Enrollment of older adults in Cancer clinical trials: US Food and Drug Administration Experience

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Enrollment of Older Adults in Cancer Clinical Trials- A Continuing Conversation

SPECIAL ARTICLE

Underrepresentation of Patients 65 Years of Age or Older in Cancer-Treatment Trials

Laura F. Hutchins, M.D., CLINICAL TRIALS

Albain, M.D.

In 1990, the five leading causes of death in older people were coronary heart disease, chronic obstructive pulmonary disease (COPD), cerebrovascular disease, cancer, and pneumonia. In 1982, the National Cancer Institute (NCI)-sponsored Clinical Cooperative Group Cooperative study trials (which included more than 8000 older patients) for the aforementioned sites was compared with the 1990 incidence data from the NCI's Surveillance, Epidemiology, and End Results program. Of the male patients enrolled in the trials, the average age of 38% were older than 65. 47.5% coparcen, 46.6% perineum, and 46.0% leukemia; whereas 23.8% of all women enrolled in trials were 65 or older (31.9% breast, 46.5% colorectal, 41.6% pancreas, and 33.4% ovary). With respect to incidence, older patients generally are underrepresented in cancer treatment trials. With the exception of the data on prostate cancer, each of the comparisons using the Z statistic gave a probability value of less than 0.01. The most significant differences were observed in colon and rectum, prostate, ovarian, and breast cancer.

Possible explanations for these findings include [1] a research focus on aggressive therapy, which may be unacceptable to the elderly; [2] presence of comorbidity in the elderly; [3] fewer trials available specifically aimed at older patients; [4] limited expectations for long-term benefits on the part of physicians, relatives, and the patients themselves; and [5] a lack of financial, institutional, and social support for the participation of elderly patients in clinical trials.

Recognizing this situation, NCI recently sponsored a project to investigate the enrollment of older adults in cancer clinical trials. The project will include a review of patient eligibility criteria, a survey of physician attitudes, and a registry of clinical trials open to older patients. The results of this project will be used to develop recommendations for improving the enrollment of older adults in cancer clinical trials.

Participation of Patients 65 Years of Age or Older in Cancer Clinical Trials

Joy H. Lewis, Meredith L. Kilgore, Dan J. Montello...

A Correction Has Been Published

Group Cancer Site

Participation in Cancer Clinical Trials

Race-, Sex-, and Age-Based Disparities

Vivek H. Murthy, MD, MBA; Harlan M. Krumholz, MD, SM; Cary P. Gross, MD

Author Affiliations

## FDA Guidance & Perspectives

<table>
<thead>
<tr>
<th>Year</th>
<th>Guidance Title</th>
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<td>1989</td>
<td>Guidance for the Study of Drugs Likely to Be Used in the Elderly</td>
<td>FDA</td>
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<td>2016</td>
<td>Evaluation and Reporting of Age, Race, and Ethnicity Data in Medical Device</td>
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<td>Clinical Studies</td>
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<td>2016</td>
<td>Enrollment of Older Adults on Oncology Trials: an FDA Perspective</td>
<td>Journal of Geriatric Oncology</td>
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Enrollment of Older Adults in Cancer Clinical Trials - U.S. Food and Drug Administration Experience

Modified from Fig 1. Enrollment of Elderly Patients in Clinical Trials for Cancer Drug Registration: A 7-Year Experience by the US Food and Drug Administration Lilia Talarico, Gang Chen, Richard Pazdur
Elderly Cancer Patients Enrolled on Clinical Trials Supporting FDA Approval Compared with SEER Cancer Incidence by Age Group

Clinical Trial Participants: FDA Approvals 2005-2015
Cancer Incidence by Age: SEER 2013
Tumor Type/Indication*

