient population where drug may be effective
- Measurements of organ dysfunction
  - LFTs and renal function
  - Exclusion may not be justified based on molecule properties
  - Potential to lose early assessment of dose adjustments that enable patients to continue treatment
- Socioeconomic (travel, family support, e.g.)
- Complicated clinical plan and assessments

# Looking forward

- NIH supported studies instituted guidelines on supported studies around inclusion and reporting on age-related enrollment
- FDA Workshop in 2018 identified key areas that impact inclusion/exclusion criteria across studies
- Enrollment in older patients
  - Prior cancer may impact but needs to be assessed on a disease by disease bases
  - Organ function
  - Co-morbidities and comedications
- Review of assessments and logistics – can we eliminate challenges to participation by older patients?