**Advanced Solid Tumors**
- early phase clinical trials
- multiple tumor types

**Hematologic Malignancies**

**Head and Neck Cancer**

**Lung Cancer**

**Melanoma**

**Genitourinary Malignancies**
- prostate cancer
- urothelial carcinoma
- renal cell carcinoma

**Gastrointestinal Malignancies**
- colorectal cancer
- hepatocellular carcinoma
- pancreatic cancer
- gastric cancer

**Breast Cancer**

**Gynecologic Tumors**
- cervical cancer
- ovarian cancer

**Other**
- healthy volunteer
- organ dysfunction
- brain tumors
- thyroid cancer
- neuroendocrine tumors
- sarcomas/stromal tumors

*Excludes pediatric studies included to support adult indications, biosimilars, supportive medications (n=176598)
Elderly Patients with Breast Cancer Enrolled on FDA Trials Compared with New Cases by Age Group

- Clinical Trial Participants
- New Cases By Age Group

- <65: 80%
- 65-74: 17% / 23%
- 75+: 4% / 19%

FDA Registration Trials 2005-2015
SEER 18 2010-2014, All Races, Females
Elderly Patients with Colorectal Cancer Enrolled on FDA Trials Compared with New Cases by Age Group

- Clinical Trial Participants
- New Cases by Age Group

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<tr>
<td>&lt;65</td>
<td>65%</td>
<td>43%</td>
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<tr>
<td>65-74</td>
<td>27%</td>
<td>24%</td>
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<td>75+</td>
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FDA Registration Trials 2005-2015
SEER 18 2010-2014, All Races, Both Sexes
Elderly Patients with Lung Cancer Enrolled on FDA Trials Compared with New Cases by Age Group

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FDA Registration Trials 2005-2015
SEER 18 2010-2014, All Races, Both Sexes
Elderly Patients with Prostate Cancer Enrolled on FDA Trials Compared with New Cases by Age Group

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Labeling – Geriatric Use Section

• Interest in including the most critical safety and efficacy information for older patients
  - descriptive information to better characterize drug and biological product use in older patients
Example #1 – Urothelial Carcinoma

Of the 119 cisplatin-ineligible patients with urothelial carcinoma treated with Drug X in Study 4, 83% were 65 years or older and 41% were 75 years or older. The overall response rate in patients 65 years or older was 23% (23/99) and in patients 75 years or older was 29% (14/49). Grade 3 or 4 adverse reactions occurred in 53% (52/99) of patients 65 years or older and 51% (25/49) of patients 75 years or older. No overall differences in safety or efficacy were observed between patients ≥ 75 years of age and younger patients.
Example #2 – Hematologic malignancies

Of the 905 patients in clinical studies of Drug X, 62% were ≥ 65 years of age, while 21% were ≥75 years of age. No overall differences in effectiveness were observed between younger and older patients. Anemia (all grades) and Grade 3 or higher pneumonia occurred more frequently among older patients treated with Drug X.
Example #3 – Melanoma

Of the 559 patients with melanoma randomized to receive Drug X plus Drug Y in Study 1, 24% were aged 65 years and older and 6% patients aged 75 years and older. No overall differences in the effectiveness of Drug X were observed in elderly patients as compared to younger patients. The incidences of peripheral edema (26% vs. 12%) and anorexia (21% vs. 9%) were increased in elderly patients as compared to younger patients.
Drug Trials Snapshot

WHAT IS THE PURPOSE OF DRUG TRIALS SNAPSHOT?

The FDA has developed Drug Trials Snapshots to provide information to the public about who participated in the clinical trials for new FDA approved drugs. Drug Trials Snapshot is part of a pilot project to provide information about the sex, age, race and ethnicity of clinical participants for a small group of recently approved drugs. In addition to information about who participates in the trial, each Snapshot also includes information on how the study was designed, results of the efficacy and safety studies and, if known, differences in efficacy and side effects among sex, race and age (referred to as subgroups).
Drug Snapshot Example- IDHIFA

Baseline Demographics by Age

Subgroup Analyses of Complete Response Rate by Age

Subgroup Analyses of Adverse Events

https://www.fda.gov/Drugs/InformationOnDrugs/ucm571802.htm
Conclusions

- Older cancer patients continue to be underrepresented in cancer clinical trials
- Most striking in ≥75 age groups
- Product Label/clinical reviews/Drug Snapshots include information on safety and effectiveness in older adults
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